Book of Abstracts

ISCOMS
science beyond borders

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Preface

Marieke Goodijk
Prof. Marian Joëls PhD

Marieke Goodijk

President ISCOMS 2020

Dear participants,

It is with great pleasure that I welcome you to the digital version of the 27th edition of the International Student Congress of (bio)Medical Sciences.

Over the past 27 years, ISCOMS has grown to become one of the world's leading biomedical student congresses. However now, for the first time in history, our congress cannot take place as planned due to the global outbreak of the coronavirus. After a year of hard work of the Organising Committee, and, most importantly, after all the enthusiasm and support you as participants have always shown us, we decided to not leave it at that.

Over the past two months, our Organising Committee has been working very hard to put together an alternative programme that all participants are able to follow from home. By doing so, we hope that ISCOMS still provides students the opportunity to present their research on an international platform, to gain knowledge by attending the programme, and to expand their network by interacting with other participants.

Our new online programme, D(igital) ISCOMS, contains a digital platform on which participants are able to attend one full day of inspiring lectures and student presentations. We will kick-off with a keynote lecture by prof. Peter van der Voort MD PhD, who serves as head of the Intensive Care unit at the University Medical Center Groningen (UMCG). In addition, Peter van der Voort serves as a member of the Dutch Senate. In his lecture, Peter will share insights on the current and future situation related to COVID-19 ICU capacity issues. In addition, he will address the challenges that intensivists, health care management practitioners and politicians face due to the COVID-19 outbreak.

In our second lecture, Dennie Jager will tell us everything about the accident that severely changed his life. A few years ago, Dennie Jager got diagnosed with paraplegia. From that day on, Dennie had only one goal in mind: to be able to walk again. In order to gather funds for his exoskeleton, Dennie became ambassador of the Walk On foundation. In his lecture, Dennie will demonstrate what it's like to walk with an exoskeleton.

Furthermore, participants are given the opportunity to interact with each other through "speed dating with participants". As such, all participants are able to make appointments with anyone of their choice. I hope that everyone takes full advantage of the possibilities that our digital platform offers.

On behalf of the entire Organising Committee, I wish you all a wonderful time and I hope you will enjoy DISCOMS as much as I did organising it!

Prof. Marian Joëls PhD

Dean/Member of the Board of Directors University Medical Center Groningen

Dear participants of ISCOMS 2020,

It is my great pleasure to welcome you all to this very special edition of the International Student Congress of (bio)Medical Sciences in Groningen. An exciting event organised by Groningen students for students from all over the world.

For many years already, ISCOMS has proved to be a true highlight of the University Medical Center Groningen academic year. But this year we faced exceptional conditions. Early on during the Covid-19 outbreak, the organizing committee had to take the inevitable but unfortunate decision to cancel the live version of the Conference. Inevitable because we cannot allow large gatherings of people for the time being and because travel across the globe is seriously scaled down. Unfortunate because the organising committee put so much effort in organizing yet another fabulous program in the welcoming scenery of the city of Groningen. Yet, theirs was the only possible decision, we can only hope that next year the situation has normalized to the extent that we can welcome many participants again on site.

After taking this hard decision, the organising committee immediately switched gears and started to organize an online version of ISCOMS, keeping some of the programme elements intact. It was an encouraging sign that most of those that had already registered fully supported the idea of such an alternative program and indicated that they would participate online. And there we are!

International contacts and collaborations are essential for progress in science. And in this era much of these contacts can take place online. The UMCG and the University of Groningen foster such international contacts, not only in their research collaborations but also at all levels of the educational system. We have strategic partnerships with many institutions across the world. ISCOMS transpires the same international spirit, by bringing students from a great variety of countries together.

ISCOMS offers a unique platform exposing participants to the best that science can offer and at the same time helps students to start new collaborations. So, although we cannot offer you those valuable moments of informal contact at the coffee table or a gala dinner in the enchanting atmosphere of one of the oldest churches of Groningen, the scientific exchange is alive and kicking.
Enjoy the science, the discussions and we hope to see many of you next year in Groningen!

Marian Joëls PhD
Professor of Neuroscience
Dean / Member of the Board of Directors
University Medical Center Groningen

Organisation

Executive Board
Advisory Board
President, Secretary, Treasurer
Scientific Programme
Sponsors and Fundraising
International Contacts
Hosting and Logistics
Public Relations
Research and Development
Ambassadors
Partners

Executive Board

The ISCOMS Executive Board consists of nine (bio)medical students of the University of Groningen and was formed in June 2019. Some of us were already part of the Organising Committee in previous editions of ISCOMS, but not everyone. During the intensive start of the year, we had to collaborate closely in our office next to the Faculty of Medical Sciences of the University of Groningen. In the first months, we accustomed ourselves to the functions and responsibilities and became close very quickly. During the meetings we had twice a week, we made sure every task was done and everyone was informed accurately.

Besides our professional collaboration, we also became friends. Despite the group is filled with completely different personalities, we made sure we complemented each other and helped each other in case it was needed.

We want to express our gratitude to the entire Organising Committee for their amazing effort they have put into this edition. Furthermore, we want to thank the advisory board and everyone who supported us during the difficult time when we had to turn the physical edition of ISCOMS 2020 into a digital one due to the global outbreak of the coronavirus.

We are honoured to welcome you to the 27th edition of the International Student Congress Of (bio)Medical Sciences on a, for the first time in the history of ISCOMS, digital platform! We wish you an extraordinary time!

Marieke Goodijk
Maartje Witsen
Niels Bloemendal
Florine Jager
Robert Pattipeilohij
Mats Kleinjan
Lotte Windt
Matthijs Han
Lisanne ter Borgh

Advisory Board

ISCOMS is a congress organised by and for students. Thirty biomedical students are responsible for all scientific, financial, and organisational aspects of the congress. As the congress is organised every year by a new team of students, the advisory board can assist in the continuity of the congress. They have helped organising ISCOMS for many years now. Their expertise, experience and contacts are of great support for the Organising Committee. The advisory board consists of three seniors from the University Medical Center Groningen (UMCG).

Advisory board:

Prof. Paul de Vos PhD
Full professor immunoendocrinology
at the University of Groningen
Advisor since 2009

Prof. Paul de Vos PhD

Matijs van Meurs MD PhD
Intensivist at the UMCG
Advisor since 2016

Matijs van Meurs MD PhD

Robert A. Pol MD PhD
Vascular and transplant surgeon at the UMCG
Advisor since 2018

Robert A. Pol MD PhD

We would like to thank the advisory board for their continuous support and useful advice.

President, Secretary, Treasurer

The president, secretary and treasurer are responsible for overseeing the Organising Committee, as head of the Executive Board.

The main task of the president, Marieke Goodijk, is to lead the Executive Board. She is responsible for the whole organisation towards and during the congress. Additionally, her task is to find suitable day chairs and jury members.

The secretary, Maartje Witsen, is the contact person of the organisation. During this year, she will work closely with the president. Besides that, she will be responsible for all of the registrations, both online and during the congress. She will manage the registration desk and will be happy to welcome you.
The treasurer, Niels Bloemendal, is responsible for all of the budgetary aspects of the congress. As treasurer, he is in charge of the incoming and outgoing money and he will manage the budget estimate for the congress.

Furthermore, we will take care of the evaluations and statistics of our congress, to improve ISCOMS for the upcoming years.

Enjoy ISCOMS 2020!

Marieke Goodijk
Maartje Witsen
Niels Bloemendal

Scientific Programme

The Scientific Programme committee consists of six young and enthusiastic (bio)medical students. It is our responsibility to organise the scientific part of ISCOMS 2020. We are in charge of the keynote lectures, workshops, pre-course, interactive operation and the ISCOMS Research Fellowships (IRF). It is our aim to make the scientific programme of ISCOMS challenging and diverse. Besides this, we also supervise the abstract selection and ensure that students can present their research in a plenary, oral or poster session.

During the pre-course, the Graduate School of Medical Sciences will tell you all about the research possibilities in Groningen at 'Your Future at the UMCG'. You will have the chance to improve your research skills in masterclasses and attend interesting speed-keynotes.

On three congress days five internationally well-established researchers will share their knowledge and experiences with us in keynote lectures. There are also a lot of exciting workshops you can participate in, ranging from practical workshops to patient demonstrations and interactive ethical workshops. Additionally, you will have the opportunity to attend an interactive operation. So even if you are not very familiar with research yet, you can visit the lectures, participate actively in hands-on workshops and gain new scientific skills.

For students who are interested in doing research in Groningen in the University Medical Center Groningen (UMCG), we organise the two-week ISCOMS Research Fellowships. These short internships will take place directly after the congress and brings you into contact with researchers. Another possibility in order to come in contact with researchers from the UMCG is the workshop "Speeddating with Researchers". This workshop will be organised during the congress and will provide you the opportunity to talk to researchers of various Research Institutes of the UMCG.

We are convinced ISCOMS is the perfect opportunity for students and young researchers from all around the world to present their recent work, meet fellow researchers and get enthusiastic about research. We enjoy creating a challenging and diverse scientific programme for ISCOMS 2020 a lot and we are looking forward to meeting you all in June 2020!

Florine Jager
Justine Zijlstra
Lennart van Koerseveld
Pieter Herings
Loïs Span
Tom Bokkers

Sponsors & Fundraising

ISCOMS cannot take place without its financial funding. The committee of Sponsors and Fundraising takes care of the financial resources. Our committee consists of four enthusiastic, dedicated students who will make every effort to make this congress financially possible. We will do our very best to contact and inform companies in order to establish a good cooperation between the sponsors and ISCOMS.

Due to the fact that we are one of the biggest student congresses for biomedical sciences within Europe and due to the numerous national and international students attending, we have a great amount of sponsoring opportunities to offer. Besides students, there will also be scientists, professors, researchers and UMCG medical specialists attending the presentations, lectures and workshops. Hence making ISCOMS very attractive for potential sponsors.

Being a sponsor of ISCOMS allows extensive prospects for both large and small companies to create more awareness for the company, subsequently acquiring new business opportunities. Our purpose is to establish an agreement of mutual benefits. Companies can present themselves with a stand or they can choose for an appearance of their logo on for example our website or our congress bag. A new initiative that has started three years ago, is the networking lunch. Selected motivated students will get acquainted with different companies during a luxurious lunch in a private space. Our sponsor program is available on the website under the heading 'supporters'.

Apart from contacting potential sponsors, we will also subscribe several funds to support ISCOMS. Besides that, one of our committee members is going to assist the treasurer with the finances during the congress. We are also responsible for the journal subscriptions which the presenting participants can win during the congress. And last but not least, we carry the responsibility to provide the participants with a full congress bag which contains a variety of gadgets, magazines and information.

If you are interested in supporting biomedical research and if you want it to be able to reach hundreds of national and international motivated (bio)medical students or if you are willing to support ISCOMS as a high standing platform to exchange in international scientific knowledge, please go to our site! If you have any questions, please contact us and we are more than willing to give you all the information you need.

__Robert Pattipeilohij__
Inga Bakker
Jort Braams
Hugo Breman

International Contacts

The International Contacts Committee takes care of the international part of ISCOMS. Our daily responsibilities include the worldwide promotion of our congress, and taking care of participants who encounter problems with their registration, Visa application, or other difficulties while organising their trip to Groningen, the Netherlands.

We take care of the promotion by e-mailing, calling, and sending promotional materials across the globe. In this worldwide promotion we are supported by our highly motivated ambassadors, who were inspired by their own ISCOMS experience. Click here to see what ambassadors do and which ambassadors you can contact in your own country. Furthermore, we are responsible for the social media community of ISCOMS, including Facebook, Twitter, Instagram, Snapchat, and many more. Besides following us on social media, you can also subscribe to our monthly news letter in order to be kept up to date about the latest progress in the organisation of our congress (click here to subscribe).

All incoming emails of students who want to submit their abstract or who are seeking additional information about ISCOMS are answered by us. We are also the committee that has contact with the embassies when aiding students in obtaining their Visa. Lastly, we are responsible for the Travel Grants for students that require financial aid in order to attend our congress.

As the International Contacts Committee we are constantly looking for new contacts around the world that would like to help us with promoting ISCOMS 2020. If you believe you can help, please send an email to iscoms@umcg.nl. If you have any other questions regarding promotion, Visas, Ambassadors, Travel Grants, and so forth, please send us an email and we will be glad to help you!
We hope to see you at ISCOMS 2020!

__Mats Kleinjan__
Laura Liethof
Thijmen Bliek
Stephanie Braunius
Willemijn van Dijk

Hosting & Logistics

The Hosting and Logistics committee is not only responsible for the social programme, but also for the accommodations, the City Tour, the Post Congress Tour and the plan of action during the congress.
The social programme is the perfect way to extend your social contacts. While enjoying dinners and informal drinks you can meet people from many different countries and cultures.

On Sunday, there will be a City Tour through the center of Groningen and a welcoming party afterwards. At this welcoming party there will be a pub quiz for both the participants and the housing providers. On Monday we will have a completely new social programme this year! Due to last year's success we have decided that the additional third congress day will remain in our programme. Therefore, on Tuesday the recreational evening will be held again. There you will be able to choose one of five activities like visiting a museum, a cheese tasting or a cycling tour.

On Wednesday there will be a formal dinner with 350 participants. This beautiful dinner will be at an historical location in Groningen. We will conclude the last congress day on Thursday with the unforgettable World Wide ISCOMS Night. At this party you can show everyone some great things your country has to offer by bringing your typical national snacks and by putting on your traditional clothing.

To finish off the excellent congress, there will be a Post Congress Tour on Friday. On this day, we will show you a piece of our beautiful country. Together with about 100 foreign participants we will enjoy a day full of fun to blow off some steam after an intense week full of science.

We, as the Hosting and Logistics committee, will provide you with options for accommodation during the congress. One of the options is 'Staying with a Student'. This gives you the perfect opportunity to get a better view of what the student life in the city of Groningen has to offer. Furthermore, you can stay at an international student accommodation or we can give you advice on hostels or hotels.

We ensure you we will do everything to make this congress memorable. We hope you are as excited as we are and we are looking forward to seeing you at ISCOMS 2020!

Lotte Windt
Tijn van Rietschoten
Dagmar Goodijk
Maaike Dam
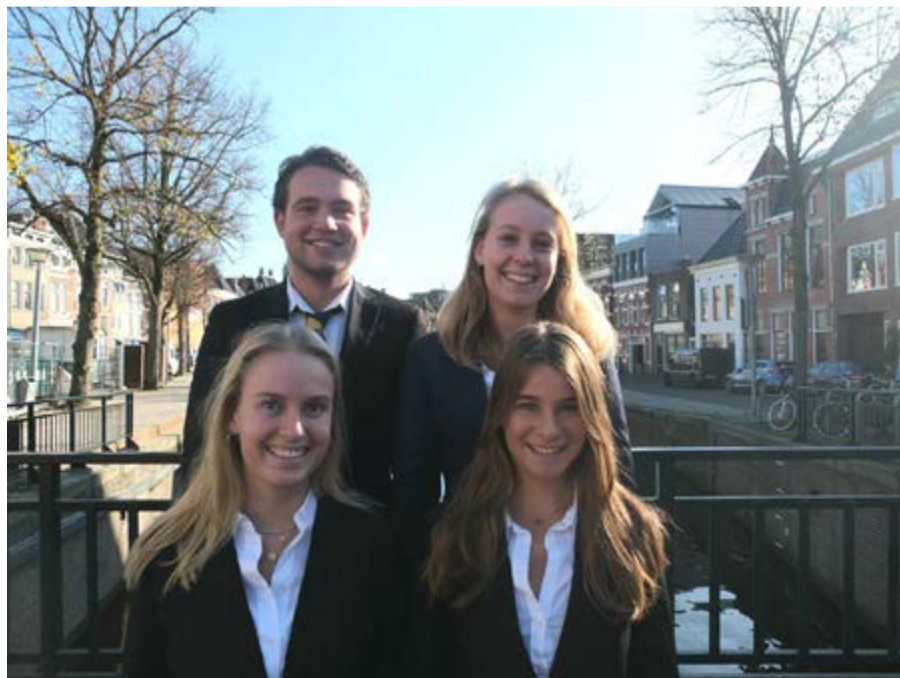
Public Relations

The Public Relations committee is responsible for the appearance of ISCOMS and for the promotion of ISCOMS in Groningen and in The Netherlands.

To reach as many students as possible we are in contact with all other (bio)medical faculties in the Netherlands. They help us to get a lot of attention to ISCOMS, for example, by hanging posters in their faculties and by posting information about the congress on their website. Furthermore we communicate with faculty coordinators to make sure they stimulate their students to visit ISCOMS. Besides this we are setting up a promotional campaign and communicate with the press.

Together, we are also responsible for the graphical design of all material that will be handed out at the congress and of all flyers, posters, booklets and cards that are spread all over the world by our colleagues from the International Contacts committee. Last but not least we compose and design the Book of Abstracts that will be handed out at the congress to all participants. This book contains information about the congress and the people involved and contains all abstracts of participants who present their research at ISCOMS 2020.

Matthijs Han
Pieter Boek
Julie Bruinsma
Catelijne Roelofs
India Hoekman

Research & Development

The main goal of the Research & Development (R&D) committee of ISCOMS is to innovate and improve every upcoming edition of the congress. We establish this by extensive evaluation that helps us determine what we can and should change. Also, we try to think of how it could be changed. The R&D committee makes sure the improvements are implemented at the upcoming congress. Brainstorming is a great part of our committee's task. Thinking of new ideas that will enhance the congress. These ideas come from the evaluation sheets that participants fill out and, for example, brainstorm sessions with the entire organisation that our committee organises.

A good example of innovation of ISCOMS is the application for smartphones that has been set up and launched five years ago. In the meantime, it has been updated by R&D and we will try to keep improving it every year.

Furthermore, R&D is responsible for the website. This means that, in addition to providing the website with its lay-out, we also keep the website up to date at all times to ensure you will receive the correct information.

We maintain partnerships, because these are vitally important to the improvement of medical congresses. Each year we evaluate these partnerships and look for possible new ones. As partners, ISCOMS tries to become an even more inspiring congress.

Each year ISCOMS chooses a charity to support. By organising activities our committee raises money to support this charity. This year we chose the UMCG Alzheimer Foundation. This foundation supports research in the UMCG to find out the cause, develop new treatments, and find ways to lower the risk of dementia. We have collected money for this foundation among others by organising a pub quiz and by participating in a run called the 'Nacht van Groningen'.

Lisanne Ter Borgh
Thomas Luchies
Jolijn Scharn

Ambassadors

The ambassadors of ISCOMS are participants or presenters from a previous ISCOMS who were so enthusiastic about the congress, that they decided to apply to become a well-respected ambassador. They play a vital role in our international promotional campaign. Each year ambassadors are selected after the congress and maintain the ambassadorship for exactly one year, until the next congress takes place. However, some ambassadors can be reselected as they provided such devotion to ISCOMS that they cannot be missed. The ambassadors start their main promotion in October. They share our social media posts and promote ISCOMS in their country by distributing posters and flyers. Some of the ambassadors even organise meetings or give presentations to explain how great their experience was at ISCOMS. The enthusiasm and excitement that we wish to bring across to everyone all around the world, is accomplished by this group of young excited scientists. We have ambassadors from over 35 countries worldwide, who we have close contact with. On the website you can find all of our ambassadors and their passion is evident in their words.

"I had the opportunity to attend ISCOMS 2019 as a poster presenter. It is a great experience, if you are looking to increase your knowledge on medicine and to meet people who share as much as enthusiasm as you do on research and medicine, around the globe. ISCOMS has a unique program with the patient lectures, workshops, keynote lectures and more. It is very well-organized by the organizing committee whom you can reach out for help anytime." Birce Ataş, a third-year medical student at Izmir University of Economics, Turkey.

For any question about ISCOMS, Visa applications, travelling to Groningen, or anything else, please do not hesitate to contact our ambassadors, as they will be more than happy to help you out. Their e-mail addresses can be found on our website.

If ISCOMS 2020 also excited you and makes you want to share your experience with others, you can apply to become an ambassador for ISCOMS 2021. Help us with our promotional campaign yourself! During the congress you can fill in an application form by contacting the ambassador coordinator or you can apply by sending an e-mail with a short motivation letter to iscoms@umcg.nl in days following the congress.

Abdulrahman Habashy

Egypt

Akinsola Akinyemi

China
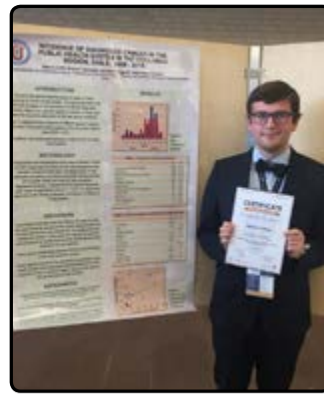
Alex Arya

Chile

Alexandra Androni

Greece

Ali Hamza

Pakistan

Alireza Majd

Iran

Andrei Polnikov

Russia

Ashwini Priyadarshini Singh

India

Avichal Dani

India

Ayat Yaseen

Sudan

Bahram Askarpour

Iran

Bendik Skinningsrud

Poland

Bernard Annan

Ghana

Birce Ataş

Turkey

Boyan Zhang

China

chhavi talwar

India

Collins Kofi Frimpong Osei Owusu

Ghana

Darya Matvienko

Russia

Waradana Viraj Virantha De Silva

Sri Lanka

Eyob Alemayehu Gebreyohannes

Australië

Faizan Akram	Felipe Calderón Salazar	George Krivoshein	Grace Thandekire Sibande
Pakistan	Mexico	Russia	Malawi
Gulfairuz Tukinova	Hanna Kumierczyk	ibrahim Abdullah Al Yaeesh	Ishani Desai
Kazakhstan	Poland	Saudi Arabia	Georgia
Ishika Mahajan	Jadesandra Haarmann	Jordan Popovic	José Israel Luna Mendoza
India	Germany	Serbia	Mexico
Kazuki Takada	Khusronasir Mohamedfaruq	Klimentsi Kamisarau	Kritika Pathak
Japan	Georgia	Belarus	India
Liubov Shilova	Liza Korniiko	Madhyra Indraswari	Mahootchi, E.M. (Elaheh)
Russia	Ukraine	Indonesië	Norway
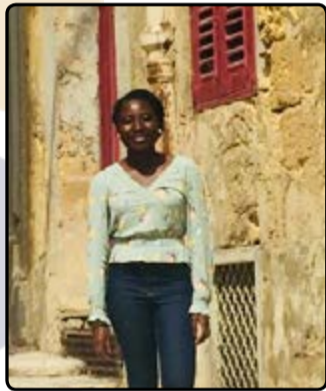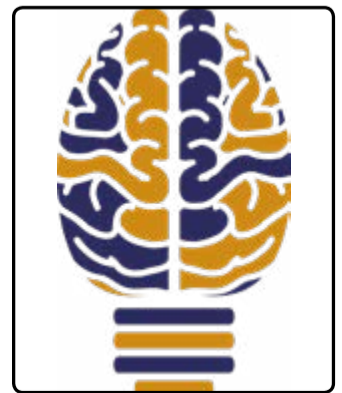
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Mahsan divanbeygi kermani	Mainak Bardhan	Martina Dietrich	Mashkur Abdulhamid Isa
iran	India	Brazil	Ukraine
Mozhdeh Mehdizadeh	Miho takemura	Milica Maleševic	Mostafa Shahin
Canada	Japan	Bosnia and Herzegovina	Arab Republic of Egypt
Nad'a Majerníková	Natalia Chepelova	Nazanin Hazrati	Nikhil Chauhan
Slovakia	Russia	Iran	Georgië
Ogechi Opara	Oguttu Benson	Omar AL Sowayigh	Omotayo Victoria Owolabi
Nigeria	Uganda	Saudia Arabia	Ukraine
Onyeka Kingsley Nwosu	Raful Navarro	Renan R souza lopes	Rene Novysedlak
Nigeria	Mexico	Brazil	Czech Republic

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Reyhan Aslancan	Riya Vaidya	Rizana Riyaz	Ruby Owusua Diabene
turkey	India	India	UK
Ruchika Sukhwal	Saeed Keshtkar	Sahira Nahari	Saif Muqdad
Kyrgyzstan	Iran	Saudia Arabia	Georgia
Samuel Ed Kwesi	Sandeep Goud Palsam	Sebastian Tauer	Shonza felicitee
Ghana	India	Duitsland	Rwanda
Sik Kwan Chan	Terje Kolltveit Skeie	Thomas Emmanuel	Tomonari Masuda
Hong Kong	Poland	Denmark	Japan
Varun Thomas	Veronika Shinkevich	Viral Dave	Wafa Munir Ansari
Georgia	Belarus	India	Pakistan
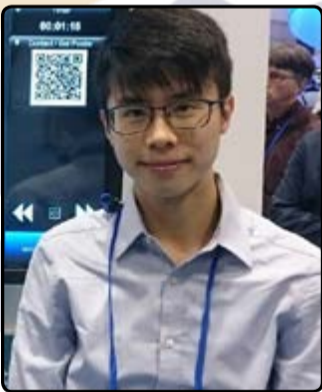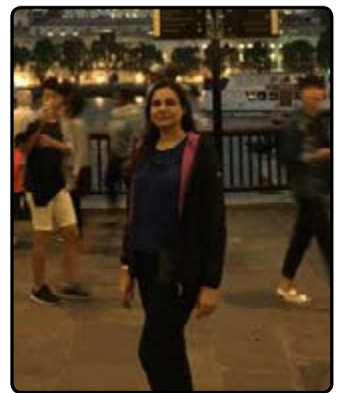
Widyan Putra

Indonesië

Yaa Owusuaa Offei-Darko

Ghana
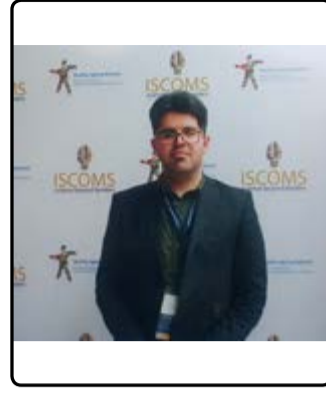
Farid Masoud

Iran
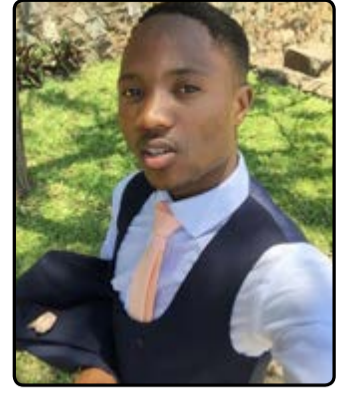
Samuel L. Mpinganjira

Malawi

Partners

AIMS

The Annual International Medical Students (AIMS) Meeting is an international medical congress hosted at the Faculty of Medicine of the University of Lisbon, entirely held by students every year during the month of March. With renowned national and international speakers and a huge range of practical workshops on several medical fields, this is one of the most complete and alluring congresses for students in Europe. Since it is a three-day congress, each day is based on a subject module and all the scientific lectures are related to it. Besides this, there are also keynote lectures, Clinical and Scientific Competitions, a Research Competition (poster, oral and plenary sessions) and a science speed dating session with doctors and researchers. It is our main purpose to promote an enriching scientific setting for learning, interaction and communication among students, health professionals and researchers alike. As we deeply value the social and cultural dimensions of the human being, the AIMS Meeting also includes a social programme and a charity programme for all its participants.

we are continuing to follow our mission of creating a global platform for innovation and medical research. For more information, visit our website www.ichams.org or contact us at ichams@rcsi.ie!

AMSA

The Asian Medical Students' Association (AMSA) International is a peak representative organisation for medical students from across Asia, the Asia-Pacific and beyond. Training doctors from 16 Member Nations and 11 Associate/Observer Nations combine to share knowledge, undertake activities and social services and create international and transcontinental friendships. AMSA was officially founded in Manila, Philippines in 1985, and from this day it has been an active, dynamic and exciting student-led, not-for-profit, non-political organisation. Today, with members and friends spanning the globe AMSA has an active student-exchange program, regularly undertakes national and regional projects, provides humanitarian assistance at times of need, produces quarterly student publications and liaises with the World Health Organisation, the Association of Medical Doctors of Asia, and many other international and regional medical student organisations. Since it was first established in 1979 and the first conference was held in Mahidol University of Thailand, the Asian Medical Students' Conferences have been a key focus for the organisation. Now it is held biannually in January/February and July/August. These events see over 700 students from across the world to learn from each other, teach their fellow peers and develop lasting friendships. The AMSA Vision is Knowledge, Action and Friendship. Three areas we continuously strive to in our members and peers through our organisational missions:

 • Knowledge: We promote scientific and medical activities to increase and expand our knowledge whilst training to become the medical professionals of the future
 • Action: As medical students, we are concerned for the community around us and endeavour to do things for the benefit and improvement of our fellow citizens
 • Friendship: As future doctors, we aim to build and maintain a good relationship among our colleagues of the Asia-Pacific and beyond

AMSA INTERNATIONAL

AMSC

The Antwerp Medical Students' Congress is a project of the European Medical Students Association in Antwerp, Belgium. The AMSC has seen 13 editions. Our congress is perfect for all students in the (para) medical field (medicine, pharmacy, dentistry, biomedical sciences and nursery) to share their knowledge with students from across the world. The 14th edition will take place from the 9th to the 12th of September 2020. We will spend the first two days sharing all knowledge gathered by research conducted by medical students, using poster and oral presentations. Afterwards, we will inform you on the top medical practice, performed here in Antwerp and Belgium, through several interesting lectures and workshops.

BRAINCOMS

Braincoms is a unique opportunity for you to include yourself in the international medical context by listening to amazing internationally acclaimed speakers, practising and improving your skills at hands-on workshops, building up a network with other medical students from everywhere, and much more! All this in an engaging atmosphere with smart people, sense of humour, outstanding scientific quality and – why not? – great food and social events! This congress has everything to add a lot to your personal and medical formation. You couldn't spend these 3 days in a better way. You can't waste this chance!!!

The next edition of BRAINCOMS will take place in São Paulo, at UNIFESP - Universidade Federalde São Paulo, Brazil, from the 13th till the 15th of August 2020.

For more information, please, check our website: http://braincoms.com/2020/

CROSS

Croatian Student Summit – CROSS is a congress organized by the Student Council of the University of Zagreb, School of Medicine that has been continuously organised for 16 years in a row.
The project was started in the academic year 2004/2005 and it also involved Dental, Veterinary and Pharmacy-Biochemistry Schools in the University of Zagreb.
The seventeenth congress in a row will take place in 2021, at the School of Medicine University of Zagreb, Šalata 3.

This year's topic is Neuroscience. (This topic is only regarding lectures.) Topics for poster presentations may differ. For more details about how to register and participate in CROSS 16 visit our website: https://cross.mef.hr/en

CROATIAN STUDENT SUMMIT
SIXTEEN

EMSA

The European Medical Students' Association (EMSA) is a politically neutral, non-governmental, non-profit and independent organisation that represents students from individual medical faculties across geographical Europe. It was established in 1991 in Brussels, Belgium and is currently uniting 96 medical faculties in 24 different European countries. European Medical Students Association seeks to improve the health and quality of care of the European citizens, by acting as a conduit for increased interaction and sharing of knowledge between European medical students in the areas of medical education, medical ethics, medical science and European integration. The main objectives of EMSA are to establish a network between European medical students in order to facilitate European integration and develop a sense of European identity, to represent and voice the opinions of medical students of Europe and to promote the highest standards in European medical education, science and ethics. Our webpage: www.emsa-europe.org

Official BlueMist blog: www.bluemist.eu

ESC

Since its foundation in 1989, the ESC has become one of Europe's most established student biomedical conferences. It is our mission to promote the scientific exchange between students, scientists, and researchers worldwide. Every year, more than 500 participants from over 50 countries take the opportunity to attend keynote lectures by renowned experts, participate in exciting workshops, present their research, and explore the vibrant city of Berlin!

For more information, visit our website at https://esc-berlin.charite.de/en/ !

ICHAMS

The International Conference for Healthcare and Medical Students (ICHAMS) is held annually at the Royal College of Surgeons in Ireland (RCSI) to allow undergraduate healthcare and medical students to present their research to peers and professionals in this field. Our mission is to create a platform for students across the globe to interact with one another in order to challenge conventional methodology and encourage innovation in medicine. The conference includes workshops offered on a variety of topics as well as keynote speakers representing incredibly impactful realms of medicine. Centred in the vibrant city of Dublin, Ireland, we also encourage our participants to embrace the rich culture via city walking tours and traditional Irish music. The first conference was held in 2011 and in 2013, the conference received the Irish Healthcare Award for student project of the year. As we continue to grow as an international conference, we are continuing to follow our mission of creating a global platform for innovation and medical research. For more information, visit our website www.ichams.org or contact us at ichams@rcsi.ie!

ICMS

ICMS – International Congress of Medical Sciences is an international event that welcomes more than 500 participants every year. The congress gives the opportunity to students and young doctors from all over the world to present their research in a set of Preclinic, Therapy, Surgery and Public Health poster and oral sessions. We aim to inspire innovation and promote academic quality through an outstanding list of hands-on workshops and keynote lectures by world-renowned scientists and doctors. The organiser of the forum is the Association of Medical Students in Bulgaria – Sofia (AMSB-Sofia).

IFMSA

International Federation of Medical Students Associations of the Netherlands (IFMSA-NL) is an organisation for Dutch medical students, situated at each of the eight medical faculties. Our mission is to offer future physicians a comprehensive introduction to global health issues. Through our programming and opportunities, we develop culturally sensitive medical students, intent on influencing the transnational inequalities that shape the health of our planet. Besides being the Dutch member organisation of the worldwide federation called IFMSA, IFMSA-NL is also part of the European Medical Students Association (EMSA). More information at: http://www.ifmsa.nl/

LIMSC

The Leiden International (Bio)Medical Student Conference (LIMSC) is the largest biennial student conference in the world. LIMSC offers the opportunity for medical, biomedical and life sciences students worldwide to present their research, to participate in various state-of-the-art workshops, to be enlightened by prominent guest speakers and to engage in networking with fellow international students and researchers. Furthermore, anyone just interested in learning about cutting-edge research at the frontiers of science can attend the whole scientific and social programme without having to present their research.

LIMSC takes pride in being able to provide a high-quality student conference since 1999 and we strive to improve LIMSC with every passing edition. The 12th Edition of LIMSC will take place 10th to 14th March in 2021.

WIMC

We believe that there is a huge need of international meetings for medical students. Such events provoke discussion, lead to cooperation, provide inspiration and encourage young scientists to further endeavours. Therefore, we would like to invite you to Warsaw International Medical Congress (WIMC) 2020 edition. Students from all over the world are welcome to register and present their research, attend workshops, keynote lectures and thematic sessions. Students can choose to present their research in 29 different scientific sessions including a Dentistry Session, Case Report Sessions and PhD Students Sessions.

WIMC offers a wide range of workshops – during the previous edition participants could choose out of 30 different fields.

The rich social programme is another reason for joining the congress – the opening ceremony, gala dinner, medical students' party and "Warsaw by night" are events that should not be missed!

Please visit our website for more details:

http://wimc.wum.edu.pl/

YES Meeting

The Young European Scientist Meeting (YES Meeting) is an annual international students conference which takes place at the Faculty of Medicine of the University of Porto, Portugal. After fourteen editions, the YES Meeting still aims to provide students with the opportunity to learn about groundbreaking and innovative discoveries from world-class scientists, and, more importantly, to hence their motivation in doing research!

Therefore, the students have the chance to present and discuss their research projects on Oncology & Molecular Biology, Neurosciences, Physiology & Immunology, Internal Medicine, Surgery, Public Health & Medical Informatics. You'll also have the possibility to improve your skills with a wide variety of workshops and enjoy the beautiful city of Porto through various kinds of social programmes, where you can enjoy Porto's great weather and its vibrant culture. We invite you all to take part in the 15th YES Meeting, which will take place between the 17th and 20th of September 2020, whether as a Presenting or a Non-Presenting student. We are waiting for you!

ZIMS

ZIMS is a medical congress that brings together medical students and young doctors worldwide. ZIMS gathers students of biomedical sciences and young doctors.
Definition of „young doctor" is taken from the statute of EMSA Europe as a person who graduated from medical studies in the last 5 years.

You can participate as active presenter (with poster presentation or oral presentation on MS PowerPoint), or as passive participant.

ZIMS is one of few conferences where young students and not yet affirmed scientists have access to the world of publishing, thus becoming the only conference in Europe where the book of abstracts is published as a supplement to a prestigious medical journal, 'Liječnički vjesnik', which is indexed in EMBASE/Index Medicus. Moreover, the best works are published as full texts.

Research in Groningen

Junior Scientific Masterclass
Graduate School of Medical
Sciences
Research Institute
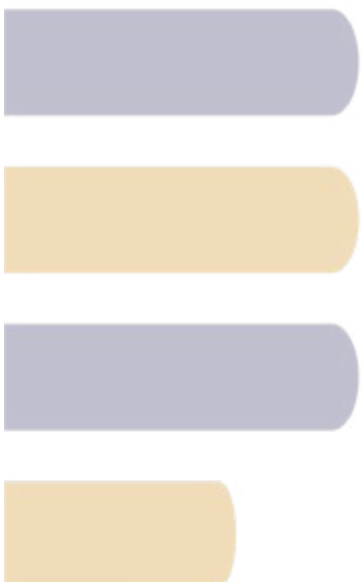
Junior Scientific Masterclass

Prof. Robert J. Porte MD PhD, Chair Junior Scientific Masterclass

The route to become a physician-scientist

Are you dreaming of becoming a physician who is trained to combine the care for patients with clinical science? The Junior Scientific Masterclass (JSM) of the University Medical Center Groningen (UMCG) presents you a unique possibility to realize this dream.

Because of the major growth in biomedical knowledge, there is a dire need for physicians who can translate fundamental insights into new clinical applications and, simultaneously, generate scientific questions based on clinical observations (i.e. translational research). In order to enforce clinical research, it is essential to immerse medical students into research during the pre-clinical phase of their curriculum. Therefore, the JSM educational programme encourages motivated students to seek research experience from the start of their medical education.

The JSM educational programme also enables medical students to apply for MD/PhD projects. The MD/PhD programme consists of clinical internships ('co-schappen') combined with a financed period of two extra years within the medical curriculum. This programme gives medical students the opportunity to successfully finish both their medical education (MD) and a PhD project within a period of eight years.

The JSM educational programme in the Bachelor phase, the 'Bachelor Honours programme', consists of two phases. The first phase entails getting familiar with research within (the Graduate School Medical Sciences of) the UMCG (GUIDE, BCN, SHARE and Kolff Institute). The second phase is meant to be a turning point and consists of a one-week course of intensive training in clinical research for a (selected) group of students, called the COMPASS week. In the second phase the students are also stimulated to choose their own line of research and apply for research grants.

The JSM programme has grown considerably since it started in 1999. In the period of 2001 until 2014, more than 850 students have been awarded Pilot Projects and 480 students an MD/PhD project. Until now, more than 200 students successfully mastered the MD/PhD programme. In 2008, the 'Mandema-stipendium' was introduced which enables young physician-scientists (MD PhD) to combine their specialist training with research and establish their own line of research.

The route to become a physician-scientist is challenging, but also highly rewarding. It represents an investment for a lifelong learning in the field of academic medicine.

Additional information: www.jsmgroningen.nl or j.s.masterclass@umcg.nl

Graduate School of Medical Sciences

Martin J. Smit MD PhD, director of GSMS

The Graduate School of Medical Sciences (GSMS) trains and educates excellent researchers and promotes excellent research. The GSMS is responsible for all Research Masters and PhD education and training programmes within the University Medical Center Groningen (UMCG), including the 'Junior Scientific Masterclass', a special research-oriented programme (BSc Honours and (D)MD/PhD programme) for talented medical and dental students. At the GSMS we are outward-looking in our approach, working with people and partners from all over the world. All of our postgraduate programmes are conducted in English and in fact half of our doctoral students are international.

Research within the UMCG ranges from fundamental to patient-oriented (clinical) research. The UMCG has organized all its research in five Research Institutes that each have developed research programmes around specific aims and objectives. The five Research Institutes collaborate in the GSMS to educate and train research masters and PhD students for future scientific leadership. We endeavour to encourage and shape students to become critical and independent thinkers. Both PhD and Research Master students have the opportunity to tailor their programme to fit their own personal research interests.

More information for international students: www.groningenbiomed.com

Do you have questions about doing a PhD in the UMCG, and you want to ask someone with experience? Please go to www.iscoms.com/about-iscoms/research-2/research-in-groningen/

Here you will find a list of students who are from abroad and came to the Netherlands to start a PhD in the UMCG. They are happy to help and answer all of your questions!

Martin J. Smit MD PhD, director of GSMS

PhD training programmes (MD/PhD, 2+2, 3 or 4 years)

The GSMS PhD curriculum has an extensive programme (choice of more than 70 courses and activities) offering each PhD student the opportunity to join courses and activities related to the Research Institute they participate in and their own specific research interest. Five Research Institutes work together to organize these courses and activities each based on their own field of expertise: 1. Behavioural and Cognitive Neurosciences (Research School BCN/Research Institute BCN-BRAIN), 2. Chronic Diseases and Drug Exploration (Research Institute GUIDE), 3. Cancer Research (Cancer Research Center Groningen), 4. Health Research (Research Institute SHARE) and 5. Biomedical Engineering (Research Institute W.J. Kolff)

The Graduate School offers different types of PhD training programmes
1. The MD/PhD programme offers medical and dental students the opportunity to combine the last two years of the Master phase with a PhD training (two additional years of research training financed by the UMCG) to obtain a (D)MD and PhD degree upon completion.
2. The Abel Tasman Talent Programme (also see below) offers PhD Sandwich Scholarships (2+2 years). First, PhD students pursue a two years PhD education and training programme at their home university followed by a two years programme in Groningen (funded by the UMCG) where the thesis will be completed.
3. Upon successful completion of their Research Master's programmes GSMS Research Master's students have the opportunity to apply for a three-year PhD education and training programme within the GSMS.
4. Finally, within the UMCG regularly regular four-year PhD positions are available (offered by individual researchers or research groups) and posted on the UMCG website.

Degree awarded: PhD

Research Master's programmes (2 years)
The Graduate School of Medical Sciences administrates three Research Master's Programmes:

1.Behavioural and Cognitive Neurosciences (BCN/BCN-BRAIN)
The Research Master Behavioural & Cognitive Neurosciences, organised by the Research School of Behavioural and Cognitive Neurosciences (BCN), concentrates on three focal and closely related areas of particular strength within the field of neurosciences: Animal and human behaviour (B-track), Cognitive neuroscience and cognitive modeling (C-track), and Molecular and clinical neuroscience (N-track).

The programme is characterized by its interactive setting, offering the unique chance of a truly multidisciplinary neuroscience education, while becoming an expert in one specialistic track. The programme is essentially tailor-made. Depending on the student's research interest (or future career aspiration) the student can design his or her own training programme.

More information:
www.rug.nl/research/behavioural-cognitive-neurosciences/education/researchmaster/

2. Clinical and Psychosocial Epidemiology (CPE-SHARE)

Clinical and Psychosocial Epidemiology (CPE) is a selective two-year research master. The programme is unique in the sense that students are encouraged to focus on their individual development as a researcher. Therefore, classes are taught in small groups. Students can choose additional courses that suit their personal interests and moreover, research will be conducted side by side with scientists who are leading experts in their field.

Mental and physical health and the reciprocal relationship between these two forms the basis of the programme. There is a strong focus on prevention, diagnosis and treatment of physical and mental health conditions. The central idea is that psychological, biological and social aspects all play a role in any physical condition. Students conduct research in several populations, including children, adults and elderly, with or without a physical or mental condition.

More information: www.rug.nl/masters/clinical-and-psychosocial-epidemiology-research/

3. Medical Pharmaceutical Drug Innovation (MPDI-GUIDE)

The selective two-year master programme Medical and Pharmaceutical Drug Innovation (MPDI) offers research-minded students small-group interactive teaching in an international and multidisciplinary environment. You will learn how to creatively apply knowledge and we will train you to become a critical and analytical scientist. You will be challenged with exciting cutting-edge research and methodologies and will learn how to critically read the literature, design novel research questions, translate hypotheses into testable research plans, and write scientific essays.

As a student you can focus on your interests and ambitions by participating in one of the following tracks after the first semester: Oncology, Medical Neurosciences and neurological diseases, Infection and immunity, Medical nutrition and metabolic diseases, Medical system biology and bioinformatics, Drug innovation.

More information: www.rug.nl/masters/medical-and-pharmaceutical-drug-innovation/

Degree awarded: Master of Science

More information:
http://www.rug.nl/research/gradschool-medical-sciences/phd-programme
http://www.umcg.nl/NL/UMCG/werken_in_het_umcg/vacatures/Pages/default.aspx

Abel Tasman Talent Programme

The Abel Tasman Talent Programme (ATTP) supports high-potential international students to excel in the field of (bio)medical or pharmaceutical sciences. Two types of financial support can be distinguished:
Financial support for students from one of our so-called 'preferred partner universities'
Financial support for exceptionally talented students from other institutions

More information: https://www.groningenbiomed.com/practical/abel-tasman-talent-programme/

Erasmus Mundus Action 2 mobility

The European Committee's programme 'Education and Training' offers many opportunities to stimulate education, training and exchange of Research Master's and PhD students of the European Union and beyond. The University of Groningen participates in many of these exchange programmes.

More information:

https://www.rug.nl/about-us/internationalization/global-focus/europe/erasmus-programme
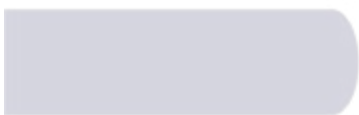
Research Institutes

Research Institute BCN-BRAIN
Director: prof. Iris E.C. Sommer MD PhD
Central theme: Behavioural and Cognitive Neurosciences

The Research Institute BCN-BRAIN was established in 2005 and is part of the Graduate School of Medical Sciences and of the Research School of Behavioural and Cognitive Neurosciences. BCN-BRAIN promotes research that is aimed at understanding the function of the healthy brain and dysfunction of the nervous system with reference to neurological and psychiatric disorders. Research is focused on translational collaboration between lab-based (molecular- and cell biological) and hospital-based (clinical) researchers integrating different levels of neuroscience research.

Research Institute GUIDE
Director: prof. Jos G.W. Kosterink PhD
Central theme: Chronic Diseases and Drug Exploration

The main asset of the Groningen University Institute for Drug Exploration (GUIDE) is the integration of clinical, biomedical and pharmaceutical research stimulating translational research and researchers with a keen eye on the complete spectrum of biomedical research: from bed to bench to drugs. Ageing is a central theme as most chronic diseases are age-dependent. Research focuses mainly on 1. Lead discovery, development of new drugs, drug delivery and advanced formulation technology and 2. Translational research on molecular and cellular mechanisms underlying disease (etiology and pathophysiology) and on research related to treatment of disease, e.g. in the context of clinical trials and by using relevant animal models.

Cancer Research Center Groningen (CRCG)
Director: prof. Mark van Vugt PhD
Central theme: Cancer Research

The Cancer Research Center Groningen (CRCG) organizes and facilitates high-quality, oncology-related research activities within the UMCG and University of Groningen. All research activities at CRCG share the overall perspective of 'healthier and longer lives of cancer patients through improved care'. Research is performed at the fundamental, translational and clinical levels and organized in a coherent and effective manner in several research programmes to achieve fundamental, clinical and societal relevant research output. Ultimately this leads to personalized cancer therapy, thus reducing the unintended side effects of treatment on normal tissues and improving the quality of life of cancer patients.

Research Institute SHARE (Science in Healthy Ageing and healthcaRE)
Director: prof. Maarten J. Postma PhD
Central theme: Prevention in Health Research

SHARE's mission is to identify determinants and consequences of illness and Healthy Ageing, conducted within inter-/multidisciplinary programmes, in close connection with societal parties and often based on observational data. The institute investigates and evaluates factors and interventions that are population-, patient- and/or healthcare-system-related.

It adds knowledge on prevention of and adaptation to disease, enhancing societal participation of patients with chronic somatic and mental disease and cost-effectiveness and efficacy of pharmaceutical, medical, life-style and psychosocial interventions.

Notably, a life-course perspective is taken, addressing research questions spanning from the preconception period, through infancy, reproductive and working ages to old age.

Research Institute W.J. Kolff
Director: prof. Yijin Ren DDS PhD
Central theme: Biomaterials

The primary objective of the W.J. Kolff Institute for Biomedical Engineering and Materials Science is to bring together pre-clinical and clinical research groups and to establish a center of expertise for the entire stage of biomedical materials science and its application involving basic materials science, medical product development and clinical evaluation that will contribute to the long-lasting well-being of patients in need of biomaterial implants and extra-corporal support systems. Research is conducted within four thematic research programmes each with their own specific theme: 1. Bioadhesion, biocompatibility and infection, 2. Nanobiotechnology and advanced therapeutic materials, 3. Restoring organ function by means of regenerative medicine and 4. Maintaining oral health and oral function.

European Research Institute for the Biology of Ageing (ERIBA)
The mission of the European Institute for the Biology of Ageing (ERIBA) is to gain more knowledge about the causes of age-related disease. Our studies are focused on the mechanisms that result in loss of cells with age and the decline in the function of old cells and tissues. We aim to develop novel strategies to prevent or combat age-related disease and to provide evidence-based recommendations for healthy ageing. Our approach is based on curiosity, communication and collaboration. Group leaders and their team working with unique model systems and technology platforms meet regularly and share their knowledge and expertise to accelerate discoveries.

ERIBA aims to become a world-class research Institute, internationally renowned for its cutting-edge basic science. It aims to attract top-level scientists of all levels of seniority. Staff scientists are expected to publish their papers in high impact journals with quality prevailing over quantity. There is ample opportunity to explore uncharted territory and embark on high-risk projects that can yield major breakthroughs. The development of novel tools and technology required to answer fundamental questions is a strategic focus. Long-term investments in developing a strong research programme are favoured over short-term activities leading to incremental results. Staff scientists define their own research agenda, but are also expected to collaborate with fellow scientists in ERIBA and its affiliated local and distant Institutions.

Education at ERIBA
Research in ERIBA is strongly connected with education and training of the future generation of Biology-of-Ageing researchers. ERIBA aims to be "the place to be" for the best students by offering comprehensive training in some of the best Biology-of-Ageing laboratories in the world. We have developed a cutting-edge graduate curriculum in Ageing biology in which students will be exposed to a wide variety of model systems and approaches. The extensive training experience of the international faculty at ERIBA in other research institutes worldwide ensures an optimal educational and research environment.

Undergraduate students

ERIBA welcomes applications from undergraduate (pre-BSc and MSc) students who wish to pursue an internship in one of the ERIBA labs. Students would typically be enrolled at a biomedical, chemical, pharmaceutical, medical or bioinformatic programme at their home University or University of Applied Sciences ("Hogeschool"). Prospective students are invited to explore the different research teams on the ERIBA website, and motivate in their application the interest for the lab of their choice. Although some short-term internshipsw may be available, we prefer rotations that last for 5 months or longer.

PhD students

ERIBA offers an exciting environment to pursue a PhD degree in the Biology of Ageing. We aim to train PhD students to become independent, creative, multi-skilled scientists. Students devote most of their time to their own research project, but will be enriched by and benefit from the complimentary research activities in neighbouring labs. A large variety of courses, all taught in English, is available for PhD students to acquire additional skills. A PhD degree from one of the ERIBA labs will optimally prepare students for the next phase in their University or corporate career. PhD students in ERIBA will be enrolled in the Graduate School of Medical Sciences and defend their thesis at the University of Groningen. PhD projects in ERIBA typically will last 4 years.

Postdoctoral fellows

We are always searching for outstanding postdoctoral candidates with a proper training in molecular or cell biology who wish to solve scientific questions in ageing science. We encourage postdoctoral candidates to directly contact one of the ERIBA Principle Investigators to explore job opportunities.

For more information, please visit www.eriba.umcg.nl

Congress

Programme DISCOMS 2020
Jury members
Awards
Keynote
Patient lecture
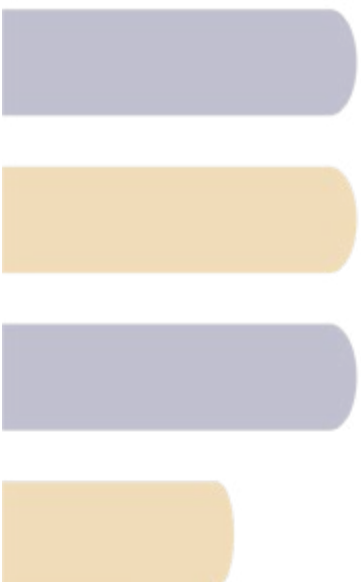
Programme DISCOMS 2020

Thursday, 4th of June 2020

12:00	Registration
12:30	Opening ceremony
12:45	Keynote Lecture: Prof. Peter van der Voort MD PhD
13:40	Short break and speed dating with participants
14:00	Plenary presentations
15:00	Break and poster presentations
16:00	Patient Lecture: the Exoskeleton
16:50	Plenary presentations
17:40	Speed dating with participants
18:00	Your future at the UMCG
18:15	Award & closing ceremony
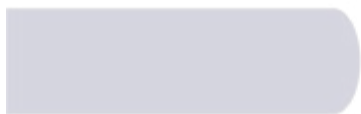
Jury members

Stefan M. Willems MD PhD

Chair of the Department of Pathology and Medical Pathology

Stefan M. Willems MD PhD (1979) graduated cum laude from medical school in Leuven (B.) and was subsequently trained as a pathologist at Leiden University Medical Center. He received his PhD on molecular genetics from Leiden University in 2011. As a Rubicon (NWO) laureate and KWF fellow, he did his postdoc at Harvard Medical School (Cell Biology, Gygi lab), and the Netherlands Cancer Institute (Berards lab). Meanwhile he became staff member at the department of pathology in the UMC Utrecht in 2010 and successfully established his own research line mainly focussing on molecular pathology of head and neck cancer. In 2018 he became head of the Molecular Pathology lab within the UMC Utrecht.

March 1st, he moved to the University Medical Center Groningen to become Chair of the Department of Pathology and Medical Pathology. His main drive is connecting people and creating a fruitful environment for his co-workers to execute the academic core tasks: providing top notch patient care, innovative research, state of the art teaching and clinical leadership. Meanwhile he leads a research group (currently eleven PhD students) and is involved in nationwide big data initiatives/organisations (e.g. PALGA, www.palga.nl). He's married to Debbie van Baarle and together they have two boys. In his free time, he likes playing field hockey and tennis.

emProf. Cees Th. Smit Sibinga MD PhD

Expert advisor World Health Organisation

emProf. Cees Th. Smit Sibinga MD PhD FRCP Edin FRCPath is a clinical haematologist and specialist of Transfusion Medicine. He is special professor of International Development of Transfusion Medicine at the University of Groningen. He was involved in the development of Transfusion Medicine, and quality systems and management in developing economies since 1980 through his work with the World Health Organization (WHO). There he has been regional coordinator of the global Quality Management Project for the Europe region. For 25 years, he has served as the Managing Director of Sanquin Division Blood Bank North Netherlands in Groningen. From 1993 until 2005 the Blood Bank incorporated the WHO Collaborating Centre for Blood Transfusion and the WFH International Hemophilia Training Centre in Groningen.

emProf. Smit Sibinga is the founder of the Dutch Blood Bank Inspection, the Accreditation Programme and the Hemovigilance system. Besides this, he is the founder of the Academic Institute for International Development of Transfusion Medicine at the UMCG. This institute used to provide a post-academic Master in Management of Transfusion Medicine, which is now part of the Master programme of the University of Groningen Graduate School of Medical Sciences.

emProf. Smit Sibinga is still intensively involved in transfusion medicine, related health sciences education and research focused on developing countries. He serves WHO Eastern Mediterranean Region as a Lead Technical Adviser in their Strategic Framework for Blood Safety and Availability 2016-2025 and its priority interventions.

Prof. Edwin Bremer PhD

Medical biologist and tenure track professor at the department of Hematology

Prof. dr. Edwin Bremer is a medical biologist and tenure track professor at the department of Hematology of the UMCG and a visiting professor at the Harbin Medical University in Harbin, China. His research is centered on the development of new cancer immunotherapeutics, from bench to bedside. The focus within his research group is on the design of strategies to re-establish effective innate and adaptive anticancer immunity, including the development of innate checkpoint inhibitors as well as Chimeric Antigen Receptor (CAR) T cell therapeutics. His research interests extend from fundamental, to translational and clinical research. Further, he is coordinator of the European training network I-DireCT, in which innovative academic and industrial immunotherapeutic concepts are merged with nanomedicine into the next-generation of cancer immunotherapeutics.

Hanno Maassen MD PhD

MD PhD student working at the department of Pathology and Medical Biology and the department of Experimental Transplantation Surgery

Hanno Maassen is an MD-PhD student working at the department of Pathology and Medical Biology and the department of Experimental Transplantation Surgery, both at the University Medical Center Groningen. His main research interest is improving renal preservation, mainly focussing on prevention of ischemic injury by using hydrogen sulphide during different stages of kidney transplantation. He started studying medicine in 2016 via the pre-master programme, before that, he worked as a physical therapist after graduating in 2014. During his research internship he got involved in the previous mentioned research and started an MD-PhD programme. His scientific career started at ISCOMS, where he presented his first research results in a plenary presentation, kick-starting his career.

Jolien de Veld

Medical student at UMCG and president of the 25th edition of ISCOMS in 2018

Dear participants,

As the president of the 25th edition of ISCOMS in 2018, I am delighted to be a jury member of the first edition of DISCOMS! Even though ISCOMS is known for its international students travelling to Groningen, I think the digital version of the congress will lift the international character to the next level. This year, students that were not able to travel to the Netherlands in the past will also have the opportunity to be a visitor at DISCOMS and take part in the wonderful programme the Executive Board and Organising Committee have created.

My name is Jolien de Veld and I am a medical student at the University of Groningen. Currently I am in my fifth year and doing my medical internships at the Isala Hospital in Zwolle, a small city south of Groningen. When I was president of ISCOMS, I had not done any internships yet. In the past eighteen months, I became aware once more how important doing research is for the biomedical world. Every day, we are getting closer to curing diseases and making certain treatments more applicable. In my opinion, everyone who visits DISCOMS, either by presenting their own research or by being interested in the results found by others, is of great value to the biomedical world.

I would like to wish all of you a great day, and do not forget to celebrate this first edition of DISCOMS at your own small world wide ISCOMS night this evening!

Kind regards,
Jolien de Veld

Awards

Plenary awards
Students who are selected to present their research during the plenary sessions, have a chance of winning one of the three plenary awards. The first prize consists of €200,-, the second prize of €150,-, and the third prize of €100,-. In addition to this, all the winners will receive a universal pass for one of the upcoming editions of ISCOMS.

You can spend the prize money on visiting biomedical congresses of your choice. All of these winners will also receive a one-year online subscription to the New England Journal of Medicine. The winners will be selected by a jury of renowned medical scientists and (bio)medical students.

Plenary presentation: audience award
The winner of this award will be determined by the audience. The presenter most appreciated by the audience will receive a cheque of €50,- to spend on visiting a biomedical congress of his or her choice.

Best oral award
This prize is awarded to the best poster uploaded in the oral category on our digital platform, judged by our jury. The winner will receive a cheque of €50,- to spend on visiting a biomedical congress of his or her choice and an universal pass for one of the upcoming editions of ISCOMS. In addition to this, the winner will also receive a one-year online subscription to the New England Journal of Medicine.

Best poster award
This prize is awarded to the best poster uploaded in the poster category on our digital platform, judged by our jury. The winner will receive an universal pass for one of the upcoming editions of ISCOMS and a one-year online subscription to the New England Journal of Medicine.

World Health award
To stimulate and acknowledge students in the research of global health issues and their contribution to global health in general, the WHO supported World Health award consists of a one-year online subscription to the Eastern Mediterranean Health Journal (EMHJ). This means that either the presenter comes from a developing country or the subject of the research affects developing countries.

Keynote

Prof. Peter van der Voort MD PhD

The current and future situation concerning COVID-19 ICU capacity and related issues

Professor Peter van der Voort MD PhD is an intensivist and politician. He is currently the head of the Intensive Care at the University Medical Center Groningen (UMCG) and serves as member of the Dutch Senate. He received his internal medicine training at the Academic Medical Center in Amsterdam and the Onze Lieve Vrouwe Gasthuis. He also earned his doctorate and a master's degree in epidemiology in Amsterdam. His research is focused on the improvement of intensive care quality and the effect of organisational change on the field. During the coronavirus pandemic the capacity of the intensive care unit of the UMCG led by professor Van der Voort was increased from 36 to 112.

The lecture will cover the current and future situation concerning COVID-19 ICU capacity and related issues. In addition, challenges for intensivists, health care management and politics will be addressed. How can health care systems be prepared for large scale, sudden and unexpected events? What does this mean for leadership, especially related to medical practice?

Prof. Peter van der Voort MD PhD

Patient lecture

Dennie Jager

Walking after paraplegia: the exoskeleton

On Saturday night the 18th of October 2014, Dennie Jager was riding on his moped home when he accidently hit the sidewalk and was thrown of his moped. During his fall he hit an electrical distribution cabinet.

Later in the hospital he was diagnosed with paraplegia and was told that his life would change forever. From that day onward he continued his life mostly in a wheelchair. After the crash they told him he had to accept the fact that he would never walk again, learn to live with it and set new goals. However, acceptation was difficult for him and he only had one goal: to walk again. He became ambassador of the foundation Walk On and has gathered the funds for his own exoskeleton.

During this year's patient lecture Dennie Jager will speak about his accident, revalidation and demonstrate walking with an exoskeleton. Make sure you don't miss this session on our digital platform!

Dennie Jager

Plenary Session

Presenters:
Nasa, A. (Anurag)
Loaiza-Cano, V. (Vanessa)
van Eekelen, L (Leander)
Kopka, M. (Michał)
Subrakova, V. (Vera)
Keller, D. (Diana)
Capendale, P. E. (Pamela)

The Human Ventral Amygdalofugal Pathway: A Virtual Game of Hide and Seek

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Introduction

The Amygdala is known to have a role in processes regulated by the limbic system such as emotion, behaviour, and memory. The ventral amygdalofugal pathway is the major efferent fibre bundle that serves as a key output of the amygdala. It divides into five branches terminating at the hypothalamus, dorsomedial nucleus of the thalamus, septal region of the cerebrum, nucleus accumbens and brain stem.

The underlying neuronal fibre connectivity has yet to be delineated with standard neuroimaging. By using advanced diffusion-weighted magnetic resonance (MR) technologies and virtual reality (VR) we present for the first time a virtual dissection of this tract in-vivo.

Materials & Methods

90 healthy subjects were scanned using High Angular Resolution Diffusion Imaging (HARDI) and high-resolution T1 (1mm isotropic) MR imaging at Trinity College Dublin (Phillips, Intega 3T). 3D amygdalar and nucleus accumbens volumes were generated by automated cortical segmentation using FreeSurfer 6.0. These digital analogues were used to extract the ventral amygdalofugal pathway and its branches through a neuroanatomically derived boolean logic protocol of the diffusion data. Post-generation tract analogues were converted in 3DS Max and visualised in a Unity3D/Oculus Rift VR environment allowing for intracerebral virtual manipulation and individual isolation of generated elements. Ethics approval was granted by St. James/Tallaght joint REC.

Results

Using our protocol, we were able to delineate the trajectory of the ventral amygdalofugal pathway and it's connections in-vivo. This demonstrates how both neuroimaging and VR techniques can synergise to inform neuroanatomy. Macroscopic and microscopic data can be calculated from these virtual tracts to provide insight on various neuropsychiatric conditions. In particular, this tract may show differences in illnesses which involve amygdalar, neuroendocrine and autonomic pathology such as depression, anxiety, PTSD and schizophrenia.

Conclusion

In summary, this is the first time the ventral amygdalofugal pathway and its major branches were virtually dissected and visualised using VR.

Evaluation of di-halogenated L-Tyrosine Derivatives as Potential Antivirals Against two Emergent Arboviruses

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Introduction

In the last decade, several regions around the world have reported the emergence and co-circulation of two mosquito-borne viruses: Zika (ZIKV) and Chikungunya (CHIKV). None of these arboviruses has specific licensed antiviral drugs or vaccines to treat or prevent the infection. These facts increase the necessity of investigation and development of new synthetic compounds with potential antiviral activity helped by in silico methods. Then, the aim was to evaluate the potential antiviral in vitro activity of di-halogenated L-tyrosine derived compounds against two emergent arboviruses and determinate the in silico interactions and toxicity.

Materials & Methods

10 synthetic di-halogenated L-tyrosine derived compounds, five bromo-tyrosines (1 to 5) and five chloro-tyrosines (6 to 10), were synthetized and tested. The cytotoxicity was assessed by MTT method. Antiviral screening (pre-trans-post infection combined treatment) was accomplished in VERO cells. The inhibitory effect against CHIKV and ZIKV was quantified by plaque assay. Suramin (500 µM) and Ribavirin (200 µM) were also evaluated at the same conditions as positive inhibition controls. The interaction between the compounds and two viral proteins of each virus, was evaluated with Autodock VINA® software and analyzed with PMV. The possible toxicity of the compounds was predicted with ADMET Predictor® software. All data were analyzed by t-student.

Results

None of the tested compounds showed cytotoxicity higher than 10% at the experimental concentration (250 µM). Compounds 1, 2, 3, 4, 7, 9 and 10 exhibited anti-CHIKV activity, being compounds 4 and 9 the most promissory antivirals (inhibition above 75%, p<0.01). The compounds 4 and 9 inhibited the infection of ZIKV, but only compound 9 had an inhibition percentage above 65% (p < 0.01). The binding energy of the compounds and viral proteins were between -4.2 and -5.8 Kcal/mol. In silico toxicity models estimated that compound 9 has less harmful effect at the endocrine system and allergenic capacity than compound 4, but higher risk of liver enzymes elevation.

Conclusion

Compounds 4 and 9 presented an antiviral potential activity. Studies in course allow to evaluate the mechanism involved in the antiviral effect.

Deep learning in hematopathology: supporting pathologists in identifying cells and diseases in bone marrow biopsies

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Introduction

Bone marrow biopsies play a central role in hematopathology for diagnosing various diseases, staging neoplasms or performing follow-up progression. It has been shown that evaluations performed by hematopathologists on biopsies are subject to significant inter- and intra-observer variability. This may result in multiple hematopathologists diagnosing some patients differently. To that end, a deep neural network was designed to categorize six cell types in bone marrow trephine biopsies. The clinical applicability of the network is shown by using its output to train a classifier to distinguish between normocellular and aplastic marrow.

Materials & Methods

24 scans of normocellular, periodic acid-Schiff (PAS) stained bone marrow trephine biopsies were used for the training and testing of the network. The network was trained by showing it examples of bone marrow with accompanying annotations provided by hematopathologists and two trained non-experts. The network consisted of 10 layers with 8.5 million parameters and was trained on a NVIDIA GTX 1080TI for a hundred epochs with a learning rate of 1e-4 and batch size of 32.

The aplasia classifier was trained and tested using 31 aplastic, PAS stained biopsies in addition to the 24 normocellular biopsies, which served as positive and negative cases respectively. Three classifiers were fitted on vectorized prediction maps from the network: a support vector machine (SVM), a k-nearest neighbor (kNN) classifier and a multi-variate logistic regression model. The classifier with the highest ROCAUC was then applied on the test set for a final performance metric.

Results

The network correctly categorizes cells across all types minimally 70 percent of the time on the test set. On average, the detection rate is 83 percent. The SVM classifier performed best on the validation set (ROCAUC = 0.999) and was applied on the test set for a final ROCAUC of 0.990.

Conclusion

The high detection rate of the network shows that is capable of categorizing most cells in bone marrow trephine biopsies. These categorizations could assist hematopathologists in identifying and delineating cells, thus reducing inter- and intra-observer variability on tasks performed while examining marrow. The AUC metric of the SVM classifier indicates that is capable of automatically identifying aplasia in bone marrow.

Shp-2 deficient CAR-NK cells exert enhanced cytotoxicity against prostate cancer cells

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Introduction

Cancer is one of the leading causes of death following cardiovascular diseases. In recent years, immunotherapy has shown great potential for cancer treatment: NK-cells are successfully used in therapy of oncological diseases. Nevertheless, because tumor cells avoid elimination by establishing an immunosuppressive tumor microenvironment, the cytotoxicity of NK-cells can be strongly affected. We aimed to improve the cytotoxic effect of NK cells against tumor cells and explored whether modification of the signaling pathway through the shp-2 gene knockout in NK cells would result in the increase of the cytotoxic activity of model NK cells.

Materials & Methods

We used CRISPR/Cas9 system to introduce mutations in the coding sequence of the shp-2 (PTPN11) gene encoding the signaling molecules of signaling pathways in NK cells, specifically YT cell line. These knock-out NK cells were additionally transduced to express a chimeric antigen receptor (CAR) that selectively recognized the antigen of interest (PSMA) on the target cell surface and generated an activating signal. Then cytolytic effects against expressing PSMA Du-145 prostate cancer cells were measured by Real-Time Cell Analysis system.

Results

Using the CRISPR/Cas9 system we obtained several derivatives of YT cell line in which biallelic deletions occurred, thus disrupting the function of the shp-2 gene. Knock-outs were also verified by western-blot analysis. It was found that CAR-YT shp-2 knockout cells exerted significantly higher cytotoxicity than CAR-YT cells with a functional shp-2 gene. To understand whether CAR-YT shp-2 deficient cells may display unwanted cytotoxicity against healthy cells, cytotoxicity assay was conducted with PBMCs isolated from a healthy donor. We observed that the percentage of dead healthy cells did not differ significantly between the CAR-YT shp-2 knockout cells and no effector cells (control) added.

Conclusion

Our experiments show that shp-2-deficient NK cells demonstrate stronger CAR-mediated cytotoxicity towards NK-resistant cell line Du-145-PSMA, unlike CAR-cells expressing shp-2. Thus, the best option for enhancing cytotoxicity of NK cells and the YT cell line in particular is to induce activating signals using CARs in combination with the suppression of inhibitory signaling via knocking out its key mediator, the SHP-2 protein

Automated MATLAB tool for morphometric analysis of nerve fibers

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Introduction

Preclinical research of neuroregeneration requires assessment of nerve fibers histol-ogy. The most reliable results contain histomorphometry parameters of axons and myelin sheaths. Manual methods are prone to human error and are time consuming. Computer-based techniques may improve the above and deliver the accuracy comparable with a experienced researcher. The study aimed to prepare a MATLAB script, with a novel approach to contrast-based method used for whole nerve section analysis.

Materials & Methods

Semithin sections of a rat sciatic nerve stained with toluidine blue were a input data. They were scanned at 40x magnifications. Firstly, the analysis includes grey-scale conversion and contrast improving modifications e.g. CLAHE. Unlike other similar methods, which analyze objects after binarization, we worked with the grey-scale image. Objects found with regionprops function were then filtered. Our protocol offers manual verification and removal of false-positive objects. Then, a rectangle enclosing each object was defined. From the center to the edge of the acquired area line segment was lead and histogram on this length was set. The border of each axon was determined in the point of highest contrast between neighbour pixels. The borders of myelin sheaths were defined likewise. This operation was repeated 360 times, around the analyzed nerve cell (radial histogram scanning and thresholding). The method resembles manual analysis since local contrast is used to mark the axon. Finally, the main morphometric parameters may be determined. Results were compared with manual measurements of 28 random nerve images, estimated by 3 researchers in ImageJ. Comparison to manual data was shown as ratios: script: manual.

Results

After optimization of brightness and contrast parameters, axon area overlay at level 1,010 and 1,009 of the myelin sheaths was achieved. Paired T-test showed no significant differences between these two methods (p-value = 0,321). Use of Neural Net enables to reach 93,6% of accuracy of axons recognition vs 3 researchers. A run time of the script is about 12 times shorter than the manual method

Conclusion

The presented script performs an accurate analysis of nerve sections on a grey-scaled image. It overcomes bias of a binarization. The method decreases time of analysis and remains repeatable.

Effects of flow-controlled versus volume-controlled one-lung ventilation on oxygenation and respiratory mechanics in normo- and hypovolemic anesthetized pigs

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Introduction

During thoracic surgery, one-lung ventilation (OLV) is frequently necessary to improve the surgical access. The risk of hypoxemia and ventilator induced lung injury is increased during OLV due to higher alveolar collapse and intrapulmonary shunt. Major blood loss resulting in intravascular hypovolemia may impair the hypoxic pulmonary vasoconstriction, increasing the intrapulmonary shunt. Flow controlled- ventilation (FCV) is a new mechanical ventilation mode that enables both inspiratory and expiratory control. The slower decrease in airway pressure during expiration in FCV might reduce alveolar collapse.

We hypothesized that OLV with FCV compared to volume-controlled ventilation (VCV) increases the arterial partial pressure of oxygen (PaO2) and reduces mechanical power in normo- and hypovolemic anesthetized pigs.

Materials & Methods

After approval of the animal welfare committee (DD24.1-5131/449/71), we anesthetized and instrumented 16 juvenile pigs. Animals were randomised to one of two groups (n=8/group): 1) intravascular normovolemia and 2) intravascular hypovolemia. For the induction of hypovolemia, 25% of the calculated blood was drawn. To mimic thoracic surgery and systemic inflammation a right-sided thoracotomy was performed, and 0.5 µg/kg/h lipopolysaccharides from E. coli continuously infused, respectively.

Thereafter, animals were randomly assigned to mechanical ventilation of the left lung of two following sequences: I VCV-FCV and II FCV-VCV (60 min/mode). Gas exchange, hemodynamics, respiratory mechanics and distribution of ventilation (electro impedance tomography) were assessed every 20 min.

Results

PaO2 did not differ significantly between FCV and VCV (P=0.881). In the normovolemia group, FCV decreased the corrected expired minute volume (P=0.022) and positive end-expiratory pressure (PEEP) (P<0.001) compared with VCV. Also, the minute volume (P≤0.001), respiratory rate (P≤0.001), total PEEP (P≤0.001), resistance of the respiratory system (P≤0.001), and mechanical power (P≤0.001) were lower during FCV than VCV irrespective of the volemia status. The distribution of ventilation did not differ between ventilation modes (P=0.103).

Conclusion

During OLV in pigs, FCV compared with VCV reduced mechanical power and increased ventilation efficency, without significant effects on oxygenation.

Following studies might investigate whether the differences in mechanical power and ventilation efficiency result in less lung damage.

3D kidney model: Mimicking the proximal tubule and its vasculature by using a co-axial bioprinting technique

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Introduction

In phase III of drug evaluations, renal toxicity accounts for almost 1/5th of all dropouts. To ensure these safety-related withdrawals are detected in an early stage, models are needed to mimic the in vivo situation of the human kidney. The currently used static 2D models poorly mimic the function and morphology of the kidney. Nephrotoxicity is mainly detected in the proximal tubule (PT) of the nephrons, where solutes are actively being reabsorbed towards the bloodstream by the PT epithelial cells (PTEC). Co-axial bioprinting is a technique that can be used to create hollow channels embedded within hydrogel microfibers. In this project, we aim to use this technique to obtain two intertwined channels within these hydrogel microfibers by optimizing the bioink and the bioprinting device. The goal is to create a 3D environment in which both the PT and its microvasculature are included to model the reabsorption of solutes and eventually to reduce renal toxicity-related withdrawals in drug evaluations.

Materials & Methods

The bioprinting device was redesigned, the properties of the bioink optimized, and the bioprint parameters adapted for the viscosity of this bioink. Conditionally immortalized PTEC and human umbilical vein endothelial cells were seeded to mimic the PT and the microvasculature, respectively. Immunofluorescent stainings, inulin-FITC migration assays, and a degradation assay were performed to visualize cell proliferation and assess the porosity and stability of the hydrogel, respectively. One-way ANOVA and Tukey test were performed to assess significant differences.
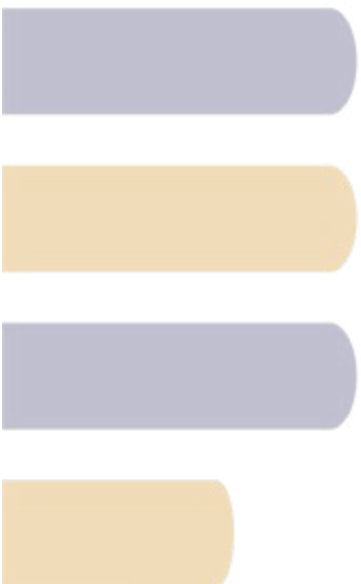
Results

We demonstrated that the optimized bioprinting setup allowed us to embed two hollow coiled channels simultaneously within one cytocompatible hydrogel microfiber. The migration assay and degradation assay showed 65% permeability for a hydrogel environment of a diameter of 100 μm compared to the 0 μm control ($P<0.05$), and no significant degradation over 4 weeks ($P<0.05$), respectively.

Conclusion

This printing device shows potential to mimic the 3D environment in which both the PT and its microvasculature are included. Further improvement of this setup and its implementation in pharmaceutical industry could eventually contribute to reduce toxicity-related withdrawals in drug evaluations.

Oral Sessions I

Cell Biology and Genetics
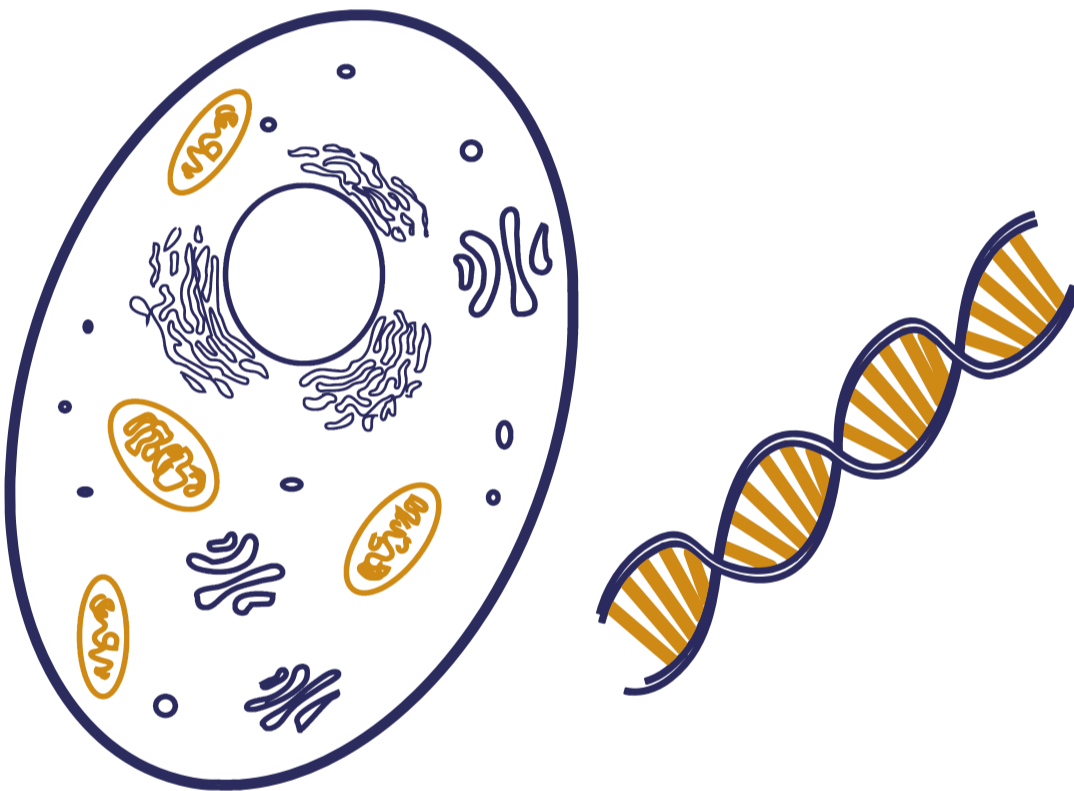
Presenters:
Ovechkina, V.O. (Vera)
Zaharija, B.
Viola, F (Federica)
van der Slikke, E.C (Kaylie)
Onyeogaziri, F.C (Favour)
Pociunaite, S.M.P (Severina)

The transgenic IPS cell model from a patient with SMA type I helps to assess the level of endoplasmatic reticulum stress

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Introduction

Spinal muscular atrophy (SMA) is a genetic disease, which characterized by the degeneration of the motor neurons in the spinal cord and further striated muscle atrophy. Although the pathogenesis bases are well observed, the molecular pathways of the disease remain unclear. There is evidence that the high-stress level of the endoplasmic reticulum (ER) has a sufficient role in SMA pathogenesis. The investigation of pathological processes in motor neurons is difficult because of the inability to safely extract them from patients as well as the postmortal neurons present the information only about the terminal stage of the disease. We aimed to make a transgenic IPS cell model with SMA type I, which allows estimation of endoplasmatic reticulum stress level.

Materials & Methods

IPSCs were generated from a SMA type I patient by using episomal vectors. The cells showed a pluripotent phenotype and could be involved in neural differentiation. The cells were transfected with plasmid vectors, containing components of a CRISPR/Cas9 system, tetracycline-controlled transactivator, and XBP-TagRFP chimeric protein. The XBP protein is a part of the ER stress response and can be used as a genetically-encoded sensor. The transgenic cells were selected with antibiotics and differentiated into motor neurons. The ER stress was induced by tunicamycin and the ER stress level was assessed with RFP fluorescence.

Results

We selected 2 subclones with the insertion of transactivator and XBP-TagRFP, which had no additional off-target integrations. Transgenic lines were differentiated in motor neurons with high efficiency. The RFP fluorescence was detected after the ER stress induction with tunicamycin on each stage of the neural differentiation. Moreover, there was no fluorescence in control groups (cells with no tunicamycin and non-transgenic IPSCs SMA type I).

Conclusion

We generated two transgenic IPS cell lines with SMA type I phenotype, which have the insertion of the ER stress sensor. After the ER stress induction, the RFP fluorescence was observed in transgenic cell lines, contrary to the negative control groups. The obtained cell model can be used in molecular studies of the SMA pathogenesis as well as a platform for drug screening.
The research was supported by RFBR grant № 20-34-70019.

Protein aggregation of DISC1 caused by its disruption in mental illness

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Introduction

Disrupted in Schizophrenia 1 (DISC1) was first implicated as a risk factor for mental illnesses such as schizophrenia, bipolar disorder and depression due to its disruption by a chromosomal translocation found in a Scottish family with high prevalence for these disorders. While it is known that the Scottish translocation affects DISC1 function, the exact mechanism of this is unclear. Recently, it has been suggested that several proteins, including DISC1, form insoluble aggregates in the brains of patients with chronic mental illness. Here, we propose that the formation of insoluble aggregates may be affected by the Scottish translocation.

Materials & Methods

Polymerase-chain reaction (PCR) was used to amplify different regions of DISC1, including those stopping at the translocation breakpoint, which were subsequently cloned into competent E. coli. The plasmids were harvested, purified and expressed in SH-SY5Y mammalian neuroblastoma cells. Data was obtained by fluorescent microscopy.

Results

Although it has been shown previously that a full-length DISC1 protein forms insoluble aggregates, which has also been confirmed in our work, the lack of knowledge about its structure has considerably impeded further studies. Taking into consideration the recently discovered DISC1 structure, we cloned multiple DISC1 regions, as well as the constructs truncated at the translocation breakpoint, and expressed them in mammalian cells. Those constructs encoding the central region of DISC1, including the ones ending at the breakpoint, have shown a clear propensity for aggregation within the cell cytoplasm. In contrast, constructs expressing only C-terminal regions of the protein did not show any indication of aggregate formation.

Conclusion

Based on our data, we were able to narrow the aggregating region of DISC1 down to a cluster of amino acids near the centre of the protein. Furthermore, DISC1 that is truncated at the Scottish translocation breakpoint may be more prone to aggregation than the full-length protein. Taking into consideration how aggregation affects the brains of patients with neurodegenerative diseases, these findings could present a powerful insight into biological mechanisms of mental illness.

Application of CRISPRCas9 technology for F8 promoter modification

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Introduction

Hemophilia A is a rare genetic disease caused by mutations in the gene coding for the coagulation FVIII. The hallmark of the disease is uncontrollable bleeding, which can be fatal if left untreated. Bleedings into joints are frequent, resulting in debilitating arthropathy. Contrarily to what was initially believed, FVIII is not produced by hepatocytes, because numerous studies have shown that hepatic sinusoid endothelial cells (LSEC) efficiently produce and secrete FVIII being the main source of FVIII. We focused our study on the FVIII promoter (pF8), finding two binding sites for the transcription factor Ets-1 involved in the angiogenesis and in the expression of endothelial genes. The aim of our study was to mutate the DNA of these cells through the CRISPR/Cas9 system removing the binding sites for Ets1, to evaluate, in subsequent studies if Ets-1 is important for pF8 activity.

Materials & Methods

We realized two guides for Cas9 complementary to the binding regions for ETS-1, these were inserted into two plasmids lentiCRISPRV2_Puro. The Colony PCR was subsequently performed using complementary primers to the guides, to evaluate if the bacterial colonies, obtained after transformation, had the plasmid with the insert. We selected the positive colonies containing the correct constructs, we purified the plasmidic DNA and the selected plasmids were sequenced with the Sanger Method. To introduce the genetic material into the cells, the plasmids were transfected into HEK293T cells through the calcium phosphate method. The positive cells were selected after Puromycin selection and the genomic DNA was isolated to evaluate through the T7 Assay if Cas9, together with the guides, had cut the two Ets-1 binding sites present on the F8 promoter.

Results

From the T7 assay it emerged that the cutting efficiency was greater than 30% for both gRNAs, so we can say that we have selected and produced efficient guides that are able to select the "on-target" sites of our interest.

Conclusion

The validated guides will be used on primary endothelial cells to further characterize the F8 promoter by a gene editing approach and verify the role of Ets1 on the functionality of pF8.

Sepsis induces mitochondrial DNA damage in the human kidney

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Introduction

Sepsis is not only associated with a high mortality during hospital admission, but also with increased long-term morbidity and mortality in survivors after hospital discharge. Although the pathogenesis of sepsis-associated organ injury is not precisely known, mitochondrial dysfunction seems to play a key role. Mitochondrial dysfunction is associated with a lowered production of ATP, but also with an increased generation of free radicals. We hypothesize that sepsis induces alterations to mitochondrial DNA, which permanently affects mitochondrial function and impairs long-term health and lifespan.

Materials & Methods

We determined mitochondrial DNA damage and assessed the mitochondrial stress response and quality control, using previously obtained renal biopsies from patients who died of severe sepsis with AKI (n = 12, department of critical care UMCG). As a control, kidney biopsies (n = 12) from non-septic patients with renal cell carcinoma were obtained.

Results

Patients who died due to sepsis had a significantly higher amount of mtDNA damage (p= <0.01) and a decrease in mitochondrial mass (p = < 0.05) compared to control patients. Furthermore markers for the mitochondrial stress response were significantly upregulated in septic patients and mitophagy, a markers for the clearance of damaged mitochondria, was increased. However, mitochondrial biogenesis markers, which implicate the genesis of new mitochondria, were downregulated during sepsis and no difference in mtDNA expression was seen.

Conclusion

Here we demonstrated that sepsis leads to mitochondrial DNA damage in the kidney. In addition these results may indicate a failure in the mitochondrial quality control system to compensate for the mitochondrial DNA damage and mitochondrial loss, causing long-term damage and health effects in patients with sepsis.

Heterogeneous, organ-dependent regulation of endothelial permeability in a mouse model of sepsis

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Introduction

Sepsis, an exaggerated host response to infection, leads to 6 million deaths worldwide yearly. In patients with sepsis, vascular permeability results in organ edema, which contributes to organ dysfunction. Under physiological conditions, vascular permeability is regulated by endothelial tight-, gap- and adherence junctions. The endothelial-specific tyrosine kinase receptor Tie2 is thought to control endothelial permeability by maintaining these junction molecules. We showed that in human and murine sepsis, Tie2 is downregulated, raising the question whether Tie2 contributes to increased permeability and organ edema. To answer this question, we used a genetically modified mouse to knock out Tie2 in the endothelium and mimicked the acute phase of sepsis by administrating the bacterial cell wall component lipopolysaccharide (LPS). We investigated the expression of endothelial junction molecules in kidney and lung, two organs that frequently fail in patients with sepsis.

Materials & Methods

mRNA was isolated and cDNA prepared from kidneys and lungs of wildtype (n=7 LPS-challenged; n=8 unchallenged controls) and Tie2 knockout mice (n=8 LPS-challenged; n=7 unchallenged controls). Expression of endothelial tight junction molecules (Ocln, Cldn5, Esam, Zo1, F11r), the gap junction molecule Gja4, and the adherence junction molecule Cdh5, was determined by RT-qPCR. Differences between groups were calculated using one-way ANOVA with post-hoc Bonferroni correction. P values <0.05 were considered statistically significant.

Results

In kidneys of Tie2 knockout mice, expression of the tight junction molecules Ocln, Cldn5, and Esam was significantly lower than in wildtype mice. Moreover, Esam expression in LPS-challenged mice was significantly lower than in unchallenged controls. Expression of the tight (Zo1, F11r), adherence (Cdh5), and gap (Gja4) junction molecules was unchanged by either Tie2 knockout or LPS challenge. In lungs, none of the junction molecules studied was affected by Tie2 knockout or LPS treatment.

Conclusion

Our data reveal a heterogeneous, organ- and junction-type dependent regulation of endothelial permeability by sepsis and Tie2 loss. The current mRNA expression analysis will be extended to liver and heart, and validated at protein level (to be presented during the ISCOMS meeting). Better understanding of the molecules that regulate vascular permeability will lead to novel therapies aimed at restoring these molecules in patients with sepsis.

Double-strand break repair dynamics in pericentromeric heterochromatin

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Introduction

Specific repair systems have evolved to protect cells from DNA damage. Although many of these systems are well studied, it is often overlooked how different chromatin domains in the nucleus influence the dynamic repair response. Euchromatin is a domain with active genes and an open conformation, whereas heterochromatin is a more compact environment harbouring silenced genes and repetitive sequences. Double-strand breaks are a particularly dangerous type of DNA damage and are often repaired by either non-homologous end joining (NHEJ) or homologous recombination (HR). Although HR is often considered the safest repair pathway, its execution in heterochromatin could be problematic. Recombination between homologous repetitive sequences on non-homologous chromosomes in heterochromatin could lead to the formation of acentric or dicentric chromosomes, often associated with tumorigenesis. DSB movement to the heterochromatin periphery has been proposed as a mechanism to prevent this aberrant recombination between repeats. Because of the specific environment and DSB dynamics in heterochromatin, we hypothesize specific chromatin changes are necessary for DSB repair in this domain. In this study we will try to determine the role of chromatin changes in DSB repair in heterochromatin.

Materials & Methods

We use locus-specific DSB systems (Janssen A et al., 2016), to study chromatin domain-specific repair responses and heterochromatin-specific dynamics in Drosophila tissue and cells. In combination with these DSB systems, we use state-of-the-art chromatin analysis as well as high-resolution live imaging to study DSB-associated heterochromatin changes and to determine their function in repair -kinetics, -dynamics and -pathway choice.

Results

Our preliminary chromatin immunoprecipitation results reveal that there is an increase in Histone H3 lysine 9 acetylation (H3K9ac) at DSBs when compared to intact DNA in pericentromeric heterochromatin. Live imaging of repair proteins upon irradiation of Drosophila cells also reveals that DSB relocalisation to the heterochromatin periphery is impaired after knock-down of H3K9 acetyltransferases (elp3).

Conclusion

These observations suggest that changes in the chromatin conformation by histone acetylation at the break site can help repair DSBs in heterochromatin by moving the foci to the heterochromatin periphery.

GI medicine and Nutrition
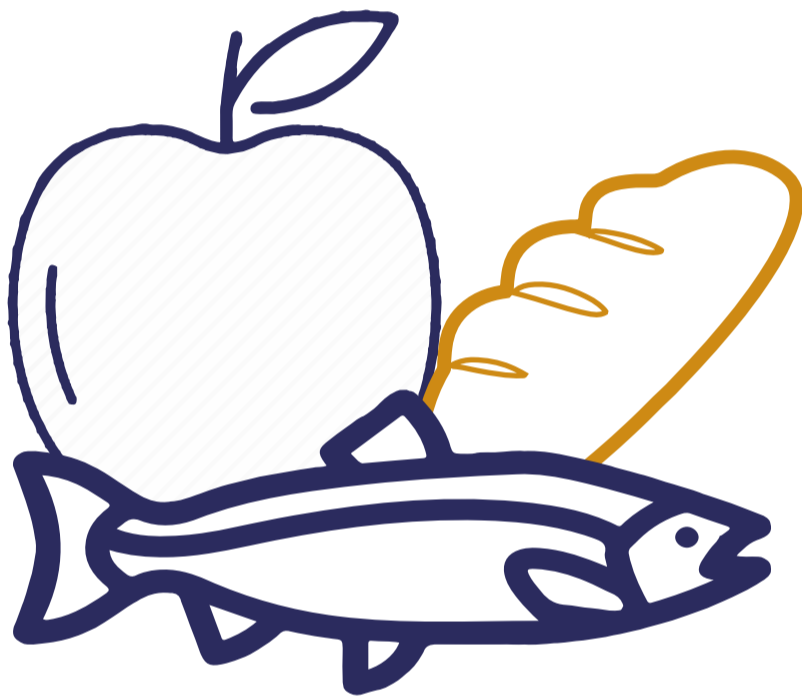
Presenters:
Mathur, K.M (Kushagra)
Ebrahimi, A. (Alireza)
Świerczyński, M. (Mikołaj)
Santaella, F. J. S. (Felipe)
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Effect of Artificial Sweeteners on Insulin Resistance Among Type-2 Diabetes Mellitus Patients

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Introduction

Incidence of diabetes mellitus has increased over the past few years, mainly due to our eating habits and physical inactivity. This also includes the use of artificial sweetening agents which have broadly replaced other forms of sugars. Studies have shown a rise in blood glucose levels in patients using artificial sweeteners(AS). Through this study, we aimed to determine if any relation between the two exists or not.

Materials & Methods

After obtaining a due clearance from Institutional Ethics Committee (IEC), a cross sectional study was conducted on patients who are a known case of type-2 diabetes mellitus. All the diabetics that presented in the OPD were divided into 2 groups based on whether they used artificial sweeteners (group A) or not (group B). Insulin resistance was calculated for each group using HOMA-IR (Homeostatic Model Assessment of Insulin Resistance) and graphs were plotted.

Results

The HOMA-IR values for Group A and B ranged from 0.9–24.33 and 0.12–10.83 respectively, with mean values of 7.39 and 2.6, showing that the ones who used AS had a higher insulin resistance as compared to those who were not taking the sweeteners. The study also showed that the duration of use of artificial sweeteners had a direct impact on serum insulin levels, that is, the ones who used AS for a longer duration, had a higher serum insulin than those who did not.

Conclusion

It can be concluded that the prolonged use of artificial sweetening agents has a harmful effect on the glucose metabolism and glycemic profile of a patient. Chronic use of AS can result in hyperinsulinemia, insulin resistance and poor glycemic control. The need of the hour is to reduce their intake and make people aware of their harmful effects in the long run. If our results match with those of other studies, evidence based practice can begin with further spread of information to a wider population in an endeavour to better the lives of the diabetic community of the world.

Comparison of the Effects of Mesalazine on the Treatment of Nonspecific Inflammatory Bowel Disease in Patients with Normal versus High Fecal Calprotectin

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Introduction

Nearly 10% of patients with inflammatory bowel disease (IBD) might show unspecified features that cannot be clearly characterized, these patients could be labeled as having "nonspecific" IBD (NIBD). In this investigation we aimed to compare the therapeutic effects of Mesalazine in NIBD patients with high and normal levels of fecal Calprotectin and assess the reduction of their symptoms during the treatment.

Materials & Methods

84 NIBD outpatients were involved in this study (42 with normal and 42 with high Calprotectin). Participants were being treated by 2 grams of Mesalazine for one month, and they were evaluated every week. Individuals' signs and symptoms were reviewed; consequently, the patients were labeled as treated/untreated.

Results

The result of presenting study demonstrated there was no significant difference between the level of Calprotectin among male or female participants (P = 0.28) or contributors with different ages (P = 0.067) or patients with dissimilar symptoms (P = 1.00). Patients who responded to Mesalazine and patients who did not had significant difference regarding Calprotectin level (P = 0.00). Patients with high calprotectin and abdominal pain showed a response rate of 94.5% to Mesalazine treatment; while patients with normal Calprotectin and similar symptom showed 36.1% of sensitivity to the drug (P = 0.000).

Conclusion

Our study showed patients with NIBD and high Calprotectin who received Mesalazine as treatment went into remission. The result of the present study also demonstrated that fecal Calprotectin can be used as a marker to predict relapse of NIBD symptoms and progression of NIBD to early stages of definite IBD, besides it can be used a sign of remission in these cases. Furthermore, fecal Calprotectin concentration monitoring in patients with symptoms that suggest the diagnosis NIBD may help us in order to early recognition of the disease before overt complaints. There was a significant correlation between the level of fecal Calprotectin and NIBD patients' response to Mesalazine; therefore, we could assume this parameter as an indicator of progression of IBD in patients with unspecified features of the disease.

Inflammation affects populations of interstitial cells in the colon in the mouse model of DSS-induced colitis

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Introduction

Inflammatory bowel diseases (IBD) are a group of chronic conditions of still not fully understood etiology. Here we hypothesize that interstitial cells: interstitial cells of Cajal (ICC) and telocytes may play a role in IBD pathogenesis. Interstitial cells are involved in intestinal motility by generating (ICC) and spreading (telocytes) impulses. Moreover, telocytes are likely to affect tissue repair, immune regulation or intercellular signaling. In this work, we evaluated the populations of ICC, telocytes and neurons in the inflamed and non-inflamed colon in the mouse model of DSS-induced colitis.

Materials & Methods

Twenty male Balb/C mice obtained from Department of Biology, University of Lodz, Poland were divided into control and DSS groups (10 mice each). The DSS group underwent a 7-day treatment with orally administered 3% DSS water drinking solution from day 0 to day 4, which was then exchanged for water. On day 7, mice were sacrificed and colon samples were taken for macroscopic evaluation of the inflammation score and immunohistochemical examination. The neurons were identified as PGP 9.5, ICC as c-kit and telocytes as CD34 and PDGFRalpha double-positive cells, respectively.

Results

Mice from DSS group had significantly higher macroscopic inflammation score than the control group. The examined cell populations of neurons and telocytes within the colon wall differed in number between the groups, with higher abundance of both cell types in the DSS group. Neurons were located mainly in muscular and external part of the wall, while the higher abundance of telocytes in the DSS compared to the control group was observed mainly in the intestinal crypts. No significant change in the number of cells was observed for the population of ICC between DSS and control groups; however, we observed differences in ICC morphology with larger, oval cells noted in the DSS group.

Conclusion

The inflammation impacts the populations of interstitial cells in the mouse colon. The number and distribution of neurons, ICC and especially telocytes suggest their role in adaptive reaction and regeneration of the mucosa during colitis. To the best of our knowledge, this is the first study on the possible role of interstitial cells in the pathogenesis of IBD.

Differential expression of miRNA 500a in patients with Crohn´s disease and ulcerative colitis

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Introduction

Inflammatory bowel disease (IBD) includes Crohn´s disease (CD) and ulcerative colitis (UC). Both are distinguished by endoscopic, histological, clinical features and outcomes. However, in almost 20% of cases, it is classified as indeterminate colitis. Recently molecular studies are gaining importance trying to discriminate between them. The B-catenin/Wnt signaling pathway is important to stem cell proliferation in the intestinal lamina propria and has an increased expression in biopsies from IBD patients. One miRNA, 500a, has been related to invasion by activation of the B-catenin/Wnt signaling pathway in lung cancer and glioblastoma. We investigated the differential expression of miRNA 500a in patients with CD and UC.

Materials & Methods

20 biopsy samples (10 CD and 10 UC) from non-treated IBD patients, were included in the study. Data were obtained using the online medical data from Sao Paulo State University hospital-Brazil. The histological features were analyzed with a gastroenterology pathology expert, with the diagnostics features from the European Crohn's and Colitis Organisation(ECCO) guidelines. Biopsy tissues were microdissected for molecular analysis. RNA was extracted with MagMax FFPE DNA/RNA Ultra kit (Applied Biosystems) and expression assessed using MegaplexTm Primer Pools for MirRna expression analysis for use with TaqMan Array Cards. We included 10 endogenous controls for normalization and 1 negative control. t-test and Mann-Whitney were used as statistical tools.

Results

There was 14 female (UC:7, CD: 7) and 6 male (UC:3, CD: 3) patients. 95% were Caucasian and 10% were smokers and alcohol consumers. The average age at diagnosis was 36,8 for UC and 31,7 for CD patients. UC presented with pancolitis in 50% and hemi-colitis in 50%. CD presented with the ileocolonic disease in 60 % and colonic disease by 40%. miRNA 500a was over-expressed in all samples from patients with CD and in 2 patients with UC ($p < 0.05$).

Conclusion

Our results demonstrated a significant increase of Mirna500a expression in patients with CD compared to UC patients. Further studies are necessary to validate this biomarker as a potential diagnostic tool.

Serological markers for early diagnosis of intestinal ischemia in strangulated small bowel obstruction

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Introduction

High lethality rate up to 30% due to acute strangulated small bowel obstruction (SBO) is connected with delays in diagnostics and treatment of intestinal ischemic injury which can be potentially fully reversible on early stages. We aimed to investigate if serological markers can be used for the early diagnosis of intestinal ischemia and evaluation of injury extent in strangulated SBO.

Materials & Methods

Twenty-two male Wistar rats (430-560 g) were randomly distributed in 4 groups: "O" - SBO (n=6); "SL" - strangulated obstruction of long loop (n=6); "S" - strangulated obstruction of short loop and "C" - sham operated (n=4). The SBO model was made by ligation of intestinal loop from both sides without mesenterium ; the strangulation - by ligation of intestinal loop with mesenterium using catheter (22G). The length of loop in groups "O" and in "SL" was 16-17 cm, in group "S" - 9-10 cm. The blood samples from femoral vein were collected before surgery and after 2 and 4 hours. In samples the leukocytes, lactate, alkaline phosphate, alanine aminotransferase (ALaT), aspartate aminotransferase (ASaT), creatine kinase (CK), C-reactive protein (CRP), intestinal fatty acid binding protein (I-FABP) were determined. Statistical analysis was performed using Statistica 13.0. For paired comparisons of continuous variables the U-criteria of Mann-Whitney was used, for multiple comparisons of dependent variables - Fridman's test. A p-value < 0.05 was considered as significant.

Results

During all period of experiment the significant increase of I-FABP, ASaT and CK in groups "S" and "SL" and lactate in all groups were detected. But the increase of CRP and leukocytes was not meaningful. In comparison between groups the significant difference was seen only in I-FABP level (p=0.017 "SL" vs. "O"; p=0.047 "S" vs. "O") and lactate (p=0.028 "SL" vs. "O"; p=0.03 "S" vs. "O") at 4 hours. In group "C" all markers were on pre-operative level.

Conclusion

Serum I-FABP seems to be a potential biomarker for detecting early intestinal ischemia in acute strangulated obstruction but its level does not reflect the extent of damaged bowel.

Double-blind placebo-controlled food challenges are of disputed value for children with non-IgE mediated cow's milk allergy

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Introduction

Cow's milk allergy (CMA) is one of the most common food allergies amongst children. Non-IgE mediated CMA is a subtype of CMA which typically causes delayed symptoms manifesting up to days after ingestion of cow's milk. The delayed manifestation of the symptoms makes establishment of the diagnosis challenging. Currently, the double-blind placebo-controlled food challenge (DBPCFC) is the reference standard for diagnosing all types of CMA. With this study, we assessed the value of the DBPCFC in diagnosing non-IgE mediated CMA.

Materials & Methods

We collected data from DBPCFCs that took place at Meander Medical Centre between January 2016 and November 2019 in children ≤5 years of age. All children were suspected of non-IgE mediated CMA. Data on symptoms after cow's milk exposure and symptoms ≤72 hours after the DBPCFC were extracted. In addition, recommendations from the pediatrician concerning reintroduction of cow's milk into the children's diets were collected.

Results

251 DBPCFCs were analyzed. 163 DBPCFCs (67,6%) were negative. Children experienced significantly more symptoms on the verum day (mean 0.61 symptoms, SD 0.99) compared to the placebo day (mean 0.37 symptoms, SD 0.73); p-value 0.003 95% CI 0.081 – 0.387. Also, delayed symptoms occurred more frequently on the verum day (mean 1.58 symptoms, SD 1.56) compared to the placebo day (mean 1.02 symptoms, SD 1.43); p-value <0.0001, 95% CI 0,261 - 0.856. Reintroduction of cow's milk after a negative DBPCFC and a positive reintroduction advice from a pediatrician, was successful in 60.5% of the DBPCFCs.

Conclusion

In over two fifths of patients, the diagnosis non-IgE mediated CMA can be rejected using a DBPCFC followed by the reintroduction of cow's milk into the diet. Numbers on false negative results of the DBPCFCs remain unknown. However, we identified reoccurring symptoms during reintroduction, parents remaining convinced that their child suffers from CMA and revision of the DBPCFC's conclusion by the pediatrician as the most important causes of unsuccessful reintroduction. This suggests an even lower sensitivity of the DBPCFC than expected, causing dispute about its value as the diagnostic reference standard.

Immunology and Endocrinology

Presenters:
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Anomah, A.V.K (Victor)
Lorenzi, V.L. (Valentina)
Amusat, Mr (Saheed Oladele)
Zhang, Z (Zedan)
Al-Mubarak, A A (Ali A.)

Alterations in thyroid hormone levels in diabetic patients and their contributions to diabetes-related atherosclerosis

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Introduction

Thyroid hormone levels often fluctuate in patients with type-2 diabetes mellitus (DM). The clinical implications of this fluctuation remain unknown. Previous research has shown that small changes in thyroid hormone levels increase the risk of DM-related complications such as atherosclerosis. Because DM-related atherosclerosis is mediated by oxidative damage, we hypothesized that thyroid hormone levels affect the anti-oxidative functions of high-density lipoprotein (HDL) in DM patients. This alteration in the anti-oxidative properties of HDL are reflected as DM-related atherosclerosis.

Materials & Methods

We conducted a case-control study that comprised of fifty DM patients with no prior history of thyroid abnormalities and fifty age-, sex-matched healthy controls. Thyroid hormone levels (free T3, freeT4) and thyroid stimulating hormone (TSH) levels were evaluated in all participants using enzyme-linked immunosorbent assay. The antioxidant properties of HDL were assessed by measuring the levels of serum paraoxanase-1 (PON-1)

Results

DM patients had significantly higher free T4 compared to healthy controls (p=0.001). Free T3 levels were significantly reduced in DM patients than controls (p=0.041). There were no group-differences in TSH levels. PON-1 levels were significantly reduced in DM patients compared to healthy controls. In addition, PON-1 levels increased with increases in free T3 levels in DM patients. No such changes were observed in healthy controls.

Conclusion

We found that thyroid hormone levels are affected in DM patients. Furthermore, thyroid hormone levels predicted alterations in anti-oxidative properties of HDL. These findings implicate the importance thyroid hormone fluctuation in DM patients and their potential contribution to DM-related atherosclerosis by reducing the anti-oxidative properties of HDL. Furthermore, this study highlights the importance to carefully manage thyroid hormone levels in patients with DM.

Thyroid dysfunction influences serum lipids concentration in chronic kidney disease patients

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Introduction

Dyslipidemia is prevalent in patients diagnosed of chronic kidney disease. Serum lipids level is regulated by thyroid hormones. Thyroid dysfunction in chronic kidney disease patients may contribute to cardiovascular complications in patients. The study aimed at determining the thyroid hormones level and lipid profile in patients with chronic kidney disease.

Materials & Methods

Participants recruited were made up of 60 chronic kidney disease patients and 65 controls. Demographics and clinical data were collected using standard questionnaire after obtaining Ethical Clearance. Serum thyroid stimulating hormone (TSH), free triiodothyronine (FT3) and (FT4) thyroxine were determined using enzyme-linked immunosorbent assay (ELISA). Serum creatinine and lipid profile were analysed using a clinical chemistry Analyzer.

Results

Patients were advanced in age than control group ($p < 0.05$). Blood pressure was higher in patients (137.77 ± 23.07) than controls 117.51 ± 15.58) ($p < 0.001$). Difference in BMI between the studied groups was not statistically significant ($p > 0.05$). Free triiodothyronine and thyroxine hormone levels in the CKD patients compared to controls were significantly elevated ($p < 0.05$). However, thyroid stimulating hormone level showed no significant change between the two groups ($p > 0.05$). Difference in serum lipids were not significant ($p > 0.05$) with exception of triglyceride and very low density lipoprotein ($p < 0.05$). Mean serum creatinine level was significantly elevated in CKD patients (339.40 ± 420.73) than the controls (78.06 ± 20.59), ($p < 0.05$), whiles creatinine clearance in patients (46.73 ± 39.08) was significantly low compared to the controls (107.12 ± 43.54) ($p < 0.001$). The mean glomerular filtration rate for the patients (53.48 ± 47.49) was also lower than the controls (132.78 ± 35.09) ($p < 0.05$). Glomerular filtration rate positively and significantly correlated with thyroid stimulating hormone levels ($r = 0.291$, $p < 0.05$). The sub-clinical hyperthyroidism in patients may be due to statin therapy but not dialysis. However, hypothyroidism is a well-known cause of secondary dyslipidemia in CKD patients and its association with atherosclerosis is well established.

Conclusion

Maintaining normal serum thyroid hormones may be important for proper management of CKD patients diagnosed of dyslipidemia.

Characterizing the effect of Dicer depletion on the heterogeneity of tumor-associated macrophages at the single cell resolution

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Introduction

Tumor-associated macrophages (TAMs) largely express an alternatively activated (M2) phenotype, which entails immunosuppressive and tumor-promoting capabilities. Reprogramming TAMs towards a classically activated (M1) phenotype may prevent immunosuppression and unleash anti-tumor immunity. Macrophages express detectable amounts of many miRNA species, which modulate macrophage differentiation and activation. Mature miRNAs are processed from hairpin-shaped precursor miRNAs by the RNAse-III enzyme Dicer.

The goal of this study was to use Single-Cell RNA Sequencing to study the effect of Dicer depletion in TAMs in a mouse model of adenocarcinoma.

Materials & Methods

Whole tumors obtained from mice in which TAMs were deficient for the Dicer1 gene and control mice were analyzed with Single-Cell RNA Sequencing. The computational pipeline assembled for the analysis of the tumor microenvironment at the single-cell resolution was the following: quality control, normalization, dimensionality reduction, clustering with graph-based methods, two-dimensional data visualization techniques, cell type annotation, marker gene detection, gene set enrichment analysis and differential state analysis. All the work was carried out in R.

Results

Dicer depletion in TAMs significantly increased the proportion of classically activated macrophages (Log Fold Change: 1.57, False Discovery Rate < 0.001), and reduced the proportion of alternatively activated macrophages (Log Fold Change: -1.25, False Discovery Rate < 0.001) in the tumor microenvironment. Classically activated macrophages were identified by the upregulation of Major Histocompatibility Complex class II antigens, while alternatively activated macrophages were characterized by the upregulation of Arginase-1. Moreover, a significant proportion of TAMs in both wild type and Dicer-KO mice showed markers of proliferation, such as histone cluster genes.

Conclusion

Suppressing miRNA activity in tumor-associated macrophages contributes to their reprogramming from an immunosuppressive phenotype to an immunostimulatory phenotype. Single-Cell RNA Sequencing also allowed for the discovery of a previously unreported population of tumor-associated macrophages that are in active proliferation in the tumor microenvironment.

Advantage of non-HDL-cholesterol as a Dyslipidemia Risk Tool

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Introduction

Cardiovascular diseases (CVDs) are the number 1 cause of death globally. According to the World Health Organization, an estimated 17.9 million people died from CVDs in 2016. Over three quarters of CVD deaths take place in low- and middle-income countries. People with cardiovascular disease or who are at high cardiovascular risk due to the presence of one or more risk factors such as hypertension, diabetes or hyperlipidaemia need early detection of their lipid profile for proper management. However, the routine lipid profile are not directly proportional to CVDs risks from empirical perspective. Therefore, this study aims to determine the suitability of non-HDL cholesterol as a dyslipidemia risk tool

Materials & Methods

This study was conducted on the lipid profile parameters of 231 hyperlipidemic subjects. The profile parameters (TC, HDL-C, and TG) were determined using enzymatic methods while the non-high-density lipoprotein (Non-HDL) cholesterol was extrapolated using Friedewald's formula and Non-HDL-C was derived by subtracting HDL-C from total cholesterol (TC) values. For statistical analysis, a normality test was first conducted to determine the distribution of the data. Then, descriptives were collected to measure central tendencies. Finally, Pearson's Correlation was employed to analyze linear relationships among the variables. All assumptions were validated at $p \leq 0.05$.

Results

The correlation analysis showed that there were significant positive relationships between TC; and HDL-C (r=0.26), LDL-C (r=0.95), TG (r=0.26) and non-HDL cholesterol (r=0.95). High-density-lipoprotein cholesterol showed a significant; negative relationship with TG (r= -0.27), and positive relationship with TC (r=0.26). Interestingly, we found that HDL-C have no correlation with LDL-C, and non-HDL-C respectively. The results also showed that LDL-C have a significant positive correlation with all the parameters except HDL-C. We also found that TG positively correlated with TC, LDL-C (r=0.14), and non-HDL-cholesterol (r=0.36). However, a negative correlation between TG and HDL-C was observed. Lastly, Non-HDL-C was found to have significant positive correlations with all the parameters except HDL-C.

Conclusion

The non-HDL cholesterol is significantly correlated with lipid profile parameters except HDL-cholesterol. Therefore, it is suggested that assessment of the risk and management of cardiovascular diseases should focus less on HDL-C, but more on non-HDL-cholesterol in conjunction with TC, LDL-C, and TG.

In vitro expanded CD8+CD28- T suppressor cells of kidney transplant recipients show allospecific suppression property

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Introduction

Human CD8+CD28- T suppressor (Ts) cells have been recently proposed to be essential for induction and maintenance of immune tolerance. The optimized novel methodology for expanding CD8+CD28- Ts cells in vitro was established based on our previous study focusing on healthy volunteers. However, whether CD8+CD28- Ts cells from transplant recipients, particularly kidney transplant recipients (KTR), could be expanded and exhibit immunomodulatory property in alloimmunity should be investigated further.

Materials & Methods

The CD8+CD28- Ts cells of KTR were expanded through coculture of CD8+T cells and antigen presenting cells (APCs) whose human leukocyte antigen class I (HLA-I) antigens well matched with that of kidney donors for 9 days in the presence of IL-15 in vitro. Then, the immune suppression properties of CD8+CD28- Ts cells were observed. Besides, the phenotypic characteristics of CD8+CD28- Ts cells were also analyzed after in vitro expansion.

Results

Under the stimulation of IL-15 and allogenic APCs, the CD8+CD28- Ts cells from KTR were expanded vigorously in vitro. The CD28-/CD28+ cells ratio was enhanced during the proliferation and differentiation of CD8+T cells (from 0.31 to 1.00). Importantly, the expanded CD8+CD28- Ts cells displayed the capacity that suppressed proliferation of CD4+ T cells from KTR, among which the suppression showed in a donor-specific manner. However, the CD8+CD28- T cells purified directly from PBMCs of KTR didn't show the inhibitory effect. Upregulated expression of TIM3 and CD132 but downregulated expression of GZM-B and perforin while exhibiting no cytotoxicity, were seen in the expanded CD8+CD28- Ts cells.

Conclusion

Our findings provide further evidence that CD8+CD28- Ts cells could be expanded from CD8+ cells of KTR and exhibit donor-specific suppression property, which suggest that the novel methodology will probably be a potent strategy for in vitro generation of such regulatory cells to induce and maintain immune tolerance in transplantation in the future.

Biomarker profile of low selenium in HF patients is associated with unfavorable immune processes

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Introduction

Selenium (Se) deficiency affects approximately one fifth of heart failure (HF) patients in Europe and has been associated with worse outcomes. The mechanisms through which this deleterious association can be explained are not completely known. Therefore, we assessed 363 blood biomarkers from multiple pathophysiological domains to identify pathophysiological pathways related to aberrant Se concentrations in patients with HF.

Materials & Methods

Serum Se was measured in 2328 patients of the BIOSTAT-CHF cohort that included patients with worsening HF. Additionally, plasma levels of 363 biomarkers from multiple pathophysiological domains were measured (Olink proteomics). Full-blood transcriptomic analyses were carried out in a subset of 887 patients to determine mRNA expression levels of the 25 known selenoproteins and used to assess the relationship between Se levels and these mRNA signatures. The ncvreg package for R-Studio v.3.6.0 was used to fit a Minimax Concave Penalty (MCP) penalized linear regression model for predicting Se levels. Potential features to be selected included clinical characteristics and all biomarkers with <10% of measurements exceeding the lower limit of detection. The ClueGo plugin for Cytoscape v.3.7.2 was used for pathway enrichment analysis.

Results

Lower Se levels were significantly associated with older age, female sex, worse exercise capacity, and elevated IL-6 levels. The MCP regression model selected 58 variables with <5% marginal false discovery rate. Differential expression analyses indicated the following biomarkers to be associated with increased Se concentration: EGFR, IFN-gamma-R1, CD4 GDF15, and IL10. Whilst biomarkers associated with decreased Se concentration included: PCSK9, SPON2 TNFRSF4, CEACAM1, ADM and PAI. Pathway enrichment analysis of the selected biomarkers identified enriched processes related to T lymphocyte regulation/proliferation, and macrophage/natural killer cell mediated-immunity. Assessment of the seleno-transcriptome showed EEFSEC (β = 0.00094; P = 0.0014), SELENOH (β = 0.0010; P = 0.011) and MSrB1 (β = -0.0021; P = 0.0014) to be significantly associated with serum Se levels.

Conclusion

Low Se levels were independently associated with a more pro-inflammatory biomarker profile in HF patients. This is supported by the association between MSrB1 expression, a regulator of immune response, and Se levels. These data suggest immunomodulatory pathways to be activated in patients with HF and low Se levels.

Infectious Diseases
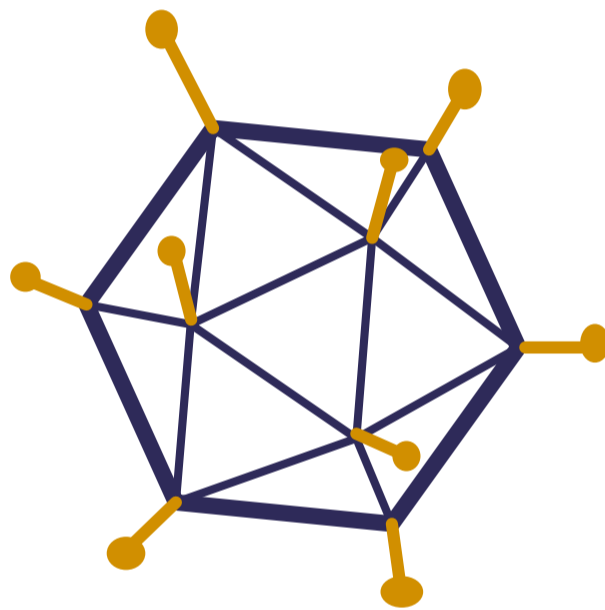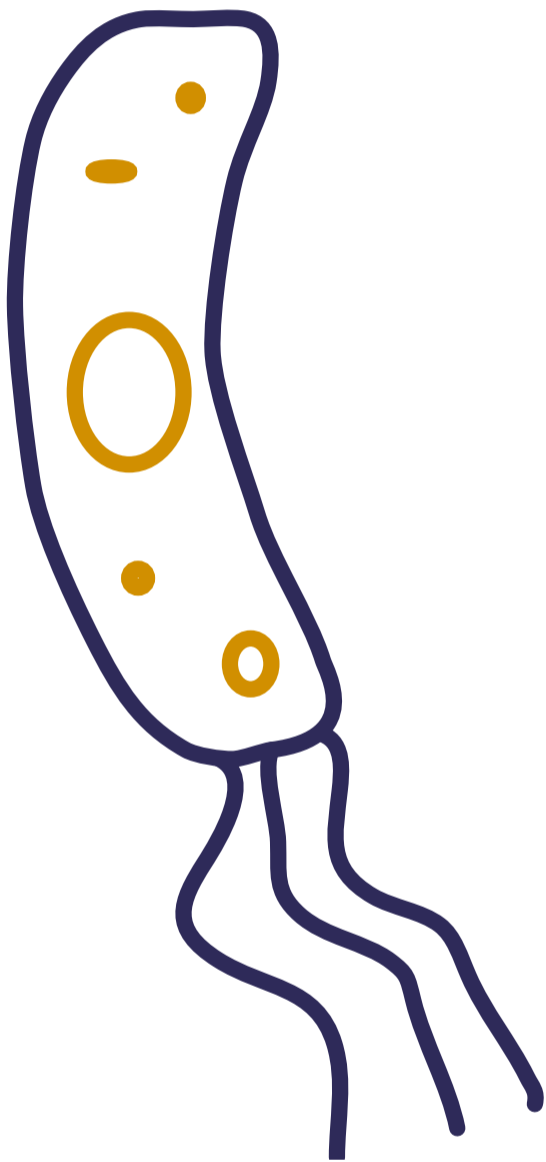
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Viscosin from Pseudomonas Fluorescens Bacteria Membrane Inhibit Streptococcus Pneumoniae Growth, Promising a Novel Pneumonia Therapy: An In Vitro and In Silico Study

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Introduction

Pneumonia is a lung infection caused by Streptococcus pneumoniae. The current treatment of pneumonia is using antibiotics, but most patients are resistant to available antibiotics. Pseudomonas fluorescens is a common bacteria that lives in soil and water which has potential in the development of a new Pneumonia treatment. In the membrane of Pseudomonas fluorescens contain Viscosin, a lipoprotein synthesized by Pseudomonas fluorescens, that serves as a medium in motility which also have antimicrobial effects that can be used as antibiotics and inhibit the biosynthesis of polysaccharides by inhibiting the LasR protein. LasR is an agent of replication and transcription of Streptoccocus pneumoniae. The purpose of this study is to use Viscosin as a treatment for pneumonia in Indonesia.

Materials & Methods

This research was conducted using two method, in-silico and disk diffusion test in in-vitro. In In-Silico, the procedure were computerized using licensed softwares such as Pymol and VegaZZ. Meanwhile in In-Vitro, the Streptococcus pneumonia and Pseudomonas fluorescens were used as the main subject. The variable used in the study are: positive control using Cotrimoxazole, negative control, and three variant doses of viscosin for Treatment 1 (75 µl), Treatment 2 (87.5µl) and Treatment 3 (100µl). The efficacy of each treatment were observed in agar plate as inhibition zone and the diameter measured using caliper in millimeters (mm).We use SPSS17 for Windows with confident interval of 95%.

Results

In silico study shows that viscosin can bind to the active side of LasR in valin 144 with a bond strength of -7.9 Kcal / mol. This bond will inhibit the replication or transcription of Streptococcus pneumoniae. In vitro study exhibited using different concentrations of viscosin, the zone of inhibition obtained using One way ANOVA was found to be statistically significant ($p=0.001$). Pearson correlation test showed a very strong and positive relationship (coefficient A = 0.776 and B = 0.119). Thus with the increasing concentration of Viscosin, the antimicrobial potential is stronger.

Conclusion

Based on this study, it can be concluded that Viscosin have prospective antimicrobial properties against Streptococcus pneumoniae bacteria. Viscosin can be potential as pneumonia treatment.

Sublethal dose of Bacillus sphaericus enhanced vector competence of Anopheles stephensi for Plasmodium yoelii by suppressing the midgut epithelial nitration

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Introduction

Malaria, transmitted by mosquitoes, is still one of the most devastating disease worldwide. Vector control is an effective way to control this disease. Bacillus shpaericus (Bs) has been used as an ideal mosquito biolarvicide because of its good biological effects. However, some mosquitoes can survive from the treatment with sublethal dose of Bs (SdBs) because of nonstandard using in reality, which would change their biological traits. This study was focused on exploring whether SdBs treatment will affect vector competence of the surviving An. stephensi to malaria, and discussing the potential mechanisms. This study will provide new ideas for blocking the spread of malaria.

Materials & Methods

Firstly, we dissected the midguts of mosquitoes in control and Bs groups, and assessd the infection rates and densities of them. Then, transcriptome sequencing was conducted to identify the expression pattern of mRNA transcripts in control and Bs groups. Bioinformatics analyses were performed to examine the biological functions of the differentially expressed genes. Finally, SYBR quantitative PCR assay was utilized to validate the differentially expressed genes.

Results

We discovered that SdBs treatment significantly increased the infection rate of Plasmodium from 92.1% (210/228) to 97.6% (202/207) (P=0.011<0.05), and enhanced the infection densities from (56.69±69.29) to (84.19±75.64) per mosquito either (P<0.01). By transcriptome sequencing, a total of 45 differentially expressed genes were identified, 30 of which were up-regulated and 15 of which were down-regulated. Bioinformatics analyses revealed that the differentially expressed genes mainly participated in innate immunity signaling pathways including Toll, Imd and JAK-STAT. Meanwhile, Bs group had a significantly lower expression level of heme peroxidase (HPX) gene and leucine rich immune protein (LRIM) gene than control group, which were confirmed by qPCR.

Conclusion

We firstly found that the SdBs treatment significantly enhanced the vector competence of An. stephensi to malaria parasites, which revealed a potential hazard to human health. Our further results indicated that SdBs treatment could remarkably inhibit midgut epithelial nitration by down-regulating the expression of HPX gene and block TEP1 from killing plasmodium by suppressing the expression of LRIM gene, resulting in an increase of malaria parasites.

Sero-prevalence and risk factors of human brucellosis among febrile patients visited Derayitu Health center and Kelewani Primary Hospital at Awra and Gulina district, Afar Region, Ethiopia

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Introduction

Brucellosis is an important neglected zoonotic bacterial disease that affect animals and humans for decades. In humans, the illness is relating to chronic debilitating infections, recurring febrile conditions, joint pains, malaise, fatigue and arthritis resulting in substantial lasting disabilities. The aim of this study was to determine the sero-prevalence and risk factors of human brucellosis among febrile patients visited health institutes at Awra and Gulina District, Afar Region; Ethiopia

Materials & Methods

A purposive cross Sectional study was conducted among febrile patients visiting health institutes at Awra & Gulina District of Afar region, Ethiopia from February to May 2019. After consent/assent obtained, demographic and clinical data were collected using structured questionnaire and 3-5ml venous blood was collected with plain vacationer tube from febrile study participants. Thick and thin blood films were prepared, Serum was separated and stored in refrigerator. Rose Bengal plate Test was performed and positive sera were confirmed using ELISA. Giemsa stained blood films were used for diagnosis hem-parasites. Data were entered in EpiData3.1, and exported to StataSE 14 to analyze prevalence and potential risk factors at 95% confidence interval. $P < 0.05$ was considered as statistically significant

Results

444 febrile individuals (female 61.1%), age ranged from 2 to 83 years (mean = 26.1, SD = ±11.8) were participated in this study. Among all individuals tested for brucellosis, 31.5% (140/444) were found reactive by RBPT and only half of the reactive (70/140) were found reactive again by ELISA. The sero-prevalence of Brucella infection based on the two tests was 15.8% (70/444). Being males (23.3%, $X2 = 13.05$; $p<0.001$), illiterate (20.4%, $X2 = 6.21$; $p = 0.045$) and rural residents (17.6%; $X2 = 3.93$; $p = 0.047$) were highly infected by Brucella infection than their respective comparison. Multivariate logistic regression model analysis revealed that drinking of raw milk (AOR=16.96, 95%CI: 2.27-126.69, p=0.006) and touching aborted fetus/discharges without protection (AOR=2.13, 95%CI: 1.08-4.20, p = 0.029) were found significantly associated with having brucellosis whereas being females (AOR = 0.42, 95%CI: 0.44 - 0.74, P = 0.003) were found associated with not having brucellosis. Of all (444) individuals, 19 (4.3%) were found positive for malaria infection (only for P. falciparum).

Conclusion

The sero-prevalence of human brucellosis among febrile patients is found high (15.8%). Consuming raw milk and touching of aborted material/fetus were found risk factors for brucellosis. Lack of awareness about the zoonotic nature of brucellosis, together with an existing habit of raw milk consumption and close contact with animals, can serve as means of infection to human beings.

HIV-1 infected patients exhibit altered expression of cholesterol transport proteins and immunomodulators molecules

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Introduction

The main mechanism associated with immune alteration during human immunodeficiency virus type-1 (HIV-1) infection is the progressive and uncontrolled inflammation, strongly induced by the inflammasome activation. This complex can be activated by several molecules, but recently some reports indicate that TXNIP and Caspase-5, alternative pathways for inflammasome activation, have an important role in this process. As antiretroviral therapy is unable to control immune activation, the study of immune modulator molecules, such as high-density lipoproteins (HDL) can provide alternative strategies to control immune activation. However, the role of HDL and molecules involved in its synthesis like cholesterol transport proteins ABCA-1 and 3 during the HIV-1 infection are still unclear. Therefore, this research aims to explore the expression of TXNIP, Caspase-5, ABCA-1 and 3 and its association with HDL levels and clinical parameters in HIV-1 infected patients.

Materials & Methods

A cross-sectional study, including 23 HIV-1-infected patients without antiretroviral treatment, and 7 healthy controls, was conducted. Viral load, CD4+ T-cell counts and serum HDL levels were quantified. The expression of TXNIP, Caspase-5, ABCA-1 and 3 was determined by quantitative real-time PCR. The data were analyzed in GraphPad software version 7.02.

Results

HIV-1 infected patients showed significantly lower levels of HDL and TXNIP than healthy controls. Interestingly, lower transcriptional expression of ABCA-3 was observed in HIV-1 infected patients with viral load >2000 copies/mL. The expression of ABCA-1 and Caspase-5 was not significantly altered in our HIV-1 patients. Finally, a positive correlation between HDL levels and CD4+ T-cell counts was found.

Conclusion

Our results suggest that during HIV-1 infection occurs an alteration in HDL metabolism and ABCA-3 expression. In addition, the alternative pathways for inflammasome activation were not relevant, at least in our HIV-1 patients. However, given the complexity of the immune response during HIV-1 infection, additional studies are needed to establish the role of HDL in the control of inflammation during HIV-1 infection in order to elucidate the precise mechanisms behind these processes.

Antiviral In-vitro effect of Lovastatin against Chikungunya virus infection

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Introduction

Chikungunya virus (CHIKV) is an enveloped emergent mosquito-borne alphavirus in America. Its transmission causes the chikungunya disease. The most of infection symptomatology disappear after the acute phase (almost a week), but some persistent neurological, ophtalmological and articular symptoms could last even years.

There are no licensed antiviral drugs against CHIKV. The many years of research and the expensive clinical studies to probe effectiveness and security for new therapies development, leads to investigate the off-label indications of the potential antiviral activity of medicines already approved by World drug agencies. Then, the aim of this study was to evaluate the potential in-vitro antiviral activity of Lovastatin against CHIKV.

Materials & Methods

Lovastatin antiviral activity was tested with the combined treatment strategies (Pre-during and post-treatment) at different concentrations (10 µM, 5 µM and 2.5 µM) on infected VERO cells with CHIKV/Acol at different MOI (5, 1 and 0.1). The individual POST-Treatment strategy was also accomplished at different concentrations (20 µM, 10 µM and 5 µM). The in vitro inhibitory effect was quantified by plaque assay in VERO cells.

Ribavirin 200 and Doxycycline 50 µM, FDA approved drugs with previous reports against CHIKV, was also researched at the same conditions as positive inhibition controls to compare the results. All data were analyzed by t-student.

Results

The combined treatment strategies with lovastatin in all the tested concentrations present an in-vitro CHIKV inhibition despite the different MOI ($p < 0.05$), and 10µM, concentration previously proved against another arbovirus (DENV), had an inhibitory effect above 3Log of the CHIKV infection. Also, the POST-treatment strategy shown a concentration dependent antiviral activity ($p < 0.05$). The inhibition controls, doxycycline and Ribavirin, shows 91 and 92%, respectively ($p < 0.05$) and a superior anti-CHIKV activity of Lovastatin was statistically significant compared with these two controls ($p < 0.05$).

Conclusion

Lovastatin is capable of a significant in-vitro inhibition of the CHIKV infection, even better than other approved drugs. Therefore, this research demonstrates that the potential off-label antiviral indication of this drug could be a possible treatment for Chikungunya disease.

The correlation of CTLA-4/CD86 signaling pathway and Epstein-Barr virus coinfection in patients suffering from chronic lymphocytic leukemia

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Introduction

Viral pathogens play a significant role in hematological cancers. Infection caused by Epstein-Bar virus (EBV) is commonly associated with an adverse prognosis in CLL, however the underlying mechanisms are still undiscovered. Herein we present a study aimed to validate whether EBV presence worsens the course of CLL by deregulation of CTLA-4/CD86 signaling pathway.

Materials & Methods

Polymerase chain reaction was used to measure the load of EBV DNA in the blood of 110 newly diagnosed, treatment-naïve patients with CLL. The expression of CTLA-4 and CD86 antigen on CD4+, CD8+, and CD19+ cells was assessed with flow cytometry. Additionally, CTLA-4 and CD86 serum concentrations were measured through enzyme-linked immunosorbent assays. We confronted the expressions of CTLA-4 and CD86 to EBV DNA amount and clinical outcomes.

Results

Fifty-nine (54%) patients had detectable EBV DNA [EBV(+)], and this group had more advanced disease at baseline. CTLA-4 and CD86 serum concentrations and their expressions on investigated cell populations were significantly higher in EBV(+) than EBV(-) patients. EBV load correlated positively with unfavorable prognostic markers of CLL and the expression of CTLA-4 on CD3+ lymphocytes (r=0.5339; p=0.027) and CD86 on CD19+ cells (r=0.6950; p<0.001). EBV(+) patients had higher risks of treatment initiation and lymphocyte doubling during a median follow-up period of 32 months (p<0.001). Among EBV(+), but not EBV(-), patients, increased expressions of CTLA-4 on CD4+ and CD8+ cells were associated with elevated risks of progression, treatment initiation and lymphocyte doubling (p≤0.020).

Conclusion

We propose that EBV coinfection causes the worse prognosis in CLL patients, partly due to EBV-induced up-regulation of CTLA-4 expression. CTLA-4 inhibitors could be promising alternatives for patients with CLL, therefore we suggest that clinical trials evaluating the use of CTLA-4 inhibitors should be considered for patients with CLL who have EBV reactivation, as those patients could have an increased risk of treatment failure.

Medical Microbiology and Haematology
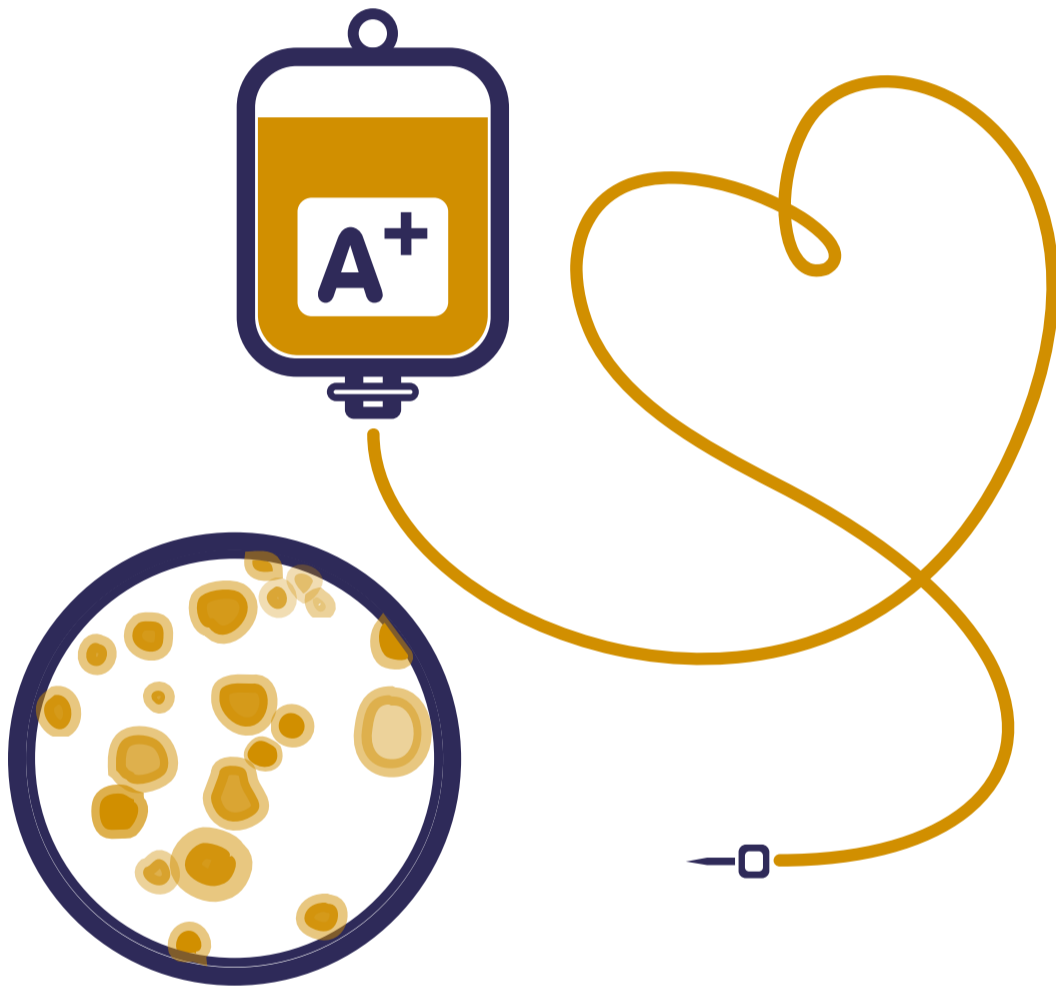
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The effect of the composition of the intestinal microbiota on immune system

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Introduction

Human microbiota plays a key role in the functioning of the immune system, the metabolism of lipids, glucose and bile acids, as well as in the defense against pathogens through competition for space and nutrients, activating the host's immune system, affecting immune cells. It is assumed that a change of intestinal microbiota is associated with the development of obesity, the occurrence of inflammatory, autoimmune, neurodegenerative diseases and the intestinal form of the «graft versus host reaction» (GVHD). We sought to evaluate the species diversity of the intestinal microbiota in children after HSCT and the control group.

Materials & Methods

The material for the study was stool samples obtained from 11 children after HSCT and 10 children of the control group. Taxonomic analysis of fecal microbiota was carried out by sequencing the V3-V4 region of the 16S rRNA gene on an Illumina MiSeq platform. Bioinformatics processing was carried out using QIIME software.

Results

The diversity of representatives of the intestinal microbiotaa was significantly reduced in 11 samples of the patients (R_Shannon = 3.51),compared with the control group (R_Shannon= 5.47). An increase in the microbiota of bacteria of the f. Enterococcaceae is observed in 7 patients after HSCT and an increase in the microbiota of bacteria of the of f. Lactobacillaceae in 8 patients. Besides, the intestinal microbiota of patients is characterized by a decrease in the proportion of the g. Blautia and g. Clastridiales.

Conclusion

The intestinal microbiota of patients is characterized by an average low diversity of intestinal microflora (R_Shannon = 3.51) than the microbiota of patients in the control group (R_Shannon = 5.47). A decrease in the diversity of intestinal microbiota usually indicates the presence of an inflammatory process. A high level of taxonomic diversity makes the microbiota more resistant to colonization by pathogens, and a decrease in diversity increases the likelihood of pathological processes.

Effects of biosurfactants in E. coli: adhesion and biofilm formation

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Introduction

The human gut is colonized by complex commensal organisms that have the ability of aiding the host's nutrition and maintenance of homeostasis. Probiotics play an important role in protecting the host from infection through a variety of mechanism including production of bacteriocin and biosurfactant to inhibit the adhesion of pathogens (ref). Bifidobacteria are probiotics who can protect the intestine from attacks by pathogens.

Aim: In this study, we investigated the effect of the biosurfactant produced by bifidobacteria on the inhibition of the adhesion and biofilm formation of Escherichia coli.

Materials & Methods

Biosurfactant produced by bifidobacteria was collected and evaluated by measuring the surface tension using Axisymmetric drop shape analysis-profile (ADSA-P). The sterilized (0.22 µm filter) biosurfactant was used to coat a surface and evaluate the effect on E. coli adhesion. E. coli was cultured in a microfluidic device (height 150 µm, width 1 mm, length 1 cm). E. coli (3×10^8 mL-1) was flown through a microfluidic device at the rate of 300 µL mL-1 for 4 h; the images of E. coli on the surface were continuously taken during the adhesion time. The number of E. coli on the surface was calculated with imageJ. After 4 h adhesion, LB growth medium was flown through the microchannel to evaluate the effects of biosurfactant on E. coli biofilm forming. After 24 h biofilm formation, the thickness of the biofilm was determined with optical coherence tomography. The images were analyzed with imageJ.

Results

When coating the microfluidic channel with the B. breve biosurfactant, it was observed that the number of E. coli adhering on the biosurfactant coated surface was ten times less than in the channel without the coating. Furthermore, it was also shown that the total area occupied by the biofilm formed after 16 h in the coated channel was 16.09% and in the non-coated channel was 45.67%.

Conclusion

Biosurfactants produced by bifidobacteria decreased the number of E. coli adhering on the biosurfactant coated surface and also reduces the biofilm thickness.

Dynamic changes in the microbiome and mucosal immune microenvironment of the lower respiratory tract by influenza virus infection

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Introduction

Influenza is a major public health concern, and the primary cause of death among the critically ill patients, especially the infants, the elderly, pregnant women and those with chronic infection, is secondary bacterial infection. Although studies have explored several molecular and cellular mechanisms underlying secondary bacterial infection post IAV infection, the role of lung microflora has been largely ignored. Recent studies have reported that the alteration of lower respiratory tract (LRT) microbiome is associated with diseases. The microenvironmental homeostasis of LRT is important for the defense against the invasion of potential pathogens. However, the microenvironment of LRT is unclear on the condition of influenza virus infection, especially on long-term observation. The objective of this study was to determine host anti-virus activity, microbial flora and metabolic mass in the LRT of mice during influenza virus infection.

Materials & Methods

Female C57BL/6 mice, aged 8 weeks, SPF intranasal inoculated with 50 µl saline/influenza virus (H1N1/PR/8, 6.2×108 PFU per mouse), and collected bronchoalveolar lavage fluid (BALF) and lung tissues. We then used a series of bioinformatics methods to analyze the microbiome, transcriptome, and metabolome of the samples.

Results

There were obvious systemic changes after influenza virus infection, such as body weight changes. And the microbiota diversity and structure of bacterial communities also changed after infection. Genomic function of microbiome indicates different periods have different immune ability. After infection, differentially expressed genes also changed a lot. KEGG pathway analysis of DEGs following H1N1 infection revealed significant pathways involved in local immune responses and cell adhesion molecules in the lung of mice. Metabolomics analysis showed metabolic changes in BALF after influenza infection.

Conclusion

Influenza virus infection induces a long-term alteration of LRT micro-environment, disrupts the LRT microbiome, alters the LRT metabolites and desensitizes the immune system of lung. The imbalance of homeostasis of LRT micro-environment may give a chance for the invasion of potential pathogens.

In-vitro Experimentation of indigenously devised Enteric String Test (K-8 spider) as a sample collection method for Pediatric Pulmonary Tuberculosis

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Introduction

Tuberculosis (TB) has the highest mortality worldwide and also the leading cause of deaths among people with HIV/AIDS. Pediatric TB suspects contribute 11% of total TB cases and are unable to produce adequate sputum which is mostly pauci-bacillary. We designed a novel, cost-effective indigenously devised enteric capsule (K-8 spider) that may provide a simple tool for obtaining gastric samples containing ingested sputum in sputum scarce pediatric patient and possibly in individuals with HIV/AIDS. The aim of this study was to investigate the in-vitro ability of K-8 spider to effectively pick up and transfer microorganism for their detection by microbiological techniques.

Materials & Methods

The ability of K-8 spider to adsorb and transfer microorganisms was tested in multi-stepwise assessment experiments starting from E.coli to H37Rv and finally replicating in-vivo conditions with fully assembled K-8 enteric capsule and patient's sputum positive sample. Objective evaluation of the analytic performance of tests, program conditions, and operational research determining the local factors affecting the tests were done.

Results

The K-8 spider demonstrated its ability to transfer E.coli by displaying growth on both nutrient and MacConkey agar. Mycobacterium tuberculosis was also transferred successfully by the K-8 spider shown by growth present on the Lowenstein Jensen slants, MGIT and presence of acid-fast bacilli on smear microscopy. The blood agar culture plate did not show any growth indicative of no contamination.

Conclusion

The K-8 spider containing capsule effectively picked up mycobacteria and has the potential to be used as a sample collection method for effective diagnosis in sputum scarce children and HIV/AIDS subjects. In a resource-limited setting novel and low-cost sample collection method like the K-8 spider will have a definitive impact on accelerating the detection of pediatric tuberculosis. This will be an inexpensive, simple to use, effective test for not only pediatric tuberculosis diagnosis but may also serve as a tool for screening HIV-TB diagnostic workup at the primary level of health care. As children represent the future burden of TB disease, these efforts could significantly reduce the overall global burden of TB in years to come.

The impact of helicobacter pylori eradication on platelet counts of adult patients with idiopathic thrombocytopenic purpura

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Introduction

diopathic (immune) thrombocytopenic purpura (ITP) is an acquired disorder characterized by autoantibodies against platelet membrane antigens. Several studies found an association between Helicobacter Pylori infection and the incidence of ITP. So far, It is still unclear whether H. pylori eradication will increase platelet counts in adult ITP patients. We conduct this study to investigate platelet recovery in ITP patients after H. pylori eradication.

Materials & Methods

This is a prospective study. The diagnostic criterion for Idiopathic thrombocytopenic purpura is: isolated thrombocytopenia, with no evidence of any underlying causes like drugs, TTP, SLE, hepatitis, HIV,CLL and… etc. We examined blood smears of all patients. We have diagnosed Helicobacter pylori infection by histological examination of several biopsies obtained from stomach and duodenum by esophagogastroduodenoscopy (EGD). If EGD was not applicable due to patient's poor situation or platelet count, H.pylori infection was diagnosed by the positivity of serum antibodies or respiratory urease test. We treated infected patients with triple therapy (omeprazole 40 mg once daily, amoxicillin 1000 mg twice daily and clarithromycin 500 mg twice daily) for 14 days. Uninfected patients did not receive any treatment. We did platelet quantification at the beginning of the study, at the end of the first month, at the end of the third month and at the end of the sixth month.

Results

This study involved 50 patients with chronic ITP, 29 males (58%) and 21 females (42%). Participants ages range between18 and 51 years (mean age = 28.60 years). We diagnosed H. pylori in 36 patients (72%), who were treated with triple therapy. At the end of the sixth month, 10 of them (27.77%) showed complete response, and 18 of them (50%) showed partial response. The 14 uninfected patients, who did not receive any treatment, did not show neither complete nor partial response. Patient sex and age were not associated with achieving response, while baseline platelet count and H.pylori infection did.

Conclusion

Helicobacter pylori eradication significantly increases platelet counts in adult ITP patients.

Optimization of biosynthesis and purification of vaccine antigen based on capsid protein (ORF2) of hepatitis E virus

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Introduction

Hepatitis E virus (HEV) is the most common cause of acute hepatitis in many areas of the world with estimated about 20 million infections, and over 70 000 deaths each year. ORF2 protein (pORF2) is the capsid protein of HEV, which is widely used for vaccine development. Although the first vaccine against HEV based on recombinant HEV genotype (GT) 1 pORF2 had been licensed in China, but it is not yet available globally. The aim of this study was to optimize the conditions of biosynthesis in Escherichia coli, purification and assembly of recombinant HEV GT3 pORF2 into immunogenic virus-like particles (VLPs).

Materials & Methods

Sequence encoding amino acids 110-660 of HEV GT 3 pORF2 was optimized for bacterial expression and cloned into an expression vector pET3a. Protein synthesis was induced by autoinduction (F. Studier, 2015) or by IPTG at concentration 0.1-1mM overnight at 20 or for 4 hours at 37 . Protein isolation was performed by 7 different protocols, both from inclusion bodies and from soluble fraction to achieve the highest yield. Protein purification and refolding were carried out using metal affinity chromatography by gradients of imidazole, pH, urea or in combination. Purification was confirmed by SDS-PAAG and Western blot with anti-His tag (Abcam) and protein-specific antibodies (Abcam). The confirmation of the VLPs assembly was performed by electron microscopy.

Results

pORF2 was mainly contained in inclusion bodies when produced in E. coli. The highest yield of pORF2 was achieved by overnight autoinduction at 37 . Inclusion bodies were solubilized and Ni-NTA affinity chromatography with urea gradient from 6M to 0M was used for protein refolding. VLP assembly was efficiently induced by dialysis against PBS buffer with 0,5M NaCl and confirmed by electron microscopy.

Conclusion

We optimized the procedure of biosynthesis and purification of recombinant HEV GT 3 capsid protein and confirmed that the protein is capable to self-assembly in vitro into virus-like particles, which can be further used as candidate vaccine antigen.

Neurology I
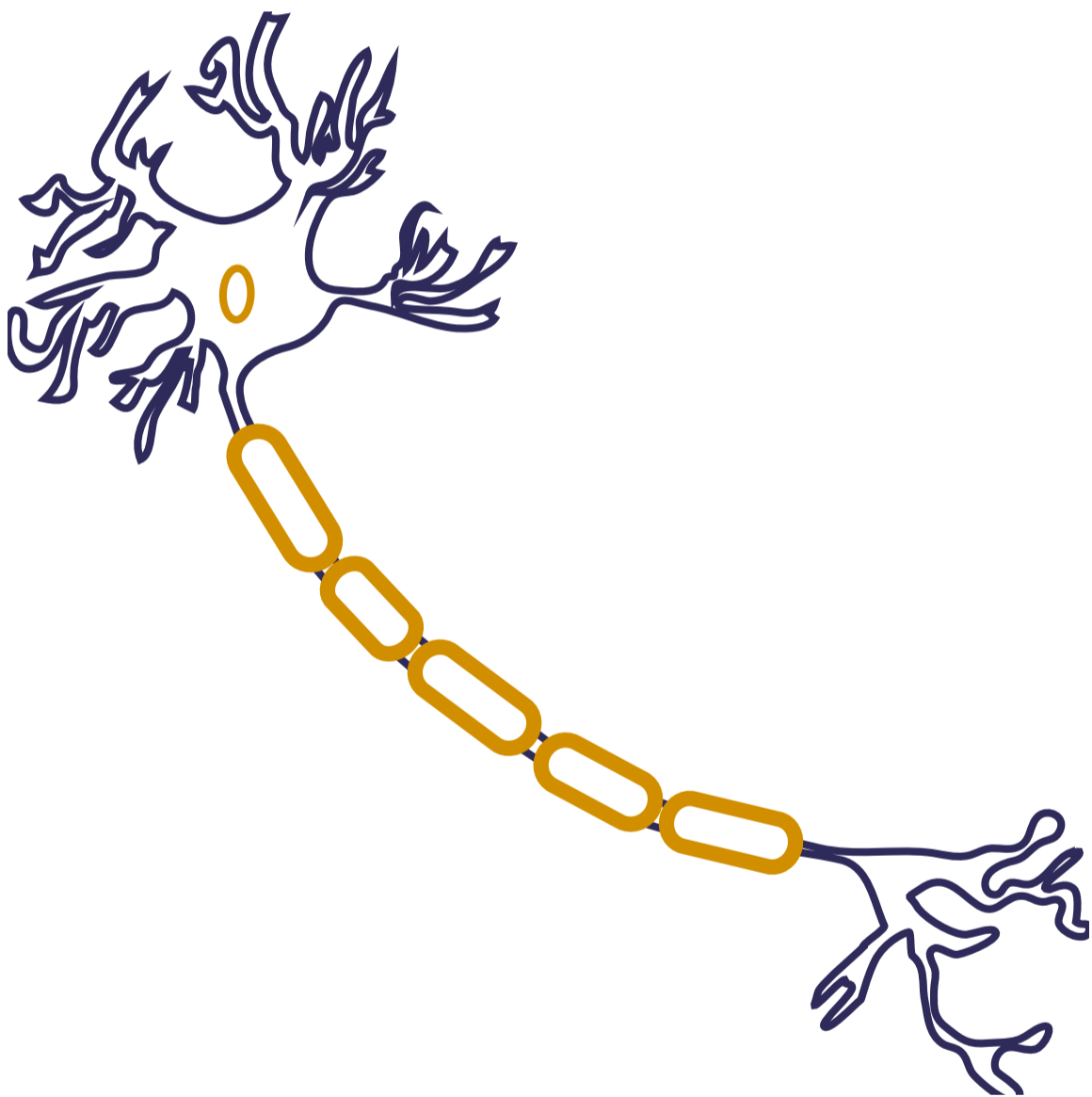
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Neurosurgical treatment of interdigital (Morton's) neuroma with radiofrequency ablation

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Introduction

Morton's neuroma is a very common cause of metatarsalgia. The purpose of this study was to investigate the effectiveness of radiofrequency ablation (RFA) in patients with chronic pain refractory to conservative therapy.

Materials & Methods

88 patients were studied. There were 6,8% of men and 93,2% of women among them. The median age was 45 years (from 20 to 68 years). All patients have previous conservative treatment. Continuous RFA was performed under ultrasound guidance and electrophysiological control by using one or more of 90 seconds cycle and with maintenance of the probe tip a temperature of 90 °C. We followed patients for a 11.1±2.2 months to assess their change in visual analogue pain scores (VAS), symptom improvement, complications. The obtained results were processed using Statistica 10.0. (StatSoft inc.). Nonparametric statistical methods were used (Mann-Whitney U-test).

Results

Mean VAS score before the procedure was 8.4±1.5. A reduction of pain intensity was achieved in 1 day after RFA (mean VAS scores 2,3±1,4), with stabilization of painful symptomatology during the following months. In 12 months after RFA mean VAS core was 1,9±0,9 (p<0.001). No patients developed complications. Overall, 93,2% of patients were either very or moderately satisfied with their outcome. 5 of 6 patients with recurrence of symptoms were undergone RFA again successfully.

Conclusion

Radiofrequency ablation is a safe and effective, minimally invasive technique for the treatment of Morton's neuroma.

Evaluation Of Therapeutic Efficacy Of Citicoline In Acute Ischaemic Stroke Patients: A Meta Analysis

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Introduction

Stroke is the third leading condition with the highest mortality and death and is a major cause of disability. The estimated number of deaths due to stroke was about 5.71 million people as per the WHO data, and estimated to peak at 7.8 million in 2030. Citicoline is believed to exert neuroprotection and neurorestoration intracellularly by supporting cellular phospholipid synthesis. Citicoline is used in AIS (Acute Ischaemic Stroke) patients, however, there is not enough statistical evidence available for the benefits of the same.

Hence, this calls for a meta-analysis of RCTs on a larger scale to generate highest level of scientific evidence regarding the controversial negative studies of Citicoline when tested against placebo.

Materials & Methods

A total of 16 studies, involving 5029 patients ($\geq$18years) were included. The studies were double-blind, randomized, and placebo-controlled clinical trials studying the effect of citicoline on patients with acute ischemic stroke. The included patients suffered from an acute ischemic stroke with a minimum therapeutic window of 6 hours. The treatments tested were either citicoline, with doses ranging from 250 to 4000 mg daily, or placebo. The duration of the treatment ranged from 10 days to 9 weeks.

The principal summary measure were the Odd's Ratio(OR) And Relative Risk(RR) (at 95% Confidence Interval). Analysis of efficacy is done by using different methods like forest plot, funnel plot.

Results

The overall pooled odd's ratio (for 5029 participants) was 1.842(random) and 1.285(fixed) [95% confidence interval (CI) 1.140 to 1.450 (fixed), P<0.0001], indicating a slight advantage of Citicoline over placebo treatment. The relative risk (for 5029 participants) was 1.339(random) and 1.168(fixed) [95% confidence interval (CI) 1.084 to 1.259 (fixed), P=0.0001], indicating a slight advantage of Citicoline over placebo treatment. Citicoline was also found to be associated with a less number of adverse events and deaths compared to placebo.

Conclusion

Citicoline is proven to be slightly more efficacious than placebo, with lesser adverse events and deaths and can be used depending on the suitability. However the margin of benefit is not very huge. Future trials comparing the same, on higher number of patients is necessary to draw a final conclusion on it.

Facilitating cortico-motoneuronal synapse excitability by pairing transcranial magnetic stimulation and spinal cord stimulation in healthy humans

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Introduction

Repeatedly pairing neuronal presynaptic depolarization with postsynaptic firing leads to changes in synaptic strength known as spike time dependent plasticity (STDP). Previous studies, using transcranial magnetic stimulation (TMS), indicated the potential of STDP to modulate spinal excitability in humans. We aimed to assess if carefully timing pairs of non-invasive cortical and spinal stimulation (sPAS) induces plasticity at two locations; the spino-motoneuronal and cortico-motoneuronal synapses. We then assessed whether this manifests functionally. The results may have implications for strengthening residual connections in spinal cord injury (SCI).

Materials & Methods

We delivered 100 paired pulses of TMS, stimulating corticospinal neurons, and transcutaneous spinal cord stimulation (SCS), stimulating Ia afferents, in 11 subjects. Motor activity in the form of focused involuntary muscle twitches were measured using EMG recordings of antagonistic muscles; tibialis anterior and soleus. Each subject was tested on two occasions during which the interstimulus interval (ISI) between the arrival of the paired pulses at the spinal cord motoneuron was either 0ms or 5ms. Before and after each protocol, subjects undertook a behavioural task; a series of explosive isometric dorsiflexions were performed, EMG activity was recorded and peak rate of force development (acceleration) was measured.

Results

A significant increase in excitability at the cortico-motoneuronal synapse was observed after 0msPAS ($t(df)$=-6.282(10), p=0.000) but not after 5msPAS ($t(df)$=-0.271(10), p=0.792). sPAS-induced plasticity at the spino-motoneuronal synapse was not observed (four-way rmANOVA; no main effects of time, session or leg and no interactions). sPAS induced potentiation of corticospinal excitability, did not affect peak rate of force development (rmANOVA; session x time (F=0.021(1,10), p=0.888)).

Conclusion

Findings suggest STDP as a likely candidate mechanism for timing dependent facilitation at the cortico-motoneuronal synapse. Further investigations are required to determine functional significance of these findings as, retrospectively, the task adapted here may not have been sensitive enough to pick up potential functional manifestations of induced plasticity. Future research should focus on the implications of these results in SCI therapy as well as the potential for these effects to be elicited by volitional movement, replacing artificial cortical stimulation.

Protective Effect of Ivermectin Against Acetic Acid-induced Colitis in Rats Through the GABAergic Pathway

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Introduction

Inflammatory bowel diseases are chronic severe conditions, which exert lots of disabilities to the patients, and also costs to the healthcare services. Studies in recent years attempted to introduce the best treatment regimen, but IBDs are not still fully resolved. Recent studies indicated the possible role of the GABAergic pathway in the inflammatory conditions. Our study aimed to investigate the role of this pathway in the protection of intestinal tissue against inflammation.

Materials & Methods

Colitis was induced in Wistar rats by intracolonic instillation of 1.5 ml 4% (v/v) acetic acid under general anesthesia, induced by ketamine and xylazine. Multiple doses of ivermectin were administrated by gavage-feeding after the recovery of rats from general anesthesia and also for four days following the surgery. In another groups, the co-administration of GABA agonist (baclofen 0.5) or antagonist (bicuculline 2 mg/kg) with ivermectin was investigated. Prednisolone was administrated as the positive control group. Control group received the vehicle by gavage-feeding. Bicuculline was injected intraperitoneally before the administration of ivermectin. On the fifth day, rats were anesthetized, and the last 8 cm of the colon was dissected in each group and were compared grossly and histopathologically. One-way analysis of variances (ANOVA) followed by Tukey's post-hoc test was utilized to compare the means.

Results

Ivermectin 0.5 mg/kg showed a significant antiulcer effect compared to the control group (vehicle-treated), grossly and histopathologically ($p < 0.001$). The co-administration of the non-effective dose of baclofen (0.2) with the sub-effective dose of ivermectin (0.1 mg/kg) also exerted a significant protective effect against colitis compared to the control ($p < 0.001$). Moreover, the non-effective dose of bicuculline (2 mg/kg) reversed the protective effect of ivermectin 0.5 mg/kg ($p < 0.001$). Baclofen 0.5 mg alone could also protect the intestinal tissue against colitis vs. the control ($p < 0.001$). Higher doses of baclofen (1 and 2 mg/kg) had similar effects to the baclofen 0.5 mg/kg group.

Conclusion

Ivermectin protects the intestinal tissue against acetic-acid colitis, probably through the GABAergic pathway. Baclofen also has a protective effect against colitis as a standard GABA agonist.

In vivo Studies on The Neuroprotective Effect of Propolis on The Bcl-2 Expression in Prefrontal Cortex of Rat (Rattus norvegicus) Induced by Social Isolation

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Introduction

Social isolation is the low quality and quantity of social relationship. Social isolation increases stress on cells through the glucocorticoid pathway which decreases Bcl-2 expression stimulating cell apoptosis. Social isolation causes neuronal apoptosis in prefrontal cortex which functions as a cognitive area, gestures planning, and learning. Prefrontal cortex is often referred as a locus with high intelligence which differs humans with other mammals. To prevent apoptosis of prefrontal cortex neurons, neuroprotective agents are needed. Propolis contains CAPE and chrysin as neuroprotective agents. This study aims to determine the effect of propolis administration on Bcl-2 expression in the prefrontal cortex of rats (Rattus novergicus) induced by social isolation.

Materials & Methods

This research is an experimental research with posttest-only control group design. This study used 25 rats (Rattus novergicus) as subjects. Positive control group (K+) was not induced by stress nor propolis, negative control group (K-) was stress-induced + aquades, treatment group 1 (P1) was stress-induced + propolis 100 mg/kg BW/day, treatment group 2 (P2) was stress-induced + propolis 150 mg/kg BW/day and treatment group 3 (P3) was stress-induced and + 200 mg/kg BW/day. Then the rats were terminated and each slice of sample was stained with immunohistochemical staining. The results were analyzed using one-way ANOVA and the Bonferroni post-hoc test.

Results

The mean of Bcl-2 expressions were 3,58±0,125 (K-), 6,37±0,168 (K+), 6,23±0,175 (P1), 6,94±0,129 (P2), and 4,54±0,096 (P3). There was a significant difference in the expression of Bcl-2 in prefrontal cortex in all groups (P=0.00) except between groups P1 and K+ (P=1.00) with 95% confidence interval. The Bcl-2 expression in P1, P2 and P3 were higher than K- (P=0.00), this result showed that the administration of propolis prevents neuronal apoptosis. The Bcl-2 expression in P1 and P2 were higher than P3 (P=0.00), this result showed that the optimal doses of propolis are 100 mg/kg BW and 150 mg/kg BW.

Conclusion

Propolis increases the Bcl-2 expression in prefrontal cortex of stress-induced rats. The administration of propolis 100 mg/kg BW and 150 mg/kg BW are the optimal doses to increase the Bcl-2 expression in prefrontal cortex of Rattus novergicus induced by social isolation.

The association between REM sleep behavior disorder and autonomic dysfunction in Parkinson's disease

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Introduction

Rapid eye movement (REM) sleep behavior disorder has characteristic clinical features including the lack of atonia and repeated episodes of vocalizations or abnormal behavior during REM sleep. REM behavior disorder (RBD) can occur either as an isolated phenomenon or because of neurodegenerative alpha-synucleinopathies such as parkinson's disease (PD) as the underlying cause. PD associated with RBD (PD-RBD) represent more severe symptoms and signs compared with PD without RBD. On another note, autonomic dysfunction in PD patients is categorized as one of the most prominent non-motor symptoms and have been lately the field of interest in research. As previous studies could not certainly determine the influence of PD-RBD on autonomic symptoms, we longitudinally studied autonomic dysfunction in PD patients with (PD-RBD) and without RBD (PD-nRBD).

Materials & Methods

This study was conducted on 420 drug-naïve PD patients included in the Parkinson's Progression Markers Initiative (PPMI) database. RBD Screening Questionnaire (RBDSQ) was used to define the presence of probable RBD. The Scales for Outcomes in Parkinson's Disease–Autonomic (SCOPA-AUT) was used to assess autonomic dysfunction and dopamine transporter (DAT) deficits on [123I]FP-CIT SPECT imaging was conducted in all patients.

Results

Out of 420 PD patients, 158 individuals (37.6%) were considered to have probable RBD (PD-pRBD) and others without RBD (PD-nRBD). Except pupillomotor function, all the autonomic symptoms were significantly more severe in PD-RBD group. Considering the association between SCOPA-AUT scores and DAT scan results, no significant correlation was observed in PD-pRBD group. However, in PD-nRBD group, caudate striatal binding ratio (SBR) was negatively correlated with SCOPA-AUT total score and gastrointestinal, urinary, pupillomotor and sexuality subscores (p values <= 0.001; correlation coefficients = -0.223, -0.204, -0.131, -0.202 and -0.246, respectively). Finally, there was a significant difference considering the longitudinal changes of SCOPA-AUT total between PD-pRBD and PD-nRBD groups, suggesting more severe autonomic decline in PD-RBD patients.

Conclusion

Our results indicates that PD-RBD patients have more severe autonomic dysfunction. These results support the theory that PD patients can be categorized based on the clinical presentation, possibly representing differences in the disease pathophysiology.

Nuclear and Technical Medicine
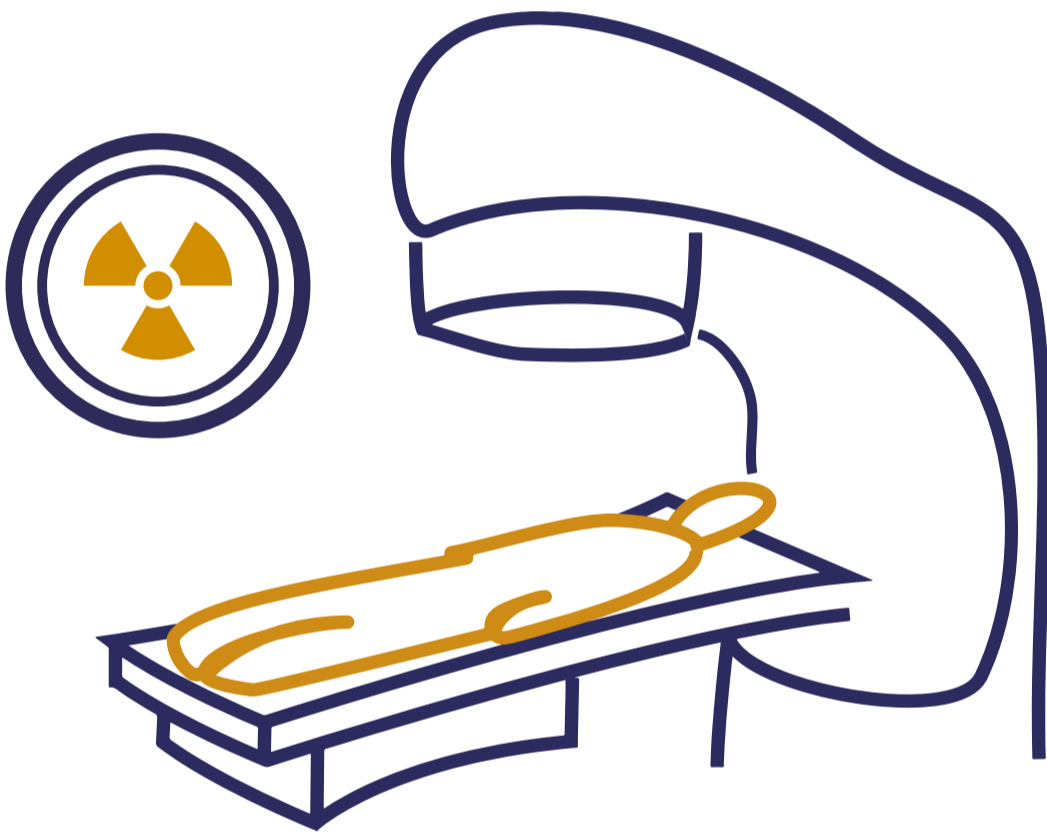
Presenters:
Bhushan, S (Saraswati)
Huiskamp, LFJ (Laura)
Fang, W (Weimin)
Erdős, S (Sándor)
Smolyarova, D. (Daria)
Born Guerra, D. (Danieli)

Biomedical functionalization of Bombyx mori silk using silver nanoparticles: understanding its fundamental effect on mechanical properties, secondary structure and anti-microbial activity of obtained silk

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Introduction

Silk produced by Bombyx mori silkworms has been widely used in biomedical applications, most notably for surgical sutures. This is due to its excellent mechanical performance, biocompatibility and tunable biodegradability. The superior properties of B. mori silk can be further improved through the incorporation of functional components into the material. An eco-friendly way to achieve this is by directly feeding functional components to the silkworms. In the present study, silver nanoparticles are fed to silkworms as a dietary supplement. Silver nanoparticles have been chosen as a functionalizing agent due to their established anti-microbial properties. The aim of this study is to understand the fundamental effect of direct feeding of silver nanoparticles on the hierarchical organization and mechanical performance of silk fibres.

Materials & Methods

Silver nanoparticles were synthesized using an ice-melting reaction and characterized by Ultraviolet-visible spectroscopy, Scanning Electron Microscopy (SEM) and Transmission Electron Microscopy (TEM). Silk properties were investigated through tensile testing, Fourier Transform Infrared Spectroscopy (FTIR), Wide Angle X-ray Diffraction (WAXRD) and disk diffusion test.

Results

Several changes in the secondary structure of silk fibroin due to nanoparticle feeding were observed. These include reduced amount of β-turns, with the β-turns being preferentially oriented with respect to the fibre axis. Furthermore, lattice expansion of the hydrogen-bonded β-sheets was observed, implying a less perfect crystal structure of nanoparticle fed group. These changes in the secondary structure appear to be correlated to their mechanical properties of lower Elastic modulus, higher stress and strain at failure and strain-hardening. No anti-bacterial properties of the silk are observed through the disk diffusion test. This warrants further investigation into the degradation behavior of silk fibroin to release nanoparticles and initiate their contact killing mechanism for antimicrobial effect.

Conclusion

This study provides an elementary understanding of the effect of silver nanoparticle feeding on the secondary structure and mechanical behavior of silk. The results obtained provide a basis and can be further developed to eventually be able to produce silk with anti-bacterial properties, in a green and eco-friendly way. Consequently, these silk fibres with high biomedical value could be utilized for anti-bacterial sutures, wound dressings, bandages and tissue engineering scaffolds.

The predictive and prognostic value of low skeletal muscle mass for dose-limiting toxicity and survival in head and neck cancer patients receiving curative concomitant cetuximab and radiotherapy

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Introduction

This study aims to investigate the predictive value of low SMM for cetuximab DLT and its prognostic value in head and neck squamous cell carcinoma (HNSCC) patients treated with concomitant cetuximab and radiotherapy.

Materials & Methods

Patients diagnosed with HNSCC and treated with primary or adjuvant concomitant cetuximab and radiotherapy were included. Clinical and demographic variables were retrospectively retrieved and SMM was measured at the level of the third cervical vertebra using pre-treatment diagnostic computed tomography or magnetic resonance imaging. An optimal cut-off value for low SMM was determined based on the lowest log likelihood associated with cetuximab DLT. A multivariate linear regression model was used to determine predictive factors for cetuximab DLT. The prognostic value of low SMM for disease-free and overall survival was analyzed using Kaplan-Meier curves.

Results

The optimal cut-off value for low SMM as a predictor of cetuximab DLT was an LSMI ≤ 45.2 cm2/m2. Of the 91 included patients, 74.7% had low SMM and 30.8% experienced cetuximab DLT. At multivariate analysis, low SMM had no predictive value for DLT (OR 0.83; 95% CI 0.27-2.56; p=0.74). The Kaplan-Meier curve demonstrated that patients with low SMM had significantly lower overall survival (Log Rank $\chi2$ = 5.87; p=0.02).

Conclusion

Low SMM is highly prevalent in HNSCC patients treated with concomitant cetuximab and radiotherapy. Low SMM has no predictive value for cetuximab DLT in HNSCC patients. However, low SMM is a negative prognostic factor for overall survival in HNSCC patients treated with concomitant cetuximab and radiotherapy.

Application of Ultrasound Elastography in the relationship between Type 2 Diabetes Mellitus and Distal Femoral Cartilage

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Introduction

Type 2 diabetes mellitus(T2DM) is a risk factor in knee osteoarthritis(OA) that accelerates degeneration of articular cartilage. Real-time ultrasound elastography (RTE) in particular can evaluate the relative hardness of tissues and non-invasively distinguish tissues of varying stiffness. We aimed to analyze the differences in distal femoral cartilage of T2DM patients and healthy controls by ultrasound elastography.

Materials & Methods

A cross-sectional study was conducted on T2DM patients and matched controls. The demographic characteristics, duration of diabetes and complications were recorded. Ultrasonography and RTE of the cartilage were conducted by an experienced ultrasound diagnostician blinded to the clinical data using an ultrasonic instrument with a 5–13 MHz linear probe. The thickness of the medial, intercondylar and lateral cartilage was measured by two-dimensional ultrasound. The strain ratios were measured in the corresponding area using ultrasonic elastography.

Results

A total of 85 subjects were included in the study, including 37 males and 48 females, with an average age of 56.2 ± 5.8 years. Mean duration of T2DM was 11.6 ± 5.9 years and mean number of complications was 1.1 ± 0.9. There were no significant differences between the two groups in terms of age, BMI, gender and activity score ($P>0.05$). The cartilage at the medial, intercondylar and lateral condyle were markedly thinner in the diabetics ($P<0.05$), and the corresponding strain ratios were higher at all positions ($P<0.05$). A negative correlation was observed between medial cartilage thickness and the number of complications, whereas the medial strain ratio of cartilage was positively correlated with the duration and the number of complications.

Conclusion

The thickness of the distal femur cartilage is decreased in T2DM patients and the strain ratio is increased. We have shown a negative correlation between T2DM and femoral cartilage integrity for the first time using ultrasound elastography. The clinical significance of two dimensional and elastic changes should be explored in future studies.

Impact of virtual reality on psychological and physiological variables in chemotherapy-treated children

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Introduction

In the case of childhood cancer besides medical treatment, the activities which improve children general well-being are equally important. Virtual reality (VR) is a greatly immersive, 360-degree artificial environment which is increasingly considered in medicine. In our pilot study, we examined the feasibility of VR into the everyday life of pediatric oncology centres and explored the psychological and physiological effects of VR during chemotherapy treatment.

Materials & Methods

For the study we included pediatric oncology patients between the age of 10 to 18 who were receiving chemotherapy treatment (n=23). During the experiment, we used a repeated measurement design where all children participated in both experimental (VR) and control conditions. Psychological and physiological variables (heart rate, blood pressure, skin impedance - EDA) were measured immediately before and after the session. Psychological variables were investigated with an individual questionnaire which contained an 11-point Likert scales, which measured variables such as mood, anxiety and patience. In the VR session, children could play Night Sky videogame on the Samsung Gear VR/Oculus Go device for 20-30 minutes, while in the control session they could play a mobile game. In the statistical analysis linear mixed modelling was used.

Results

VR session significantly improved children's mood compared to the control condition (p=0.042). Furthermore, anxiety was significantly reduced in both conditions (p=0.017). However, we did not find a significant interaction effect between occasion and condition. We did not experience significant effect on patience or nausea. In one case, we detected symptoms of kinetosis. No significant interaction effect was found for physiological variables.

Conclusion

We had a positive experience with the feasibility of VR, which was confirmed by both the parents and the nurses. According to our results, VR has greater positive effect on children's mood than a mobile game. Further investigations are needed to determine, how much this effect belongs to the novelty or specificity of VR. However, in the meantime, it can be safely used as part of their treatment.

Fluorogenic biosensor for hydrogen peroxide detection

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Introduction

The role of hydrogen peroxide in cells is not limited to oxidative stress as it is for most reactive oxygen species. Hydrogen peroxide is an important signaling molecule that is involved in aging, regeneration, inflammation and other biological processes. For intracellular hydrogen peroxide detection in space and time highly specific sensors with different spectral characteristics are needed.

We aimed to develop a new type of HyPer biosensor that is a widely used tool in redox research. New sensor consists of two parts: fluorogenic protein, that interacts with different GFP-like chromophores which are not fluorescent without protein, and bacterial OxyR – hydrogen peroxide-sensitive regulatory domain, that forms disulfide bond only after oxidation under hydrogen peroxide.

Materials & Methods

We made libraries of genetic constructions with different circular permutated fluorogenic proteins that was integrated via 1-3 amino acid linkers into the OxyR. Then we tested the ability of each construction to interact with hydrogen peroxide and chromophores with help of high throughput screening in E.coli, selected the construction with the best fluorescent enhancement during oxidation, improved it with random mutagenesis and defined the properties of the final biosensor in vivo and in vitro.

Results

The new fluorogenic biosensor in complex with chromophore 4-hydroxybenzylidene-rhodanine outcomes existing HyPerRed by its spectral properties: it is brighter and provides better resolution because of 9-12 times enhancement of fluorescence compared reduced and oxidized states in HeLa Kyoto cell culture. We also determined in vitro properties: brightness, interaction constant and proved high selectivity to hydrogen peroxide.

Conclusion

The new biosensor has significant advantages compared with HyPer biosensors based on GFP-like proteins: renewable fluorescent signal and less photobleaching due to rapid reversible interaction with chromophore, modifiable spectral properties due to compatibility with various chromophores with different spectral properties and it gives an opportunity for anaerobic studies because it does not require oxygen for maturation of intrinsic chromophore as GFP-like proteins do. The last property allows hydrogen peroxide analysis during hypoxia. In addition, new sensor enables hydrogen peroxide detection in super-resolution mode because of rapid photoswitching and also it has potential for drug screening.

Investigation of radiosensitization process assisted by gold nanoparticles in cellular systems irradiated with high energy photons and charged particles.

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Introduction

Oncological radiation therapy is the process by which cancer cells are eliminated within a tumor volume prescribing an appropriate dose of radiation, seeking to preserve the surrounding healthy tissues as much as possible. One strategy to improve dose discrimination between tissues is to use nanoparticles (NPs) as radiosensitizers. There are still several details about the effects of the presence of NPs in a radioactive field within a biological system that need to be clarified, especially for the case of charged particle beams.

Materials & Methods

AuNPs were synthesized by reducing chlorouric acid. Their physicochemical properties have been characterized, including its morphology, optical properties and colloidal stability in cell culture medium. In a second step, the toxicological effects of the treatment with AuNPs with different cell lines were evaluated by in vitro assays. Cell morphology after exposure to treatment and internalization of NPs were analyzed by transmission electron microscopy (TEM). Clonogenic assays were carried out in order to investigate the influence of AuNPs on the reproductive viability of cells after exposure to ionizing radiation.

Results

The average diameters of the resulting NPs were around 5 and 19 nm, depending on the reducing agent used. The results regarding the citotoxicity indicated acceptable values of cell viability for gold concentrations from 0.05 to 1 mM. TEM images revealed that NPs are internalized by cells in large quantities, and are concentrated in the cytoplasm, mainly involved by endosomes. The clonogenic assays indicate a reduction in the reproductive capacity of the cells in the presence of AuNPs.

Conclusion

The tests performed showed that the presence of AuNPs led to a reduction in the reproductive viability of cells after irradiation, showing that they have great potential as radiosensitizers.

Oncology I

Presenters:
Neumann, N. (Nina)
Román, A.L.T. (Ana)
Singh, R (Rageshwari)
Avdoshina, D. (Daria)
Elassall, M., G. (Gena)

Maspin Deficiency Promotes Carcinogenesis in a Knock out Mouse Model

Neumann, N. (Nina)[1], Nahra, N. (Nadine)[1], Bernardo, M. (Margarida)[1,2], Sheng, S. (Shijie) Ph.D.[1,3,2]

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Introduction

Maspin is an epithelium-specific tumor suppressor, the loss of which has been shown to reprogram the epigenetic profile of tumor cells toward malignant progression. Homozygous Maspin gene deletion is embryonically lethal. However, a particular breeding scheme for conditional Maspin knockout-out (KO), using the C57BL6 mouse strain, yielded viable Maspin KO mice in our laboratory. The question herein addressed is: what is the effect of maspin knock out on the overall well-being and longevity of these animals, with particular emphasis on carcinogenesis.

Materials & Methods

At different ages, ranging from 4 weeks to end of life, maspin KO mice were sacrificed, dissected and organs were formalin-fixed and paraffin-embedded. Same age wild type (wt) mice were used as controls. Tissues were sectioned and subjected to Haematoxylin & Eosin (H&E) staining. The stained sections were examined by board-certified Pathologists.

Results

The health condition at the end of life between female Maspin KO mice and the wt/wt counterparts is striking as the wt/wt mice were sacrificed without any visual health problems. Female mice lived for up to 26 months and outlived male mice by up to 7 months. Moreover, male mice exhibited life-threatening phenotypes over a narrower time window (2 months) compared with the female counterparts (6 months). The most apparent male mice phenotypes were asymmetrical seminal vesicles, enlarged prostates, and dry bladders. Examination of H&E stained sections revealed extensive angiogenesis, hemorrhaging, reactive stroma and adenocarcinomas in the mice prostate lobes, particularly in the dorsal-lateral lobe. In female mice the most prominent phenotypes were mammary gland angiogenesis and hemorrhaging, which impaired mobility. Mammary gland H&E staining revealed hyperplasia and basal cell adenocarcinomas. Intra-alveolar hemorrhage, lymphoid aggregates and adenocarcinoma were also apparent in the lungs of both male and female animals.

Conclusion

These findings show a dramatic effect of maspin on mice longevity, and carcinogenesis particularly in reproductive organs.

Oleamide induces cell death of the rat glioblastoma RG2 cell line but not of primary astrocytes in an independent cannabinoid receptor mechanism

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Introduction

Glioblastoma is considered the most aggressive tumor of the central nervous system, however, its treatment is unsatisfactory due to poor survival of patients. In this sense, endocannabinoid system (ECS) inhibits proliferation by activation of cell death mechanisms evaluated on murine and human tumor cell lines. Oleamide is an endogenous agonist of ECS which is firstly, recognized as a gap junction inhibitor in cancer cells, however, its effect under proliferation and survival on glioblastoma cells remains unknown. In this study we evaluated the anti-proliferative effect of oleamide on the tumoral rat glioblastoma cell line RG2 compared with normal primary 8 days postnatal rat astrocytes from cerebellum.

Materials & Methods

RG2 cell line and primary astrocytes were treated with ODA at different concentration (25µM, 50µM, 100µM and 200µM) and culture times (12, 24 and 48h). To evaluate the anti-proliferative effects of ODA, we evaluated morphological changes using phase contrast microscopy, the cell viability by MTT assay (mitochondrial cell viability) and the mechanisms of cell death using necrosis/apoptosis markers, as well as the inhibition of the cell cycle by flow cytometry. In addition, the role of cannabinoid receptors in ODA signaling was explored by treatment with antagonists.

Results

The appearance of polygonal morphology and its cytoplasmic polarization was observed in somatic compartments in RG2 cells treated with [ODA 100 µM] for 24h, contrary to this, astrocyte primary cultures formed clusters. ODA [100 µM] decreases viability to 46.38% vs. control in RG2 and 88.09% vs. control in astrocyte cultures, both effects at 24 h. Experimental flow cytometry demonstrates an increase in apoptotic cell death after 24h of treatment with ODA [100µM]. Cell cycle flow cytometry results demonstrates also, that cell death active mechanisms occurred on G1 phase on RG2 cells with ODA. None of the treatments with antagonists/inverse agonists significantly recovered cell viability compared to treatment with ODA [100 µM].

Conclusion

This study suggests that oleamide have anti-proliferative effects on glioblastoma RG2 cell line compared to normal primary astrocytes and that it is exerting its death effect through independent mechanisms of cannabinoid receptors. Oleamide could be used as co-treatment with standard care in glioblastoma tumors.

A study of CD56 expression in papillary carcinoma thyroid and its follicular variant in comparison with other solitary follicular patterned lesions of the thyroid

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Introduction

Follicular variant of papillary carcinoma of thyroid (FVPTC) has differential diagnoses varying from non-neoplastic, benign to malignant lesions. Studies have explored the use of morphology and immunohistochemical(IHC) studies to diagnose true positive cases. The purpose of our study was to analyse the expression of CD56 in papillary thyroid carcinoma (PTC) and follicular patterned lesions and establish CD56 as a marker to differentiate FVPTC from other solitary follicular patterned mimics.

Materials & Methods

This study is a retrospective 2-year study conducted in a tertiary care hospital in South India following approval from the institutional ethics committee. 74 thyroid lesions- PTC and solitary follicular patterned lesions were studied. Slides and blocks retrieved from archives were evaluated. IHC with CD56 was performed on selected cases. A positive result was defined as moderate-strong membranous immunostaining in ≥ 10% of epithelial cells; <10% was considered negative. Data analysis was done using statistical package for social sciences- version 20. Chi square test was used to determine the association of CD56 expression in FVPTC and its mimics.

Results

74 lesions were studied-hyperplastic nodule (n=14), follicular adenoma (n=11), hurthle cell adenoma (n=1), follicular carcinoma (n=8), hurthle cell carcinoma (n=4), PTC(n=30), FVPTC(n=3) and noninvasive encapsulated follicular variant of papillary carcinoma(NIFTP) (n=3). Chi square test showed statistical significance in CD56 expression between FVPTC and its mimics (P value 0.008) and between PTC and benign lesions (P value less than 0.0001).

Conclusion

CD56 is a reliable negative marker of PTC and can be used as an adjunct to morphology to differentiate FVPTC from other solitary follicular patterned lesions of the thyroid.

Overexpression of synthetic genes for rat telomerase reverse transcriptase or its reverse transcriptase domain in murine adenocarcinoma cells suppresses their growth and metastatic activity

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Introduction

Telomerase reverse transcriptase (TERT) is a classical tumor-associated antigen overexpressed in many cancers, which turns it into attractive target for therapeutic cancer vaccines. Considerable progress in therapeutic vaccination against cancer has been achieved with DNA vaccine technology: immunization with DNA which directs expression of immunogens in the host inducing a desired immune response. For cancer vaccines, this implies overexpression of tumor-associated antigen which raises safety concerns. Within a project on TERT-based DNA vaccine against cancer, we evaluated possible adverse effects of overexpression of the full-length TERT or its reverse transcriptase domain (rtTERT) by tumor cells in vitro and in vivo.

Materials & Methods

Synthetic expression-optimized genes for rat TERT and rtTERT were cloned into lentiviral vector pRRLSIN.cPPT.PGK (Addgene). Resulting lentivirus was used to transduce 4T1luc2 cells (Perkin Elmer) generating subclones overexpressing TERT (n=4) or rtTERT (n=4). Number of TERT/rtTERT genomic inserts was determined by ddPCR. Gene expression was assessed by the levels of TERT/rtTERT mRNA determined by real-time RT-PCR. Subclones were characterized by population doubling time. Cell cycle analysis was performed using DRAQ5 (Abcam) staining. Subclones were ectopically implanted into BALB/c mice; tumor growth was monitored by in vivo bioluminescence imaging (BLI; Spectrum, PerkinElmer). Metastatic activity was assessed at the experimental endpoint by ex vivo BLI of mouse organs. Statistical analysis was performed using GraphPad Prism 8.

Results

The overall doubling time of all derivative subclones was similar to that of the parental 4T1luc2 cells (p>0.05). Cell cycle analysis for both TERT and rtTERT-expressing clones showed an increased proportion of cells in S phase (p<0.05), possibly due to the prolonged checkpoint surveillance. All subclones showed reduced tumorigenic potential. They either did not form tumors (rtTERT) or formed significantly smaller tumors than the parental cells (TERT; p<0.05). Metastatic activity of the derivative clones was reduced compared to that of 4T1luc2 (p<0.05).

Conclusion

Overexpression of TERT or rtTERT by murine adenocarcinoma cells does not make them more aggressive, on contrary, it reduces their tumorigenic and metastatic activity. Thus, expression of TERT or rtTERT in the context of DNA vaccine is not a risk factor enhancing aggressiveness of cancer cells.

Analgesic effect of pectoral nerve block (PECS) in patients undergoing breast cancer surgery: A systematic review and meta-analysis

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Introduction

According to the American Cancer Society, Breast cancer is the second leading cause of death in women worldwide. Surgical Intervention is the most effective management in such cases. General anesthesia, thoracic paravertebral block, erector spinae plane block and intercostal nerve block are the usual analgesic techniques used in this surgery. Due to their insufficient role, surgeons developed new techniques as pectoral nerve block I and II. This systematic review and meta-analysis aim to compare the safety and efficacy of (PECS) I and II with other analgesic techniques used during breast cancer surgeries.

Materials & Methods

Four databases were systemically searched (PubMed-Cochrane library-Scopus-Web of science (WOS)) for all relevant randomized controlled trials. All data were combined in the analysis under random-effect-model.

Results

Our metanalysis included 36 eligible studies. Four of these trials compared PECS with one of the usual analgesic procedures and some studied the effect of dexmedetomidine addition to PECS. Regarding PECS II vs. GA, results showed that PECS II was significantly better in intraoperative (p=0.009) and postoperative (P<0.00001) consumption of opioid, first time for requiring analgesia (P<0.00001) and pain score at 0,6,12,24h with (P<0.00001, P=0.01, P=0.01 and P=0.0007) respectively. It was also superior to PVB in postoperative consumption of opioid (p=0.0001) and insignificant in first time for requiring analgesia, PONV and pain score at 6h. We demonstrated its superiority over erector spinae plane block regards postoperative consumption of opioid (p<0.00001). Furthermore, Dexmedetomidine addition to PECS II showed remarkable results versus using PECS II alone for postoperative consumption of opioid (p<0.0001), first time for requiring analgesia (p=0.05) and pain score at 12h (p=0.006). PECS I was reported to be much better than GA in number of patients requiring analgesia (P=0.008). Its combination with serratus plane block revealed beneficial effects in intraoperative consumption of opioid (p=0.0001), PONV (P<0.001) and pain score at 24h (p=0.04) compared to GA.

Conclusion

Our study suggests that pectoral nerve block I and II are superior than GA, PVB and ESP regards most of the recorded outcomes. The results also demonstrate better effect for PECS I and II when combined with Dexmedetomidine.

Pharmacology
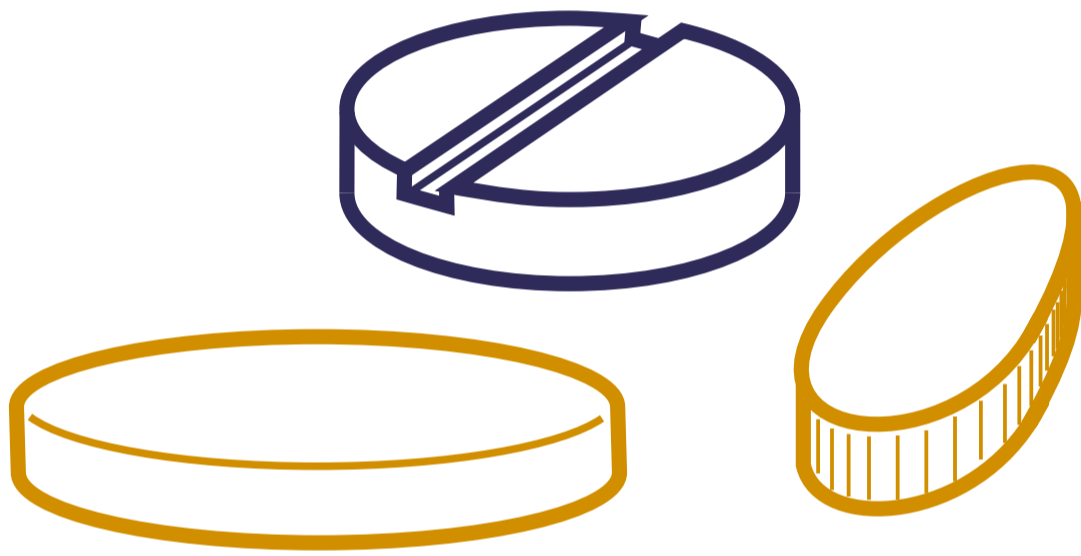
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Syzygium aromaticum L. ameliorates the post-operative peritoneal adhesion possibly through regulating the inflammatory cytokines, oxidative factors, and fibrosis and angiogenesis biomarkers

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Introduction

Post-operative adhesions are regarded as the major complication following abdominal surgery. Syzygium aromaticum L. (clove) and its constituents possessed anti-oxidative and anti-inflammatory properties in previous studies. Therefore, we aimed to evaluate the anti-inflammatory and anti-oxidant effects of clove on the formation and development of post-operative abdominal adhesions in a rat model of peritoneal adhesion.

Materials & Methods

Thirty 6-weeks old Wistar rats (220 ± 20g) were divided into 5 groups of 6: normal group, without any surgical procedures (negative control), vehicle group without clove treatment, and 3, 4 and 5 experimental groups with 2 ml of 1%, 0.5% and 0.25% w/v of clove treatment, respectively. Peritoneal adhesions were examined macroscopically and also the levels of inflammatory cytokines (IL-6, and TNF-α), growth factors (TGF-β1 and VEGF), oxidative (NO and MDA) and anti-oxidative (GSH) factors were evaluated.

Results

The results of this study revealed that the vehicle group markedly increased adhesion score, IL-6, TNF-α, TGF-β1, VEGF, NO and MDA levels as well as diminishes GSH level compared to normal group. Moreover, Clove treatment at concentration of 0.25 % w/v notably ameliorates all measured parameters following post-operative abdominal adhesions compared to vehicle group (p<0.05 to 0.001 for all cases). However, other applied concentrations of clove significantly reduced the biochemical parameters; they had no observational healing effects.

Conclusion

Interestingly, our results revealed that clove at low concentrations can ameliorate the post-operative peritoneal adhesion through alleviating adhesion score through regulating the inflammatory cytokines, oxidative factors, fibrosis and angiogenesis biomarkers as well as stimulating anti-oxidative factors. Therefore, clove can be considered as a potential candidate for the management of post-operative peritoneal adhesion.

Comparison of three doses of intrathecal morphine to placebo in terms of reducing pain and need for analgesics after total knee replacement: A meta-analysis

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Introduction

Delivery of morphine with spinal anaesthesia has showed its effectiveness in reducing the need for pain killers after total knee replacement (TKR). To minimize side effects produced by morphine administration, a low-dose protocol was encouraged. We aimed to assess pain scores and need for rescue analgesia when using three doses of intrathecal morphine at different time periods, post-TKR.

Materials & Methods

A computer-based literature search of PubMed, Cochrane Central, Scopus, and Web of science was performed. We included randomised controlled trials (RCTs) that used low doses of intrathecal morphine for providing analgesia after TKR. Data were extracted from eligible studies and pooled as standardised mean difference (SMD) under the random effects model, using the Review Manager software. For single arm studies, we used the Open Meta-analyst software.

Results

Analysing data from nine RCTs, including 544 patients, showed that intrathecal morphine doses of 0.1 mg, 0.2 mg, and 0.3 mg had lower Visual Analogue Scale (VAS) pain scores compared to placebo one hour, four hours, 24 hours, and 48 hours after TKR ($p<0.05$). However, there was no significant difference between placebo and intrathecal morphine after 12 hours (SMD= -0.65, 95% CI [-1.35, 0.05], p=0.07), or between placebo and the 0.3 mg dose of intrathecal morphine after eight hours (SMD=0.288, 95% CI [-0.345, 0.921], p<0.05). Cumulative dose of patient controlled analgesia (PCA) was significantly lower in the intrathecal morphine group post-TKR after one day (SMD= -1.16, 95% CI [-1.60, -0.73], p>0.0001).

Conclusion

Based on the results obtained from this meta-analysis, low doses of intrathecal morphine were efficient in reducing pain after TKR, in addition to decreasing the doses of PCA. Careful watching of commonly expected side effects of morphine, particularly respiratory depression, is essential.

Melatonin Ameliorates Ischemia/Reperfusion-induced Myocardial Apoptosis via Modulating the Ubiquitin Proteasome System

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Introduction

Apoptosis is believed to be one of the main pathogenesis of myocardial ischemia/reperfusion (I/R) injury. Previous studies have demonstrated that melatonin protects against I/R injury through ameliorating myocardial apoptosis. However, the mechanisms have not been fully clarified. It has been reported that the ubiquitin proteasome system (UPS) dysfunction is closely related to apoptosis. With the STAT3 signaling activation, the UPS activity was increased to exert anti-apoptotic effect in I/R injury. Here this study aimed to investigate whether the UPS mediated by STAT3 plays a role in the effect of melatonin inhibition on I/R-induced myocardial apoptosis.

Materials & Methods

Adult male C57BL/6Cnc mice treated with or without melatonin (20mg/kg) were performed to ligate left anterior descending coronary artery (LAD) as an in vivo I/R model. Cardiac function and myocardial infarct size following by I/R were evaluated with echocardiography and Evan's blue/TTC staining. Apoptosis was detected by TUNEL staining and expression of apoptosis-related proteins Cleaved Caspase-3, Bax, Bcl-2 in the presence and absence of the proteasome inhibitor Bortezomib (BTZ) and the STAT3 inhibitor S3I-201. Also the activity and expression of proteasome were measured.

Results

In this study, we found that melatonin treatment improved cardiac function, reduced the myocardial infarct size and decreased the number of TUNEL-positive cardiomyocytes. And melatonin inhibited the elevation of Cleaved Caspase-3 protein levels and the Bax/Bcl-2 ratio induced by I/R, respectively. However, these anti-apoptosis effects of melatonin were abolished by BTZ. Also melatonin up-regulated the proteasome activity, as well as the protein levels of β1i and β5i. Suppression of STAT3 blocked the inhibition of melatonin on apoptosis resulted from I/R.

Conclusion

Taken together, these results indicate that melatonin ameliorates I/R-induced myocardial apoptosis, at least in part through the activation of STAT3 signaling and subsequent the activation of UPS. Our findings provide novel intrinsic mechanism insights into the cardioprotection of melatonin, predict melatonin is a promising therapeutic drug for the prevention and treatment of myocardial apoptosis.

Ivermectin Increases Skin Flap Survival in the Random-Pattern Skin Flap Model in Rat: The Novel role of GABA-A and GABA-B Receptors

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Introduction

Ivermectin is a well-known anti-parasite drug from the avermectin family. Ivermectin acts through many mechanisms including the stimulation of the GABAergic system. GABAergic system has been shown to play a role in ischemia-reperfusion injury (I/R injury) in the central nervous system. In this study, we aimed to introduce Ivermectin as a new drug for pharmacologic pre-conditioning of skin flap, as well as introducing the novel role of GABAergic system in the I/R injury in the skin.

Materials & Methods

Ninety Wistar male rats were used in this study. Multiple doses of Ivermectin (0.02, 0.05, 0.1, 0.2, 0.5, 1 mg/kg) were injected intraperitoneally (i.p) prior to the surgery. Baclofen (GABA-B agonist) and bicuculine (GABA-A antagonist) were administered to evaluate the involvement of the GABAergic system. The control group received the vehicle. All drugs were injected i.p. Histopathological evaluations were performed by Hematoxylin and Eosin, Masson's trichrome, and CD31 immunohistochemical staining. Western-blot was performed to show the expression of GABA-A and GABA-B receptors in the treatment groups.

Results

Ivermectin 0.05 mg/kg was the effective dose among treatment groups when compared to the control group (Mean necrotic area: $10 \pm 2\%$ and $70 \pm 10\%$ in the treatment group vs control, $p < 0.001$). Baclofen 0.2 mg/kg and the co-administration of Baclofen 0.1 mg/kg with Ivermectin 0.02 mg/kg (sub-effective dose) increased flap survival (Mean necrotic area: $15 \pm 5\%$ and $10 \pm 5\%$), while co-administration of bicuculine with Ivermectin decreased flap survival (Mean necrotic area: $50 \pm 10\%$).

Conclusion

Ivermectin increased skin flap survival through mediating GABA-A and GABA-B receptors. The result of this study shows that the GABAergic system plays a role in I/R injury of the skin.

Ganciclovir Therapeutic Drug Monitoring in Transplant Recipients

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Introduction

Ganciclovir and valganciclovir are indicated for prophylaxis and treatment of cytomegalovirus and human herpes virus-6 which can be a major risk for transplant recipients. Due to the narrow therapeutic range of ganciclovir, potential toxicity and threat of resistance, therapeutic drug monitoring (TDM) may be a suitable tool to optimize therapy. The aim of this study was to evaluate TDM guideline application in University Medical Center Groningen (UMCG).

Materials & Methods

An observational cohort study was conducted in the UMCG. Solid organ and stem cell transplant recipients (aged ≥ 18 years) who received (val)ganciclovir for CMV prophylaxis or treatment, or for HHV-6 prophylaxis were enrolled in the study. Before the start of the study, a (val)ganciclovir dosing and TDM guideline had been introduced in the UMCG, which implied routine performance of TDM of (val)ganciclovir. Ganciclovir 5 mg/kg and valganciclovir 900 mg were given twice daily as therapy or once daily as prophylaxis in adults with a normal kidney function. The predefined therapeutic window for prophylaxis and treatment were 1-2 mg/L and 2-4 mg/L respectively.

Results

From June 2018 to April 2019, 63 patients (26 treatment, 37 prophylaxis) were included. Only part of patients received the initial appropriate dose according to the guideline in both prophylaxis (56,7%) and therapy (65,4%) group. Overall, 254 (val)ganciclovir trough concentrations (108 treatment, 146 prophylaxis) were measured with a median of 3 (IQR 4) per patient resulting in 34% trough concentrations (48 therapy, 37 prophylaxis) within target; this was either after a first dose, or after dosage adjustment. However, more than 50% of trough concentrations were too low (47 treatment, 83 prophylaxis). Initial concentrations were subtherapeutic in 9 treatment patients (53%) and 16 prophylaxis patients (80%) who received correct guideline doses. Five treatment patients and seven prophylaxis patients with normal renal function who had low initial levels had not received any loading dose.

Conclusion

Current dosing regimens did not result in predefined concentrations. Instead, too often, low trough concentrations in both initial and subsequent concentrations were attained. A loading dose is required to avoid low exposure. Therefore, the dosing guideline, loading dose and target concentrations have to be evaluated.

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Effects of Lavender Oil Inhalation on Anxiety and Pain in Patients Undergoing Coronary Angiography

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Introduction

Cardiovascular diseases alone account for 48% of deaths in the world. There is a high rate of coronary angiography for the early diagnosis of such diseases. Not only do patients suffer from anxiety because of the invasive nature of this procedure but also they experience pain and discomfort for several hours after the procedure. We conducted this study to assess the effects of the inhalation of lavender essential oil on anxiety and pain in patients undergoing coronary angiography.

Materials & Methods

This clinical trial was performed at Rajaie Cardiovascular, Medical, and Research Center, Tehran, Iran. Eighty patients who were hospitalized for coronary angiography participated in this study. The patients were divided into 2 groups: control (n = 40) and intervention (n=40). Data collection tools included the 3 forms of demographic information, standard Spielberger questionnaire, and visual analog pain scale, which were completed by both groups before and after aromatherapy with lavender oil. The collected data were analyzed with SPSS software, version 16.0. (Armonk, NY, USA) using the χ^2, McNemar, Wilcoxon, Mann–Whitney, and t tests.

Results

The 2 groups were comparable apropos age, sex, marital status, and education level. After aromatherapy, the level of anxiety in the intervention group decreased significantly ($P < 0.05$) in comparison with the control group. Additionally, the extent of pain in the 2 groups showed a significant difference ($P < 0.05$).

Conclusion

Smelling the scent of lavender significantly reduced anxiety and pain in our patients, before and after coronary angiography.

Resveratrol Adjunct Therapy for Negative Symptoms in Patients with Stable Schizophrenia: A Double-Blind, Randomized Placebo-Controlled Trial

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Introduction

Patients with schizophrenia can generally manifest a broad variety of primary negative symptoms. The current study aimed to assess the efficacy and tolerability of resveratrol add-on therapy in the treatment of negative symptoms in patients with stable schizophrenia.

Materials & Methods

In a randomized, double-blind and placebo-controlled setting, schizophrenia patients were assigned to receive either 200 mg/day resveratrol or matched placebo in addition to a stable dose of risperidone for 8 weeks. Patients were assessed using the positive and negative syndrome scale (PANSS), the extrapyramidal symptom rating scale (ESRS), and Hamilton depression rating scale (HDRS) over the trial period. The primary outcome was considered as the change in PANSS negative subscale score from baseline to week 8 between the treatment arms.

Results

Fifty-two patients completed the trial (26 in each arm). Baseline characteristics of both groups were statistically similar (p values > 0.05). Despite the statistically similar behavior of positive symptoms between the groups across time (Greenhouse-Geisser corrected: $F = 1.76$, $df = 1.88$, $p = 0.180$), the resveratrol group demonstrated greater improvement in negative, general psychopathology, and total scores (Greenhouse-Geisser corrected: $F = 12.25$, $df = 2.04$, $p < 0.001$; $F = 5.42$, $df = 1.56$, $p = 0.011$; $F = 7.64$, $df = 1.48$, $p = 0.003$). HDRS scores and its changes, ESRS score, and frequency of other complications were not significantly different between resveratrol and placebo groups.

Conclusion

Adding resveratrol to risperidone can exhibit remarkable efficacy and safety in terms of management of schizophrenia-related negative symptoms.

Brain electrical activity related to an attentional task in members of families with genetic risk for Alzheimer's disease

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Introduction

Alzheimer's Disease (AD) is a neurodegenerative disease being the most prevalent form of dementia in the world. The pathological features of AD are the formation of amyloid-beta (Aβ) plaques and neurofibrillary tangles that leads to a synaptic dysfunction in preclinical stages of the disease. The Event-related potentials (ERP) allows to study the modulation of the brain electrical activity related to a cognitive task in neurodegenerative processes. The study of ERP in familial early onset AD allows to identify early neurophysiological changes that could be preclinical biomarkers of the disease.

Materials & Methods

A sample of 86 participants, belonging to families with genetic risk for AD by PSEN1 E280A mutation was included. They were distributed in three groups: asymptomatic carriers (AC, n=28), asymptomatic non-carriers (ANC, n=35) and a group with Mild Cognitive Impairment (MCI, n=23). High-density Electroencefalography (EEG) was used for recording the brain electrical activity. The participants performed a visual Odd-Ball paradigm for ERP, P300. The Peak amplitude, the latency, the Positive and Rectified Area were obtained using Matlab's ERPLab toolbox. For each component, mixed repeated measures ANOVA of group (3), condition (2) and electrodes (PZ, P2, P4) was performed.

Results

The MCI group show lower amplitude than AC in P2 and P4 electrodes (p<0.05). There aren't differences in the amplitude between the asymptomatics groups. A greater latency was observed in ANC than the AC (p=0.072). AC show more Positive Area compared to ANC (p<0.05), but there aren't differences in the Rectified Area between the groups.

Conclusion

The changes observed between AC and ANC can show the differences in the modulation of the brain electrical activity associated to the pathophysiological mechanisms of the disease and the continuum until clinical stages as MCI. In the future, new measures of P300 may be plausible neurophysiological biomarkers that could serve as a method to diagnose AD.

Association between permissive parenting style and high-risk behaviors among young adults: an analytical cross-sectional study

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Introduction

Young adults are mainly susceptible to high-risk behaviors (HRBs) because they are in a critical period of development wherein mortality rates are high, the health needs are unique, and where challenges and milestones are distinct from both adolescents and adults. It is a period of transitioning. In relation to this, studies have shown that parenting influences the development of a child. Therefore, parenting style may affect a young adult's decision in engaging in high-risk behaviors, and can directly affect their overall health and well-being. This study aims to determine the presence of association between permissive parenting style and HRBs among young adults in the Philippines.

Materials & Methods

An analytical cross-sectional study design was used. The study population was comprised of undergraduate college students, aged 19-24 years old, in selected areas in the Philippines, recruited using convenience, non-probability sampling. Prevalence Risk Ratio and Chi-Square Tests were computed using IBM SPSS Software.

Results

At 95% confidence interval, PRR values >1 were obtained for permissive parenting in mothers and HRBs for alcohol and drug use, sexual behavior, and diet/food intake. For permissive parenting style in fathers, PRR values >1 were obtained with HRBs for alcohol and drug use and for diet/food intake. P-values for all the results were >0.05.

Conclusion

Results reveal that respondents with mothers utilizing permissive parenting have higher odds of developing HRBs for alcohol and drug use, sexual behavior, and diet/food intake as opposed to those whose mothers do not use permissive parenting. Likewise, respondents with permissive fathers are more likely to develop HRBs for alcohol and drug use and diet/food intake. However, all computations had p-values greater than 0.05, rendering the results statistically insignificant. This can imply that the results of previous studies proving the association of permissive parenting style and HRBs do not apply to the context of the Philippines or possibly countries with similar profile. Likewise, it can also be attributed to Filipino culture, especially how Filipino children understand the concept of permissive parenting.

Medicine undergraduates caught in the web of internet! Effect on affect, mental and social health

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Introduction

The widespread use of internet a tool for e-learning and education, information exchange, communication, and recreation, is now an indispensable adjunct in the lives of young adults. With the ease of access, internet users account to more than three billion people worldwide. Extensive unrestrained time consuming usage disturbing a person's daily life with detrimental effects on physical and psychological wellbeing is termed as internet addiction (IA).

The prevalence of IA among undergraduates ranges from 4% to 18%, and 30.1% amongst medicine undergraduates. Internet addiction has emerged as a serious mental health issue of the present decade. Students with potential IA need to be identified as the addiction can coexist or result in other psychological problems. The aim of our study was to assess internet addiction in medical undergraduates using a validated questionnaire and correlate it with somatic symptoms, anxiety and insomnia, social dysfunction and depression.

Materials & Methods

A descriptive cross sectional questionnaire based study was conducted involving undergraduate students of medicine, aged 18 years and above. A validated self-report online questionnaire using Google documents to assess internet dependence and somatic symptoms, anxiety and depression, insomnia, social dysfunction was administered. The significance level set at 0.05. Collected data was analyzed by frequency, percentage, Karl Pearson correlation coefficient and student t-test.

Results

Of the 215 students, age range 18 to 23 years, who consented and answered the questionnaire there were 126 internet users grouped as normal. High addiction scores were observed in 89 (41.1%) of whom 21(9.8%) had severe addiction. There was significant association between internet addiction and altered sleep, somatic and social functions (p value 0.000). Those with high scores for internet addiction also had highly significant correlation for anxiety and depression (p value 0.000).

Conclusion

Internet addiction among students is a source for concern and should be given more attention. An awareness program for students with provision for a 'safety network' could be prepared to detect students at risk of internet addiction before it becomes pathological.

A maternal high-fat diet during pregnancy leads to decrease antioxidant capacity with working memory deficits

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Introduction

Modern human societies have been subjected to a unprecedented rise in the availability of highly palatable and low-cost foods that are high in saturated fat. The widespread availability of these type foods has led to a drastic increase in the exposure to dietary fat during the fetal and early-life period, which is a highly sensitive developmental window; however, the mechanisms by which a maternal HFD causes these deficits are not fully elucidated.

Materials & Methods

We used 40 pups: 20 pups from a mother fed balanced diet (BD) (6.2% fat energy) and 20 pups from a mother fed an HFD (42% fat energy) during pregnancy. The pups were fed with a BD. At PND 28 to 42, using the Eight-Arm Radial Water Maze, was assessed working memory. After the behavioral evaluation, a blood sample was collected and blood serum was obtained. Subsequently, the ELISA technique was performed to identify the serum GSH levels. The normality of data was confirmed with the Shapiro-Wilks test. The SPSS v25.0 software was used for statistical analysis and the statistical significance was set at $p < 0.05$. The effect of the interaction between variables were analyzed with the two-way ANOVA test.

Results

The offspring born to dams fed with an HFD showed significantly major errors with respect to their counterparts ($t = 7.843$, $p < 0.002$, 95% CI) and a significantly lower serum GSH levels ($t = 8.135$, $p = 0.001$, 95% CI). A correlation was found between the GSH serum levels and the correct working memory errors ($r = 0.81$, $p < 0.05$).

Conclusion

Exposure to a maternal HFD during pregnancy cause working memory deficits and decrease the GSH levels in the offspring. Therefore, we could hypothesize that this is one mechanisms causative that affect the environment of the developing offspring. Given the high rates of obesity and high fat diet consumption in pregnant women, it is vital establish nutritional recommendations for pregnant women, which could contribute to the prevention of cognitive deterioration in the offspring.

Urology and Nephrology
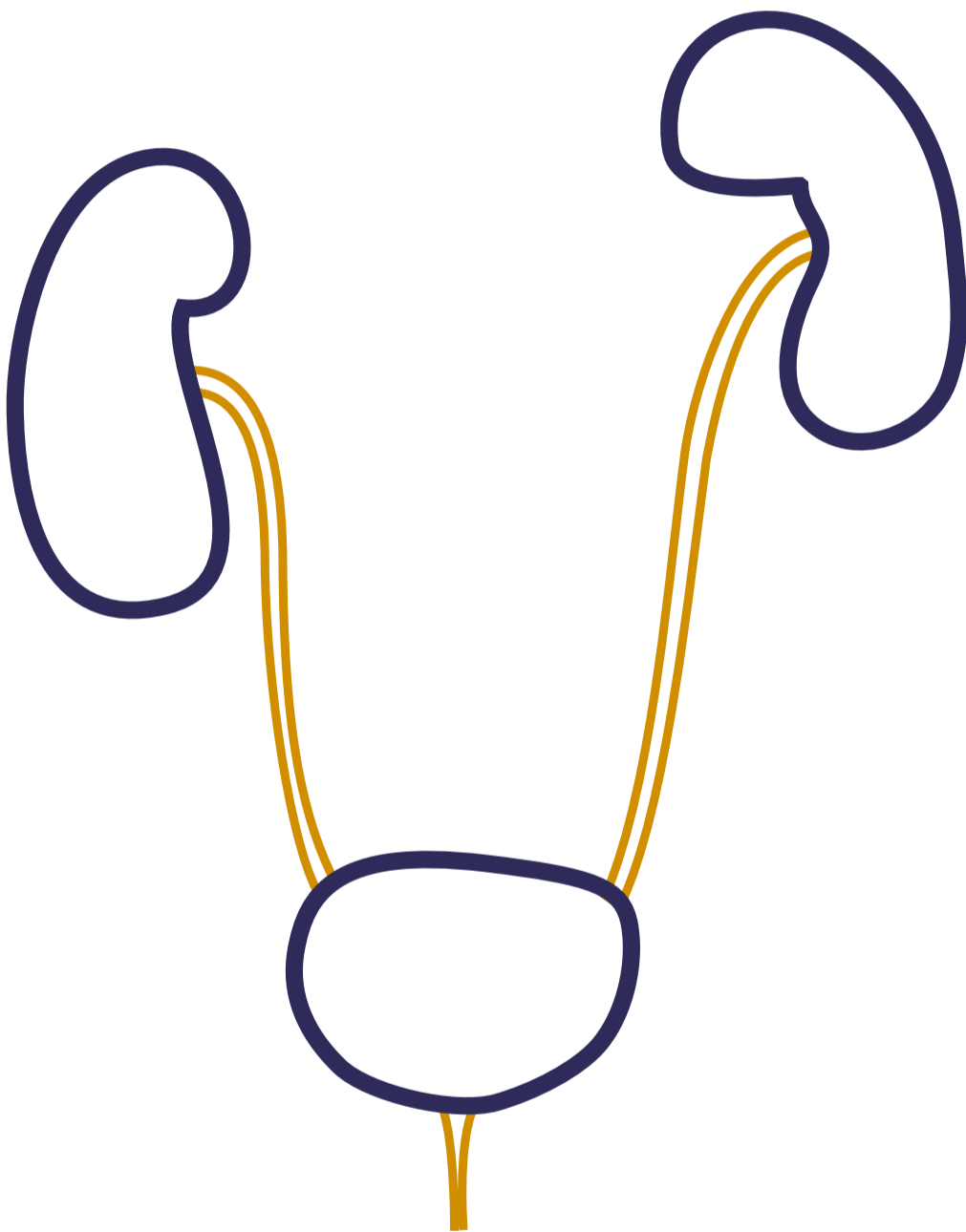
Presenters:
Siwi, G. N. (Gita Nur)
El-Qushayri, A (Amr Ehab)
Khavandi, M.M.K (Mohammad Mahdi)
Pakniyat, A (Abdolghader)
Purnomo, A.F. (Athaya Febriantyo)
Lammerts, A

Effects of Moringa oleifera (LAM.) seed extract on kidney function and glomerular volume in metabolic syndrome rats

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Introduction

Metabolic syndrome (MetS) has been associated with kidney disease markers including reduced glomerular filtration rate, proteinuria and/or microalbuminuria. The phytochemicals found in Moringa oleifera, Lam. seed could potentially decline the progressivity of renal pathology caused by MetS. This study aimed to assess the phytochemical effect of Moringa oleifera, Lam. seed extract for metabolic syndrome rat's kidney function and pathology.

Materials & Methods

This study was an experimental study on 28 adult male albino Wistar rats. The rats were divided into four groups each comprising of seven rats. Rats group I (control group) (G1) received standard diet without Moringa oleifera, Lam. seed extract. Rats group II (G2) received high fat and high sugar diet without Moringa oleifera, Lam. seed extract. Rats group III & IV (G3 & G4) received high fat and high sugar diet with oral administration of 150 and 200 mg/kg bodyweight of the ethanolic extract of moringa oleifera seed. The combination of high fat and high sugar diet was given for 53 days to induce metabolic syndrome in rats.

Results

The combination of high fat and high sugar diet on rats for 53 days had resulted in metabolic syndrome state in rats. Friedman test and One Way ANOVA test show oral administration of Moringa oleifera, Lam. ethanolic seed extract on MetS rats with the dosage of 150 mg/kgBB and 200 mg/kgBB for 28 days could lower the serum creatinine level (p=0.028 and p=0.018) and lower the glomerular volume (p=0.000 and p=0.000).

Conclusion

Oral administration of the ethanolic extract of Moringa oleifera, Lam. seed could lower the creatinine serum level and decrease the glomerular volume of MetS Wistar rats.

Fournier's gangrene mortality; A 17- year systematic review and meta-analysis

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Introduction

Fournier's gangrene (FG) is a rare necrotizing soft tissue infection involving the perineal, perianal and genital areas. Despite the significant improvement in the therapeutic modalities, mortality from FG is still high. We carried out this study to provide better management of the disease through identifying the mortality-associated comorbidities and the common etiologies of deaths.

Materials & Methods

We performed a systematic search through twelve databases for selection of relevant articles. We included all studies that report comorbidities and the specific causes of mortality among FG patients. There were no restrictions on study design, country, language or publication date. Meta-analysis was used to pool the results.

Results

We included 38 articles after screening of 1186 reports. Mortality rates were higher in patients with diabetes, heart disease, kidney disease and renal failure with the risk ratio (RR) and 95% confidence interval of 0.72 (95%CI 0.59-0.89), 0.39 (0.24-0.62),0.34 (95%CI 0.16-0.73) and 0.41 (95%CI 0.27-0.63), respectively. However, we did not find a significant association between the survival status and co-morbid hypertension, lung disease, liver disease and malignant disease (p > 0.05). The most common causes of deaths were sepsis (76%) and multiple organ failure (66%), followed by the observed mortality rates due to respiratory (19.4%), renal (18%), cardiovascular (15.7%) and hepatic (5%).

Conclusion

The results of our paper highlight the influence of comorbidities on the survival of FG patients, therefore Fournier Gangrene Severity Index (FGSI) should be modified to include comorbidities as a significant prognostic tool which will aid clinicians for better management of the dangerous disease. Additionally, more attention should be devoted towards the main cause of death regarding the selection of the proper therapy.

Glatiramer acetate potentially is protective against renal ischemia reperfusion injury: Results of an animal study

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Introduction

Chronic renal failure can ultimately lead to kidney transplantation. This is associated with renal ischemia reperfusion. The subsequent processes of kidney ischemia reperfusion can lead to irreversible damages to the kidney tissue. The purpose of this study was to evaluate the protective and therapeutic effects of Glatiramer acetate on reducing the damages arising from kidney ischemia reperfusion. The anti-inflammatory effects of this drug have already been proven in some inflammatory models and some diseases, such as MS.

Materials & Methods

In this study, 42 male Wistar rats are used which divided into 6 groups: normal (saline), sham, control (I/R), Glatiramer 0.5 mg / kg + I / R, Glatiramer 1 mg / kg + I / R, Glatiramer 2 Mg / kg + I / R. Both renal arteries are clamped bilaterally, and for 45 minutes the kidneys suffered with ischemia, and then the clamps are removed and the reperfusion process continues to 24 hours. In the following, the animals were killed, and then the serum and both kidneys were separated for analysis.

Results

: In the control group, inflammatory factor TNF-α and functional markers such as BUN, Creatinine, and LDH were significantly increased, but in the treatment groups, especially the Glatiramer 2 mg / kg group, a significant decrease was observed, in the lipid peroxidation marker, such as MDA, similar effects were obtained. IL-10, which was considered as an anti-inflammatory factor, was significantly increased in the treatment group of Glatiramer 2 mg / kg. Histopathological studies also demonstrated the protective effect of this compound.

Conclusion

The results of this study indicated that Glatiramer can causes the protective effects on kidney ischemia reperfusion by reducing inflammatory and oxidative damages.

Intranasal ketamine and IV morphine in renal colic: A clinical trial study

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Introduction

Intranasal pathway is a mucosal way for absorbing agents to directly affect in brain via olfactory sheets, bypassing first pass metabolism and the blood brain barrier. This study was aimed to compare the effect of intranasal ketamine vs. intravenous morphine on renal colic.

Materials & Methods

In this clinical trial study, 100 patients with renal colic were entered into the study and randomly divided into two groups. Patients in treatment group received intranasal ketamine (1.5 mg/kg), and the other group was given intravenous morphine (0.1 mg/kg). The pain was measured at 0, 5, 15, 30 and 60 minutes after medication administration.

Inclusion criteria :

known history of renal stone, acute renal pain with score ≥four based on VAS , and with age between 20 to 50 years and with no other underlying diseases.

Exclusion criteria:

drug addiction based on patient's own declaration, pregnant and lactating women, narcotic allergy, nasal obstruction, systolic blood pressure less than 100 mmHg, respiratory distress, history of seizure, history of glaucoma, previous use of the pain-killer drug before visiting the hospital, and critical diseases such as aortic dissection.

The relationship between variables measured using T and Chi-square tests, and determining changes in pain score over time repeated ANOVA test was used at the significance level of 0.05.

Results

In this study, 32% of patients were female and 68% were male. Also, the difference between the initial pain with pain at all subsequent times in the two groups were significant ($P < 0.001$). The duration of the ketamine effect to control pain was longer, but with the administration of morphine, a faster effect on pain relief was achieved.

Conclusion

Low-dose ketamine is considered as an analgesic with low side effects; Especially that the use of this drug via intranasal is simple and uncomplicated and its analgesia is comparable with intravenous administration, in the pre-hospital condition reduces the need for establishing IV access and so that the risk of the needle stick. According to the results, the use of intravenous morphine to reduce the renal colic pain has a faster effect than intranasal ketamine, and its use in these patients should be given priority.

Comparison between Intravesical Epirubicin or Mitomycin-C after TURB and TURB alone with Recurrence Rate of Non-Muscle Invasive Bladder Cancer : Meta-Analysis

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Introduction

Bladder cancer is still a burden on the world of oncology medicine, which every year affects about 3.4 million people globally with 430,000 new cases per year. It is the fourth most common cancer in men and eighth most common women malignancy in the world. This makes bladder cancer a "silent killer" and it needs appropriate treatment planning. Single immediate instillation of chemotherapy after transurethral resection of the bladder (TURB) is recommended by EAU guideline, but its use remains a controversy. Study aimed to analyze benefit of intravesical chemotherapy following TURB in terms of recurrency of non-muscle invasive bladder cancer (NMIBC).

Materials & Methods

Systematic review and meta-analysis of randomized controlled trials comparing the efficacy of a single instillation after TURB with TURB alone in NMIBC (pTa-pT1) patients was conducted. Studies searched throughout Medline, PubMed, Embase, and Cochrane in December 2018. Keywords were intravesical chemotherapy, combination, transurethral resection, bladder cancer. Inclusion criteria were RCT studies, subjects in study were treated single immediate chemotherapy instillation after TURB compared to TURB alone in patient with pTa-pT1 urothelial carcinoma of the bladder. Trials with additional treatment prior to first reccurence were not eligible. Studies using recurrence rate as dependent variable. Total 11 studies were eligible for this meta-analysis.

Results

From those 11 studies, it is shown that intravesical chemotherapy using Epirubicin and Mitomycin-C following TURB showed significant decrease of recurrence rate of bladder cancer even to progression of the disease compared to TURB alone (p<0.05) with pooled Risk Ratio were 0.69 and pooled heterogeneity (I2) were 26.6%.

Conclusion

This meta-analysis study showed that combination therapy of intravesical chemotherapy after TURB is superior to TURB alone in showing the recurrence rate of NMIBC

The effect of different haemoglobin concentrations during normothermic reperfusion of porcine DCD kidneys on oxygen consumption, renal sodium handling and oxidative stress

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Introduction

Donor kidneys derived from donation after circulatory death (DCD) suffer ischemia when the oxygen supply stops. Reperfusion in post ischemic kidneys causes ischemia-reperfusion injury (IRI), which is associated with the incidence of delayed graft function (DFG). The mechanism most commonly involved in IRI and therefore an important contributor to adverse outcomes in kidney transplantations is oxidative stress. Normothermic machine perfusion (NMP) is a relatively new technique for pre-transplant preservation, assessment and conditioning of marginal donor kidneys. An adequate oxygen supply during NMP is required to maintain renal metabolism and to minimize hypoxic-related damage. However, the optimal conditions in terms of sufficient oxygen supply during NMP are not established. The aim of this study is to evaluate the effects of different haemoglobin concentrations on oxygen consumption, renal sodium handling and oxidative stress markers during ex vivo kidney NMP.

Materials & Methods

Porcine kidneys obtained from an abattoir were subjected to 35 minutes of warm ischemic time. Thereafter, the kidneys were preserved with oxygenated hypothermic machine perfusion for 3 hours. Subsequently, they were reperfused for 4 hours in a normothermic, pressure-controlled, setup with an autologous blood-based solution containing either 2,2 mmol/L (n=6), 4,5 mmol/L (n=3) or 5,6 mmol/L haemoglobin (n=4). Oxygen consumption, fractional sodium excretion and creatinine clearance were measured. Additional experiments and analyses are ongoing.

Results

Total oxygen consumption was the highest in the 5.6 mmol/L group and significantly higher compared to the two other groups. Improved fractional sodium excretion levels were observed in the highest haemoglobin group. Glomerular filtration rate assessed by creatinine clearance showed no significant differences. More in-depth analyses on adenosine triphosphate (ATP), oxidative stress and injury markers are ongoing to investigate mitochondrial function.

Conclusion

This preliminary data suggests that low haemoglobin levels result in insufficient oxygen delivery to support renal sodium reabsorption during NMP. Whether this is due to mitochondrial malfunction remains to be investigated.

Oral Sessions II
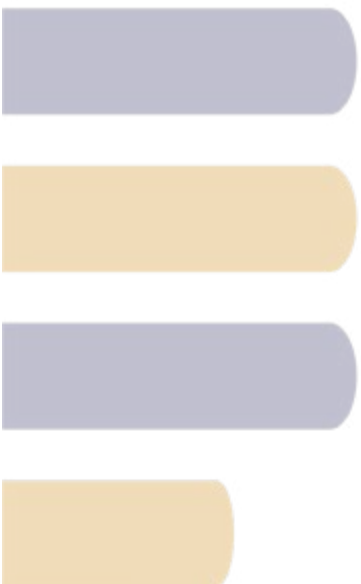
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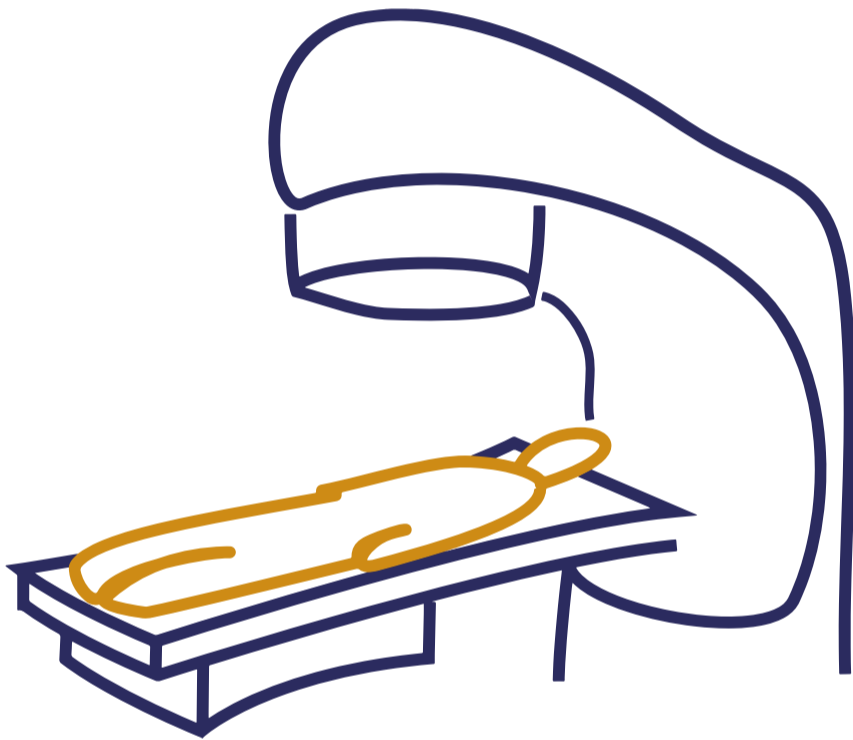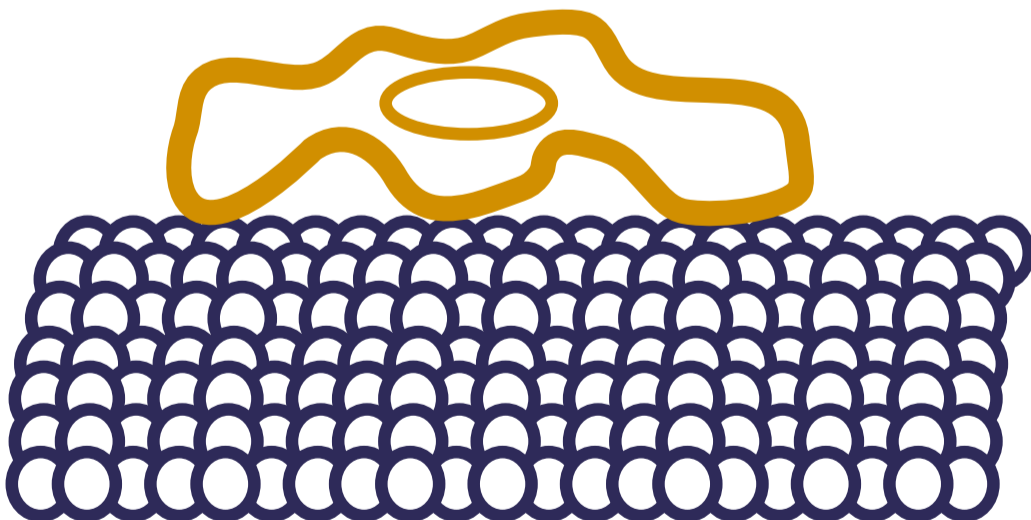
Presenters:
Tang, X. (Xiongfeng)
Badri, MB (Mohammadali)
N. (NIKITA)
Capendale, P. E. (Pamela)
Deb, DS (Shramana)
Wenardy, C.J.W. (Celestine)

Automatic Knee Joint Segmentation and Quantitative Analysis from MR Images in Normal and Osteoarthritic Subjects: A Deep Learning-Based Approach

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Introduction

To improve the accuracy of deep learning-based methods to automatically segment human knee joint tissue from MRI, and analysis biomarkers morphology index for the assessment of Osteoarthritis (OA) pathological progression.

Materials & Methods

This retrospective work involved the analysis both SKI10 dataset (150 knee MRI images) and our private dataset which collected from the local hospital (637 knee MRI images). We first employed a deep learning-based model to jointly segment six tissues from knee MRI, including femur, tibia, femoral cartilage, tibial cartilage, lateral meniscus and medial meniscus. Then, we calculated morphologic biomarkers: joint spacing distance, the thickness and the volume of cartilage and meniscus from another dataset of 100 images which consists of the OA group (54 subjects, KL grade>1) and the normal group (46 subjects, KL grade=0). Finally, we analyzed the statistical difference of these biomarkers between the two groups.

Results

Our segmentation model demonstrated relative highly precision in quickly generating accurate performance in the test group, with mean Dice similarity coefficient (DSC) 0.948 for femur, 0.919 for tibia, 0.781 for femoral cartilage, 0.707 for tibial cartilage, 0.820 for lateral meniscus, and 0.818 for medial meniscus. The whole segmentation pipeline took around 5s on NVIDIA DGX workstation. Based on the high accuracy segmentation results, we find no significant difference with respect to meniscal volume and thickness between normal and OA, but joint space distance, cartilage volume and thickness have a moderate correlation between normal and OA subjects.

Conclusion

In this work, we proposed a deep learning-based method based on 3D-CNN for multiple object segmentation from knee MRI and developed several biomarkers to analyze morphological changes of tissues in the knee joint at different pathological progression of OA.

Establishing a novel approach of micro-fluidic devices in determining factors in vascularisation

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Introduction

Vasculogenesis is the de—novo formation of vessels from cells derived from the mesoderm. This can be sub—divided into pre—natal and post-natal vasculogenesis depending on whether it occurs prior to or after birth (Ribatti et al., 2001). On the other hand, angiogenesis is described as a sprouting ' of new capillaries from pre-existing vessels resulting in new capillary networks (Risau, 1997). Vasculogenesis requires a complex series of molecules to orchestrate the formation of blood vessels from endothelial cell differentiation. Here the aim of this study is to establish a novel platform to use in vitro microfluidic devices as to identify certain vascularisation factors.

Materials & Methods

For harvesting required medium, we collected 15 ml of fibroblast conditioned media and epithelial growth factor-2 (EGM-2), using Easypet3. After incubations, we used Ultrafree-15 filter sit to concentrate collected EGM-2 conditioned media. At last, we took 150 µL from appropriate media and load it into each well of our baked silicone gel microfluidic device. After aspirating of each well, we added 80µl of paraformaldehyde (PFA) to fix HUVEC cells loaded in the central chamber to visualise lumenisation of epithelial cells.

Results

The study conducted with two main experiments. While the first experiment examined 6 different concentration of epithelial growth medium, in second experiment the idea was to identify the angiogenic factors. The results showed that the factor is potentially a protein (F= 52.19, p-value <0.001) while fractionation results indicated the potential protein could be VEGF-165 (F=130.8, p-value <0.03) from 6 different repeats, including all possible confounding factors in the medium.

Conclusion

In summary, both fibroblast growth factor-2 (FGF-2) (Cox and Poole, 2000) and vascular endothelial growth factor (VEGF) (Carmeliet et al., 1996) are required for mesodermal differentiation into angioblasts. Although, there were few studies available on using microfluidic devices, however, our results confirm the potential application of microfluidics in studies of vascularisation.

A grafted copolymer-based topical nanomicellar formulation targeting the posterior segment of the eye for effective treatment of Uveitis

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Introduction

The therapeutic agents administered through oral and i.v. routes cannot reach targeted ocular tissues. Also, diseases affecting the posterior segment of the ocular tissue are difficult to treat via topical administration of drugs due to various ocular anatomical and physiological barriers. Therefore, the present work is aimed to overcome the ocular barriers via the preparation of Everolimus loaded nanomicelles (EVR-NMs) using a grafted copolymer that could incorporate the hydrophobic drug in the core and hence improved permeation through ocular epithelia with minimal or no irritation ultimately leading to enhanced ocular bioavailability at the posterior segments of the eye for the treatment of uveitis.

Materials & Methods

The Evr-NMs formulation was developed by the solvent evaporation method. The concentration of the polymer was optimized by determining the CMC and Evr-NMs were prepared and characterized for particle size, PDI, drug entrapment efficiency, surface morphology, and drug release. The EVR-NMs with best characteristic features were selected and evaluated for in-vitro ocular irritancy and anti-inflammatory test by HET-CAM assay, and ex- vivo permeation study using goat cornea, confocal laser scanning microscopy. In addition to this, the efficacy of Evr-NMs in treating the uveitis was studied using a rat model and the biochemical estimation of pro-inflammatory mediators in rat vitreous humour and serum was determined.

Results

The prepared EVR-NMs were found to be <70nm in size and showed more than 95% entrapment efficiency. The surface morphological studies by TEM, SEM, and AFM analysis showed that the micelles were spherical and homogenous. The in-vitro ocular irritancy test confirmed that the EVR-NMs did not result in any irritation and significantly reduced the inflammation (p<0.001). Ex-vivo permeation study confirmed that the EVR-NMs showed better permeation than that of EVR solution. Biochemical estimation confirmed that EVR-NMs significantly reduced the increased inflammatory mediators in rats with uveitis (p<0.001).

Conclusion

The results of nanomicellar formulation demonstrated the significantly higher accessibility and improved drug bioavailability of EVR at the posterior segment which could lead to a promising therapeutic outcome in immunosuppressive drug therapy for uveitis.

Hemodynamic Response Analysis for Mind-Driven Type-writing Using a Type 2 Fuzzy Classifier

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Introduction

The current prospects of cognitive neuroscience unfolds the mental utterance of vowel sounds known as 'vowel sound imagery', primarily recognized through temporal and frontal activation in real time Electroencephalography (EEG) apparently produces excellent temporal response, however EEG acquired from the channel is often found to be contaminated by neighborhood signal sources, which intrigues us to find the scope of functional near infrared spectroscopy (f-NIR) as a substitute to EEG for the present application.

Our study attempts to detect vowel sounds (A,AA,AeA,EE,O,Ae,UU) from brain activation in frontal/prefrontal and temporal cortices due to vowel sounds imageries.

Materials & Methods

10 healthy volunteers (22-30yrs) with normal eyesight were included. A codebook was prepared to describe consonants by a part of vowel sounds in a space between them (e.g. A_A denotes B) We used 21-channels (international 10/20 system)EEG device (500Hz) & f-NIR device (penetration depth-1.25cm) having 4 Infra-red emitters with 10 detectors .Initially, our study attempts to detect vowel sounds by experimentally determining the maximum and relatively longer activation in frontal/prefrontal areas during vowel sound imaginations using acquired EEG signal analysis by e-LORETA software. Then we captured prefrontal/frontal vowel sound imagery using f-NIR device to extract certain statistical features. We used, a differential evolution-based feature selection algorithm to reduce the large dimension of extracted features into a reduced set of data, which is then used to design an interval Type-2 Fuzzy Classifier to classify the vowel sounds from prefrontal/frontal f-NIR responses to vowel sounds imagination. This proposed classifier is used to detect these vowel sounds () from prefrontal/frontal activities secondary to vowel sound imageries. Statistical analysis was performed using well known McNemar's Test.

Results

We found, through experiments undertaken, that the proposed classifiers outperform its competitors in a classification accuracy for each vowel sound imagery class along with further confirmation that the f-NIR based classification out-stands EEG based modality for better capture of brain activation.

Conclusion

As consonants here are specially encoded with a two vowel sounds with a space between them, thus the proposed technique can effectively used for mind driven type writing for both vowels and consonants for the peoples with vocal deficiency.

Accurate non-invasive blood glucose concentration monitoring via thermal and light technology

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Introduction

Due to the painful and unsustainably costly nature of invasive glucose meters on the market, many diabetics suffer from complications as they opt not to monitor their glucose levels. Thus, this study aims to explore novel and relatively affordable approaches in non-invasive glucose monitoring, and implement these methods into a functional prototype.

Materials & Methods

Thermal and light technology as a method of estimating glucose concentration was explored. The thermal technology utilises the correlation between the heat capacity of skin, and thus the rate of change of temperature given a constant emission of heat, and blood glucose concentration. On the other hand, the light technology leverages the dependance of the refractive index of the interstitial fluid on blood glucose concentration. (As the refractive index changes with glucose concentration, the amount of light reflected in a certain area will also change.) These mechanisms utilise thermistors and LDRs respectively to measure heat/light dependent resistances which are then mapped onto a calibration curve to obtain readings. 229 readings from this noninvasive prototype were obtained and plotted against true glucose concentration – the R^2 value was calculated to measure accuracy, in addition to Clarke error grid analysis.

Results

The R^2 value obtained from the 229 readings was 0.883, indicating a strong correlation which in turn reveals that the prototype is highly accurate. Furthermore, Clarke error grid analysis (which divides the graph of measured v. true glucose concentration into 5 zones of 'accuracy') signifies that 95% of points are clinically acceptable. These values are significantly higher than the majority of clinical trials in noninvasive glucose monitoring over the past 30 years. In terms of affordability, the unit cost of this design totals at approximately $30 (0.6% of what the average previous model costs).

Conclusion

In conclusion, thermal and light technology can be used as an accurate method of measuring blood glucose levels non-invasively and affordably. In the future, this research will be aimed towards transforming this glucose monitor into a wearable, as well as enabling the monitor to predict future glucose levels based on previous collected data and trends.

Cardiology
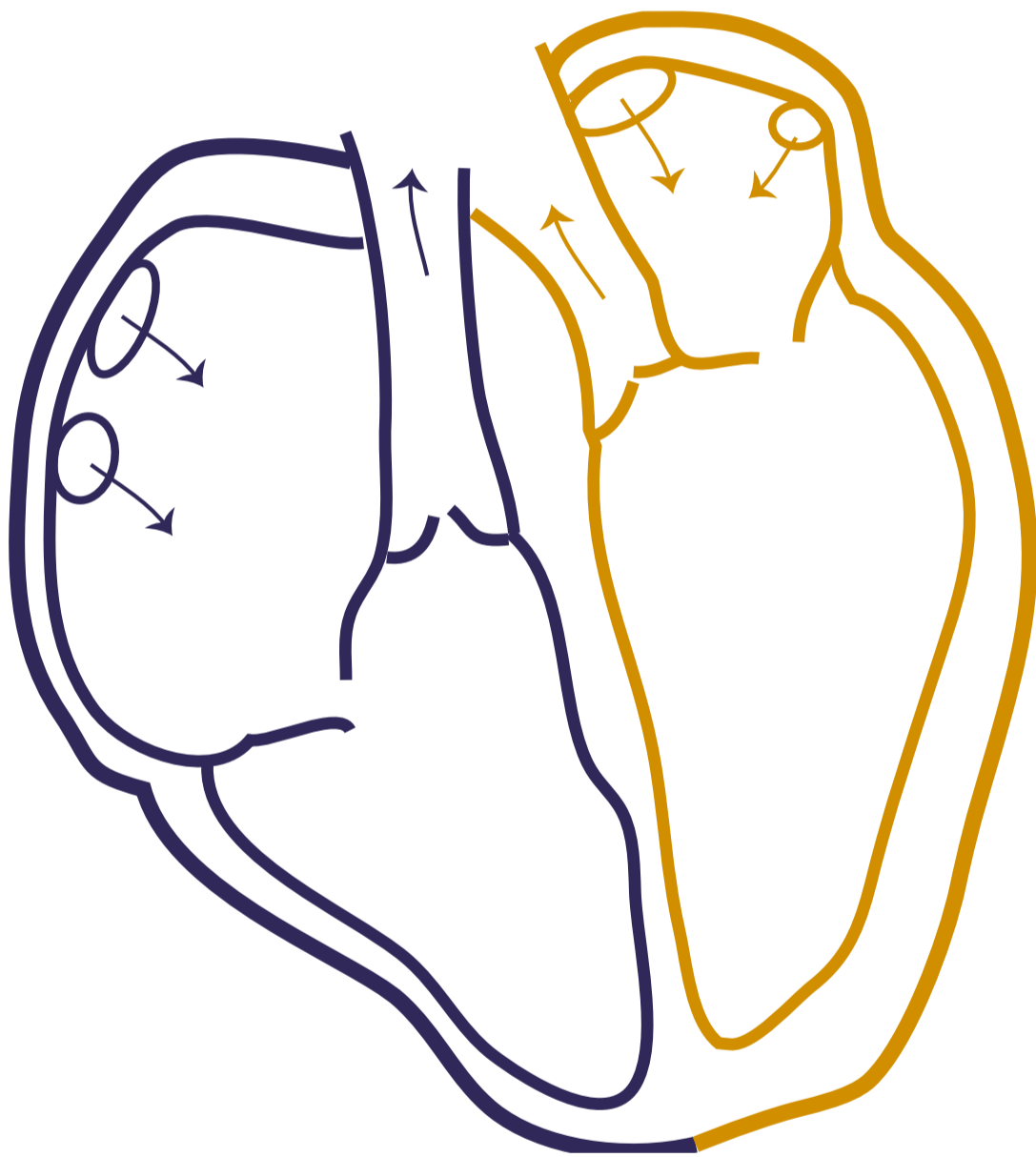
Presenters:
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Davarian, A (Ali)
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The Value of N-Terminal Pro B-Type Natriuretic Peptide in Evaluating Obstructive Sleep Apnea in Patients With Coronary Artery Disease

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Introduction

Natriuretic peptides have been identified as biomarkers of increased myocardial wall stress in the context of obstructive sleep apnea (OSA) in the general population. However, the relationship between N-terminal pro B-type natriuretic peptide (NT-proBNP) and OSA remains unclear in patients with coronary artery disease (CAD). Hence, we aimed to investigate the clinical value of NT-proBNP in evaluating OSA in a large population of patients with CAD.

Materials & Methods

Consecutive patients with CAD were prospectively enrolled between February 2015 and March 2018. Portable respiratory monitoring was applied to facilitate the diagnosis of sleep apnea. Patients were as assigned to the non-OSA (when the respiratory events index [REI] or 3% oxygen desaturation index [ODI] < 15 events/h) and OSA (when the REI or 3% ODI ≥ 15 events/h) groups. Multivariate analyses were used to explore the independent association between NT-proBNP levels and OSA.

Results

A total of 1,292 consecutive patients were included with a mean NT-proBNP value of 826.57 εg/L. Patients with high levels of NT-proBNP experienced increasing severity of OSA in those with CAD (P =.0004). Univariate analysis demonstrated that NT-proBNP was a risk factor for OSA (odds ratio [OR] 1.10, 95% confidence interval [CI] 1.03–1.18, P =.005). In addition, multivariate analysis revealed that NT-proBNP was independently associated with the presence of OSA (OR 1.11, 95% CI 1.02–1.20, P = .012) even after adjusting for other confounding factors.

Conclusion

Elevated levels of NT-proBNP were independently associated with a higher likelihood of OSA in patients with CAD. Periodically screening for NT-proBNP levels may provide early identification of OSA.

Fabrication of Engineered Heart Tissue as a New Tool for Drug Screening and Diseased Heart Studies

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Introduction

Culturing cardiomyocytes in a collagen matrix creates a coherently contractile 3D tissue named as engineered heart tissue (EHT) which serves as a model of normal or diseased heart. This could provide a reliable in vitro model for drug testing and as a novel treatment for salvaged myocardium after infarction. We herein developed an EHT from chick embryonic cardiomyocytes for the first time in Iran.

Materials & Methods

The cardiac cells were isolated from 11-day old embryonic chicken by enzymatic digestion and then engrafted in collagen matrix. These cells then were casted in 8-well polycarbonate mold with a 5x106 cardiomyocyte density in each well (mold, N=4). Tissue formation process was observed using inverted microscope. In order to evaluate tissue characteristics, mono-phasic Action Potential Duration (APD), Sinus Rate (SR) and Contractile force measurement were done for each tissue before and after injection of a β-adrenergic drug (Epinephrine 0.1 μM). Electrophysiological tests were recorded using silver electrodes. Contractile forces of EHTs were measured by an isometric force transducer.

Results

The EHTs started to beat spontaneously after 4-6 days with a rate of 120-140/min. The contractile force measures significantly increased from 0.2±0.001 μN to 0.4±0.0014 μN in response to β-adrenergic stimulation (p<0.01). Tissue recordings revealed that SR decreased from 839.8±3.07 ms to 437.7±3.45 ms (p<0.0001) before and after epinephrine and action potential duration (APD) decreased from 206.6±6.73 ms to 187.9±2.05 ms (p<0.02).

Conclusion

It seems that EHT contains many physiological characteristics of a cardiac tissue and acts as a functional model, suitable for being considered to use in regenerative medicine and a platform for drug tests.

Meta-analysis of the association between sarcoidosis and cardiovascular comorbidity

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Introduction

Cardiovascular involvement is one of the critical and lethal problems that sarcoidosis patients may ever experience, if they are not caught early and managed properly. We aimed in this systematic review and meta-analysis to quantify the burden of cardiovascular comorbidities (CVS) and their association with sarcoidosis.

Materials & Methods

Nine databases were search comprehensively to retrieve relevant articles discussing CVS in sarcoidosis patients. The National Institute of Health quality assessment tool (NIH) was used to assess the quality of the included studies, and meta-analysis was conducted to pool the results of the individual studies.

Results

There were 2208 reports screened, of which 14 studies were included in the final analysis. Hypertension appeared to be the most common CVS (28.8%), followed by heart failure (9.3%) and non-specified arrhythmia (8.1%). Sarcoidosis patients were significantly more prone to heart failure and hypertension as compared to controls (OR = 2.10, 95%CI (1.65 - 2.69), $p < 0.01$) and (OR = 1.27, 95%CI (1.02 - 1.59), $p = 0.036$), respectively. We were unable to find a significant association between sarcoidosis and cerebrovascular disease, ischemic heart disease and ventricular tachycardia ($p > 0.05$).

Conclusion

Some cardiovascular comorbidities appeared to be prevalent and associated with sarcoidosis. As a result, a thorough cardiovascular examination in sarcoidosis patients is crucial to decrease its cardiovascular-specific mortality.

The Comparison between Cryoballoon and Radiofrequency Ablation for Rhythm Control in Atrial Fibrillation: A Meta-Analysis of Studies from the Last Decade

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Introduction

Pulmonary vein isolation (PVI) is still be the main approach of catheter ablation for atrial fibrillation (AF). The superiority of cryoballoon ablation (CBA) over radiofrequency ablation (RFA) for PVI is still less clear.

The objective of this study is to investigate the superiority of CBA over RFA for AF in terms of safety and efficacy profile.

Materials & Methods

From October to November 2019, a meta-analysis was conducted. Articles comparing CBA ablation and RFA for AF published between 2010 to 2019 were collected from Embase, PubMed, and ProQuest. Correlation and effect were determined by the fixed or random-effect model.

Results

A total of 15250 patients (CBA, n = 6634 vs. RFA, n = 8616) with AF from 24 studies were involved in this meta-analysis. Procedure-related complications between CBA and RFA was not significantly different (7.55 % vs 6.91%; OR [95% CI] = 1.18 [0.88-1.57], P = 0.27; I2 = 53%, Phet = 0.005). CBA was related to higher risk of phrenic nerve paralysis (PNP) (3.1 % vs 0.1%; OR [95% CI] = 15.39 [8.42-28.1], P = <0.00001; I2 = 4%, Phet = 0.4) and lower risk of pericardial effusion or cardiac tamponade (0.9 % vs 2.15%; OR [95% CI] = 0.39 [0.28-0.54], P = <0.00001; I2 = 16%, Phet = 0.31) than RFA. Procedure time was shorter in CBA compared with RFA (WMD [95% CI] =-24.98 min [-35.44 to -14.52], P = <0.00001; I2 = 97%, Phet = <0.00001).

Conclusion

PVI using CBA was not inferior to RFA in terms of safety and efficacy profile. Compared with RFA, CBA increased the risk of PNP, decreased the risk of pericardial effusion or cardiac tamponade, and revealed a shorter procedure time.

Small dense low-density lipoprotein-cholesterol (sdLDL-C) as a predictor in young acute coronary syndrome patients with normal low-density lipoprotein-cholesterol (LDL-C) - a prospective observational study

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Introduction

Coronary artery disease (CAD) is the leading cause of death worldwide and is expected to remain so for the next 20 years. CAD occurs earlier in the Indian population, is more advanced at present, and has different dyslipidemia patterns compared to western population. LDL-C levels have been identified as one of the strongest risk factors for CAD and are used as a diagnostic tool. The study aims to determine the role of sdLDL-C as a predictor of acute coronary syndrome (ACS) in patients having normal levels of LDL-C.

Materials & Methods

A total number of 100 normolipidemic ACS patients within the age group of 20-50 were included in the study. Blood samples of 5ml was drawn from patients and collected in plain vials (without any anticoagulant) for estimation of serum lipids (total cholesterol, triglycerides, and high-density lipoprotein cholesterol) and sdLDL. Small dense-LDL was quantified by the modified method of Tsutomu Hirano et al (in mg/dl).

Results

A correlation was established between serum sdLDL and other risk factors such as age, gender, cardiac markers namely Troponin, CKMB & CRP. In females, the mean sdLDL level was lower than in males. Of the total sdLDL patients, 79 were >25mg/dl and 21 were <25mg/dl. The Manwhitney test showed a positive correlation between the values of Troponin and sdLDL (with a p value of 0.036). Gender-based analysis using the Manwhitney test was highly significant with p values 0.009 and 0.062 respectively for both females and males. For each level of sdLDL, TG (p=0.002), HDL (p=0.001), CRP (p=0.008), CKMB (p=0.000) were significant. While LDL, VLDL, TC were not significant. The majority of subjects with Double Vessel disease, and Triple Vessel Disease had elevated sdLDL (>25mg/dl) levels. A graded and gradual trend was observed between mean sdLDL levels and severity of Coronary artery disease.

Conclusion

There is a positive correlation between sdLDL and ACS events in normolipidemic patients. In terms of clinical application, sdLDL is a stronger predictor of cardiovascular events than LDL-C and can be suggested as a marker for better prognosis of ACS.

Prospective study: Reduced global strains in asymptomatic female carriers for Duchenne muscular dystrophy gene using feature tracking

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Introduction

Duchenne muscular dystrophy (DMD) is a X-linked recessive disease manifested in males predominantly by skeletal muscle wasting but also dilated cardiomyopathy (DCM). Heterozygous female carriers often have normal echocardiographic findings. Nevertheless, untreated may develop during 4th and 5th decade of life into cardiomyopathy, probably due to progressive myocardial fibrosis. Cardiac magnetic resonance (CMR) allows fibrosis quantification due to high sensitivity even in early stages. CMR-FT is an innovative technique that measures the myocardial wall deformation and could help to detect the contractile impairment in asymptomatic patients and may identify carriers at higher risk of developing DCM later in their life.

The aim of this prospective study was to assess left ventricular systolic function (LV) in DMD female carriers compared to healthy controls (HC) using CMR-FT.

Materials & Methods

Global longitudinal strain (GLS), global circumferential strain (GCS) and global radial strain (GRS) were evaluated by CMR-FR. The end-systolic volume (ESV), end-diastolic volume (EDV) LV and ejection fraction (EF) LV were also measured by CMR-FT. There were 37 carriers and 20 HC enrolled in the study. The data distributed by the Gaussian curve were compared using a t-test, followed by Benjamini-Hochberg correction.

Results

Groups of carriers and HC did not differ in basic demographic data (age: 39.5 ± 9.1 vs. 39.1 ± 10.7 years). In contrast, there were found statistically significant differences in EF LV (56 ± 5 vs. $60 \pm 3\%$), and all strain parameters (GLS (-19.4 ± 2.4 vs. $-22.3 \pm 2.2\%$), GCS (-26.8 ± 3.3 vs. $-29.5 \pm 2.0\%$) and GRS (59.8 ± 12.9 vs. $70.9 \pm 14.8\%$, all $p < 0.05$)).

Conclusion

To our best knowledge this is the first study comparing structural myocardial changes in asymptomatic carriers to HC, using CMR-FT. Carriers had significantly lower values of global strains compared to HC using CMR-FT, although presenting preserved global EF LV. CMR-FT could be beneficial for early diagnosis of developing heart disease in asymptomatic patients with a genetic predisposition.

ENT, Opthalmology and Dermatology
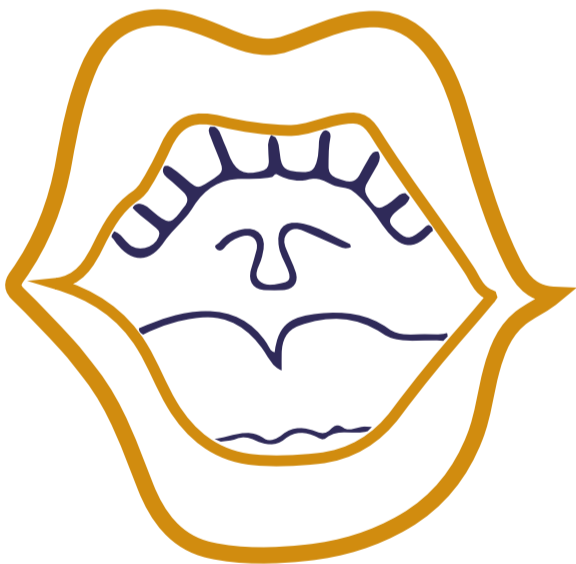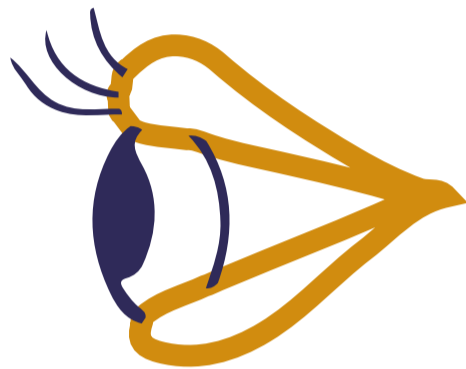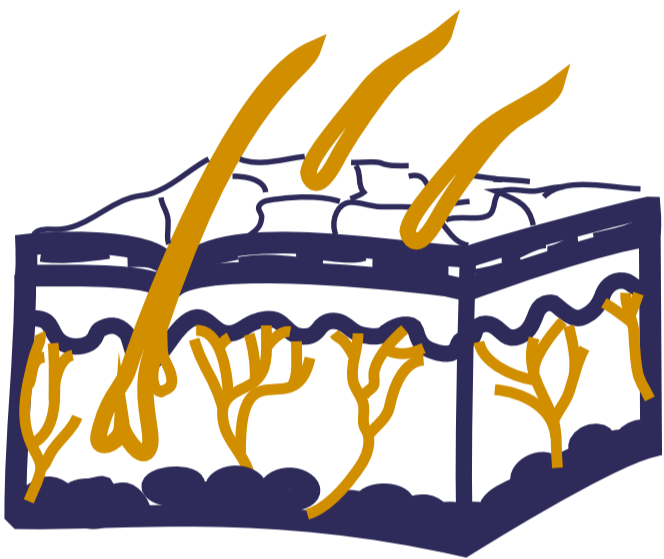
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The effect of losartan on dermatological symptoms of psoriasis in animal models

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Introduction

Psoriasis is a lifelong immune-mediated disease. The dermatological complaint is the most disturbing manifestation of the disease. Chronic inflammation is one of the suggested pathogenesis of psoriasis. In recent studies, losartan was shown anti-inflammatory actions through AT1 receptors. This study aimed to investigate the anti-inflammatory effect of losartan on the animal models of psoriasis.

Materials & Methods

Mice were examined for any visible dermatological disorder prior to the experiment. Psoriasis model in mice was induced by a daily topical dose of 62.5 mg Imiquimod (Aldara) cream on the shaved back for 6 consecutive days. Topical treatment with 1% losartan was used twice daily in mice models of psoriasis. The placebo group received urea containing cream that was used as a base to make the 1% losartan cream. Psoriasis Area and Severity Index (PASI) scores were used to compare the groups visually. PASI scores were analyzed with GraphPad Prism 8.0 by one-way analysis of variance (ANOVA) along with Turkey's multiple comparison test. On the last day of the experiment, mice were sacrificed in order to collect the skin samples for histological analysis.

Results

Application of imiquimod for 6 consecutive days successfully induced psoriasis in mice models. Topical 1% losartan significantly (p-value=0.0031) decrease the PASI score in comparison with the group that received imiquimod. Histological analysis revealed decreased infiltration of neutrophil and lymphocyte in the treatment group in comparison to the imiquimod group. The average neutrophil count was $25.17*10^3$ in the treatment group, $29.86*10^3$ in the imiquimod group and $14.02*10^3$ in the placebo group. The average lymphocyte count was $17.18*10^3$ in the treatment group, $25.78*10^3$ in the imiquimod group and $11.74*10^3$ in the placebo group. The volume of the epidermis layer decreased significantly in the treatment group. The average volume of the epidermis was 87.94 mm^3 in the treatment group, 114.78 mm^3 in the imiquimod group and 68.23 mm^3 in the placebo group.

Conclusion

Losartan can improve the dermatological symptoms caused by imiquimod-induced psoriasis in animal models via the anti-inflammatory process.

A potential alternative approach for the treatment of androgenetic alopecia: a randomized clinical trial study

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Introduction

The most common type of hair loss, androgenetic alopecia(AGA), is mostly caused by the miniaturization of androgen-sensitive hair follicles. Conventional therapy for AGA presents many side effects and disadvantages due to long-term treatment. However, herbal compounds characterized by more significant adaptation to the patient, fewer side effects, easy availability, and more mechanism of action in the treatment. This study aimed to evaluate the efficacy of topical herbal solutions(THS) in patients with AGA and comparison with 5% minoxidil.

Materials & Methods

In this randomized, double-blind, clinical trial study, 24 volunteer male patients (aged 23–43 years) with mild to moderate AGA selected from patients referred to the dermatology clinic. Participants were randomly assigned (1:1) into two groups. The group A received 5% minoxidil topical solution(MTS), and group B received 5% minoxidil + the topical herbal solution(MTS+THS). Participants received 1mL of solutions at morning and evening intervals for nine months. Primary outcomes were measured hair diameters at baseline and repeated at weeks 12, 24, and 36. Secondary outcomes included the patient's self-assessment questionnaire, and each follow-up visit, adverse events recorded. All statistical tests were 2-sided and performed at a significance level of $P < .05$. The study logistics complied with the Declaration of Helsinki and approved by the Ethics Committee.

Results

The MTS+THS group was significantly superior to the MTS group in terms of change from baseline in hair diameter and treatment benefit after 36 weeks of therapy. At week 36, compared to baseline, the mean hair diameter of the MTS + THS group increased compared to the MTS group (p=0/001), and hair loss decreased in MTS + THS group versus MTS group (p<0/001). In both groups, neither all-cause mortality nor serious adverse events reported.

Conclusion

The results from this study establish that THS has a significant improvement in AGA with a high degree of patient satisfaction and the development of their quality of life. The application of this new herbal solution for the treatment of AGA should be recommended. Because THS in humans is safe and THS beneficially affects all known fundamental mechanisms of AGA, it should, therefore, be used clinically to prevent or treat AGA.

Prediction of Cyanosis in Complex Congenital Heart Disease Children Using Retcam Retinal Images in Neonatal Stage

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Introduction

Complex congenital heart disease (CHD) patients can develop cyanosis as the result of low cardio-pulmonary function. Cyanotic CHD patients often present with growth retardation which affects their prognosis and quality of life. The vessel malformation on the retina of CHD patients with cyanosis was previously described. The objective of this study was to predict the appearance of cyanosis in complex CHD patients before adolescence using their neonatal Retcam retinal images.

Materials & Methods

114 eyes from 57 children with complex CHD were included in this retrospective study. 48 eyes were from children with cyanotic CHD while 66 eyes from children without cyanosis. Detailed medical history of each subject was collected with the consent of their guardians. Retcam retinal photography was conduct on each subject. The retinal images that contain optic disk were analyzed with an end-to-end deep-learning based cyanosis predictor (DLCP). The model consists of a deep convolutional neural network (DCNN) and a radial basis function neural network (RBFNN). Input images were first enhanced and segmented as vessels and background. Data augmentation based on random rotation was then applied. In the end, a total of 912 images were used to train the model, 228 images were set aside for validation. Experiments were complemented using PYTHON (3.6.3). All calculations were performed under a Linux on a machine with GPU NVIDIA Pascal Titan Xp, and 12 GB of RAM.

Results

To assess the predictive power of DLCP model, receiver operating characteristic (ROC) curve was drawn and area under the curve (AUC) values was calculated. With segmented vessels as image input, the model provided acceptable accuracy of predicting cyanosis (mean AUC at 0.797, the AUC ranged from 0.726 to 0.874). Mobilenet and Resnet50 were set as references and were less accurate than the proposed model (AUC of Mobilenet ranged from 0.631 to 0.737, AUC of Resnet50 ranged from 0.622 to 0.730).

Conclusion

This study, for the first time, utilized neonatal retinal images to predict congenital disease development. The results demonstrated that early stage retina vessels can be a predictor of cyanosis on complex CHD patients before adolescence.

The potential of MSCs therapy for restoration of the vocal folds scars: experimental study

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Introduction

The vocal folds scars result from different pathologies, including iatrogenic trauma. Currently there is no treatment that can provide full restoration of the ultrastructure of the damaged vocal folds which is extremely important for vibration characteristics and voice formation. The aim of the study is to assess the potential of mesenchymal stem cells (MSC) to restore the structure of damaged vocal folds.

Materials & Methods

The study involved 12 rabbits which were divided into control and experimental groups. Six intact larynx of rabbits from biobank were used for comparison. After 3 months of the scar application, the vocal fold scar was excised with simultaneous implantation 0,6 mL (6·10*5 cells) of autologous bone-marrow derived MSCs or saline for the experimental or control groups respectively. After 90 days from first surgery tissue regeneration was assessed by morphological examination, scar tissue measurement, and atomic force microscopy (ATM).

Results

Morphology showed that there is a group with saline implantation showed lack of fibroblasts, irregular architectonics of collagen fibers, density of collagen fibers with the prevalence of alteration in the control group (p-value 0.086). In this group scar tissue was formed by randomly interlaced bundles of collagen fibers, while scars in MSC-treated group often had a parallel architecture of collagen fibers. The AFM study revealed a statistically significant increase in the average Young's moduli (p-value 0.013) in the control group and returning to their initial values (p-value 0.59) in the MSC-treated group. In this group there was a tendency to return to its initial values after MSC therapy due to almost no difference in fibrils thickness from the intact tissue.

Conclusion

Immediate implantation of autologous bone-marrow derived MSCs to the mature vocal fold scars facilitates the healing of the mucosa. The MSC-treated group showed a smaller thickness of their own lamina mucosa, lower packing density of collagen structures and thinner fibrils than untreated scars. The defect does not regenerate completely but the tendency to the restitution is observed.

Voice rehabilitation by voice prostheses after total laryngectomy: a systematic review and network meta-analysis for 11918 patients

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Introduction

Total laryngectomy is accompanied by a mandatory loss of voice. Therefore, the gold standard approach is tracheoesophageal puncture with voice prostheses (VPs). We aimed to assess different VPs to detect which one considered the best from all devices reported in the literature, besides, to assess factors that influence these VPs quality.

Materials & Methods

On 14 September 2017, 15 databases were searched with the inclusion of all randomized controlled trials (RCTs), then a new search term was done on 11 May 2019 in the same databases to include all study design articles as to include all VPs sub-types allowed in market stores. Network meta-analysis (NMA) was applied to all available 27 outcomes in included articles, besides NMA partial order setting was done by using Hasse scatter plots. P-scores were used in NMA, where the best VPs nearer to one and the least nearer to zero. Meta-analysis was done for the rest outcomes which could not be included in NMA.

Results

One hundred and twenty-three articles were eligible for analysis (N = 11918) from 211 finally included articles. Provox 2 was significantly the best device with the most preference [OR 33.88 (0.65, 1762.24) (P-score = 0.92)], the least dislodgement [RR 0.27 (0.13, 0.57) (P-score = 0.79)], the least airflow resistance [RR 0.42 (0.08, 2.11) (P-score = 0.84)], the least VPs inaccurate size [RR 0.77 (0.23, 2.61) (P-score = 0.66)]. Heat and moisture exchanger (HME) addition showed a significant increase in maximum phonation time (MPT) and breathing experience, with P-scores (1 and 0.59) respectively. While HME addition showed a significant decline in stoma cleaning frequency, coughing frequency, forced expectoration, sputum production, sleeping problems, and loosening of adhesive, with P-scores (0.99, 0.72, 0.69, 0.96, 1, and 0.96) respectively.

Conclusion

Provox 2 is considered the best choice as being the most preferable for patients. Besides, Provox 2 had the least dislodgement, airflow resistance, VPs inaccurate size. The addition of HME on top of Vps increased MPT and breathing experience. While the addition of HME declined VPs complications as stoma cleaning frequency, coughing frequency, forced expectoration, sputum production, sleeping problems, and loosening of adhesive.

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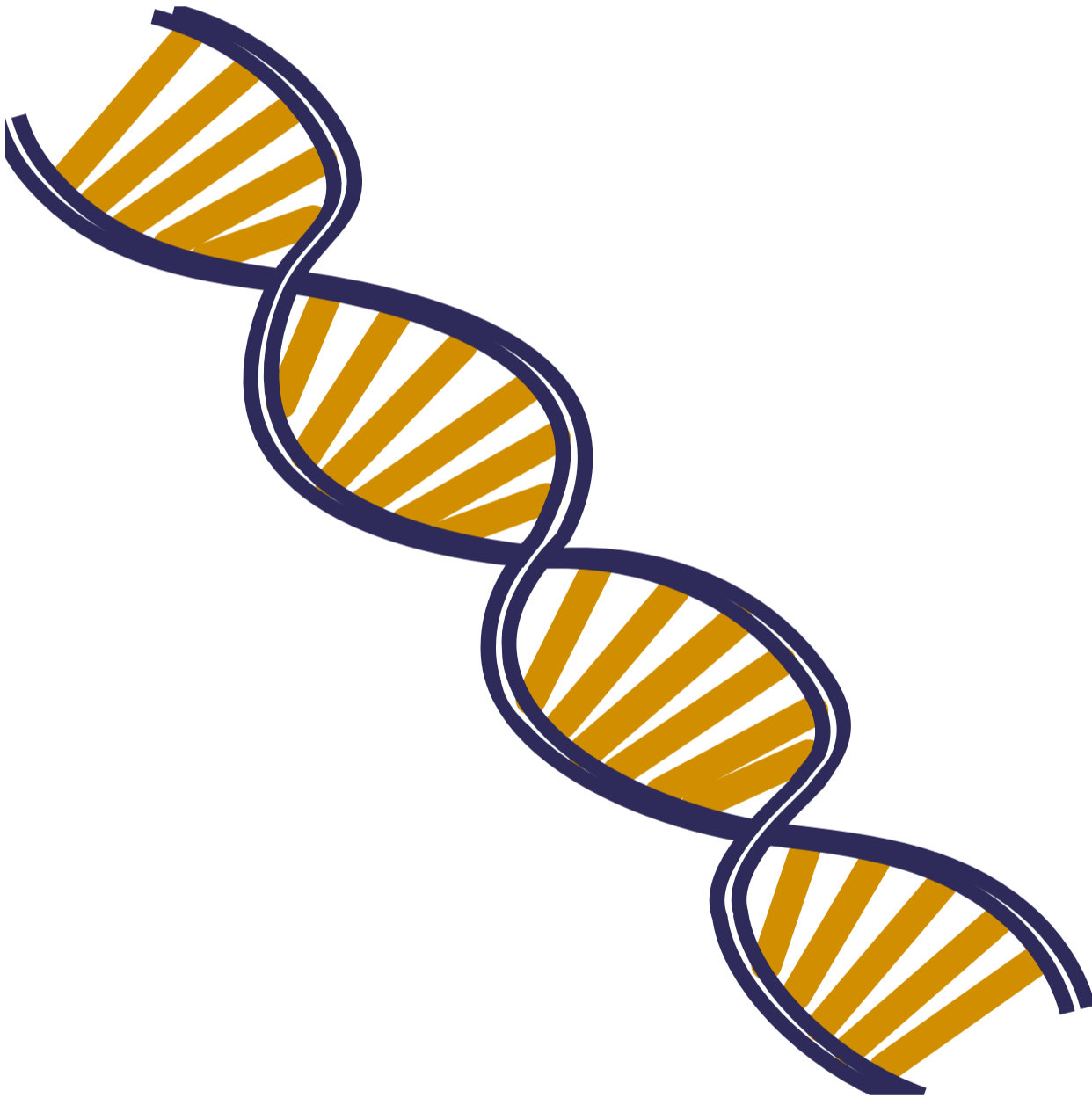
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Generation and characterization of human iPSC line with a truncating deletion at the GPKOW locus

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Introduction

Mutations in the GPKOW gene have been associated with an X-linked recessive condition consisting of developmental defects, microcephaly and embryonic lethality. Although GPKOW's role in alternative splicing has been reported, the absence of relevant model systems has led to the lack of knowledge about the molecular consequences of its ablation in neurodevelopment. The present study aimed to generate and characterize an iPSC line harbouring a truncating deletion at the GPKOW locus (designated UUIGPi012-A-2), as a resource for studying the effect of GPKOW mutations in male lethal microcephaly.

Materials & Methods

A control iPSC (46, XY) was nucleofected with paired gRNAs targeting the initial exons of the GPKOW gene, and cloned by serial dilution. A clonal line with the expected deletion at the GPKOW locus was genotyped and further characterized in terms of pluripotency, by expression of stemness markers; off-targets effects, by PCR and sanger sequencing; and expression at mRNA and protein levels, by qPCR and western blotting, respectively. Finally, a construct comprising a fusion GPKOW-GFP protein was generated for future rescue experiments.

Results

The generated iPSC line presents a 1 kbp deletion within the GPKOW gene, leading to accumulation of the truncated protein within the cell. This can be concluded from an increase in mRNA transcripts and protein amount in the edited cell line, as compared to its isogenic control. Further, no off-target effects were observed in the iPSC line, as confirmed by sanger sequencing at the predicted off-target sites. Finally, line pluripotency was verified by expression of stemness markers and qPCR targeting markers for the three germ layers, upon Embryoid Bodies generation.

Conclusion

The UUIGPi012-A-2 human iPSC line represents a powerful in vitro resource for studying GPKOW role in male lethal microcephaly. The implications of truncated protein accumulation in the edited cells are currently under study. Similarly, the effect of the lack of wild-type GPKOW protein in early neurodevelopment.

Many hands make light work: CNV of GSTM1 effect on oral cancer risk

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Introduction

Genetic variations are an important key for the oral cavity carcinogenesis comprehension as well as the prediction of the tumor risk, which can improve the prognostic of patients. The copy number variation (CNV) of several genes was described to be associated in the oral cancer development, but no study considered the CNV of GSTM1 and GSTT1, whose enzymes detoxify an established risk factor of the disease: cigarette carcinogenic compounds. Furthermore, it is not fully understood how each gene copy is involved individually in the detoxification process. We determinated the CNV of GSTM1 and GSTT1 and evaluated the contribution of each copy number of these genes to oral cancer risk.

Materials & Methods

A case-control study was performed with 235 oral cancer patients and 422 controls, which were recruited at the same period from the same hospital. CNV of the genes were determinated through Real-Time PCR (qPCR) using TaqMan Gene Copy Number Assay and the Copy Caller software. The multivariate logistic regression analysis was carried out to estimate odds ratio (OR) and 95% confidence interval (95% CI) values on Statistical Package for the Social Sciences (SPSS) software.

Results

The determination of CNV of GSTM1 revealed that two or three copies of the gene were detected in high frequency among controls (11.4%) than among oncologic patients (6.8%), result that was associated with a decrease of 53% of the oral cancer risk (OR 0.47; 95% IC 0.24-0.92). Although 47.7% of controls and 42.6% of cases carried one copy of GSTM1, the analysis yielded no association between one copy of the gene and the tumor risk. According to CNV of GSTT1, tumor patients presented higher frequency of two or three copies of the gene (33.6%) than controls (18.7%), and the distribution of one copy of GSTT1 was similar between cases (50.2%) and controls (48.7%). These findings resulted no association with the risk of oral cancer development.

Conclusion

Two or three copies of GSTM1 were associated with a decreased risk of oral cancer, which may be a result of the detoxification process reinforcement. Moreover, the determination of CNV of GSTM1 could improve the prediction and surveillance of the disease.

Do familiality, environmental risk or gender influence symptom networks in major depression?

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Introduction

Major depression (MD) is a heterogeneous disorder with a variety of presentation and course. Familiality, environmental risk, and gender might influence depression risk through different mechanisms. In the network approach, MD is considered as a network of interacting symptoms, which influence each other directly. For example, insomnia may lead to fatigue, which may lead to depressed mood, which leads to more insomnia, etc. Previous studies suggest that different risk factors may lead to different connections between symptoms, and thus different symptom networks. We hypothesize that exposure to specific risk factors causes symptom networks to diverge.

Materials & Methods

In a general population sample (Lifelines), we ascertained MD in 9110 participants and determined the presence of symptoms associated with MD. Cases were divided into subgroups based on familiality (family history, age at onset), environmental risk (exposure to stressful life events) and gender. Using the permutation-based network comparison test, we determined whether symptom networks diverge between subgroups.

Results

We found significant differences in symptom endorsement between groups (32/72 of comparisons at Bonferroni-corrected $\alpha=0.0005$). For instance, women reported crying twice as often as men did (70.2% vs 34.3%). Furthermore, participants with an age at onset ≤ 21 years reported more suicidal ideation compared to a later age at onset (42.7% vs 23.7%). We found no significant differences between symptom network structure and strength. A small number (0.009%) of individual symptom associations were significantly different between networks.

Conclusion

In our general population sample, symptom networks in MD did not diverge across familial and environmental risk, and gender. This suggests that these risk factors do not influence depression at the level of symptom networks. Despite the heterogeneous nature of MD and clear differences in endorsement, the syndrome of MD is robust – contrary to expectation. Further studies should assess the effect of risk factors longitudinally, as well as the effect of individual stressful life events, as these might be associated with diverging networks, and potentially identify causal pathways leading to MD.

Genetic variations in DNA repair gene ERCC4 contribute to the gastric cancer susceptibility

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Introduction

Gastric cancer (GC) is an aggressive disease with poor prognosis and high mortality rates. Its course is characterized by nonspecific symptoms and is therefore difficult to diagnose in the earlier stages. Identification of potential biomarkers, detectable in blood, could lead to better understanding of this disease and earlier diagnosis. GC is often characterized by genomic instability. It has been postulated that these changes could be a consequence of genetic variations in DNA repair genes. Given enough time, altered DNA repair ability could lead to malignant alterations. Therefore, we aimed to assess selected polymorphisms in the ERCC4 gene in GC patients.

Materials & Methods

We conducted a case-control study comparing 309 GC cases and 376 healthy controls. Genotyping of polymorphisms rs3136038, rs1800067, rs2276464, and rs2276466 was performed using RT-PCR. The impact of genotypes on disease risk was examined by χ2 statistics and genetic model analysis (IBM SPSS25). Survival was estimated using Kaplan-Meier analysis.

Results

Statistical analyses indicated that rs3136038, rs1800067, rs2276466 could be associated with GC risk, metastasis development and survival. Carriers of rs3136038 TT genotype had increased GC risk in recessive genetic model (OR=2.56, 95% CI 1.51-4.32, p=0.001). Rs1800067 GG genotype was associated with higher GC risk in both men and women (χ2=38.92, p=0.000). In recessive genetic model AG genotype also contributed to the increased risk (OR=3.1, 95% CI 2.11-4.54, p=0.000). Polymorphism rs2276466 was associated with the invasion of malignant cells into the lymph nodes. Patients with CG genotype had lymph node metastasis more frequently than expected (χ2=9.43, p=0.012). Rs3136038 and rs180067 genotypes showed moderate association with poorer survival rates. Shorter survival was also associated with diffuse GC type and local metastasis.

Conclusion

We demonstrated the influence of selected ERCC4 polymorphisms on cancer risk, metastatic disease and survival rates, indicating that these genetic variations could be useful as biomarkers for GC.

Stress sensitivity and exposure and their genetic overlap with cardiovascular function

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Introduction

The effects of stress on the cardiovascular system, particularly on hypertension, have received much attention. Despite this, the causal pathways are not well understood. In addition to the well-known genetic effect on hypertension, surprisingly, exposures to stress such as stressful life events and long-term difficulties are also partly heritable. The overlap of genetic influences between hypertension and stress exposure could be an alternative pathway explaining their association. We aimed to determine to what extent the associations between stress exposure, stress sensitivity (neuroticism), blood pressure and other cardiovascular function markers can be explained by common genetic influences.

Materials & Methods

We applied linear mixed models in ASReml software to the baseline family data of the Lifelines Cohort Study to decompose the variance of total stress exposure (stressful life events + long term difficulties), stress sensitivity (neuroticism), systolic/diastolic blood pressure (SBP/DBP) and heart rate variability indexed by the root mean square of the successive differences (RMSSD), in its genetic and environmental components. In a second step, we will fit a bivariate genetic model to estimate genetic correlations in order to estimate shared genetic influences between stress and cardiovascular function markers.

Results

A total of 152,728 (58.4% female) adult participants were analyzed with mean age 44.63 y (SD: 13.13). We found significant heritability estimates for RMSSD, SBP, DBP, total stress exposure and neuroticism, 0.17 (SE: 0.0092), 0.25 (SE: 0.0089), 0.29 (SE: 0.0092), 0.06 (SE: 0.0085) and 0.22 (SE: 0.0224), respectively.

Conclusion

Both stress exposure and sensitivity (neuroticism) are partly heritable, therefore they are not fully determined by environmental factors and as expected, cardiovascular function markers have substantial heritable components. In a second step, we will obtain genetic correlation estimates to determine the amount of shared genetic factors between SBP/DBP/HRV/HRV and total stress exposure/neuroticism.

GGTA1 Knockout HLA-G Expressing Porcine Islet Xenotransplantation Under Mice Kidney Capsule

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Introduction

Human Leukocyte Antigen G (HLA-G), a non-canonical Class I Major Histocompatibility Complex (MHC-I) protein, promotes maternal-fetal tolerance by suppression of maternal lymphocytes. Generating genetically engineered porcine organ donors expressing HLA-G could extend xenograft survival. In our study, we used α-1-3-galactotransferase (GGTA1) Knockout (KO) transgenic HLA-G porcine pancreatic islets to assess survival and functionality in a xenotransplant environment.

Materials & Methods

Transgenic HLA-G was expressed using Clustered Regularly Interspersed Palindromic Repeats (CRISPR)/CRISPR Associated Protein 9 (Cas9) gene-editing technology among porcine ROSAßgeo26 (ROSA26) locus by Homology Directed Repair (HDR) with simultaneous KO of the GGTA1 gene. Genetically engineered porcine fetal fibroblasts were subjected to Somatic Cell Nuclear Transfer (SCNT) for piglet production. The insertion of HLA-G at the ROSA26 locus and GGTA1 KO (GTKO) were confirmed by Sanger's sequencing and supported the GGTA1-/-/ HLA-G+ cell surface phenotype analysis. Seahorse assay was used to analyze the quality of islets prior to transplantation under the kidney capsule of Streptozocin (STZ) induced diabetic nude mice. Blood glucose monitoring was used to assess the viability and function of islets. Confocal microscopy was used to demonstrate insulin and HLA-G under the capsule of the transplanted kidneys following nephrectomy.

Results

A total of six pigs were used as donors (two HLA-G and GTKO; two GTKO; two domestic wild type pigs as controls). High spare capacity and low non-mitochondrial respiration on seahorse assay were characteristics for the validation of transplanted islets. Four mice with transplanted GTKO islets and three mice with GTKO and HLA-G islets demonstrated islet viability and functional capacitance, establishing normoglycemia. The results are comparable to the survival and functional activity of transplanted wild type control islets. All cured mice returned to hyperglycaemic conditions following nephrectomies. Immunofluorescence imaging demonstrated the localization of insulin and punctate HLA-G expression on the surface of the islets under an intact kidney capsule corresponding to cure rates.

Conclusion

Xenotransplantation of transgenic HLA-G and GTKO porcine islets under the kidney capsule of nude mice demonstrates adequate viability and cure rates with acceptable glycaemic control. We look forward to using transgenic HLA-G and GTKO porcine islets to establish long-term xenograft acceptance and survival in an immunocompetent non-human primate model.

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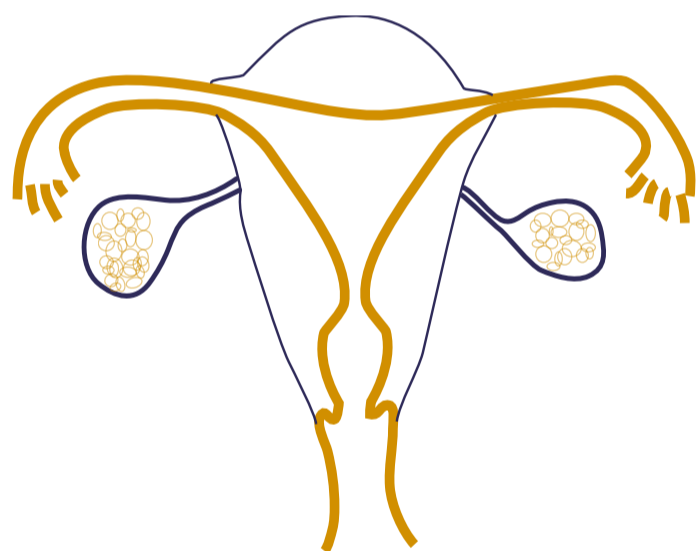
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CD34 and Bcl-2 as predictors for the efficacy of neoadjuvant chemotherapy in cervical cancer

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Introduction

Successful neoadjuvant chemotherapy (NACT) could improve the surgical resection rate and prognosis of patients with cervical cancer, but only a subset of patients benefits. Therefore, identifying the predictive biomarkers are urgently needed. The aim of this study was to evaluate the predictive value of CD34 and Bcl-2 in the NACT effectiveness for cervical cancer.

Materials & Methods

Sixty-seven patients with locally advanced cervical cancer (FIGO stages IB3, IIA2 or IIB) were classified into two groups based on effective (n=48) and ineffective (n=19) response to NACT. Immunohistochemistry was employed to identify CD34 and Bcl-2 expression before and after NACT. We analyzed the associations between the pre-NACT expression of these two biomarkers and the response of NACT. The expression of these two biomarkers before and after NACT was also assessed and compared.

Results

More patients were CD34 positive expression before NACT in effective group compared to ineffective group (p=0.005). However, no statistically significant difference in Bcl-2 expression before NACT were found between two groups (p=0.084). In NACT effective group, the expression of both CD34 and Bcl-2 after NACT are down-regulated ($p<0.001$ and $p<0.001$, respectively), while there are no statistical differences between the pre- and post-NACT expression of CD34 and Bcl-2 in NACT ineffective group (p=0.453 and p=0.317, respectively).

Conclusion

The positive CD34 expression before NACT may serve as a predictive biomarker for NACT of cervical cancer, but the pre-NACT expression of Bcl-2 is not an independent predictor. The down-regulated expression of these two indicators after NACT may indicate effective NACT.

Evaluation of FTIR ability to differentiate various embryonic days of mouse fetal life

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Introduction

Teratology is a complex science in which the defects that occur for the fetus are examined. Lack of enough technique to explore fetus adventures and disorders has limited the depth and use of this science.

FTIR spectroscopy has recently become an excellent method for the examining of biological samples; this method allows us to study biological changes at the level of biomolecules that might potentially provide a dominant opportunity to investigate the mechanism of many fetal malformations right from their initiations. During this experiment, we have used FTIR biospectroscoy to differentiate different days of the mouse fetal development.

Materials & Methods

Pregnant mice were used in this study, the fetuses were dissected on days 5-15 of gestation and then fixed by fixative solution, embryos were then dehydrated with upward percentage of ethanol and embed with paraffin, paraffin blocks were cut and FTIR microspectroscopy was performed. Preprocessing and data analysis were done by our developed routines on MATLAB software.

Results

Preprocessing and processing were done for each of the resulted spectra on different days then unsupervised with no labeling PCA analysis were done. Results confirmed that each day spectra can be separated from each other.

PCA plot showing separation of embryonic growth in 5th and 7th (included data 93%, PC1 85%, PC2 8%), 8th and 10th days (included data 97%, PC1 83%, PC2 14%), 11th and 13th days (included data 94%, PC1 82%, PC2 12%), 14th and 15th days (included data 90%, PC1 77%, PC2 13%). However, differentiation is better and stronger during the first days of different organs generation and less during the final days of pregnancy, most probably due to the development of similar tissues in various organs in late fetal life.

Conclusion

FTIR spectroscopy with mathematical analysis can develop a new method for studying fetal development with potential use in medicine and the promising technique in teratology experiments.

Evaluation of the effects of taking Evening Primrose Oil (EPO) capsules from 38th week of pregnancy in nulliparous women (labor / induction / outcomes)

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Introduction

Evening Primrose (Oenthera Biennis) is a medical plant . Evening Primrose Oil (EPO) contains Gamma-Linolenic Acid (GLA) that stimulates the production of prostaglandins in body . It is believed initiate cervical ripening due to EPO .The aim of this study was to evaluate the effects of taking EPO from 38th week of pregnancy in nulliparous women on the type of delivery , induction need , duration of induction , labor duration , neonatal outcomes , quality of labor and maternal complications.

Materials & Methods

In double-blind randomized controlled trial performed in Sanandaj Besat Hospital , 440 nulliparous pregnant women in 38th week of pregnancy and with bishop score of <6 were divided randomly in to two groups (220 in each) . first group took EPO 1g Q12h and next group took placebo . In the other part of the study women that did not enter to labor phase until 40th week of pregnancy from both groups , were evaluated during the induction by oxytocin to check the effects of EPO on induction and outcomes.

Results

Normal labor (vaginal or cesarean delivery) without needed of induction was occurred in 134(60.9%) women of EPO group (15 C/S (11.19%) and 119 NVD (88.80%)) and 122(55.45%) women of placebo group (21 C/S (17.21%) and 101 NVD (82.78%)) . Frequency of cesarean section deliveries decreased significantly in EPO group compared with placebo group . 86(39.09%) women from EPO group and 98(44.54%) women from placebo group needed induction (oxytocin) for delivery , that the rate of successful vaginal delivery was significantly higher in EPO group and duration of active phase , second stage and third stage of labor were shorter in EPO group . No significant difference of neonatal factors and outcomes (such as 1st and 5th min apgar score / need for NICU admission ..) were found between the EPO and placebo groups.

Conclusion

This research showed significant positive results of taking EPO capsules from 38th week of pregnancy in nulliparous women , on the type of delivery (decrease cesarean section) , length of labor , need for induction , duration of induction and success rate .

The combination of hemina and cinaciguat modifies the structure of resistance pulmonary arteries in chronically hypoxic and pulmonary hypertensive newborn lambs

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Introduction

Pulmonary Hypertension of the Newborn (PPHN) presents significant morbi-mortality, with a prevalence of 2-6 per 1,000 live births. The available treatment is inhaled nitric oxide (iNO), effective only in 60% of the cases. Thus, new treatments are required. We propose that treatment with cinaciguat-hemina in high altitude pulmonary hypertensive hypoxic newborn lambs will decrease the wall thickness of resistance pulmonary arteries (RPA). Our objective is to determine by histology if cinaciguat-hemina decreases the RPA remodelling, by assessing the adventitia and muscle layer thickness; and cell proliferation of RPAs in lambs with PPHN.

Materials & Methods

An animal experimental study was performed. 12 newborn lambs born 3600masl were intervened. Hematoxylin-eosin, van-Gieson, and Ki-67 stains were used in lungs of 6 lambs treated with cinaciguat-hemin and 6 controls. The muscular and adventitial layer thickness were calculated. The number of total and Ki-67 stained nuclei from muscle and adventitia layer were analyzed. Project approved by the Animal-Bioethics-Committee-CBA#0643.

Results

The muscle layer of cinaciguat-hemin group was thinner than control (44±1.7%vs.48±1.0% for 50-100µm, 34±1.1%vs.40±2.1% for 101-150µm, p<0.05). In contrast, the adventitia layer of cinaciguat-hemin group was thicker than control (55±1.7%vs.44±1.0% for 50-100µm, 52±1.4%vs.46±0.5% for 101-150µm, p<0.05). Moreover, cell proliferation showed no statistical differences in both muscle layer (6,5%±0,6% vs. 5,1%±1.1%, p=0,305), and adventitia (8,7%±1,2% vs. 9,2%±2,7%, p=0,675), compared to control.

Conclusion

A decreased muscle layer thickness correlates with lower baseline pulmonary vascular resistance (PVR) in cinaciguat-hemin group. In contrast, the increased adventitia thickness, determines a lower elasticity, and relates to an increased PVR in hypoxic conditions. Since cell proliferation showed no statistical difference, it's arguable that neither hypoplasia nor hypertrophy were the main mechanisms in which the muscle layer decreased thickness, or the adventitia increased thickness, respectively. These results do not support the use of combined therapy of cinaciguat-hemin for the treatment of PPHN, because, although it decreases the muscle thickness, it increases the adventitia layer, so the final effect in PVR is not clear.

Oxytocin potentially enhance cognitive status after Hysterectomy: Results of an animal study

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Introduction

Premature hysterectomy with or without oophorectomy has been a problematic issue according to its impacts on cognition status including memory, depression, learning and etc. Longitudinal and basic studies have emphasized on effects of premature hysterectomy on incidence of dementia and cognition attenuation. However, there is no exact mechanism known as a key clarifying the role of estrogen or hysterectomy on cognitive pathways. Engagingly, animal models have shown enhancement of cognitive status after bilateral oophorectomy (BSO) accompanying hysterectomy albeit there was still room for improvements comparing to normal baseline. Furthermore, numerous roles have been suggested for critical effects of Oxytocin on cognitive status including cholinergic pathways. In this study we have aimed the effects of Oxytocin this time on cognitive attenuation after hysterectomy.

Materials & Methods

Virgin female Wistar rats were selected for this study. Animals were divided into 5 groups including Sham operated, Control hysterectomy (Hx), Control hysterectomy + bilateral salpingo-oophorectomy (Hx + BSO), treated Hx and treated Hx + BSO. 6 weeks after surgeries, all animals underwent behavioral and cognitive studies including Morris Water Maze (MWM), Y-maze and foor shock test. Treated animals received Oxytocin (0.1 mg/kg intraventricular) started 7 days after surgery and control animals received normal saline same manner.

Results

MWM analysis indicated significant fading in spatial working memory after hysterectomy ($p = 0.002$) while BSO could relief this effect ($p = 0.03$). Interestingly, chronic administration of Oxytocin could rehab spatial learning in both Hx and Hx + BSO ($p = 0.02$ & 0.012 respectively). In addition, while Y-maze analysis indicated same configuration in control groups ($p = 0.003$ & 0.045 in Hx and Hx + BSO respectively), there was no significant alteration in short term recognition memory after administration of Oxytocin ($p = 0.098$ & 0.65 in Hx and Hx + BSO respectively).

Conclusion

Our study figured unique impacts of isolated hysterectomy on cognitive status while apparently being accompanied with BSO relief this effects. Meanwhile, chronic administration of Oxytocin seemed to be beneficial against attenuation of cognition. However, precise mechanisms of action need further evaluation based on possible cholinergic-estradiol pathways.

Correlation of Postpartum Depression with Type of Delivery, Maternal and Newborn factors: A cross-sectional study

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Introduction

In India, while providing maternal healthcare, emotional & mental aspects of the mother's health are less emphasized. As a result, a lot of suspected cases of postpartum blues remain subclinical which may progress to postpartum depression. This study was aimed at screening postpartum depression within first 7 days after labor & to study its association with type of delivery, maternal & newborn factors.

Materials & Methods

This observational, cross-sectional study included 47 mothers. By administering Edinburgh Postnatal Depression Scale(EDPS), data was collected. In EDPS, lower score suggests better mental health. While a score of 10 or more suggests possible depression. Data was analyzed using the standard error of proportions, unpaired t-test, and Pearson correlation coefficient test.

Results

17% of mothers reported possible depression (score>10). The difference between the mean total score of 24 C-section (7.417±5.641) and 23 normal vaginal delivery (3.217±3.643) is significant (P < 0.05) with a 95% confidence interval. The incidence of possible depression was thrice in C-section compared to normal delivery. The difference between the mean total score of 10 mothers with previous abortion/s (9.9±5.441) and 37 mothers with no previous abortions (4.13±4.262) is significant (P < 0.0001) with a 95% confidence interval. Nearly 43% of mothers felt restless during the perinatal period. Not even a single mother from 47 knew about Postpartum Depression.

Conclusion

Mothers who had C-section had a higher risk of Postpartum Depression compared to mothers who had undergone normal delivery. Mothers with a previous abortion history had significantly poor mental health as compared to mothers with no previous abortions. Physicians need to address such aspects of mother's health & give preliminary knowledge about this condition. If our results are confirmed by others, it could change the dynamics of screening in Postpartum Depression, by focusing more on mothers with C-section or previous history of abortion. This study will help in improving maternal & newborn health.

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The role of E-type prostaglandin receptor EP3 in acute renal injury induced by ischemia-reperfusion

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Introduction

According to reports, the incidence of acute kidney injury (AKI) can be as high as 28-35%, and about 2 million patients die directly or indirectly from AKI each year worldwide. Ischemia-reperfusion (I/R) injury is one of the main causes of acute kidney injury in the kidney. Prostaglandin E2 (PGE2) is produced by the metabolism of arachidonic acid (AA) catalyzed by cyclooxygenase-1/2 (COX-1/2), which regulates physiological processes through downstream EP1, EP2, EP3 and/or receptors. Studies have reported that EP3 receptors play different roles in ischemia-reperfusion injury in different tissues and organs. Our research is to evaluate the role of EP3 receptors in renal ischemia-reperfusion.

Materials & Methods

C57BL/6 wild type (WT) and EP3-/- mice (n=12) were subjected to sham operation or I/R treatment (unilateral renal artery and vein occlusion for 30 min followed by 24 h of reperfusion). The serum levels of blood urea nitrogen(BUN), serum creatinine (Scr) and the kidney levels of tumor necrosis factor α (TNF-α) interleukin-1β(IL-1β) and interleukin-6 (IL-6) were assessed. Blood flow and histopathological changes were detected by laser Doppler method and HE staining, respectively.

Results

After I/R injury, the function of kidney in EP3-/- mice was protected compared with wild type. The histopathologic evaluation also showed a reduction of acute tubular damage in EP3-/- mice. The levels of tumor necrosis factor α (TNF-α) interleukin-1β(IL-1β) and interleukin-6 (IL-6) in were decreased in EP3-/- kidney after I/R. However, deficiency of EP3 receptor has no effect on renal blood flow and apoptotic factors in this model.

Conclusion

Depletion of EP3 receptor has a protective effect in mouse model of I/R induced AKI via suppression of inflammation.

Beta Vulgaris Extract Can Improve Liver Enzymes in Patients with Non-Alcoholic Fatty Liver Disease

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Introduction

Non-Alcoholic Fatty Liver Disease (NAFLD) has been increased among population during recent decades. There are some challenges in the efficacy and side effects of drugs used for treatment of NAFLD. Therefore, new treatment methods and modalities are needed. The aim of this study was to determine the effect of Beta vulgaris extract on treatment of NAFLD.

Materials & Methods

This is a double-blind randomized clinical trial which conducted during the period of November 2018 to April 2019 in Shahid Beheshti Hospital, located in Kashan, Iran. Among 143 NAFLD patients who met the study criteria, 120 patients agreed to participate in the study. Subsequently, they were divided into two equal groups by simple randomization. The Beta vulgaris group received Beta vulgaris extract alongside standard treatment of NAFLD including vitamin E and Silybum marianum extract named as Livergol. Also, Placebo group received standard treatment of NAFLD and placebo instead of Beta vulgaris. The aspartate transaminase (AST), alanine transaminase (ALT), alkaline phosphatase (ALP), fasting blood sugar (FBS), low density lipoprotein (LDL) and high density lipoprotein (HDL) were evaluate and compared among groups. The variables were measured at the beginning of the study, 3th and 6th months.

Results

Among all participants, 52% of participants were male and 48% were female. The mean (SD) age for beta vulgaris and placebo groups were 47.5 (10.5) and 46.4 (8.7) years old, respectively. Results of between groups analysis revealed that AST significantly reduced in Beta vulgaris group compared to placebo group (P=0.04). However, ALT reduction was not significant among groups. Nevertheless, significant interaction between time and groups indicated that the effect of Beta vulgaris on ALT will be increase over time (P<0.001). Also, ALP, FBS, LDL and HDL significantly were improved in Beta vulgaris group compared to placebo group (P<0.05).

Conclusion

Addition of Beta vulgaris extract to the standard treatment of NAFLD can significantly improve AST, ALP, FBS, LDL and HDL. Also, this study revealed that the effect of Beta vulgaris on ALT will be increased over time. It is recommended that future studies try to find the side effects of Beta vulgaris on ALT in the longer period than six months.

Therapeutic and biotechnological potential of micromycete Tolypocladium inflatum for thrombotherapy and vascular medicine

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Introduction

Thrombolytic therapy proves to be one of the most important pharmacological approaches, mediated by blood clots lysis inside the vascular bed in order to restore the normal blood flow through it. However, most modern drugs for such severe disorder treatment are not able to guarantee a safe outcome for the patient in case of thrombosis, because of unpredictable possible side effects, including massive bleedings, cardiogenic shock, various allergic reactions and other cardiovascular disfunctions. One of the promising approaches to expanding of the pool of thrombolytic drugs is the use of more specific and safe proteinases, obtained from micromycetes for such a treatment. In this study was examined the therapeutical potential of the micromycete Tolypocladium inflatum.

Materials & Methods

The preparation of proteinases was obtained by culture fluid proteins precipitation with acetone, followed by drying stage on the sixth day of cultivation, performed with thermostatically controlled shaker in a deep culture conditions on a selected medium. The protein fractions separation of the drug was conducted by the method of liquid isoelectric focusing. Proteolytic and plasminogen activator activity was measured by fibrin plates method. Thrombolytic potential was examined in a fibrin thrombus lysis model (evaluation the weight loss of fibrin clot after the exposition with the preparation of proteinases).

Results

In experiments with the fibrin thrombus lysis model the preparation of T. inflatum proteinases demonstrated high efficiency of fibrin clot thrombolysis (34,6 % of fibrin clot weight elimination after 30 min; 67,1 % after 1 hr; 90,6% after 3 hrs). The measurement of fibrinolytic and plasminogen activator activity with a fibrin plates method revealed the fibrinolytic activity - 816,5 U/ml and the plasminogen activator activity – 314 U/ml, which is comparable to well-known plasminogen activators (e.g. urokinase) or preparations, obtained from investigated plasminogen activators, such as Sarocladium strictum.

Conclusion

The obtained data indicate that the proteinases preparation, obtained from the culture fluid of the micromycete Tolypociadium inflatum, demonstrates the pronounced thrombolytic, fibrinolytic and plasminogen activator activities, which allows to suggest the therapeutical potential in thrombosis treatment in vascular medicine and, what is more, the biotechnological potential for the development of diagnostic kit for hemostasis system disorders monitoring

Phosphodiesterase 2 overexpression protects against cellular arrhythmia during beta-adrenergic stimulation

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Introduction

Phosphodiesterase 2 (PDE2) plays a key role in degrading cyclic nucleotides in cardiomyocytes. Being upregulated in end-stage human heart failure, PDE2 protects myocardium from excessive sympathetic activation. Consequently, under beta-adrenergic stimulation PDE2 overexpressing transgenic mice (TG) revealed less ventricular tachycardia and better surviving after myocardial infarction. Here, we examined antiarrhythmic PDE2 effects at cellular level in isolated cardiomyocytes.

Materials & Methods

Ventricular cardiomyocytes of both wildtype mice (WT) and TG were investigated using whole-cell patch clamp technique. Cellular action potentials (AP) were recorded upon stimulation at 0.125 Hz following a pacing at 1 Hz and 4 Hz to provoke arrhythmia. Experiments were performed under basal conditions as well as beta-adrenergic stimulation with isoprenaline (Iso, 10 nM) and specific PDE2 inhibition via BAY60-7550 (BAY, 100 nM).

Results

PDE2 overexpression did not affect resting membrane potential and AP morphology including AP amplitude, upstroke velocity and AP duration. After applying the pacing protocol, cellular arrhythmia in cells from WT and TG were quantified. The incidence of delayed afterdepolarizations (DAD) and spontaneous AP (sAP) was increased in WT from 6.19 basal to 44.78 under Iso (95%CI: 35.34-54.22, p<0.001). Interestingly, cardiac specific PDE2 overexpression significantly blunted the arrhythmogenic Iso induced DAD and sAP from 3.17 basal to only 9.44 under Iso (95%CI: 3.45-15.44, n. s.). Incubation with BAY and Iso resulted in similar occurrence of cellular arrhythmia in TG as observed in WT under Iso (53.42, 95%CI: 33.36-73.38). Recently, we generated a cardiac specific PDE2 knockout line which is expected to show more cellular arrhythmia.

Conclusion

Cardiac specific PDE2 overexpression exerts antiarrhythmic effects under beta-adrenergic stimulation at the cellular level. Occurrence of DAD and sAP was diminished in TG under Iso but not under simultaneous PDE2 inhibition via BAY. These results indicate potential use of PDE2 stimulation as a novel therapeutic strategy against arrhythmia during heart failure.

Assessment Of Risk Of New Onset Diabetes Mellitus Associated With Statins: A Meta Analysis

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Introduction

Statins have shown to be highly beneficial in primary and secondary prevention of cardiovascular disease (CVD) in several trials. However, current reports of increased risk of type 2 diabetes with statin use are an area of concern. Given the immense utility of statins in managing cardiovascular diseases and keeping blood lipid levels under control, it is important to quantify any potential long-term risks to help patients and physicians make informed choices. Overestimation of clinical benefit or underestimation of risk is potentially hazardous and of major public health importance. This study will help us reassess the current guidelines with special emphasis on at-risk individuals.

Materials & Methods

All language search was conducted on MEDLINE, COCHRANE, EMBASE and GOOGLE SCHOLAR following PRISMA guidelines till August 2019. The following search strings and MESH terms were used: "statins", "new-onset", "DM" "RCTs". After matching studies for inclusion and exclusion criteria, Revman v5.3 was used for appropriate statistical tests. Fixed and Random Effect Model Test was used and p value<0.05 was considered statistically significant. Biases were assessed for each study using the Cochrane Collaboration Criteria.

Results

A total of 13 RCTs (46,262 individuals on statins/ 46,170 individuals on placebo) were included in this meta-analysis. Patients on statins were shown to have a significantly higher incidence of new-onset DM as compared to those only on placebo for fixed-effects model (RR=1.109, 95% CI=1.045-1.178, p=0.001) as well for the random-effects model (RR=1.104, 95% CI= 1.019-1.195, p=0.015). At-risk individuals were shown to be strongly associated with new-onset diabetes mellitus on statin use as compared to those only on placebo (RR=1.115, 95% CI=1.042-1.192, p=0.001) for fixed-effects model and (RR=1.116, 95% CI= 1.029-1.210, p=0.008) for the random-effects model.

Conclusion

Statin use was associated with a significantly higher risk of new-onset DM as compared to placebo.

Development and Screening of Novel Peptides for Type 1 Diabetes Therapy

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Introduction

Type 1 diabetes (T1D), a disease with no known cure, accounts for 10-15% of all diabetes cases. This disease affects roughly 463 million people, and costs $760 billion in healthcare globally (IDF Diabetes ATLAS). Stemming from a loss of insulin production, serious complications include blindness, kidney disease, cardiovascular disease, and amputation of limbs due to hypertension (D. M. Nathan, 1993). Interest in peptide-based therapies has been growing recently, due to their specificity and targeting abilities (A. C. Conibear et al., 2016). Stabilization, however, is usually required due to their susceptibility to proteases.

Materials & Methods

In order to identify potential therapeutic agents, we synthesized 7 novel peptides based off modifications to the known insulin promoter, the islet neogenesis associated protein (INGAP). These peptides were engineered with the aim of attaining a more stable and more bioactive compound than INGAP. It is suspected that the C-terminal region is involved with the binding mechanism, and so this becomes an area of focus for modifications.

Synthesized peptides were characterized and purified, then screened (in vitro) as potential therapeutic agents on living human pancreatic islets, obtained from organ donors. Insulin secretion was quantified for islets stimulated by high glucose solutions containing each of the prepared peptides and compared to positive and negative controls. Each of the 7 peptides were tested on cells from 3 different donors, in triplicate each time.

Results

Following synthesis, peptides were characterized via mass spectrometry, and purified via HPLC to 95% or higher. Insulin quantification of in vitro islet tests revealed that all peptides increased the release of insulin as compared to high glucose alone. Comparing with known insulin promoter exendin-4 (EX4), 3 of our synthesized peptides are implicated for an even greater enhancement of insulin expression. Among these, tyrosine modifications to the C-terminal, and addition of hydrophobic amino acids were included.

Conclusion

We engineered and synthesized bioactive peptides, identifying candidates for therapeutic benefit. Further gene expression analysis will be carried out to elucidate the mechanisms of binding and secretion. These results offer preliminary support to the hypothesis that INGAP related peptides can be modified to increase their bioactivity for human pancreatic islet insulin expression.

Neurology II
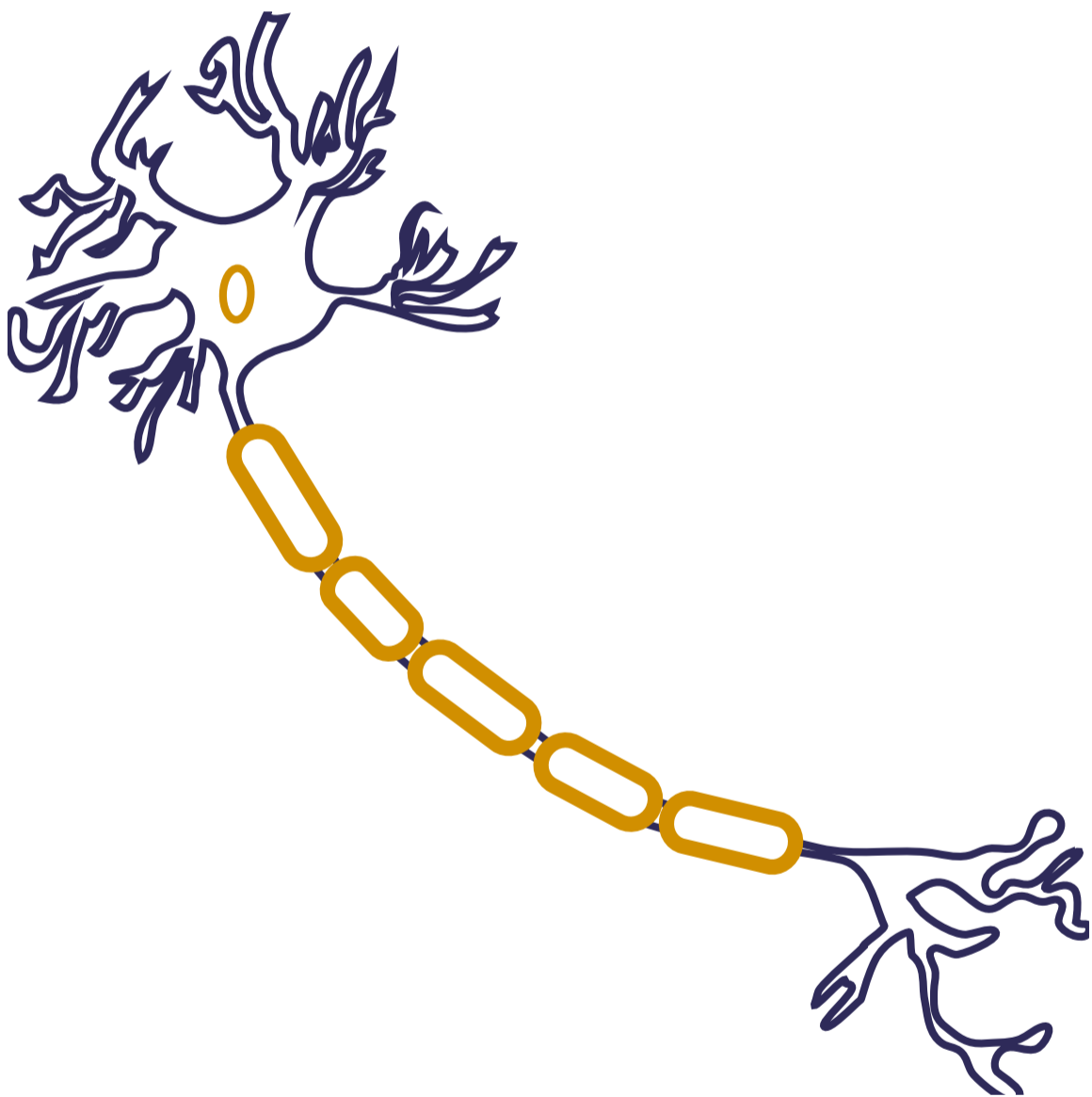
Presenters:
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Padvoiskaya, N. (Natallia)
Ciputra, E. (Edward)
Zapekin, S.Z. (Savva)
Stratilová, Ms. (Mária)

Attention and gaze desynchronization affect the performance of P300 BCI

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Introduction

Brain-computer interface (BCI) technology provides a functional connection between user's brain and external electronic devices. Various BCIs can be utilized by persons whose ability to communicate with the world is lost due to disease (e.g. amyotrophic lateral sclerosis) or trauma. Among the most well-established brain-computer interface systems is P300 BCI speller, based on P300 event-related potential component. The presented study investigates the effects of user's active attention and gaze on P300 BCI performance. It is highly relevant for the clinical application of P300 BCI, because while user's eye movements may be impaired or lost, the system should interpret his or her intentions correctly.

Materials & Methods

Eye movements data was collected from 22 healthy volunteers, with one subject participating twice. They were using 6x6 P300 BCI speller system under two experimental conditions. The subjects were instructed either to focus their gaze and attention on the same yellow-framed stimulus ('classic' condition), or to focus their gaze on red-framed stimulus, while shifting the attention to a green-framed one ('desynch' condition). During the experiment, exact gaze positions were controlled by the researchers via the SMI RED500 eye-tracker. Collected data was processed with the Prism software.

Results

According to paired t-test, error rate increases dramatically under 'desynch' condition ($p<0,0001$). Also, in this condition fixation number on a target stimulus increases ($p=0,0487$), while mean fixation time on a target stimulus decreases significantly ($p=0,0242$). The results suggest that desynchronization between gaze and attention can significantly affect the performance of P300 BCI.

Conclusion

The results imply that the performance of the P300 matrix speller in healthy subjects can be affected in considerable measure by desynchronization between user's gaze and attention. They may provide a direction for the further improvement of P300 BCI technology, including the adaptation for persons with impaired gaze control.

A neural network model for prediction of adverse events in patients with spontaneous dissection of the brachiocephalic arteries

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Introduction

Spontaneous dissection of brachiocephalic arteries (BCA) is a serious pathology that leads to adverse events of a cerebrovascular nature with neurological deficits. In this regard, the choice of the optimal intervention strategy associated with the lowest risk of possible adverse outcomes is an urgent task of interventional neuroradiology. The use of neural networks capable of analyzing hidden patterns can provide significant assistance in predicting cerebrovascular events in the long-term postoperative period in such patients.

Materials & Methods

The aim of the study was to develop a mechanism for predicting adverse outcomes using artificial neural networks in patients after endovascular interventions for spontaneous BCA dissection in the long-term postoperative period (6 months).
The neural network was created in the Java NetBeans programming environment. A multi-layer perceptron with 5 input neurons and 2 output neurons was developed. The baseline data were gender, age of the patient, degree of dissection, degree of residual stenosis, and adherence to double antiplatelet therapy (using Morisky-Green-Levine test). 217 patients were selected for the study group, and 57 patients were selected for the cross-validation group.

Results

After the ROC analysis, the area under curve (AUC) of the predictive model was 91.65% when using cross-validation. According to the expert scale of AUC values, this indicator corresponds to a predictive model of excellent quality.

Conclusion

The proposed method for predicting adverse cerebrovascular events in patients with spontaneous BCA dissection based on the mathematical apparatus of artificial neural networks allows obtaining a reliable prognosis in the long-term postoperative period by processing diagnostic information.

Effect of Epigenetic Regulation by Antidepressants Valproic Acid, Imipramine, and Fluoxetine in Neurogenesis of Neuronal Cell

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Introduction

An antidepressant agent has been associated with the management of major depressive disorder or MDD. The use of antidepressants inhibits the neurotransmitter reuptake, resulting in the stabilization of neurotransmitter circuits and improvement in neuroplasticity in MDD patients. However, the mechanism of action of antidepressants that contribute to neuroplasticity is not clearly elucidated, since the effect has both acutely and long-lasting. Herewith, we hypothesized that the long-lasting effects of antidepressant agent induces epigenetic modification that contributes to neuronal proliferation and differentiation. In this study, the expression of epigenetic and neurogenesis marker was evaluated upon treatment with three types of antidepressants, valproic acid, imipramine, and fluoxetine in vitro.

Materials & Methods

Three types of cell lines were used in this experiment, including cortical primary neuron cell, neural stem cell, and neuroblastoma SH-SY5Y. These cell lines were treated with three different antidepressants, valproic acid, imipramine, and fluoxetine for 24 & 48 hours. The expression of the neurogenesis (Nestin, GFAP, TUJ-1, MAP-2, BrdU) and epigenetic marker (H3, Acetylated H3, HDAC1) then evaluated by immunocytochemistry analysis and western blotting analysis.

Results

Different type of antidepressants treatment leads to changes in expressions of neurogenesis marker and epigenetic marker. Valproic acid treatment leads to a decrease in HDAC1 expression and an increase in acetylated H3 level. It leads to an increase in Nestin and MAP-2 and decreases in TUJ1 expression. Imipramine treatment leads to an increase in both acetylated H3 and HDAC1 expression. While an increase in TUJ1, Nestin, BrdU expression and decrease in MAP2 and GFAP expression were observed. Fluoxetine treatment did not significantly change the epigenetic marker expression. However, the increase in TUJ1 and MAP2 expression was observed, followed by a decrease in Nestin, BrdU, and GFAP. The effect generated was identified as concentration-dependent.

Conclusion

Antidepressant treatment with valproic acid and imipramine alter the global histone acetylation that contributes to neuronal proliferation and differentiation. While fluoxetine was demonstrated to affect neurogenesis in an epigenetic independent mechanism. For further confirmation, studies are needed to address the epigenetic effect in specific residues within histone for long-lasting effects of antidepressants.

Gut microbiota and clinical features of Parkinson's disease: a correlational study

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Introduction

Modern antidepressants and anxiolytics are commonly effective, but these drugs are frequently associated with serious side effects. At the same time our understanding of the human microbiota role in neuropsychiatric disorders has been increased. Even though recent studies suggests correlation between certain bacterial orders and depression. All this allows us to assume that potentially more effective pharmaceutical strategy may be developed trough the innovative way of psychobiotics. In our study we aimed to find correlations between human gut microbiome and levels of anxiety, depression and motor dysfunctions in patients with Parkinson's disease.

Materials & Methods

We used data collected from 89 patient diagnosed with PD in our study. Emotional-affective part was examined using Beck's Depression Inventory (BDI) and Hospital Anxiety and Depression Scale (HADS). Degree of motor changes was measured using Unified Parkinson's Disease Rating Scale (UPDRS).

Isolation of DNA was performed in accordance with the method described. Preparation of libraries and amplicon sequencing of bacterial 16S rRNA genes was conducted on MiSeq device (Illumina) according to manufacturer's standard protocol. Filtering readings by quality and their taxonomic classification were carried out using QIIME version 1.9.0 software. Statistical differences was counted using IBM SPSS Statistics 23.1 software.

Results

As a result, we have identified significant correlation between certain bacteria genera and measured scales.

Thus UPDRS 3 (motor examination) showed positive correlation with Pyramidobacter (0,355) and Roseburia (0,333) genus (p=0,01). UPDRS 2 (motor experiences of daily living) correlated positively with quantity of Oribacterium (0,334) and Lactobacillus (0,433) (p=0,01). Patients with clinically significant anxiety (HADS anxiety) had higher abundance of Prevotella (0,358), Solobacterium (0,370) where patients with depression (HADS depression) showed connection with Lachnoclostidium (0,329), Veillonella (0,329) and negative with Peptoniphillus (-0,392) (p=0,01). Also patients with depression (BDI) had negative correlation with quantity of Desulfovibrio (-0,304) and Pseudomonas (-0,336) genus (p=0,01).

Conclusion

Based on this data we can say that these microorganisms might not only be the part of the PD pathogenesis but also play considerable role in anxiety and depression genesis and, thus, require more clinical research in order to find new methods of altering microbiome composition and correcting dysbiosis states to improve disease outcome.

Intracranial aneurysms: Contribution of Inflammatory Changes to their Rupture

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Introduction

Rupture of intracranial aneurysm is the most common cause of non-traumatic subarachnoid hemorrhage with serious clinical consequences. Commonly used neuroimaging methods allow accidental detection of unruptured intracranial aneurysms. However, the decision regarding management in individual patients remains difficult because the underlying mechanisms of aneurysm development and rupture are still not well understood. One important factor leading to rupture could be the inflammation. We compared structural changes of the aneurysm wall and its infiltration by inflammatory cells between ruptured and unruptured aneurysms.

Materials & Methods

Forty aneurysm wall samples were studied (thirteen ruptured aneurysms, twenty-seven unruptured aneurysms); eleven samples from similar locations of Willis circle without aneurysms were used as a control. The structural changes were evaluated using basic histological staining. The presence of lymphocytes was quantified by LCA antibody. Macrophages in the aneurysm wall were quantified and defined as M1 (pro-inflammatory subtype) and M2 (reparative subtype) using HLA-DR antibody and CD163 antibody, respectively. Data were analyzed by the Mann-Whitney U test.

Results

In ruptured aneurysms marked structural changes such as hypocellularity, thin wall of aneurysm without intimal lamina and the absence of internal elastic lamina were observed in addition to significantly higher proportion of M2 macrophages (p<0.05, compared to unruptured ones) accompanied by increased lymphocytes infiltration (p<0.02, compared to unruptured ones). In contrast, in unruptured aneurysms only mild to moderate changes were found including fibrosis, non-linear arrangement of smooth muscle cells, disruption of the intimal lamina with the absence of internal elastic lamina and the predominant infiltration by M1 macrophages accompanied by lymphocytes. In the control group no previously, mentioned changes were found.

Conclusion

Increased inflammatory cells infiltration and change of macrophage subtype proportion in the aneurysm wall could be important factor responsible for the rupture of intracranial aneurysm and initiation of subarachnoid hemorrhage.

Oncology II

Presenters:
Araujo, G.H.M. (Gabriel)
Zhuang, X.S. (Xiaosheng)
Sannikova, V.S. (Valeria Sergeevna)
Zwart, A.T. (Aniek)
Maguire, A.L. (Alice)
Mielnik, M. (Michał)

The antitumoral effect of metformin: lytic cell death induced by the biguanide on tumoral hepatocytes

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Introduction

Metformin is a biguanide that is manly used to treat insulin resistance. However, the use of this drug is associated with decreased risk in several types of cancer due to its inhibitory actions over proliferation, metastasis and favor cell death of many cancer models. Hepatocellular carcinoma (HCC) is one of the mostly common and deadly, and its highly associated with others chronical diseases. However, little is known about the action of metformin on HCC. For this purpose, the aim of this study was to investigate whether the metformin induces lytic cell death in tumoral (Hepa 1c1c7) and non-tumoral cells (AML-12).

Materials & Methods

To analyse the influence of metformin on HCC, Hepa and AML, were treated with increasing concentrations of metformin (0.19mM to 100mM), in different times (24H, 48H and 72H). Cell viability was analysed by MTT, Lactate Dehydrogenase (LDH) release and pore membrane formation using spectrophotometry. The death assays were analysed by Annexin/PI, cell cycle by PI intake, FAM-FLICA assay and lipid droplets formation by Bodipy using flow cytometry.

Results

Our results showed that metformin decreased the cells viability of tumoral cells at higher concentrations and latter times, and at the same conditions favorers the membrane pore formation and arrests the cell cycle in G1 phase (significant differences were calculated with T-test, $p < 0.05$), it also increases the release of LDH (****$p<0.0001$). The lipid droplets formation wasn't modulated, however both cell death assays and FAM-FLICA assay (*$p < 0.05$, compared to control, as determined by paired One-way ANOVA test), were in dose and time dependent manner able to modulate and led the cells to a lytic cell death profile.

Conclusion

Taken together, our data suggest that metformin decreases cell viability, arrests cell cycle and promotes lytic cell death independent on caspase-1 on liver cancer cells in vitro.

A Nomogram to Predict Breast Tumour Regression Patterns after Neoadjuvant Chemotherapy Based on Baseline Characteristics

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Introduction

Breast cancers show different regression patterns after neoadjuvant chemotherapy. Certain regression patterns are associated with more reliable margins in breast-conserving surgery. This study aims to develop a nomogram based on baseline clinicopathological factors and laboratory indexes to predict regression patterns in breast cancers.

Materials & Methods

We retrospectively reviewed 320 patients with stage I-III breast cancers who received neoadjuvant chemotherapy and had definitive surgery in our cancer center from January 2016 to December 2019. Tumor regression patterns were categorized as type 1 (concentric regression + pathologic complete remission) and type 2 (multifocal residues + stable disease + progressive disease) based on mass pathological results. Two breast cancer pathologists were responsible for evaluating regression patterns. Multivariate logistic regression models were applied to identify predictive factors for types of tumor regression. A nomogram was developed according to the logistic model and internally validated using the bootstrap resampling method.

Results

Among the 320 patients enrolled, 111 (34.7%) were hormone receptor-positive, HER2-negative (HR+HER2-) breast cancers, 77 (24.1%) were HR+HER2+ breast cancers, 70 (21.8%) were HR-HER2+ breast cancers and 62 (19.4%) were HR-HER2- breast cancers. HR+HER2- breast cancers have a significantly higher rate of type 2 regression compared to other subtypes (24.3% vs 12.4%, p=0.006). No significant difference in the rate of type 2 regression was seen between HR-HER2+ and HR-HER2- breast cancers (11.4% vs 12.9%, p=0.067). Factors with a p-value <0.05 in the univariate logistic regression were included in the multivariate logistic analysis. Multivariate logistic regression identified five independent indicators: menopausal status, estrogen receptor status, T stage, N stage and lymphocyte to monocyte ratio. The nomogram established based on these factors showed its discriminatory ability, with an area under the curve (AUC) of 0.70 (95% confidence interval 0.62 - 0.78). The calibration curve and Hosmer-Lemeshow test showed that the predictive ability of the nomogram was a good fit with actual observation.

Conclusion

HR+HER2- breast cancers are more likely to have type 2 regression after neoadjuvant chemotherapy. Five baseline factors, including clinicopathological factors and laboratory indexes, were incorporated to establish a nomogram, which exhibited a sufficient discriminatory ability for predicting different patterns of tumor regression.

Anticoagulation therapy could be a potential prevention of cancer recurrence

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[1] Sechenov university, Obstetrics and Gynecology, department of Clinical Institute of Children's Health named after N.F. Filatov, Moscow, Russian Federation

Introduction

The bidirectional relationship of cancer and hemostasis are well-known: they interact in a "vicious cycle", where cancers overexpress thrombin, which in turn promote both prothrombotic potential and tumor growth, invasion, and spread. Indeed, venous thromboembolism occurs frequently as a paraneoplastic event. Thus, anticoagulants could be accepted not only as a classic treatment for prevention thrombotic complications, but also as an anti-cancer therapy.

Materials & Methods

In our case-control study, 168 patients with advanced ovarian epithelial cancer were examined. All of them underwent neoadjuvant chemotherapy, surgical treatment, and postoperative chemotherapy according to standard schemes. 11 patients were excluded because of the non-compliance with the criteria: confirmed distant metastases, thrombosis in anamnesis, development of thrombotic complications during treatment. In concordance with the identified risk of thrombosis (Khorana and Vienna CATS scale), as well as the presence of genetic thrombophilia (FV Leiden, Prothrombin mutation, MTHFRG mutation), the first group of patients (n=69) with a high risk of thrombosis received anticoagulant therapy (LMWH and NOAK), the second group (n=88) did not. Patients were under our supervision for 60-72 months. ANOVA and the independent t-test were used to compare our groups.

Results

Our study showed that the group taking anticoagulants performed a significantly lower recurrence rate than the group of patients who did not receive regular anticoagulant therapy: 30.4% and 67% respectively. However, thrombotic complications, even with anticoagulant therapy, were more common in the first group - 15.9% versus 7.95%. in the second group. It is necessary to emphasize that the first group were patients with a higher risk of thrombosis than in the second.

Conclusion

Available data confirm the role of the hemostatic system in the growth and metastasis of cancer, but we cannot confidently assert that anticoagulation therapy should be included in the secondary cancer prevention. The duration of the study was sufficient, but the number of patients involved in the study needs to be expanded to draw fulfilled conclusions.

CT-measured low skeletal muscle mass from neck scans to recognize frail patients diagnosed with head and neck cancer

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Introduction

Skeletal muscle depletion or sarcopenia is related to multiple adverse clinical outcomes. However, frailty questionnaires are currently applied to identify patients who are potentially (un)suitable for treatment, but are time-consuming and straining for patients and the clinician. Screening for sarcopenia in patients with head and neck cancer (HNC) could be a promising fast biomarker for frailty. Our objective was to quantify sarcopenia with pre-treatment low skeletal muscle mass from routinely obtained neck CT-scans at level of third cervical vertebra in HNC patients and evaluate its association with frailty.

Materials & Methods

A total of 112 HNC patients with stage III-IV disease were included from a prospective databiobank. Skeletal muscle mass was retrospectively defined using the skeletal muscle index (SMI). Correlation analysis between SMI and continuous frailty data, and the observer agreement were analysed with Pearson's r correlation coefficients. Sarcopenia was present when SMI <43.2cm2/m2. Frailty was evaluated by Geriatrics 8 (G8), Groningen Frailty Indicator (GFI), Timed Up and Go (TUG) and Malnutrition Universal Screening Tool (MUST). An univariate and multivariate logistic regression analysis was performed for all patients and males separately to obtain odds ratios (ORs) and 95% confidence intervals (95% CIs).

Results

The cohort included 82 males (73%) and 30 females (27%), with a total mean age of 63 (±9) years. The observer agreement for measurements on CT were excellent for intra- (r=0.99, p<0.001) and interobserver variability (r=0.98, p<0.001). SMI correlated best with G8 frailty score (r=0.38, p<0.001), and did not differ per gender. Sarcopenia was present in 54 (48%) patients, whereof 25 (46%) males and 29 (54%) females. Prevalence of frailty was between 5% and 54% depending on the used screening tool. The multivariate regression analysis for all patients and males separately isolated the G8 questionnaire as the only independent variable associated with sarcopenia (OR=0.76, 95%CI 0.66–0.89, p<0.001 and OR=0.76, 95%CI 0.66–0.88, p<0.001 respectively).

Conclusion

This is the first study that demonstrates that sarcopenia is independently associated with frailty based on the G8 questionnaire in HNC patients. These results suggest that in the future screening for sarcopenia on routinely obtained neck CT-scans may replace time consuming frailty questionnaires, which is highly clinically relevant.

Drug-radiotherapy combinations: Deltarasin and PI-103 exhibit significant radiosensitising effects on the A549 lung adenocarcinoma cell line

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Introduction

Lung cancer presents as the most common cancer in men and women globally, yet is by far the most lethal. Lung adenocarcinoma is the most prevalent type of lung cancer comprising 38.5% of all tumours. KRAS, a proto-oncogene, is frequently mutated in lung adenocarcinoma. In patients, mutated KRAS is associated with a poorer prognosis. There are limited targeted therapies in place for mutated KRAS gene products. Therefore, treatment for these cancers currently relies on chemotherapy, surgery and radiotherapy. This project aims to evaluate deltarasin, a KRAS pathway inhibitor; and PI-103, an inhibitor of the PI3K/mTOR signalling pathway, for use as radiosensitisers on the A549 lung adenocarcinoma cell line.

Materials & Methods

Cell proliferation assays were performed to obtain IC50 for each compound in irradiated and unirradiated cells. Drug concentrations around the IC50 were tested in clonogenic survival assays to measure radiosensitisation by each drug. A radiation enhancement ratio (RER) was calculated for each repeat. Autophagy and cell senescence assays were performed on the KRAS-dependent A549 cell line to observe the effects of the drug on these mechanisms of cell survival and death. Significance of the observed effects was evaluated on three independent repeats of each experiment using Graphpad Prism for student's t test.

Results

RER for 3µM deltarasin was 1.52 (p=≤0.05), RER for 0.5µM PI-103 was 1.47 (p=≤0.05). Preliminary results suggest radiosensitisation at lower concentrations of PI-103 (0.25µM) did not reach statistical significance, unlike the higher concentration for deltarasin (6µM). Autophagy staining showed autophagy induction increased with drug concentration, and higher staining intensity for combined drug/ radiation treatment, than for either treatment alone. Preliminary results also indicate drug-dependent and radiation-dependent induction of cell senescence.

Conclusion

Deltarasin has significant radiation enhancing effect on the A549 cell line. This may be due to prolonged autophagy during the combined treatment. PI-103 showed significant radiation enhancement and a potent autophagy-inducing effect upon the A549 cell line. For future work, deltarasin could be combined with an autophagy inhibitor, to determine whether this would counteract it's radiosensitising effect.

Brain-derived neurotrophic factor expression predicts polyneuropathy and overall survival in multiple myeloma patients

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Introduction

Brain-derived neurotrophic factor (BDNF) belongs to proteins stimulating the growth, survival and differentiation of neurons and blood vessels. It plays an important role in the pathogenesis of many malignancies, including multiple myeloma (MM). BDNF promotes angiogenesis and osteoclastogenesis induced by cancerous plasma cells. There are also reports that it is relevant to the development of chemotherapy-induced polyneuropathy.
The aim of the study was to determine the predictive and prognostic value of BDNF in patients with multiple myeloma treated with bortezomib and / or thalidomide-based chemotherapy regimens.

Materials & Methods

The study group consisted of 91 patients with newly diagnosed MM treated frontline with thalidomide, cyclophosphamide, dexamethasone (CTD), bortezomib, cyclophosphamide, dexamethasone (VCD) or bortezomib, thalidomide and dexamethasone (VTD) triplet chemotherapy regimens. Median follow-up was 24 months (range 1-56 months). Severity of polyneuropathy was assessed according to the National Cancer Institute Common Toxicity Criteria (NCI-CTC) scale. The Mann-Whitney U test was used to compare differences in BDNF concentration according to response to treatment. Correlation assessment was carried out using the Spearman correlation test. The Kaplan-Meier estimation method and Cox logistic regression were used to assess probability of survival and disease progression.

Results

A statistically significant negative correlation between BDNF concentration and age (rho=-0.308, p=0.0209) and ISS staging (rho=-0.294, p=0.0311) was observed. There was a positive correlation between BDNF and eGFR (rho=0.318, p=0.0375) and the degree of polyneuropathy (rho = 0.289, p=0.0463). Significantly higher BDNF values were noted in patients who responded to treatment (medians: 30.02 vs 24.58; p=0.0326). BDNF level proved to be a useful marker to predict lack of response after 8 cycles of treatment (sensitivity - 100%, specificity - 61.5%; AUC = 0.821, 95% CI: 0.553-0.963l; p=0.0142), and on multivariate analysis, low BDNF level was significantly associated with reduced overall survival (OS) (HR = 2.52, 95% CI: 0.86-7.43; p=0.0404). Cox multivariate analysis showed that low BDNF concentration is an independent, unfavorable prognostic factor (HR = 5.49, 95% CI: 1.30-23.26, p=0.0214).

Conclusion

In the era of new anti-myeloma drugs, serum BDNF level may play a role as a prognostic factor, and constitute a useful biomarker in predicting the development of drug-induced peripheral neuropathy.

Public Health and Epidemiology
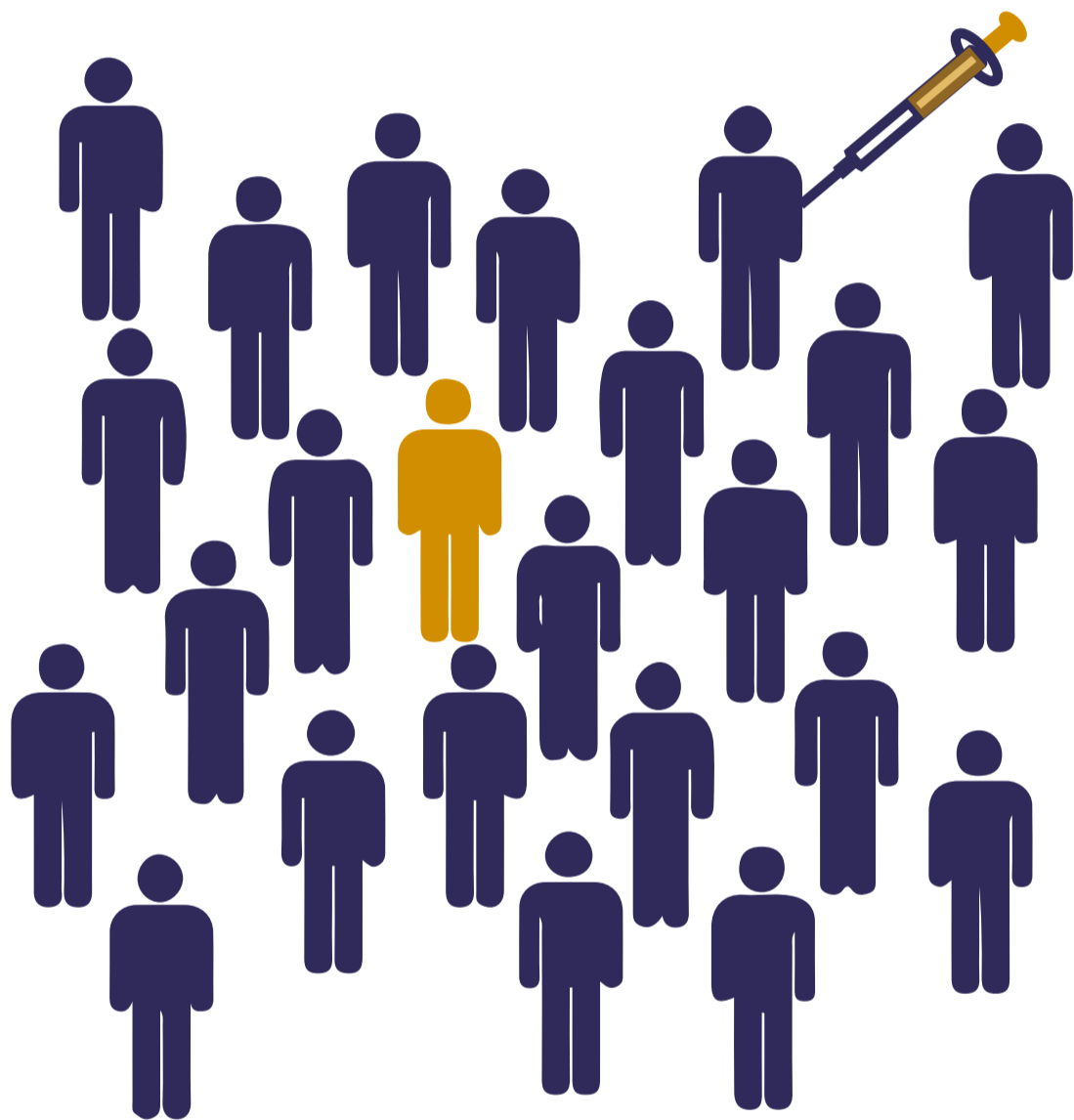
Presenters:
Balouchi, A (Abbas)
Yadav, S.Y. (Sneha)
Rodriguez Rocandio, K.E. (Karla Elena)
Reddy, R (Rahul)
Chan, S.K. (Sik Kwan)
Straathof, E.J.M. (Lilian)

Prevalence and Device Related Causes of Needle Stick Injuries among Health Care Workers: A Systematic Review and Meta-Analysis

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Introduction

Healthcare workers (HCWs) are being exposed to needlestick injuries (NSIs) every day. Needle stick injuries (NSIs) are one of the most important occupational hazards among healthcare workers (HCWs) globally. Despite the individual studies, accurate statistics on the global prevalence of NSIs do not exist. The aim of this study was to determine the global prevalence and the causes of NSIs among HCWs.

Materials & Methods

In this systematic review and meta-analysis, three databases (PubMed, Web of science, and Scopus) were searched for data from January 1, 2000 to December 31, 2018. Keywords of the search included: Prevalence OR "Needlestick Injury" OR "sharp injuries" OR "health care workers" OR "health professionals". The random effect model was used to determine the prevalence of NSIs among HCWs. Hoy et al.'s instrument was employed to evaluate the quality of the included studies. The all stages include search in databases, data screening, study selection, quality assessment, data extraction were conducted by two researchers separately.

Results

A total of 87 studies performed on 50,916 HCWs in 31 countries worldwide were included in the study. One-year global pooled prevalence of NSIs among HCWs was 44.5% (95% CI: 35.7, 53.2). The highest prevalence of NSIs was in the South East Asia region at 58.2% (95%, CI: 36.7, 79.8). Considering HCWs' job category, the prevalence of NSIs was the highest among dentists at 59.1% (95% CI: 38.8, 79.4), and the most common cause of NSIs was the hypodermic needle at 55.1% (95% CI: 41.4, 68.9).

Conclusion

In spite of various preventive programs, the high prevalence of NSIs suggests a revision of current plans to better manage global NSI rate.

Evaluation of Association of Psychosocial Stress and Hypertension in Adults > 30 Years of Age: A Community-Based Case Control Study from Rural Central India

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Introduction

Hypertension has multi-factorial causation. Stress has chronically been cited as an imperative cause of hypertension among other risk factors such as sleep abnormalities. The interrelation between psychosocial stress and hypertension has been significant though the exact association remains debatable. The aim of this study was to evaluate the association of psychosocial stress and other factors like family and social support, sleep abnormalities, physical activity and addiction with hypertension in adults > 30 years of age.

Materials & Methods

A community-based case-control study with 90 incident hypertensive cases aged >30 with 90 age and sex-matched controls selected from rural populations in central India. Study participants were examined and interviewed regarding their socio-demographic characteristics, psychosocial stress(ICMR psychosocial stress scale), family and social support(ICMR scale), quality of sleep(Pittsburgh sleep quality index), history of addiction(WHO ASSIST) and physical activity(GPAQ). Data collection was done using KOBO and multivariate analysis using binomial logistic regression was done using SPSS version 21.

Results

Psychosocial stress had a highly significant association with hypertension (AOR=8.198, 95% C.I. 2.85 – 23.52). Participants having compromised family and social support (AOR=3.0, 95% C.I. 1.41 – 6.34), Poor quality of sleep (AOR=4.429, 95% C.I. 1.78 – 10.96) and Low physical activity (AOR=2.92, 95% C.I. 1.22 – 6.98) had significantly higher odds of developing hypertension. Other parameters like sedentary occupation, lower socioeconomic status, body mass index (BMI) ≥ 25 kg/m2 were found to have an association with hypertension. Tobacco or alcohol addiction did not show any association.

Conclusion

This study highlights a significant number of undiagnosed or untreated cases of psychosocial distress in the community. Thus calling for immediate attention towards psychosocial stress as an important etiological determinant in the causation of hypertension. This indicates the need for interventions to prevent and manage psychosocial stress through systematic screening and awareness program informed by locally generated evidence. A comprehensive public healthcare initiative that would promote family care, strengthen social support coupled with effective risk communication would go a long way in offering primary counselling to prevent the development of hypertension.

Prevalence and associated risk factors of "Cognitive Frailty" in older adults

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Introduction

Physical frailty is known as a loss of reserve and resistance to external stressors and cognitive impairment as a state of reduced cognitive reserve. There is a new entity that was introduced in 2013 by a consensus group, "cognitive frailty", which is defined as the presence of both, physical frailty and cognitive impairment, excluding dementia. We aimed to find the prevalence of cognitive frailty in a sample of older adults and identify those risk factors associated.

Materials & Methods

Older adults aged over 60 years were included in this cross-sectional study. Cognitive impairment was defined using the Mini-Mental State Examination. Frailty was assessed using Fried/ Cardiovascular Health Study criteria that include slow gait velocity, weight loss, low physical activity, weakness and fatigue/exhaustion. Additionally, nutritional status was measured by the Mini-Nutritional Assessment and a clinical questionnaire was examined. Univariate and multivariate analyses by logistic regression were used, the odds ratios (95% confidence intervals and p-value) of the model were calculated. Statistical analyses were performed using SPSS (v25.0, IBM Corporation).

Results

Nine hundred nine older adults were evaluated, (mean age 68.4 years, SD 5.9). According to Fried's criteria, 68.9% were prefrail and 15.1% frail. The prevalence of cognitive impairment was 15.6% and 13% were affected by cognitive frailty. In logistic regression analysis, we found conditions that presented elevated risks associated with cognitive frailty.

Patients at risk of malnutrition or malnourished (OR 2.6 [95%CI 1.4-4.9] p=0.002), an age over 67 years (OR 1.8 [95%CI1.1-2.8] p=0.01), presence at least, of one comorbidity (OR 1.9 [95%CI 1.1-3.2 p=0.01] and two or more comorbidities (OR 1.8 [95%CI 1.1-2.8] p=0.01), this model adjusted by sex.

Conclusion

The prevalence rates we found are similar to the rates that have been reported in the literature. In those older adults with an altered nutrition state, presence of comorbidities and advanced age, we can see increasing risk to present cognitive frailty. This entity has been proposed, not only as a dementia predictor but also of other geriatric syndromes that affect the older adult's functionality, quality of life and predisposes to adverse outcomes. Identification of modifiable risk factors is important and preventive interventions to risk factors are needed.

Knowledge and Practice of First-aid among Police Personnell and Traffic Police in Road Traffic Accident Victims of Sunsari, Nepal

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Introduction

Proper first aid care to road-traffic accident victims during the "golden hour" (First Hour after incident) saves lives. Police personnel and traffic police are one of the first hand responders in road-traffic accidents. The objective of this study was to assess knowledge and practice of first aid among police personnel and traffic police in road-traffic-accident victims; and to correlate their knowledge with various socio-demographic factors

Materials & Methods

It is a descriptive cross-sectional study done over a six-month period by interviewing 121 police personnel and traffic police of Sunsari, Nepal using a purposive sampling technique.

Results

Out of 121 respondents, there were 109 civil policemen and 12 traffic policemen, with their mean age of 33.12 ± 7.133 years. Forty-three percent of the respondents had formal training on first aid. Knowledge about handling trauma victims, airway management, cardio-pulmonary resuscitation (CPR), primary care of fracture injury and management of bleeding wound was present in about 66%, 23%, 35%, 59% and 93% of the respondents respectively. Respondents with higher level of education had better knowledge about handling trauma victims ($p= 0.021$), airway management ($p= 0.010$), CPR ($p= 0.004$), and approach to unresponsive victim ($p= 0.044$). Respondents with higher rank had better knowledge on prioritizing airway ($p= 0.001$), handling trauma victims ($p= 0.026$), CPR ($p= 0.038$) and approach to unresponsive victim ($p= 0.032$). Respondents with formal training on first aid had better knowledge on airway management ($p<0.001$) and CPR ($p= 0.007$).

Conclusion

Knowledge and practice of proper first aid among police personnel and traffic police was low. Respondents with higher educational level, higher rank and having formal training had better knowledge and practice of first aid.

Pembrolizumab is not Cost-effective in Second Line Treatment of Hepatocellular Carcinoma: A Cost-effectiveness Analysis

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Introduction

Recently, checkpoint inhibitors have been approved for the second-line therapy of hepatocellular carcinoma (HCC) in patients who previously received Sorafenib. Pembrolizumab has demonstrated substantial anti-tumor activity and favorable toxicity profile as second-line treatment of HCC. However, considering the high cost of Pembrolizumab, there is a need to assess its value by considering both efficacy and cost. We aimed to evaluate the cost-effectiveness of Pembrolizumab vs. placebo (best supportive care alone) [BSC] as second-line treatment in hepatocellular carcinoma (HCC) patients from the US payer perspective.

Materials & Methods

We developed a Markov model to compare the lifetime cost and effectiveness of Pembrolizumab plus BSC vs. BSC in the second-line treatment of HCC. Health states were defined for initial treatment, progression, and death. Rates for drug discontinuation, frequency of adverse events, disease progression, and death obtained from the KEYNOTE-240 randomized control trial, which included 413 patients and compared Pembrolizumab plus BSC vs. BSC as second-line therapy of HCC, were used to determine the likelihood of transition between states. Deterministic and probabilistic sensitivity analyses were conducted to evaluate model uncertainty.

Results

Life-years, quality-adjusted life-years (QALYs), and lifetime costs were estimated, at a willingness-to-pay threshold of $100,000 to $150,000 per QALY. Pembrolizumab every 3 weeks was more effective but much more costly than BSC. Pembrolizumab provided an additional 0.73 QALYs, at a cost of $178,867 per QALY. Sensitivity analyses found the results to be most sensitive to overall survival hazard ratio (0.66; 95%CI, 0.46-0.87). Other variables, such as the cost and utility values of pembrolizumab had a moderate or minor influence on model results.

Conclusion

In this model, Pembrolizumab plus BSC was estimated to be NOT cost-effective compared with BSC as second-line therapy in HCC patients at willingness-to-pay threshold from $100,000 to $150,000 per QALY.

Prevailing head position to one side in early infancy - a population-based study

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Introduction

Proper head control is a prerequisite for young infants to learn and explore their environment, but needs time to fully establish. Impaired head control is regarded as a manifestation of neurological non-optimality. A common clinical sign of impaired head control is a prevailing head position to one side (PHP). Professional awareness of a possible association between PHP and conditions impeding typical development as well as caregivers' concerns about asymmetric infant motor behavior, frequently result in referral to paediatric physical therapy. However, knowledge about the current prevalence of PHP in the general population and its actual association with functional abilities and perinatal risk factors, is limited and outdated. Therefore, the aim of this study was to determine the prevalence of PHP in early infancy and to evaluate its associations with reaching performance, neurological condition and perinatal and socio-economic factors.

Materials & Methods

We performed an observational study in 500 infants (273 boys) 2-6 months corrected age, representative of the Dutch population (median gestational age 39.7 weeks (27-42); birthweight 3438 g (1120-4950). PHP and reaching performance were assessed with the Infant Motor Profile (IMP); neurological condition with the Standardized Infant NeuroDevelopmental Assessment (SINDA). Socio-economic and perinatal information were obtained by questionnaire and medical records. Associations were analysed with uni- and multivariable statistics.

Results

PHP was observed in 100 infants (20%), and its prevalence decreased from 49% at 2 months to 0% at 6 months. Only in infants aged 4-5 months PHP was significantly associated with worse reaching and an at-risk neurological score. Prevailing head position to one side was weakly associated with prenatal recreational substance exposure, post-natal admission to a paediatric ward and paternal native Dutch background.

Conclusion

Prevailing head position to one side at 2-3 months is a frequently occurring sign with limited clinical significance. Yet, PHP at 4-5 months is associated with a worse functional and neurological condition. Therefore, PHP at 4-5 months could serve as a red flag indicating possible challenges in later development.

Pulmonary Medicine
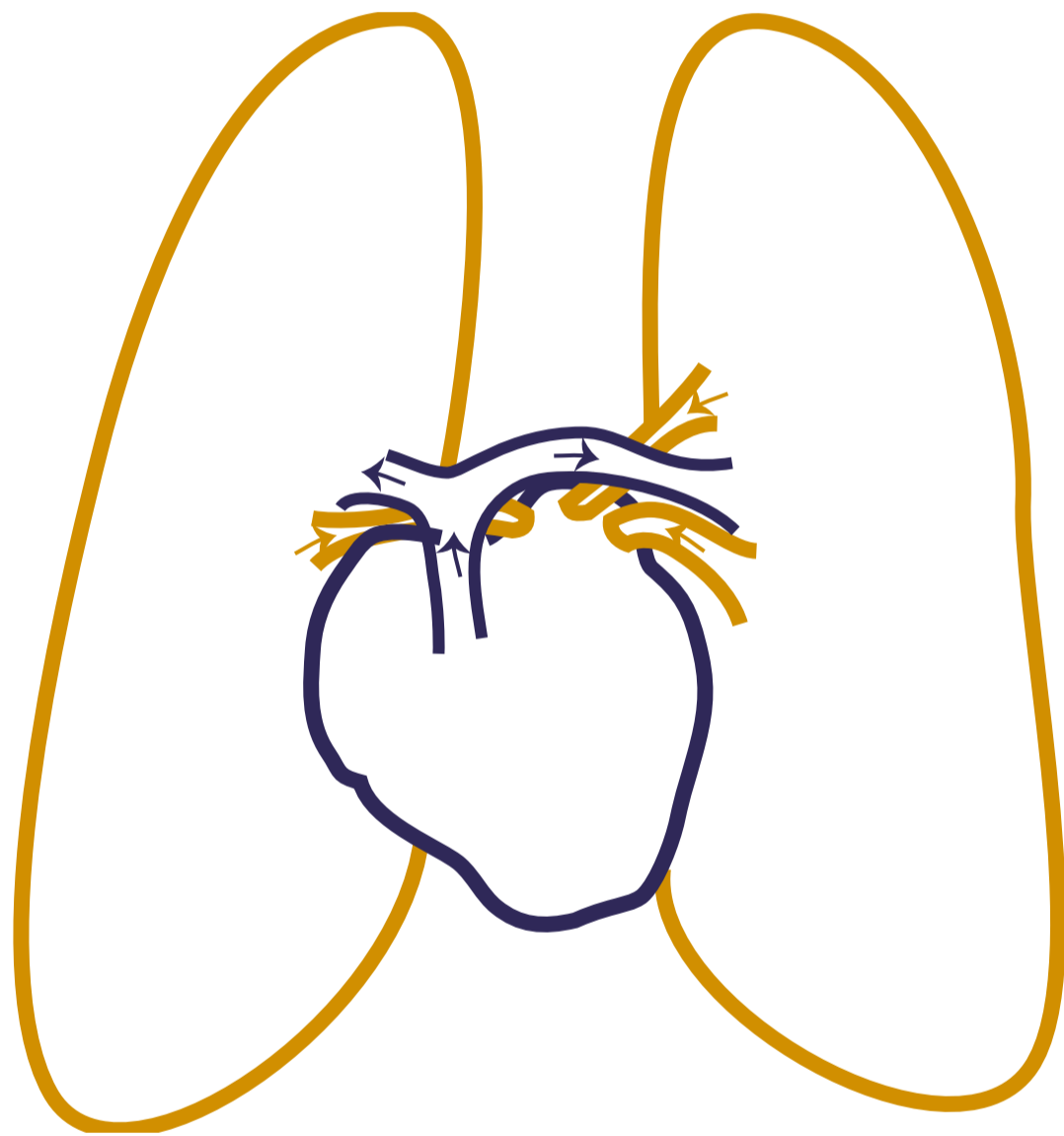
Presenters:
Eck, G.W.A. van
Fischer, J.J. (Joel)
Keny, G. J. K. Miss (Greeshma)
Lourenço, J.D. (Juliana)
Ramos, M.M.A.
Grover, S.G. (Shekhar)

Microplastic fibers and their effect on lung cells: an unexplored topic

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Introduction

Microplastic fibers are abundant in air and are inhalable. They were found in human lung tissue 20 years ago in a single study. Although exposure to nylon has been associated with interstitial lung disease in nylon flock workers, the effects of microplastics on lung tissue have never been studied and their effects on lung cells are unknown. In this study, we aimed to determine the effects of microplastic fibers on organoids grown from pulmonary epithelial cells and fibroblasts.

Materials & Methods

Nylon and polyester microfibers were cut in sizes of 11.3x30.4 µm and 14.5x53.0 µm, respectively. Murine primary epithelial cells and CCL206 fibroblasts were co-cultured in Matrigel in the presence or absence of nylon and polyester microfibers to form organoids that resemble airway structures. Numbers of airway organoids were counted, and their sizes measured after 14 or 21 days.

Results

Exposure of developing organoids to nylon or polyester microfibers for 14 days resulted in significantly fewer organoids (control: 77±9; nylon: 22±4; polyester: 57±10) of smaller size (control: 337±12µm; nylon: 186±12µm; polyester: 299±12µm). A 7-day exposure of already developed organoids on day 14 to either type of fiber did not affect their number or size. Exposure to fiber-conditioned medium (from nylon or polyester) resulted in fewer developing organoids but did not affect developed organoids.

Conclusion

Exposure to nylon and polyester microfibers caused a significant reduction in the number and size of airway organoids. Interestingly, this effect was mainly observed in developing organoids, rather than in developed organoids. Similar effects were seen for treatment with fiber-conditioned medium. This suggests that additives leaching from these microplastics are harmful to epithelial outgrowth and repair, but not to mature fully grown epithelial cells. Further studies will concentrate on identifying these additives and the mechanism behind their effect. Importantly, wider investigations into the presence of microplastic fibers in human lung tissue are urgently needed to determine the actual risk of these fibers to human health.

Psychological Stress and Lung Function and the Role of Genetic Susceptibility

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Introduction

It is well established that prolonged chronic stress can lead to serious damage in various physiological systems. The respiratory system is an important general health indicator and a potential target for physiological damage, however, the literature on the direct link between psychological stress and lung function is scarce and partly contradicting. In addition, previous research did not account for individual susceptibility to stress due to genetic differences. This study aims to clarify the relationship between stress and lung function and investigates potential genetic modifiers.

Materials & Methods

We used baseline data from adults in the Dutch Lifelines cohort (N = 99,402; mean age = 44.0 (sd = 12.2); 58.7% females). Stress was measured by the long-term difficulties inventory (LDI) for chronic stress and the list of threatening life events (LTE) for acute stress exposure. Lung function was measured by spirometry. We performed linear regression to test the stress-lung function associations. Additionally, genome-wide gene-by-stress interactions were tested using PLINK. All models were adjusted for socio-economic status, sex, smoking, height, and age.

Results

Higher stress levels were significantly associated with lower FEV1 for both LDI (b=-1.72) 95% CI [-3.05; -0.39] and LTE (b=-6.04) 95% CI [-8.44 ;-3.63]. Higher levels of chronic stress were also associated with lower FEV1/FVC (b=-0.0003) 95% CI [-.001; -.00015] and FEF25-75 (b=-0.0048) 95% CI [-.007; -.002]. A higher number of experienced threatening life events was significantly associated with lower FVC (β=-0.0094) 95% CI [-.007; -.002]. Preliminary results for genome-wide interaction terms hint at some genetic modifiers.

Conclusion

Psychological stress exposure at baseline is associated with lower lung function. The potential genetic modifiers highlight the importance to identify susceptible individuals for both clinical practice and prevention. Future studies should focus on the mechanism by which stress may impact the respiratory system by investigating if this association is mediated by systemic inflammation.

Assessment of respiratory morbities among shopkeepers and vendors in a semi urban area

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Introduction

Rapid urbanisation has increased the risk factors related to respiratory morbidities leaving the general population vulnerable. The potentially damaging agents are numerous, and thus, any damage to defense mechanisms sets in signs of respiratory morbidities. Shopkeepers and vendors in the semi urban area who mostly work outdoors at ground level, are continuously exposed to unhealthy environment and practices, and majority are unaware about the situation. Thus, on humanitarian grounds it is necessary to assess the respiratory morbidities in them. Our study will help identify the prevalence of respiratory morbidities and the risks related to them. Thus appropriate measures could be taken which in turn could impede the respiratory morbidities.

Materials & Methods

A cross-sectional study was carried out among 260 shopkeepers and vendors. Subjects who had been working for more than a year were included, and ones already on medication for respiratory illness excluded. Demographic and occupational details, general and systemic examination, presenting complains, history, habits were obtained using a questionnaire and PEFR was calculated. Excel was used for data tabulation and Chi-square tests for the significance, with the level of significance at $\alpha = 0.05$.

Results

High prevalence of respiratory morbidities with 64.62% of the study population showing one or more respiratory morbidities was noted. Cough (23.85%) followed by breathlessness (22.31%) were highly prevalent, and 31.03% had a family history of asthma. The study revealed significant associations of PEFR with age($p=0.02175$), BMI($p=0.0261$), Total Exposure Period($p=0.0078$), respiratory morbidities($p=0.0366$) and addictions($p=0.0034$). However, no significant association was found between PEFR and the type of shop($p=0.0774$), whereas, prevalence of respiratory morbidities was high in roadside as compared to the ones in closed shops.

Conclusion

An increase in TEP and the presence of respiratory morbidities, both showed a decrease in the PEFR. However, the type of shop had no effect on PEFR and thus the subjects in closed, roadside or open shops were equally exposed. But, the high prevalence of morbidities in subjects in roadside shops over those in closed shops reveals that TEP plays a major role followed by the type of shop. Therefore the population must be made aware about their surroundings along with some possible solutions.

STAT and SOCS proteins expression and their role in Th17/Treg differentiation in lung tissue and peripheral blood leukocytes of COPD patients

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Introduction

The Signal Transducer and Activator of Transcription (STAT) and Suppressor of Cytokine Signaling (SOCS) are a family of proteins that participates in the signaling pathways for many cytokines, mediate the differentiation of immunological responses and are involved at the COPD development. In this study, we aimed to compare the gene expression of SOCS and STAT proteins and their role in the T helper (Th) 17 and T regulatory (Treg) cells differentiation in both lung tissue and peripheral blood leukocytes of COPD patients.

Materials & Methods

Lung and blood samples were obtained from Smokers with COPD GOLD I and II (COPD I and II) and Non Obstructive Smokers (NOS). We also obtained blood samples from Smokers with COPD GOLD III and IV (COPD III and IV). The gene expression of STAT3, STAT5, SOCS1, SOCS3, Retinoic-acid-related orphan receptor (ROR T) and Forkhead Box P3 (FOXP3) was evaluated using Real-Time PCR, and the expression of interleukins-10 and -17 was obtained by ELISA. The comparisons were made using Student's t-test or One-way analysis of variance for parametric data, and Mann-Whitney or Kruskal Wallis test for non-parametric data.

Results

The analyses of lung tissue homogenate demonstrated an increase in gene expression of SOCS3 (p=0.03), STAT3 (p=0.005), ROR T (p=0.001) and FOXP3 (p=0.02) of COPD I and II patients compared to NOS group. We also observed an increase in SOCS3 (p=0.001), STAT3 (p=0.0004), STAT5 (p=0.0007) and ROR T (p=0.002) on the peripheral blood leukocytes from COPD III and IV patients compared to the other groups, although we found a decrease in FOXP3 gene expression (p=0.008) in both COPD groups and a decrease of IL-10 expression (p=0.008) in COPD III and IV group compared to COPD I and II.

Conclusion

There is an increase in gene expression of mediators involved in Th17 and Treg response such as STAT3, RORYT and SOCS3 both in tissue and peripheral blood leukocytes of COPD patients. However, we observed that on the peripheral blood leukocytes, these changes occur only in more advanced stages of the disease, accompanied with a decrease in FOXP3 and IL-10 expression, demonstrating a failure in Treg response.

Influence of 17β-Estradiol in lung injury and in the expression of nitric oxide synthase after aortic ischemia and reperfusion in rats

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Introduction

Ischemia and reperfusion (I/R) generates a systemic inflammatory response. Endothelial cell dysfunction is a key step for the reperfusion injury. Endothelial cells produce endothelin and nitric oxide (NO) among others which modulate vascular response. Female sex hormones exert influence on I/R process and their effects are protective. Objective: To evaluate estradiol treatment in lung inflammation after I/R and its effects on the expression of NO synthase isoforms in lung tissue.

Materials & Methods

60-days-old Wister rats underwent proximal descending aorta occlusion with the inflation of a Fogarty® 2F intravascular catheter. Animals were divided into 3 groups: SHAM (control animals that did not undergo aortic occlusion), IR (animals submit to aortic occlusion) and E2 (animals treated with 17β-estradiol 30 minutes before ischemia and reperfusion). After 20 minutes of occlusion and 2 hours of reperfusion, lung and blood samples were obtained. iNOS, eNOS and endothelin protein expression were quantified by immunofluorescence and IL-1 serum concentration was determined.

Results

No difference was found on eNOS expression among the groups. iNOS expression was found increased in IR group compared to SHAM and the treatment prevented it (SHAM 9.621 ± 0.8613, E2 8.983 ± 0.5142 vs. IR 13.42 ± 1.220). The analyses of endothelin from IR group showed an increase regarding the SHAM group $P < 0.05$ and E2 was also able to prevent it (SHAM $4,740 \pm 0.6914$, E2 5.808 ± 0.5064 vs. IR 7.133 ± 0.6428). The concentration of IL-1 was increased by I/R in comparison to SHAM group $P < 0.05$. E2 prevented the increase in IL-1 concentration (SHAM 16.38 ± 1.481, E2 23.32 ± 5.069 vs. IR 50.57 ± 13.75).

Conclusion

17β-estradiol treatment was able to prevent the inflammatory effects of I/R, reducing iNOS and endothelin molecules and IL-1 release. This treatment should be considered a potencial tool to reduce remote I/R induced inflammation.

Tobacco use amongst adolescents and youth in India: evidence from Global Adult Tobacco Survey-2 (2016-17)

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Introduction

Tobacco use is a serious public health concern affecting the youth and adolescents world over. A vast majority of tobacco users initiate well before the age of 18 years. Due to enormous psychosocial and health effects of tobacco on adolescence and youth, it is pertinent to understand the burden of tobacco use and its socio-demographic correlates for formulating effective tobacco control measures. Objective: The present study analyses the Global Adult Tobacco Survey 2016-17 (GATS-2) to estimate the prevalence of individual forms of tobacco use among adolescents and youth aged 15-24 years; and to assess the association of socio-demographic factors with tobacco use.

Materials & Methods

The source of data was a cross-sectional GATS-2 survey in India (analysed in SPSSv17.0) which utilised a multistage, geographically stratified cluster sampling method. Unadjusted Odds ratio was calculated for evaluation of possible association with socio-demographic factors, and adjusted Odds Ratio (bivariate logistic regression analysis) identified independent factor correlation (adjusted for confounding factors) (95% CI, *p<0.05).

Results

There were 13,329 respondents (44.9% boys and 55.1% girls) aged 15-24 years. The calculated prevalence of smoking and smokeless tobacco use were 5% and 10.9% respectively. There were 2% respondents reporting dual use. Overall, 11.9% respondents were using 'any' form of tobacco (one in eight). On comparison with socio-demographic factors, the odds of using 'any' tobacco was significantly higher among respondents aged 20-24 years [OR: 2 (1.76-2.77)], rural areas [OR: 1.36 (1.2-1.54)], and unmarried [OR: 1.56 (1.37-1.88)]. The odds of using 'any' form of tobacco was significantly lower among females [OR: 0.21 (0.19-0.24)], literate individuals [OR: 0.33 (0.29-0.37)] and unemployed/students/retired/homemakers (occupation) [OR: 0.44 (0.39-0.50)].

Conclusion

The overall tobacco use of approx. 12% among 15-24 year olds is a matter of concern. Also, many socio-demographic factors were significantly associated to tobacco use, implying the need for targeted intervention strategies to combat the situation.

Surgery and Rehabilitation Medicine

Presenters:
Dehdashtian, E. (Ehsan)
Khemka, M.K. (Meenakshi)
Aryannejad, A. (Armin)
Elhusseiny, H. M. (Hussein Mohamed)
Zepeda Carrillo, C.A. (Carol A.)
Kardan, M.H.K (Mohammadhossein)

Effect of various patient positions on endotracheal tube cuff pressure after adult cardiac surgery

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Introduction

To avoid microaspiration or tracheal injury, the target endotracheal tube cuff pressure must be maintained 20–30 cmH2O. Changing in patients' positions may effect on endotracheal tube cuff pressure. The aim of this study was to investigate the effect of various patients' positions on endotracheal tube cuff pressure after adult cardiac surgery.

Materials & Methods

This prospective, interventional study was conducted on 25 adult patients with orotracheal intubation for the cardiac surgery. Patients' endotracheal tube cuff pressure was assessed after surgery in a neutral starting position during an end-expiratory hold, and cuff pressure was regulated at 25 cmH2O. Then, ten changes in head position were performed: anteflexion, hyperextension, left and right lateral flexion, left and right rotation, semi-recumbent position (head elevation in 45°), recumbent position (head elevation in 10°), horizontal supine position, and finally, Trendelenburg position (10°). The observed cuff pressures were compared with the basic cuff pressure at the starting position.

Results

Of total 250 measurements (25 participants in 10 positions), 109 (43/6%) were greater than the upper target limit of 30 cmH2O. In contrast, no measurements were less than the lower target limit of 20 cmH2O. 141 (56/4%) measurements were between the target limit of 20–30 cmH2O. All ten changes of patients' head position lead to statistically significant increase in endotracheal tube cuff pressure ($P < 0.05$).

Conclusion

Simple changes in intubated patients' position could significantly increase in endotracheal tube cuff pressure that may potentially damage tracheal mucosa.

Interaction of Breast Pain Severity with Anxiety and Depression in Patients of Mastalgia

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Introduction

Breast pain (Mastalgia) is a common complaint of women attending the General Surgery Out Patient Department (OPD) of IPGME&R and SSKM Hospital, Kolkata. Considerable psychosocial distress is seen among Mastalgia patients. A grave fear of malignancy is noted. Definite data on the interaction of Mastalgia with anxiety and depression from our OPDs is unavailable. We aim to assess the severity of breast pain with anxiety and depression among patients.

Materials & Methods

A Descriptive Observational Cross-sectional Study in 101 Mastalgia patients, selected by Purposive Sampling was conducted. A predesigned structured questionnaire including the Numeric Pain Rating Scale, Hamilton Anxiety Scale (HAM-A) and Hamilton Depression Scale (HAM-D) was used. Data was summarized by routine descriptive statistics. Cross-tabulation of pain severity, anxiety and depression was done. Chi-square test and chi-square test for trend was employed for intergroup comparison of categorical variables. Linear association between age, pain severity, anxiety and depression were explored through scatterplots and quantified by calculating Spearman's rank correlation coefficient Rho.

Results

101 Mastalgia patients, ages 18-70 years, (mean 34.79, median 34 and S.D 9.430), proportion of subjects with:

Anxiety- 80/101 (79.21%); (HAM-A Score Mean 23.12, Median 23, S.D 11.195); Depression- 86/101 (85.15%); (HAM-D Score Mean 11.91, Median 12, S.D 5.103).

Pain scores range from 3 to 10 on the Numeric Scale (Mean 6.44, Median 6, S.D 1.982). Significant association seen between pain severity-anxiety and depression: Pearson's chi-square test p value: 0.020 (severity of pain-anxiety levels), 0.004 (severity of pain-depression levels). Chi-square for trend p value: 0.0017 (severity of pain-presence of anxiety), <0.001 (severity of pain-presence of depression).

Poor linear association (Spearman's rank correlation coefficient) is seen between pain severity-anxiety and depression; age- anxiety and depression:

Pain-HAM-A: Rho 0.191&p=0.0553
Pain-HAM-D: Rho 0.224&p=0.0242
Age-HAM-A: Rho -0.137&p=0.1730
Age-HAM-D: Rho -0.136&p=0.1749

Conclusion

This study shows that a high proportion of Mastalgia patients, irrespective of pain severity and age, suffer from psychosocial distress. Even patients with low/moderate pain levels report considerable anxiety, depression due to a fear of malignancy. Counselling strategies adopted to alleviate psychosocial distress may help in treatment as well as better functioning of health care facilities by reducing the daily patient load in developing countries.

Protective Effect of Modafinil on Skin Flap Survival in the Experimental Random-Pattern Skin Flap Model in Rats: The Role of ATP-Sensitive Potassium Channels and Nitric Oxide Pathway

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Introduction

Skin flaps are now widely used as a solution to skin defects, mainly due to tumor excisions, skin wounds, burns, trauma, and also congenital defects. Despite advances in surgical techniques, flap necrosis remains the most dreadful complication of skin flap surgeries. Modafinil is a brain-stimulating agent used in narcolepsy for years. It was also shown to possess an anti-ischemic effect in the heart, brain, intestine, and testis in previous studies. Some of its effects are mediated by nitric oxide (NO) and ATP-sensitive potassium (KATP) channels. Besides, recent studies have indicated that the NO pathway and KATP channels are involved in the survival of random-pattern skin flaps. So, we investigated the efficacy of modafinil on skin flap survival in rats by the possible involvement of NO pathway and KATP channels.

Materials & Methods

Ninety Wistar male rats were used in our study. Multiple doses of modafinil (10, 25, 50, and 100 mg/kg) were injected intraperitoneally (i.p) prior to the surgery. L-NAME (non-selective nitric oxide synthase [NOS] inhibitor), Aminoguanidine (inducible NOS [iNOS] inhibitor), 7-Nitroindazole (7-NI) (neuronal NOS [nNOS] inhibitor) were administrated alone or prior to modafinil. The role of KATP channels was determined by the co-administration of glibenclamide (KATP channel blocker) or cromakalim (KATP channel opener) with modafinil. The control group received the vehicle. All drugs were injected i.p. Histopathological evaluations were performed by Hematoxylin and Eosin, Masson's trichrome, and VEGF immunohistochemical staining. Nitrite concentrations were measured by the Griess reaction test. We performed statistical analyses using one-way analysis of variances (ANOVA) followed by Tukey's post-hoc test to compare the means.

Results

Modafinil 25 mg/kg was the most effective dose among the treated groups vs. the control group ($p < 0.001$), while 10 mg/kg was the sub-effective dose vs. the control group ($p < 0.05$). All NOS inhibitors significantly reversed the protective effect of modafinil ($p < 0.001$). Non-effective dose of cromakalim had synergistic effect with the sub-effective dose of modafinil (10 mg/kg), while glibenclamide reversed the effect of modafinil (25 mg/kg) ($p < 0.001$). Histopathological examinations showed significant improvements in the modafinil 25 mg/kg group.

Conclusion

Modafinil protects skin flap survival, probably mediated by the NO pathway and KATP channels.

Glycerolized Bovine Pericardium Versus Polypropylene Mesh for Reconstruction of Large Abdominal Wall Defects

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Introduction

Reconstruction of Abdominal Wall Defects relied over years on using different Prosthetic implants as Polypropylene Mesh (PPM), Polyester, Dacron and expanded Polytetrafluoroethylene (ePTFE). Using such biomaterials becomes facing several drawbacks as they are non-bioabsorbable, therefore they remain inside the body as permanent foreign materials have the potential to serve as an infection nidus. On the long run, they undergo calcification restricting their elastic function. They are unable to grow with patients' organs and unsuitable for tissue remodeling. Our previous study improved that Glycerolized Bovine Pericardium (GBP) was biocompatible, biodegradable, strong, elastic and could resist post-operative infection. In this study, we aimed to study its application on different domestic animals with different types of hernias preluding to its use in human.

Materials & Methods

Eighty clinical cases of different animal species (Ovine, Bovine, and Equine) with different types of large abdominal wall defects (Umbilical, Abdominal, Inguinal, and Scrotal Hernias) were randomly assigned to one of two groups. Defects were repaired using GBP (n=35 cases) in the first group and PPM (n=45 cases) in the second group. All Characteristic details and ultrasonography of these cases were recorded before surgery. Qualitative and gray scale quantitative ultrasonography including Implant Gray Scale (IGS) and Subcutaneous Gray Scale (SGS) were adopted post-implantation. Follow up of the cases was carried out for three months.

Results

Ultrasonography revealed significant (P<0.05) improvement of both IGS and SGS in GBP group than PPM group. IGS and SGS showed a significant (P<0.05) time-dependent increase in GBP group than PPM group. All cases in GBP group showed successful healing without major complications. Delayed healing (7 cases, 15.56%), recurrence (4 cases, 8.88%) and deep implant infection with implantation failure (2 cases, 4.44 %) were recorded in PPM group.

Conclusion

Results of this study revealed priority of GBP over PPM for repairing large abdominal wall defects. It is cost-effective, available, easily processed, with good incorporation and has less postoperative complications. The ultrasonographic examination provided a satisfactory tool not only for pre-surgical diagnosis of different abdominal wall defects but also for evaluation of their healing process post-surgery.

Safety Of Lipo-Graft Enriched With Vascular Stromal Fraction Derived From Adipose Tissue For Treatment Of Digital Articular Fibrosis And Ischemic Digital Ulcers Caused By Systemic Sclerosis

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Introduction

Systemic sclerosis (SS) causes functional disability and a poor quality of life because skin fibrosis and its osteoarticular consequences. The current therapeutics are insufficient to prevent these functional outcomes. The local application of adipose tissue-derived Stromal Vascular Fraction (ADSVF) is an alternative. We aimed to evaluate the safety of the administration of the autologous ADSVF in the hands of patients with SS.

Materials & Methods

This was an open-label and prospective clinical trial. We randomly assigned patients diagnosed with SS (ACR 2013) into a control (n=10) and an experimental (n=10) group. Fatty grafts plus ADSVF were applied in fingers, back, and palm of one hand in the experimental group. The mean follow-up of the patients was 6 months. Every patient was evaluated with manual and biomechanical goniometry; Kapandji test; numerical pain rating scale (NPRS); frequency and duration of the Raynaud Phenomenon (RP); Digital percutaneous oximetry; videocapilaroscopy; cell surface markers; and Rodnan, COCHIN, SHAQ, and SF36 scales. Their statistical analysis was with using Student´s t-test or Mann-Whitney rank sum test. Differences were calculated using ANOVA. the statistical differences ($p<0.05$).

Results

The cellular population of SVFAT varied from 39 to 543 x106 with viability from 95 up to 99% . Stem cell markers into the ADSVF was: CD34- in the 0.6%; CD44+ in 87% and CD105+ in 64%. In the experimental group no adverse events occurred during the procedure and the follow up. Compared with the patient status before the intervention, the patients in the experimental group presented lower pain (p=0.029), lower frequency and intensity of the RP (p=0.001) and a lower SHAQ scale (p=0.03). When compared with the control group, the patients in the experimental group trend to an improvement in the overall outcomes, but without statistical significance.

Conclusion

ADSVF administration and lipograft were well tolerated by the patients, lowered the pain, the frequency and intensity of the RP, and increased the hand functionality. However there was not difference with statistical significance between groups, although there was an important clinical improvement in the experimental group. It needs further analysis to be certain about the clinical relevance of this new therapy.

The efficacy of William's Flexion Exercise plus Core Muscle Training Exercise in patients with Spinal Canal Stenosis: A randomized, controlled, trial

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Introduction

Spinal Canal Stenosis is one of the most common causes of pain and muscle atrophy in people over 50 years old. Therefore, the object of this experiment was to compare the efficacy of William's Flexion Exercise plus Core Muscle Training Exercise versus William's Flexion Exercises alone for degree of pain reduction and lower limbs muscle weakness improvement.

Materials & Methods

This randomized clinical trial was conducted on 60 untreated patients aged 50 to 80 years old with spinal canal stenosis grade II and III between March and September in 2019 in kermanshah's red crescent physiotherapy Clinic. The degree of spinal canal stenosis was affirmed by a medical radiologist through magnetic resonances imaging (MRI). 30 Patients were randomly assigned into Experimental Group (EG) as well as 30 patients were considered as Control Group (CG). Experimental Group performed William's Flexion Exercise plus Core Muscle Training Exercise versus William's Flexion Exercises alone in Control Group three times a week under the supervision of a physiotherapist for 8 weeks. Pain reduction was assessed by Visual Analogue Scale (VAS: Grade 0 to 10) and Manual Muscle Test (MMT) (MRC Scale: Grade 0 to 5) was recruited to determine the Power of Muscles at the end of week 4 and week 8 and 1 month after the end of the study in both groups.

Results

42 patients (20 EG and 22 CG) succeeded in completing the training protocol. The statistical analyses proved that Experimental Group showed statistically significant pain reduction (P= 0.001) [The means of VAS scores before (EG:6.6 vs CG: 7.1)and after (EG:3.5 and CG:4.2) exercise sessions] but not significant Muscle Power improvement compared to control group as evidenced by student's t- test[The means of muscle power scores before (EG:3.9 vs CG : 4.0) and after (EG:4.2 vs CG:4.3) the experiment].
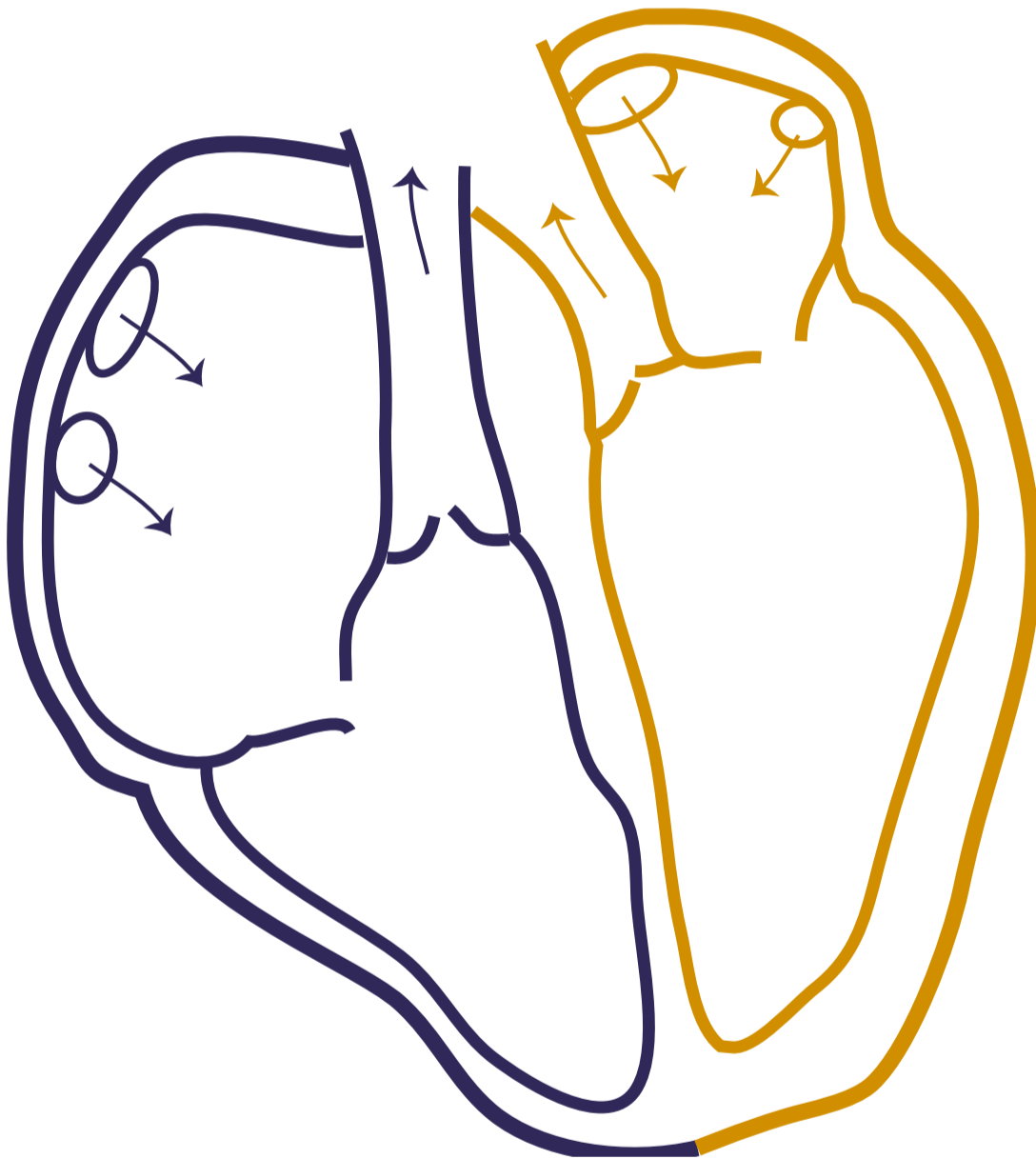
Conclusion

This study did confirm more pain reduction in patients performed William's Flexion Exercise plus Core Muscle Training Exercise simultaneously. Moreover, there was no significant difference between groups in muscle power improvement.

Poster Sessions I
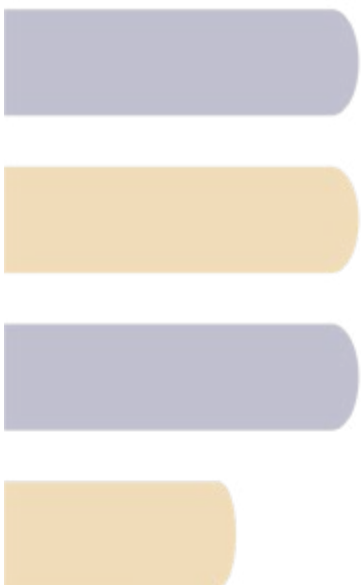
Cardiology I

Presenters:
Mohammad Hosein, M.H.Y (Yazdanpanah)
Said, F. (Fatema)
Joosen, R.S
Shah, K.N. (Kinjal)
Dani, A.S. (Avichal)
Jarosz-Popek, J. (Joanna)
Soplinska, A
Aminorroaya, A. (Arya)

Upper body fat mass was related with prolonged corrected QT interval on the electrocardiogram in men: A Fasa PERSIAN Cohort Study

Mohammad Hosein, M.H.Y (Yazdanpanah)[1], Ehsan, E.B. (Bahramali)[2], Mojtaba, M.F. (Farjam)[2], Maryam, M.M. (Mobasheri)[1], Shiva, S.D. (Dadvand)[1]

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Introduction

Previous studies suggested that obesity and fat mass are associated with QT interval prolongation but the role of different body parts' fat mass is unclear. The association between arms fat mass(AFM), legs fat mass(LFM), trunk fat mass(TFM), total fat mass(FM) and corrected QT interval(QTc) was investigated for the first time worldwide.

Materials & Methods

In this cross-sectional study using Fasa PERSIAN cohort Study data, 3,217 subjects aged 35-70 entered our study. Body fat mass was assessed by bioelectrical impedance analysis and QTc interval calculated by the QT interval measured by Cardiax® software from electrocardiograms and Bazett's formula. QTc > 450 milliseconds in males and QTc >470 milliseconds in females considered as prolonged QTc. The fat mass index (FMI) was calculated using fat mass(kg) divided by the square of height(m). Uni- and multi-variable linear and logistic regression was performed in IBM SPSS Statistics v23.

Results

In males, means of AFM, TFM, and FM were significantly higher in the prolonged QTc group. Also, FMI was higher in the group with longer QTc interval(P-value<0.005). The correlation of QTc interval and AFM(B=0.124), LFM(B=0.107), TFM(B=0.147) and FM(B=0.136) was statistically significant with P-value < 0.001. Also, FMI was at a positive correlation with the QTc interval (B=0.136 P-value < 0.001). All of these correlations remained significant after multi-variable adjusting for conventional cardiovascular risk factors. Surprisingly, none of these relationships between fat mass and QTc interval was not seen in females.

Conclusion

Our study suggested that body fat mass, especially AFM and TFM as upper body fat mass are related to QTc prolongation in males. Our study implies that upper body fat mass may be an independent risk factor for higher QTc interval and consequently more cardiovascular events. The main mechanism of this relationship should be investigated further.

Sex differences in response to cardiac resynchronization therapy

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Introduction

Cardiac resynchronization therapy (CRT) is an established therapy for patients with heart failure with reduced ejection fraction (HFrEF) to improve cardiac function and symptoms. Women appear to respond better to CRT, yet it remains unclear whether this is due to the female sex, or whether sex is a marker of other patient characteristics. In this study, we aim to investigate sex differences in response to CRT and sex-specific predictors of response.

Materials & Methods

This is a retrospective analysis of a prospective, observational, multicenter study in the Netherlands, including 240 patients with HFrEF and a class I indication for CRT. The primary outcome parameters are response to CRT, defined an increase in left ventricular ejection fraction (LVEF), and decrease in left ventricular end systolic volume (LVESV) at 6 months follow-up. The secondary outcome measure is defined as all-cause mortality. All analyses are adjusted for BSA and etiology.

Results

In the entire cohort (36% women), 70% of the women were responders (defined as a decrease >15% in LVESV) at 6 months, compared to 55% of the men (P=0.03). Women showed a greater decrease in LVESV %, LVESV index %, and increase in LVEF compared to men (all P<0.05). Significance was however lost after adjustment for BSA and etiology. In the non-ischemic subgroup (55% women), the response parameters at 6 months did not differ between sexes. In univariable Cox regression analysis, female sex was associated with a 85% lower risk of death (hazard ratio (95% confidence interval) 0.154 (0.020-1.204)), however, this did not reach statistical significance. Similarly, in the non-ischemic subgroup, there was no difference in survival between men and women.

Conclusion

Women showed a greater response to CRT at 6 months follow-up. However, in the non-ischemic subgroup, no differences were found in LV function parameters at 6 months, or survival itself. These results suggest that the non-ischemic etiology, rather than the female sex, is responsible for greater response rates in women treated with CRT compared to men.

Predictors of right ventricular dysfunction in patients with left coronary artery disease

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Introduction

Right ventricular (RV) dysfunction is an independent predictor of mortality in patients with ischemic heart disease (IHD). In addition to RV dysfunction after right coronary artery (RCA) related myocardial infarctions, RV dysfunction is also observed after left coronary artery (LCA) disease. The etiology of the latter, however, remains incompletely understood. The aim of this study is to assess the predictors of RV dysfunction in patients with LCA stenosis.

Materials & Methods

This is a retrospective analysis of 191 patients whom underwent percutaneous coronary intervention of the LCA, cardiac magnetic resonance imaging and echocardiography. Patients with significant RCA stenosis were excluded. 91 patients had a left ventricular ejection fraction (LVEF) below 50% and were divided into a group of patients with RV dysfunction (RV ejection fraction (RVEF) < 50%) and preserved RV function (RVEF ≥50%). 100 matched patients with LVEF ≥50% were used as a control group.

Results

32% of the patients with LVEF ≤50% showed RV dysfunction, in contrast to 2% of the patients with preserved LV function (p < 0.001). In patients with RV dysfunction, RV hypertrophy and dilatation were limited. In case of low LVEF, RVEF was related to LVEF (R = 0.64; p <0.001). RV function was similar in patients with septal and lateral infarctions. RV dysfunction was not associated with mitral regurgitation, tricuspid regurgitation or bundle branch blocks. After correction for age, gender and systolic pulmonary artery pressure, RV dysfunction was independently predicted by LVEF <50% (ß = 0.045; p< 0.001).

Conclusion

RV dysfunction in patients with IHD due to LCA stenosis is independently predicted by low LVEF. The results suggest that RV dysfunction may be related to interventricular mechanical dependency.

Role of Tolvaptan in Heart Failure: A Meta-analysis

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Introduction

Heart failure is a life threatening disease affecting millions worldwide. Tolvaptan is the first FDA approved orally active non peptide vasopressin 2 receptor antagonist to be used in hypervolumeic hyponatremia, heart failure, cirrhosis etc. In clinical trials, tolvaptan is seen to impact short term improvement in increasing water excretion, restoring Na+ and dyspnoea. The objective of the study is to analyse the effects of tolvaptan in existing cases of heart failure.

Materials & Methods

We conducted a database search of the MEDLINE, Embase and Cochrane Central Register of Controlled Trial and RCTs till 1st September 2019 were included after being with matched with inclusion and exclusion criteria. 21 RCTs were included with 7,357 patients receiving tolvaptan and 7,273 patients being the control group. We used the MESH strings such as 'tolvaptan', 'vasopressin V2 receptor blocker', 'acute heart failure', 'acute decompensated heart failure'.

Results

Meta-analysis showed that tolvaptan was associated with a significant reduction in edema (RR = 1.052, 95% CI = 1.019–1.085, p=0.002); body weight (SMD = -0.43, 95% CI = -0.471 to -0.388, p<0.001). On the other hand, it was also associated with significant decrease in serum sodium levels (SMD = 0.678, 95% CI = 0.609 to 0.748, p<0.001). However, there was no significant decrease in all-cause mortality and worsening renal function in heart failure.

Conclusion

Although, tolvaptan may significantly reduce edema and congestive symptoms by decreasing body weight, it has no impact on all-cause mortality and worsening renal function in heart failure.

A Meta-analysis on Clinical Outcomes of Triple anti-platelet therapy versus Dual anti-platelet therapy in patients undergoing Drug-Eluting Stent Implantation

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Introduction

Studies have shown that addition of cilostazol to the recommended dual anti-platelet therapy consisting of aspirin and clopidogrel is more effective in preventing stent thrombosis. However, the usage of cilostazol is limited due to various drug-related side-effects. Hence, the objective was to compare the effects of both regimens on cardiovascular outcomes.

Materials & Methods

A total of 13 RCTs following PRISMA guidelines till August 2019 and matching inclusion and exclusion criteria were collected. The following search strings and MESH terms were used: "TAPT vs DAPT", "cilostazol, drug-eluting stent implantation". The primary end point was major adverse cardiac events (MACE), including all-cause mortality, MI, TLR etc. Stent thrombosis and bleeding were taken as safety end points. RevMan 5.3 was used for appropriate statistical tests. Fixed and Random Effect Model Test was used and $p<0.05$ was considered statistically significant.

Results

Meta-analysis showed that TAPT was associated with a significant reduction in MACEs (RR = 0.631, 95% CI = 0.504–0.789, $p<0.001$); TLR (RR = 0.599, 95% CI = 0.459–0.782, $p<0.001$); TVR (RR = 0.833, 95% CI = 0.698–0.996, p=0.045). However, TAPT recorded significant increase in risk of minor bleeding (RR = 1.937, 95% CI = 1.176–3.190, p=0.009) and drug-discontinuation due to adverse effects. There was no significant increase in major bleeds.

Conclusion

Addition of cilostazol to aspirin and clopidogrel was found to have significantly reduced the incidence of cardiovascular events in patients undergoing DES implantation. However, it was associated with higher rates of drug discontinuation due to adverse effects and increased risk of minor bleeding. Data can be used to initiate the appropriate management and promote guideline-based medical therapy.

Canonical signaling pathways dysfunctions in the development of major cardiovascular complications, the prognostic value of circulating microRNAs and their link to inflammation in diabetic patients

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Introduction

Cardiovascular disease (CVD) is a major cause of mortality among people with type 2 diabetes (T2DM). For this purpose, we performed gene expression profiling (GEP) using plasma samples from patients with T2DM that had developed a major cardiac events during 6 years follow up, compared to patients that had not. We also assessed the prognostic ability of selected circulating microRNAs to predict cardiovascular complication during the follow up.

Materials & Methods

Six patients per group were randomly selected, from 304 T2DM patients participating in a randomized, open-label AVOCADO (Aspirin Vs./Or Clopidogrel in Aspirin resistant Diabetics inflammation Outcomes) study. Plasma RNA was extracted by mirVANA PARIS Kit and quality of RNA was assessed by fluorometric assay. GEP analysis was performed using the Clariom D pico chips, analysed on the Affymetrix platform. RT-PCR was performed in order to validate the miRNAs in 238 patients by using the Taqman universal protocol. MiRNA related to platelet function/antiplatelet treatment were chosen among those with the most relevant modulation between the groups. Independent t test was performed for miRNAs comparison with primary endpoints.

Results

Profiling results showed a significant modulation involved in: i) EIF2 ii) EIF4 and iii) mTOR signaling in the development of cardiovascular complications. A highly significant differential expression was found both at unpaired and paired analysis after matching samples for sex, age and cardiovascular risk profile. MiR-223, miR-126, Let-7e, miR-16, and miR-125a-3p were measured in 238 patients. We found that miR-126 ($p < 0.000$), Let-7e ($p < 0.000$), miR-16 ($p = 0.003$), and miR-125a-3p ($p = 0.001$) were able to predict future occurrence of the primary endpoint. MiR-16 and miR-125a-3p showed week positive correlation with hsCRP levels ($r = 0.190$, $p = 0.005$ and $r = 0.166$, $p = 0.013$, respectively). MiR-223 were also positively correlated with HbA1c ($r = 0.147$, $p = 0.027$).

Conclusion

Our results demonstrate a strong association between dysfunction of key canonical pathways such as EIF2, EIF4 and mTOR signaling pathway and the risk of major cardiovascular complications in T2DM patients. Additionally, miR-126, Let-7e, miR-16, and miR-125a-3p might be useful for the clinical risk assessment during the follow up in high risk patients with chronic inflammatory conditions, like diabetes, reflecting the residual risk to guide their clinical management.

The lack of prognostic biomarker value of gut microbial metabolites, trimethylamine N-oxide in patients with acute coronary syndromes undergoing percutaneous coronary intervention

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Introduction

Myocardial infarction (MI) is the leading cause of mortality among those. Gut microbial metabolites have been implicated as novel risk factors for cardiovascular events. The strength and consistency of associations between blood concentrations of the gut microbial metabolites, trimethylamine-N-oxide (TMAO) and its precursor TMA, with major adverse cardiovascular events (MACE) or death have not been comprehensively assessed. We aimed to quantified associations of blood concentrations of TMA and its precursor TMAO with risks of MACE in patients with acute coronary syndrome (ACS).

Materials & Methods

We assessed plasma TMAO and TMA levels and analyzed the data, biospecimens, and MACEs (myocardial infarction, stroke, need for revascularization, or all-cause mortality) from prospective, observational, multicenter ATLANTIS-SWITCH sub-study to assess its value in 344 consecutive ACS patients undergoing percutaneous coronary intervention (PCI).

Results

Contradictory to the previous publications multivariate analyzes revealed that plasma TMAO levels were not significantly related with MACE (p=0.254), despite, TMA was slightly significantly related with MACE over 365 days [adjusted OR 0,938, 95% CI 0,887-0,992; P =0.025] of follow-up independently of traditional CV risk factors.

Conclusion

Previously, increased plasma TMAO levels were found to be associated with an increased risk of incident MACE. The negative effect of TMAO on the cardiovascular system was demonstrated. However, not all clinical studies have confirmed association between high TMAO and increased cardiovascular risk. Our study shows that elevated concentrations of plasma TMAO metabolite adds to evidence of lack of prognostic value in patients with ACS undergoing PCI. Funding Acknowledgements : This study was financially supported by Ministry of Science and Higher Education. Grant = NN 4.0 = DIR.ZPZSW.640.299.2019/W5

Effects of Treatment with High Dose Atorvastatin before Elective Percutaneous Coronary Intervention on Periprocedural Myocardial Infarction and One-Year Major Adverse Cardiovascular Events; a Randomized Clinical Trial

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Introduction

Some studies have demonstrated that post-percutaneous coronary intervention (PCI) elevation of cardiac enzymes is associated with worse clinical outcomes. Furthermore, it is hypothesized that statins may exert rapid cardioprotective effects via their pleiotropic effects. In this study, we aimed to determine if treatment with high-dose of atorvastatin before planned elective PCI reduces periprocedural myocardial infarction (PMI) or major adverse cardiovascular events (MACE) at follow-up.

Materials & Methods

In this single-blind randomized clinical trial, patients with stable coronary artery disease who were indicated to undergo an elective PCI were studied. We randomly allocated participants to receive 80 mg atorvastatin 12 hours and 40 mg 2 hours before PCI (group A) or 40 mg atorvastatin daily as the routine protocol (group B). Blood samples were obtained before and 24 hours after PCI to measure high-sensitive troponin T. All patients were followed regarding MACE (the combination of death, re-hospitalizations for acute coronary syndrome, and unplanned coronary revascularization) during one year after PCI.

Results

We studied 207 patients, 97 in group A and 110 in group B. The rate of PMI was lower in group A (5.2 %) compared to group B (10.9 %); nonetheless, this 56% relative reduction did not reach statistical significance (OR=0.44, P=0.14; Adjusted OR=0.45, P=0.18). Moreover, the occurrence of MACE was comparable in both groups (11.3% in group A vs. 10% in group B; HR for the occurrence of MACE in group B was 1.20, P=0.67; Adjusted HR=0.67, P=0.43).

Conclusion

Pretreatment of patients with stable angina who were planned to undergo an elective PCI with 120 mg of atorvastatin before the procedure confer them the same benefit as 40 mg routine daily dosage of this statin does in terms of PMI and MACE.

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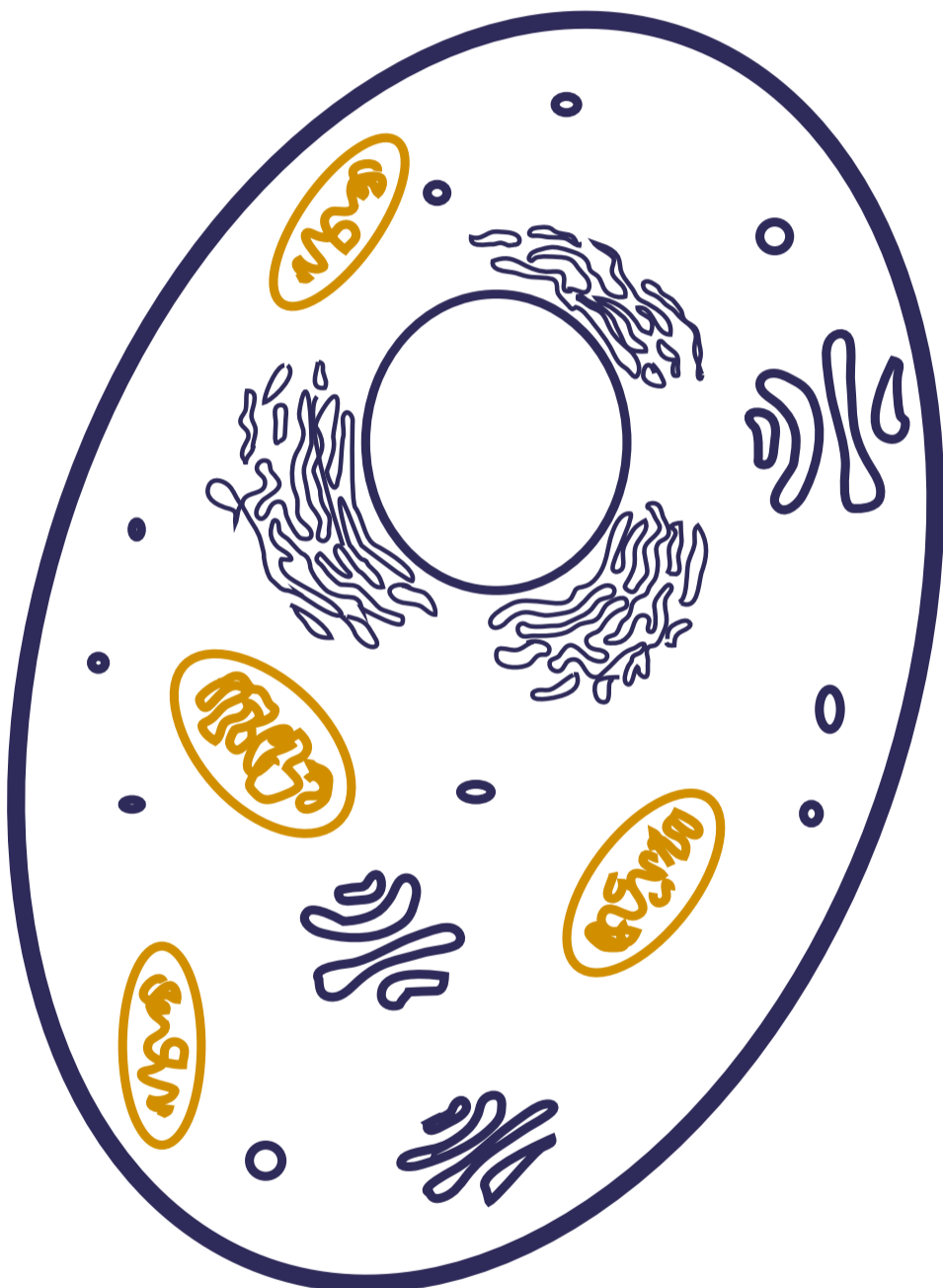
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ArtRD Protein Encoded by an Annotated Long-non Coding RNA Promotes VSMC Phenotype Switching through Transcriptional Regulation

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Introduction

Long non-coding RNAs (lncRNAs) have critical roles in gene regulation through either epigenetic regulation or producing functional small peptides. Dysregulation of lncRNAs have causal effects in pathogenesis in cardiovascular system. Interestingly, we recently discovered that not only small peptides but also proteins can be concealed within annotated lncRNAs.

Materials & Methods

LncRNA microarray was used to identify differentially expressed lncRNAs in the aortae tissue from Spontaneously Hypertensive Rats (SHRs) and normotensive counterpart WKY rats. Open reading frame (ORF) screening software was used to identify peptides hidden in candidate lncRNA2. The direct impact of a 117aa novel protein ArtRD on vascular smooth muscle cells (VSMCs) phenotype switching was characterized by testing contractile gene expression, proliferation and migration. RNA-sequencing was used to test the transcriptome changed by ArtRD. In vivo function of ArtRD was analyzed in ArtRD knockout rats using carotid artery balloon injury. Immune-precipitation followed by LC-Mass Spectrometry was used to find the interacting proteins of ArtRD, which was validated by co-immunoprecipitation and immunostaining.

Results

We identified a highly conserved vascular tissue-specific lncRNA to be significantly up-regulated in the aortae after hypertension development. This lncRNA encodes a 117aa-long protein, which we named ArtRD, being enriched expression in VSMCs nucleus. Expression of ArtRD can change global VSMC gene expression, particularly genes involved in VSMC phenotype switching. Functionally, ArtRD is sufficient to promote the rat VSMC phenotype switching from contractile to proliferative phenotype. While inactivation of ArtRD significantly attenuated VSMC phenotype switching both in vitro and in vivo. Mechanistically, we identified and confirmed ArtRD interacts directly with the C-terminal domain of YBX1. YBX1 knockdown abolished the repression of ArtRD on VSMC contractile gene expression, including a-SMA, suggesting ArtRD and YBX1 serve as co-repressors for VSMC contractile genes. Their interaction regulates VSMC phenotype switching.

Conclusion

We identified a VSMC-enriched lncRNA encoding a protein ArtRD, which induces VSMC phenotype switching through interacting with transcriptional-repressor YBX1. This highlights the possibility that large proteins concealed in RNAs currently annotated as noncoding could have important functions. Targeting both lncRNAs and the protein products generated from these lncRNAs will provide ultimate therapeutic solution for vascular disease.

Effectual delivery of Nef-MPER-V3 fusion protein using LDP12 cell penetrating peptide as a HIV-1 vaccine candidate

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Introduction

Human immunodeficiency virus (HIV) which causing acquired immune deficiency syndrome (AIDS) is one of the main universal health concern. In spite of using antiretroviral treatments, there are no authorized HIV preventative or therapeutic vaccines. The development in using therapeutic proteins is affected by the limitation on permeability and selectivity of cell membranes. Thus, utilizing cell-penetrating peptides (CPPs) as protein transfection reagents or protein transduction domains (PTDs) has been expanded. In addition, heat shock proteins (Hsps) as intracellular chaperones, are extremely immunogenic, causing humoral and cellular responses to viral antigens. Herein, Hsp27 was utilized as an adjuvant to motivate efficient immune responses.

Materials & Methods

The recombinant HIV-1 Nef-MPER-V3-LDP12 gene was prepared in expression vector pET-28a (+) in NdeI/XhoI restriction sites. Then the confirmed plasmid construct was expressed in both Escherichia coli Rosetta (DE3) and BL21 (DE3) strains using IPTG inducer reagent. Following by verifying the protein expression applying SDS-PAGE and western-blotting, the target protein was purified on Ni-NTA agarose column under native and denaturing situations, dialyzed and evaluated by Nanodrop spectrophotometry. For transfection, HEK-293T cells (4 × 10000 cells/well) were seeded into a 24-well plate supplied by complete DMEM medium which was supplemented with 5% FBS. Then LDP12-Nef-MPER-V3, Nef-MPER-V3 as a negative control, Hsp27-GFP-TurboFect and GFP-TurboFect as a positive control were applied to each well. The efficacy of transfection was assessed by western-blotting.

Results

The presence of the gene was confirmed by digestion with XhoI/NdeI as a 825 bp band moved on agarose gel and also sequencing. Moreover, western-blot analysis indicated a desired expression of Hsp27-GFP, GFP, LDP12-Nef-MPER-V3, and Nef-MPER-V3 with the clear bands of ~54 kDa, ~27 kDa, ~37 kDa, And ~35 kDa, respectively. These bands were not observed in the non-transfected cells. Our data showed the significantly expression of fusion constructs in Rosetta (5 mg/L) and poorly in BL21 strain. Also, the fusion protein was accurately purified under denaturing condition in comparison with the native situation.

Conclusion

Briefly, this stable construct (LDP12-Nef-MPER-V3) with high cellular penetrance and low toxicity could be used as a favorable procedure in HIV-1 vaccine strategy, that is sufficiently capable of inducing specific strong immune responses.

Mechanism of aggregation of NPAS3, which is implicated in mental illnesses

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Introduction

Several proteins have been implicated to form insoluble aggregates in the brains of patients suffering from mental illness, including Neuronal PAS domain protein 3 (NPAS3). NPAS3 belongs to the bHLH-PAS superfamily of transcription factors and it is involved in the regulation of neurogenesis, metabolism, and circadian rhythms. It contains three distinct regions: a basic helix-loop-helix (bHLH) region, the PAS domains and a transcriptional activation domain (TAD). The PAS domain contains a V304I mutation which was found to aggregate in postmortem samples of brain of patients with diagnosed with schizophrenia and major depressive disorder, as well as in mammalian and bacterial expression systems.

Materials & Methods

Our research involved overexpression of NPAS3 vectors in neuroblastoma cell culture. Plasmids containing different regions of NPAS3, including mutated NPAS3, were expressed in SH-SY5Y cells. Their expression was confirmed by Western blot, and their aggregation was investigated by fluorescent microscopy.

Results

Previous studies showed that mutated NPAS3 was insoluble in mammalian cells upon overexpression, suggesting it to be aggregating. Our research confirmed that mutated NPAS3 V304I forms visible aggregates in neuroblastoma cell culture, unlike full-length wild type NPAS3. We have also seen that the bHLH1 region is capable of aggregation alone, despite it not containing the mutation. Other tested regions showed no signs of aggregation by themselves. Additionally, overexpression of a combined bHLH and PAS region showed no aggregation, implying that PAS region to have a stabilizing effect.

Conclusion

The V304I mutation in found in the PAS region of NPAS3, but we have now also seen aggregation after overexpression of a non-mutated region (bHLH) which is stabilized by presence of the PAS region. Therefore, our results strongly imply that aggregation could also occur through other mechanisms (if other mutations or cellular stresses interfered with the function of the PAS region). Currently, we are investigating aggregation of NPAS3 in post mortem brains samples. Future research in this field could give some insights into the mechanism of aggregation for other proteins implicated in mental illness.

Cultivation in spheroids of human mesenchymal stem cells increases the expression of vascular endothelial growth factor (VEGF)

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Introduction

Mesenchymal stem cells (MSCs) secrete a huge variety of growth factors, cytokines and other molecules, and accumulating evidence suggest, that this paracrine activity defines their therapeutic effect. One of the most important factors with angiogenic, trophic and anti-apoptotic effects is vascular endothelial growth factor (VEGF). It is known that MSCs with VEGF secretion have a positive therapeutic effect in the treatment of heart attacks and strokes. Therefore, the study of necessary conditions of the MSCs cultivation to enhance the paracrine effect of VEGF has a great scientific and practical importance.

Materials & Methods

We used endometrial mesenchymal stem cells received from three health donors and cultivate them on plastic flasks as monolayer culture and in 96-wells plates with round non-adhesive bottom for spheroids. Viability was evaluated by MTT and Western-blot assays, expression of VEGF mRNA was evaluated with qRT-PCR and its secretion – with ELISA. Wound-healing assay was used to compare the effect of exogenous VEGF and VEGF from spheroid conditional medium.

Results

It was shown that MSCs in 3-5 passages from different donors has different basal levels of VEGF secretion (0 – 120 pc/ml/104 cells). During monolayer cultivation of MSCs, VEGF secretion rapidly decreased. Cultivation of MSCs even on late passages in spheroids increased VEGF secretion up to 1500 pc/ml/104 cells. An increased level of secretion was accompanied by increased expression of VEGF mRNA and transcription factor HIF-1 in spheroids. VEGF production in spheroids increased with an increase in the number of cells in the spheroid (2500 – 30000 cells) and cultivation time up to 7 days. A decrease in serum concentration in the medium to 1% didn't reduce the production of VEGF. Exogenous VEGF (10 ng/ml) increased the viability of MSCs but didn't stimulate proliferation. The conditioned spheroid medium (1%) enhanced MSCs migration in the wound-healing test in the same way as exogenous VEGF, while the conditioned spheroid medium after treatment with the antitumor drug doxorubicin wasn't effective in this test.

Conclusion

Culturing MSCs for 2-7 days in 3D-spheroids increases VEGF secretion and cell viability.

Is tropomyosin one of the critical regulators of cell morphology?

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Introduction

The cell cytoskeleton is similar to the foundation of an apartment building. It defines cell compartments, e.g., cell body, dendrites, or axons in neurons. It is suspected that various populations of microfilaments play a pivotal role in the determination of compartment borders and the cell shape. Recent studies, in turn, suggest that numerous isoforms of tropomyosin (Tpm), an actin-binding protein, can be responsible for microfilaments' diversity. We aimed to understand whether Tpm isoforms modulate cell morphology, have microfilament population-specific localization, and thus regulate cell activities.

Materials & Methods

We used four cell lines (MIN6, 1.1B4, the primary culture of cortical neurons, and glial cells) with overexpression of different Tpm isoforms. Super-resolution microscopy (STORM) and confocal microscopy enabled us to observe the localization of Tpm isoforms fused with self-labelling SNAP- or Halo-tag and to determine changes in the cells' morphology. We also applied various physicochemical methods to study changes in microfilament properties: stiffness by optical trap, stability by temperature-dependent dissociation and Tpm affinity to actin by cosedimentation assay.

Results

Overexpression of various Tpm isoforms led to a significant change in cell morphology: usually rounded 1.1B4 cells with Tpm3.1, 3.5 formed branches or with Tpm1.5, 3.4 built large and not-branched protoplasmic extensions. The same result was observed in three other studied cultures. Protrusions caused by Tpm1.5, 3.4 were similar to stress fibrils – the most stable structures in cells. The formation of these structures was accompanied by the fact that complexes of actin-Tpm1.5 or Tpm3.4 had an increased actin stiffness in optical trap experiments in contrast to Tpm3.1, 3.5. The second part of our work was dedicated to the determination of isoforms localization. We found that isoforms' distribution can overlap: all studied Tpm presented in every cell compartment of neurons. Although the level of isoforms in dendrites or axons was different. The coexpression of two isoforms in neurons showed that their position could slightly vary: several Tpm isoforms tend to localize in the premembrane area (Tpm3.1, 3.4), and others do not present there.

Conclusion

The presented data confirm that Tpm isoforms have specific localization features, affect microfilaments' properties, and thereby contribute to the formation of cell morphology.

Electrophysiological effects of 4-chloro-2-(2-chlorophenoxy) acetamido) benzoic acid (CBA) in canine left ventricular cardiomyocytes

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Introduction

Little is known about the electrophysiological role of calcium activated transient receptor potential melastatin 4 (TRPM4) ion channels in ventricular myocytes. Our earlier results showed the lack of selectivity of 9-phenanthrol, so CBA have been chosen as a new, potentially selective inhibitor. Our aim was to elucidate the effect and selectivity of CBA in canine left ventricular cardiomyocytes.

Materials & Methods

Experiments were carried out in enzymatically isolated canine left ventricular cardiomyocytes most resembling the electrophysiological properties of human ones. Ionic currents were recorded with action potential (AP) voltage clamp tehcnique in whole-cell configuration at 37 °C. 10 mM BAPTA was used in the pipette solution to exclude the potential activation of TRPM4 channels. AP was recorded with conventional sharp microelectrodes. CBA was used in 10 µM concentration.

Results

The value of AP duration measured at 90% of repolarization and its short term variability were significantly reduced by CBA. Moreover, AP amplitude was increased and phase 1 was reduced by the drug. In AP clamp measurements, using either own or canonical AP as a stimulus waveform, CBA-sensitive current contained a small, early outward and mainly a long, inward current. These effects of CBA were mainly reversible upon washout.

Conclusion

Based on our results the reduction of phase 1 might be due to the inhibition of transient outward potassium current (Ito). The AP shortening might be caused by the inhibition of inward currents (delayed sodium and/or L-type current) seen in AP-clamp recordings. CBA is not selective for TRPM4 channels, so similarly to 9-phenanthrol, it cannot be used to test the contribution of TRPM4 channels to cardiac electrophysiology in ventricular cells.

TGF-β stimulation reduces PTPRσ expression in murine neonatal cardiac fibroblasts

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Introduction

Heart failure as a consequence of chronic myocardial ischemia poses a major global health problem. Following myocardial infarction, remodeling is initiated to preserve form and function of the ventricle. TGF-β as an ubiquitarian cytokine influences proliferation, differentiation, migration and apoptosis in different cell types. It is upregulated in the post ischemic heart and regulates fibrosis. The Receptor-type tyrosine-protein phosphatase sigma (PTPRσ) belongs to a subgroup of transmembrane receptor-like PTPs, that function as an interface between the extracellular environment of a cell and its intracellular signaling pathways for cell motility, matrix interaction and apoptosis in the nervous system. We therefore asked if PTPRσ could play a role in myocardial fibrosis.

Materials & Methods

Left ventricular tissue from 25 patients undergoing LVAD implantation due to ischemic (ICM) and dilated cardiomyopathy (DCM) removed to insert the inflow cannula was utilized for analysis of mRNA expression. Five non-failing hearts not accepted for transplantation were used as control (ethical committee MHH approved: Nr 1842-2013). Neonatal cardiomyocytes and cardiac fibroblasts were isolated from 1-3 day old pups (project number GT TSG4(3)). Cells were transfected with scrambled or small interfering RNA targeted at PTPRσ. After stimulation with 10nm TGF-β for 24 hours cells were harvested for RNA- (using Trizol) and protein isolation (using RIPA-buffer). Samples were analyzed by rtPCR (using ΔΔCT-Method). Statistics were performed using paired t-test or Kruskal-Wallis test and Dunn´s Multiple Comparison Test if more than two groups were compared.

Results

PTPRσ was consistently upregulated in human ICM and DCM samples. It was expressed in both murine neonatal cardiomyocytes and cardiac fibroblasts. TGF-β stimulation reduced PTPRσ expression by 47% ($p=0.0159$) in murine neonatal cardiac fibroblasts. SiRNA knockdown for PTPRσ led to a decrease of Col1a1 expression by 42% ($p<0.05$).

Conclusion

PTPRσ seems to be involved in myocardial remodeling by regulating the deposition of extracellular matrix proteins after myocardial infarction and thereby influence fibrosis. Further research is needed to examine the functional and regulatory role of PTPRσ.

Dermatology and Pathology
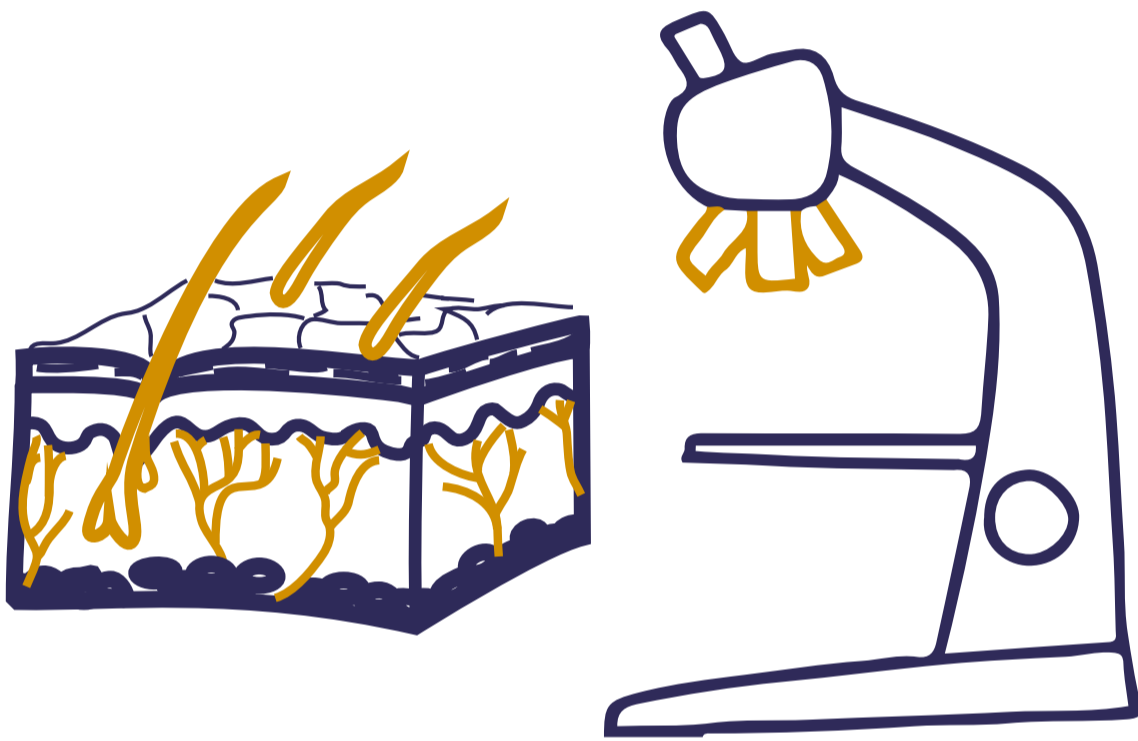
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Contemporary aspects of the epidemiology of paraneoplastic dermatoses

Martynenko, D. (Daria) student[1]

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Introduction

Paraneoplastic dermatoses (PD) are a group of skin conditions caused by the tumor's influence on the metabolism, immune and regulatory systems and can be one of the early signs of cancer. The incidence of PD varies from 7 to 15%. Taking into account the extreme rarity of the obligate PD, it is important to diagnose the facultative PD and the transformation of the quotidian dermatoses against the background of cancer.

Materials & Methods

In 2015-2019 2508 patients aged 27 to 83 years with dermatoses were examined at the Department of Dermatology and Venereology, First Moscow State Medical University and P.A.Herzen Cancer Research Institute. 303 patients had a combination of dermatoses and cancer and were divided into 3 groups: 1st- 147 patients (p) with their first diagnosed dermatoses; 2nd- 85p with chronic dermatoses before diagnosing cancer; 3d- 71p who have been retrospectively observed in 2012-2015.

Results

In all groups the symptoms of chronic dermatoses (eczema, psoriasis, lichen planus(LP), skin itch) had been aggravated 6 months before and within 4-5 months after cancer diagnosis. It was discovered in 42.3% of metastatic colorectal cancer p. (mCRC), 23.1% of the breast cancer p., 22.4% and 12.2% of the p. with cancer of the genitourinary and bronchopulmonary(CBP) systems respectively. There were only 11.8% (n=36) of obligatory PDs (paraneoplastic pemphigus and Dühring's dermatitis), reflecting them for early cancer diagnosis. There was a significant change in symptoms of atopic eczema in combination with breast cancer (42.8%), CBP (25%) and psoriasis in combination with mCRC (19.5%), CBP (16.2%), the development of a verrucous form of LP in 25.3% in the cases with genitourinary cancer. The skin lesion's increase was observed in 86.4%, a doubling of exacerbations in 65%.

Conclusion

A marked decline in the aspects of chronic dermatoses may be a manifestation of the paraneoplastic process and an indirect marker of the development of an oncological process.

Histopathological Changes of Umbilical Cord Blood Vessels in Diabetic Pregnancy

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Introduction

Prenatal and postnatal morbidity and mortality remains a serious problem threat the fetus life during diabetic pregnancy with an increased risk of congenital malformations. The umbilical cord (UC) plays a crucial role of normal growth and development of the fetus. A cross sectional study was designed to identify the main histopathological changes of UC blood vessels in pre-gestational diabetes mellitus (PGDM) and gestational diabetes mellitus (GDM) for maintain normal structure of the UC.

Materials & Methods

A total of (75) UC samples were collected from Aljalaa Maternity Hospital, Tripoli – Libya, from March to December 2017. Out of them (25) were from non – complicated pregnancies, (25) were complicated from PGDM and (25) were complicated from GDM. Segments of UC were taken at 3 cm from fetal, central and placental attachments for each group. The umbilical cords were weighted on an electronic scale in grams. All tissue segments were stained by special stains and examined under light microscope.

Results

The mean weight of UC was larger in PGDM (53.52±17.17) than GDM (50.24±20.56) and non – complicated (34.96±11.20) respectively, (p = 0.000). The tissue segments of central attachments of PGDM in comparison to GDM showed degenerative changes of umbilical blood vessels with an extensive hemorrhage of Wharton's Jelly, thickening basement membrane of UC amniotic epithelium, widely edematous spaced smooth muscle cells, more increased amount of collagen and elastic fibers, glycogen, proteoglycans and glycosaminoglycans molecules. Hugely dilated and discordant umbilical arteries were observed in fetal attachments of GDM.

Conclusion

In despite the enhancements made in the diagnosis and management of diabetes mellitus, histopathological changes of UC blood vessels are still observed in diabetic pregnancy particularly in PGDM.

CD68+ Tumor Associated Macrophages (TAMs) And Their Significance In Gastric Carcinomas

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Introduction

Gastric cancer (GC) is the 5th most common cancer and the 3rd most common cause of cancer related mortality worldwide. Tumor associated macrophages (TAMs) are associated with a diverse group of cancers like myeloma, cancers of the breast, prostate and pancreas. They promote invasion, angiogenesis and thereby, progression of tumor. They also enhance tumor immunity by evading host tumor responses and increasing growth signals. Hence, presence of TAMs is touted to be a poor prognostic factor in cancers. Macrophages express surface antigens like CD68, CD163, CD204, or CD206. Role of TAMs in GCs is being studied in various parts of the world, however, so far no studies have been published from India. We aimed to study the importance of the same in this study

Materials & Methods

A retrospective study was conducted on 60 Histopathology samples. A minimum of four tumor slides per case was scanned and the block with maximum tumor was retrieved and stained with CD68 antibody. The density of TAMs was scored by infiltration density in tumor nests and stroma. All statistical analyses were done using Statistical Package for Social Sciences version 22.0. Chi square test and Fisher's exact test were used to associate the variables. $P<0.05$ was considered statistically significant

Results

TAM infiltration significantly correlated with tumor size > 5cm (p=0.057), tumor infiltrating lymphocytes (p=0.021), pT3/T4 stage (p=0.007), presence of lymph node metastasis (p=0.000), and clinical staging (p=0.009). Follow up was available in 60 cases, of which maximum disease free survival observed was of 25 months. Parameters like age, gender, Laurens classification, WHO grade, lymphovascular invasion, perineural invasion, and distant metastasis were not associated with TAM density.

Conclusion

We assessed the importance of TAMs in relation to other clinicopathological parameters and prognosis. Assessment of TAMs density could be useful in GC, to decide on adjuvant immunotherapy targeting TAMs as it correlates with advanced clinical stage. Future studies on TAMs could help in incorporation of this parameter in routine histopathology reporting of GC biopsy and resection specimens. Along with stage, it could be used as a tool for risk stratification, to predict prognosis, decide follow up and to give any intervention counseling.

Methanolic Leaves Extract of Ficus religiosa (Banyan Tree) Exhibit Complete Diabetic Wound Closure in Streptozotocin-Induced Diabetes Rat Model

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Introduction

Diabetes is a metabolic disease characterized by an uncontrollable increasement in blood sugar levels. In advance, diabetes can cause complications and one of them is an untreatable wound caused by the inhibition of wound healing process. Currently, 80% of Diabetes patient suffering diabetic wound will lose their limbs. Methanolic leaves extract of Ficus religiosa has a potential in diabetic wound treatment, based on HPLC and GCMS analysis it contains various compounds that have antimicrobial, antioxidant, and analgesic effects altogether which beneficial for the treatment. Thus the objective of this study is to observe the efficacy and effective dose of Methanolic leaves extract of Ficus religiosa as diabetic wound treatment in diabetic rat model.

Materials & Methods

This research was using Rats (Rattus novergicus) which divided into 5 groups: negative control, positive control, treatment 1 (ointment 5%), treatment 2 (ointment 10%), and treatment 3 (ointment 15%). Induction of diabetes in rats were using Streptozotocin 40 mg/KgBW IP. All groups were performed with wound excision of 3 cm2. Wound closure was observed four times within 3 days interval, Fasting Blood Glucose (FBG) two times on pre and post-treatment, meanwhile, epithelization and fibroblast at day 12 using microscope. The results were analyzed using mean comparison and correlation in SPSS 18.0 program with confident interval of 95%.

Results

Wound closure observed in day 12 shows significant closure in ointment dose 5% compared with controls and other treatment groups with a final area of 0.18 cm2 (0.956 ± 0.05, p= 0.001). FBG shows diabetic blood glucose value (>126 mg/dL) in all treatment groups and positive control meaning that all groups are in diabetic condition. Epithelisation and fibroblast shows significant development of epithelial formation and fibroblast proliferation in ointment 5% compared with controls and other treatments (p=0.002 and p=0.005).

Conclusion

Based on this study, can be concluded that ointment 5% has the best effect in diabetic wound healing and also the most effective dose of methanolic leaves extract of Ficus religiosa ointment. Despite the great result of ointment 5%, the other doses of 10% and 15% showed negative results and considered as toxic dose range.

Development of topical hydrogel containing triple combination of herbal drugs in a nanoemulsion for the treatment of psoriasis

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Introduction

Nanoemulgel formulations are said to have various advantages over the conventional formulations. The purpose of this study was to develop a stable Curcumin, Resveratrol and Thymoquinone loaded nanoemulsion gel and for topical use in Psoriasis to improve cutaneous deposition and local effect

Materials & Methods

Triple drugs loaded nanoemulsion were prepared by aqueous phase titration method, using oleic acid, Tween 20, PEG 200, and distilled water as the oil phase, surfactant, co-surfactant and aqueous phase, respectively. A nanoemulsion was characterized by quality attributes. Nanoemulgel was prepared by adding 0.5% carbopol 940 as a gelling agent. The topical drug delivery ability of triple drug from the nanoemulgel was evaluated by in vitro permeation and skin deposition study. Nanoemulgel was further evaluated for spreadability, viscosity, and in vitro efficacy in A-431 cell line, and anti-angiogenesis activity through HET-CAM testing. In vivo performance was evaluated on psoriasis model in BALB/c mice induced by imiquimod.

Results

The result shows that optimized nanoemulsion formulation was composed of Smix in the ratio of 2:1. The optimized Nanoemulsion was found to be relatively uniform in size of 76.20 ± 1.67 nm, with a polydispersity index (0.12 ± 0.05). The nanoemulgel showed improved in vitro permeation ability with better drug deposition capacity compared to triple drug solution and gel. The nanoemulgel exhibited desirable spreadability with sustained release pattern (biphasic). A-431 cell line studies exhibited higher % of growth inhibition of drug-loaded NE as compared with the triple drug solution and blank formulation. It is also evinced good antiangiogenic by inhibiting blood vessels formation through HET-CAM testing which manifested an antipsoriatic potentiality. Imiquimod induced psoriatic BALB/c mice revealed significantly higher anti-psoriatic activity of nanoemulgel as compared to free drugs solution and marketed formulation. The developed formulation showed negligible skin irritation despite increased penetration into the skin.

Conclusion

Results indicate that in the treatment of psoriasis, the triple combination of herbal drugs in a Nanoemulgel could be a potential topical formulation.

Evaluation of mismatch repair (MMR) proteins and human epidermal growth factor receptor 2(HER2) expression in hepatobiliary cancers: Our experience from a tertiary care hospital in Western Maharashtra, India

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Introduction

Biliary tract cancer is an uncommon cancer type with an overall poor prognosis and limited therapeutic options. Cancers of biliary tract include adenocarcinomas of gallbladder, ampulla of Vater, and cholangiocarcinomas. These malignancies are often diagnosed late due to their non specific symptoms and slow growth. Microsatellite instability(MSI) results from a build up in mutations at microsatellite sequences due to insufficiency of DNA mismatch repair (MMR) proteins, and is complimentary for immune modulating therapy. We aimed to retrospectively study the prevalence of DNA mismatch repair function and HER2 by immunohistochemsitry(IHC) in cancers of biliary tract.

Materials & Methods

This was a retrospective cross-sectional study carried out in the department of Pathology at a tertiary care hospital in Western Maharashtra, India. Archival formalin fixed paraffin embedded blocks of patients who were diagnosed to have hepatobiliary cancers from 01 Jan 2017 to 31 Dec 2019 were retrieved and stained for MMR proteins (MSH2, MSH6, MLH1 and PMS2) and HER2 by IHC. Slides were studied for retained nuclear signal in MMR proteins with normal cells and lymphocytes acting as internal controls. The current guidelines for MSI IHC screening and HER2 assessment in colonic and gastric cancers respectively were followed.

Results

Among a total of 26 archival blocks studied, 8/26 patients (30.8%) had gallbladder carcinomas, 13/26 (50%) and 5/26 (19.2%) had intrahepatic and extrahepatic cholangiocarcinomas respectively. HER2 expression was score 0 in all 26 cases. Staining for MSI markers(MSH2, MSH6, MLH1 and PMS2) showed expression of all MMR proteins in 16/26(61.5%) cases. Deficient expression of at least one MMR protein was seen in 10/26(38.5%) cases. All of these 10 patients were more than 60 years of age, thus signifying more loss of MSI associated with increasing age. Deficient PMS2 expression was most frequent (7/26;26.9%), followed by MLH1 (4/26; 15.4%). MSH2 and MSH 6 were found expressed in all cases.

Conclusion

These findings support that HER2 testing may not be indicated in biliary tract cancers. Deficient MMR protein expression in 38.5% cases highlights the potential importance of immunotherapy in these patients. However, the findings in the present study need to be supported with larger studies including molecular methods.

Histopathological Study of Carcinogenic effect of formaldehyde in Renal Tissue in Rats

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Introduction

Formaldehyde is radical methylene glycol and monomeric hydrate in diluted solution. It is found in multiple natural, medical and industrial products. It has been proved that Formaldehyde can produce toxic or metaplastic changes to several rat tissues in vivo. However, it is controversial that it can cause carcinogenic effect on renal tissue. The aim of the study is to determine the carcinogenic effects on renal tissue by exposure to formaldehyde.

Materials & Methods

A 2-weeks-old experimental study on 36 Sprague dawdle rat, divided to four groups study. A novel grouping method had been used according to literature review in which divided the rats to two control and two formaldehyde groups. Physical parameters will be measured weekly and sacrifice of the rats done at end of the study for histopathological examination. Data on body weight was evaluated by a one-way analysis of covariance. The histopathological changes were examined by Fisher's exact probability test "(two-sided). Ethical approval was taken from IRB, College of medicine, King Faisal University. Strict pain management plan was kept during the period of the study.

Results

Histologically, there was multiple changes observed such as loss of orientation of glomerulus, Intratubular vessels congestion, disappearance of bowman spaces, at places tubules are swollen, vacuolization and about to disappear and tubule are thick and disturbed in comparison with control group. Gross examination in formaldehyde group shows yellowish pigmentations in both male and female skin associated with significant weight reduction and loss of apatite and body built in comparison to the control group.

Conclusion

Formaldehyde do cause multiple histological toxic changes on short term exposure to formaldehyde. However, it can cause preneoplastic changes on long term exposure which will end up by carcinogenic transformation.

Findings that has been observed upon histopathological study of a two-week-experiment. Although it needs more time to approve the hypothesis. We recommend to increase the period of exposure to formaldehyde with keeping pain management plans into consideration. Further methods of examination is recommended to end up with accurate results to be recorded.

Endocrinology
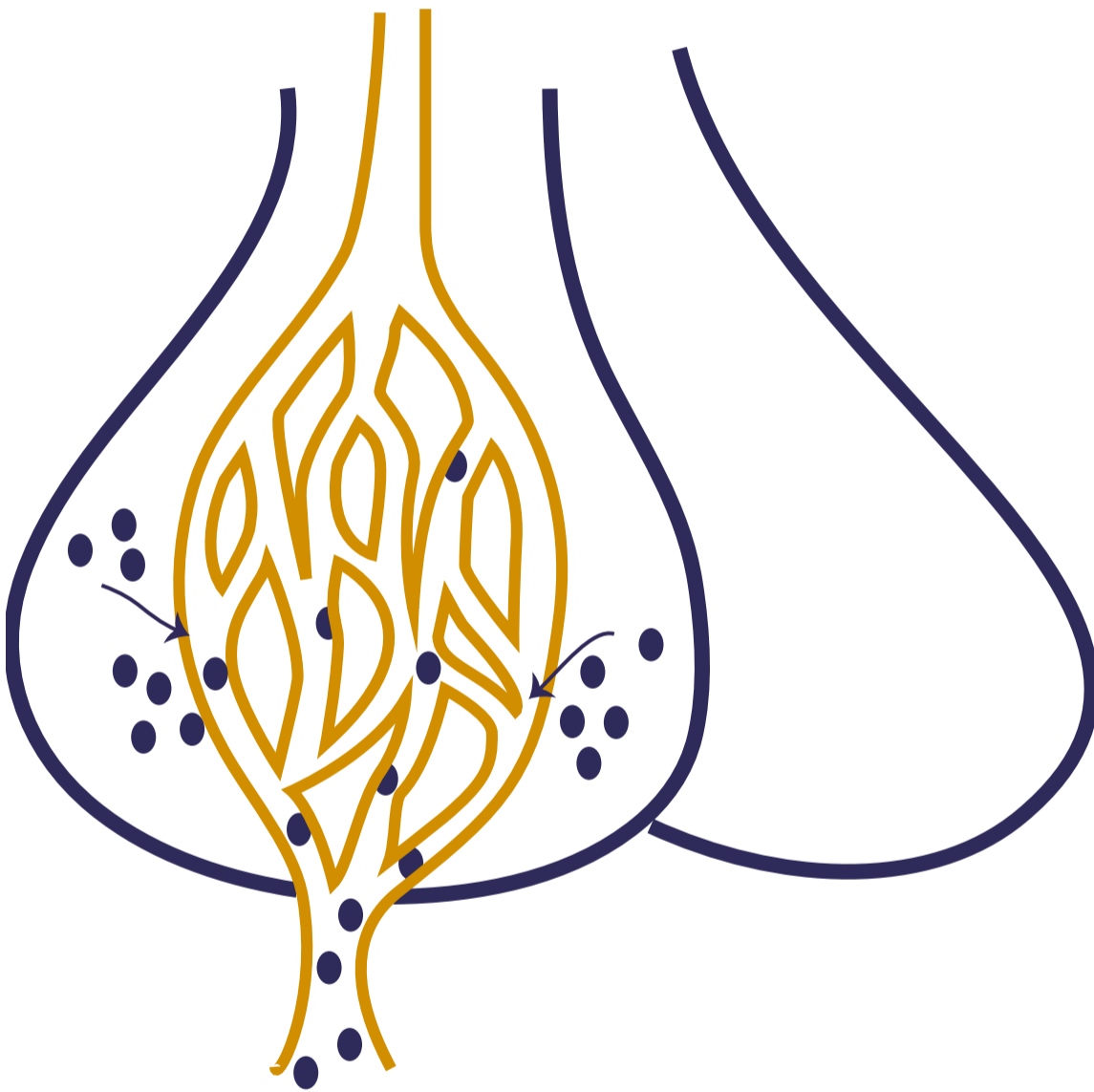
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Glycemic control influence on psychological status of patients with diabetes mellitus

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Introduction

The modern concept of managing people with DM perceives this disease as a «lifestyle» which they have to adjust to, using internal sources in order to compensate for the available disruptions and to achieve better clinical, social and psychological prognosis. The aim of the study is to evaluate the psycho-emotional characteristics of patients with DM, depending on the glycemic control (assessed by the level of HbA1c) and to determine whether patients should be screened for psychological disorders.

Materials & Methods

Patients with both T1DM and T2DM were analyzed (n=80), mean age 59 ± 11.2, mean duration of diabetes – 8.8 ± 5.48, male/female ratio 54.5%/45.5% (43/37). (T1DM – 27% (n=21), T2DM – 73% (n=59). The following tests were used to assess the psychological status of the patients: 1) method of the assessment of attitude towards disease developed in V.M. Bekhterev Research Psychoneurologic Institute, Sankt-Peterburg; 2) SF-36 to evaluate the health-related quality of life (HRQoL); 3) The Minnesota Multiphasic Personality Inventory (MMPI), 4) Patient health questionnaire – 2 (PHQ-2).

Results

Patients with good glycemic control show better results of psychological adjustment and positive attitude towards disease ($p < 0.05$). Patients with average glycemic control show worse results of psychological adaptation and lower level of HRQoL ($p < 0.05$). Patients with bad glycemic control show a high level of depression, negative attitude towards disease, and the lowest level of HRQoL. Hyperglycemia is associated with the anxiety of diabetic patients ($p < 0.05$). There were no significant associations between age, sex, diabetes types, HbA1c levels, duration of diabetes and the results of PHQ-2 ($p > 0.05$).

Conclusion

There is a tight relationship between the level of glycemic control and the psychological status of the patients, therefore the management of diabetes should include psychological aspects to improve the psychological well-being and health-related quality of life. However, our study shows that PHQ-2 is not sufficiently sensitive to be integrated into the clinic.

The interaction of COX-2 and pyroptosis mediates high glucose injury of MC3T3-E1 Osteoblasts

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Introduction

Diabetic osteoporosis is a disorder of bone metabolism due to long-term high glucose injury, in which osteoblasts play a critical role. Necroptosis and COX-2 have been determined as pathways of high glucose injury other cells, so we hypothesized that the interaction of both pathways also contribute the malfunction and decreased survival of osteoblasts due to high glucose.

Materials & Methods

Different levels of glucose is used to treat MC3T3-E1 cells to induce COX-2 and neroptosis, while COX-2 and necrosis were reduced by pharmaceutical inhibition of NS398 and Neccostatin-1 respectively. The cell viability was determined by CCK-8 assay. COX-2, RIP1, RIP3 expression were measured by Western blot. PGE2 expression was detected by ELISA. The intracellular level of reactive oxygen species (ROS) were detected by 2′,7′ -dichlorfluorescein diacetate staining followed by photofluorography. Mitochondrial membrane potential (MMP) was examined by rhodamine 123 staining followed by photofluorography. The alkaline phosphatase(ALP) level was determined by ALP assay kit. The number of mineralized nodes is examined via alizarin red staining.

Results

After the MC3T3-E1 osteoblasts were treated with 45 mmol/L glucose 24 h, the expression levels of COX-2, RIP1, RIP3 proteins and the levels of PGE2 were significantly increased. In addition, treatment with 45 mmol/L glucose causes decreased cell viability and a series of injury including increased ROS generation, loss of MMP and reduction in the differentiation and mineralization(evidenced by the decrease in ALP activity and the number of mineralized nodes. However, cell viability increased significantly and all of the above effects were reversed with both NS398 and Necrostatin-1. In addition, the blockage of COX-2 via NS398 can decrease the expression of RIP1 and RIP3, while Necrostatin-1 can also reduce the expression of COX-2 and PGE2.

Conclusion

The interaction of COX-2 and necroptosis mediates high glucose-induced injury in MC3T3-E1 Osteoblasts.

Effect of hormonal supplementation on pain tolerance in women

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Introduction

Female gonadal hormones influence pain sensitivity.Oestrogen strongly influences nociceptive actions, whereas progesterone prevents neuropathic pain. However, there is little evidence on direct effect of hormonal based drugs on experimental pain response. Therefore the aim of the study is to analyse the difference in response to pain stimulus in terms of - pain threshold, pain tolerance, pain intensity, pain unpleasantness between women on OCP pills, normal menstruating women and age matched men using cold pressor test.

Materials & Methods

Total of 50 females (20-35 years age group) on COCP pills, age matched 50 normal menstruating women and 50 healthy males were enrolled in the study. Cold pressor test was used as a stimulus source. The participants were instructed to hold their least dominant hand in the water bath (maintained between between 0°C and 2°C) as long as possible and were requested to inform the first sensation of pain which denoted the participants' pain threshold. Time from pain threshold to the point where participants could no longer cope with pain and indicate stop, was recorded as pain tolerance. At this point participants were directed to note pain intensity and unpleasantness on the visual analogue scale.Statistical analysis of data was done using standard SPSS software. Data was represented as mean standard deviation. Chi-square test was done and p values < 0.05 were considered significant.

Results

Average pain tolerance was significantly (p<0.00) higher in women on COCP therapy compared to naturally menstruating women. But men and women on COCP pill therapy do not differ significantly in average pain tolerance. The average pain threshold did not differ significantly between any age groups. The average pain unpleasantness was less in females taking hormonal pills compared to men and naturally menstruating women establishing the role of increased levels of sex hormones in reducing the discomfort and unpleasantness. There was no significant difference in average pain intensity between men and normal women but it differed significantly between normal women and women on COCP therapy.

Conclusion

The use of COCP affects the pain reporting of subjects and this should be made a note of while eliciting pain sensation in clinical practice.

No significant correlation exists between vitamin D and glycated hemoglobin (HbA1c) in type 2 diabetes mellitus patients: A cross sectional study

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Introduction

Globally, an estimated 422 million adults are living with diabetes mellitus of which 90% suffer from type 2 diabetes. Vitamin D is known to perform numerous functions in our body including regulation of insulin secretion.Therefore, vitamin D can be postulated to have a relationship with insulin resistance. However, the causal relationship between vitamin D levels and type 2 diabetes is not readily established and available clinical data is largely inconsistent, warranting further studies. We aimed to assess vitamin D levels in patients with type 2 diabetes and to correlate them with the levels of glycated hemoglobin (Hba1c).

Materials & Methods

The current cross sectional study included 100 patients with type 2 diabetes mellitus being treated at an outpatient clinic of a tertiary care hospital. Patients with known medical conditions and on medications affecting vitamin D levels were excluded. Estimation of vitamin D was done using ELISA based on principle of competitive binding and that of glycated hemoglobin (HbA1c) done using ion exchange chromatography. The data was analyzed using t test.

Results

Out of the 100 diabetic patients, 54% patients were having sufficient vitamin D levels (30-100ng/ml), 22% had vitamin D deficiency (< 20ng/ml), 9% had vitamin D insufficiency (20-30ng/ml) and 15% had toxic levels of vitamin D (> 100ng/ml). The levels of vitamin D ranged from 5- >150 ng/ml with a mean of 55.84 ± 41.730 ng/ml. No statistically significant correlation was found between vitamin D & glycated hemoglobin (HbA1c) levels (r= -0.52 & p= 0.610).

Conclusion

The results of the study reflect that majority of patients were vitamin D sufficient with a significant minority having vitamin D toxicity. It can also be concluded that no statistically significant correlation exists between vitamin D and glycated hemoglobin (HbA1c) levels. Further studies using larger patient cohort are needed given varying conclusions by different authors.

Association of visceral lipid accumulation derived by Lipid Accumulation Product (LAP) with urine albumin creatinine ratio (UACR) in type-II diabetes mellitus

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Introduction

Diabetes is the seventh leading cause of death in India, rising from the eleventh rank in 2005. Diabetic complications including the vascular abnormalities seem to be correlating with visceral obesity and insulin resistance The study was carried out by using LAP index to measure visceral fat as a simple bedside, cost-effective tool to highlight an association of visceral obesity with urine albumin excretion rate in diabetic patients. Though previous studies have highlighted the association of visceral fat with various insulin-resistant states, there is a dearth of studies regarding the association of LAP index as a marker for visceral adiposity and microvascular complications of type-2 diabetes mellitus in the form of increased UACR.

Materials & Methods

In this cross-sectional study, 38 subjects were recruited from the out-patient department. LAP was calculated with the following formula: (Waist Circumference-65) x Triglycerides for males, (Waist Circumference-58) x Triglycerides in females. Data of the study was compiled in a master chart prepared in MS Excel 2010. Statistical analysis was performed using SPSS software (2019 version).

Results

This is the Preliminary result obtained on the available data. Linear regression analysis was between LAP and UACR which was found out to be $r^2=0.033$ was obtained which is very low to be considered significant to evaluate the beta coefficient. Using Spearman's correlation LAP was correlated with UACR, for males (p=0.063, r=0.375) and for females (p=0.314, r=-0.276). The value for LAP is t(28.850)=-0.990, p=0.330; UACR is t(20.486)=1.047, p =0.307.

Conclusion

Association of declining renal function with LAP is better than other obesity indices indicated. A study conducted in China was suggestive of a positive correlation between chronic kidney disease and LAP in non-diabetic patients. A similar pattern of positive correlation was observed between UACR with LAP in diabetic patients in this study. A larger set of data is being collected to arrive at a conclusive result.

Evaluation of Flash Glucose Monitoring technology on summer camp

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Introduction

The Flash Glucose Monitoring (FGM) technology offers opportunity to perform frequent non-invasive measurements of interstitial fluid glucose concentration rivals current standard of self-performed blood glucose monitoring (SMBG) for patients with type 1 diabetes (T1D). Recently, a new generation of FGM sensors has entered the market. It offers better accuracy of measurements than the previous generation and is one of the few systems approved by FDA as equivalent to SMBG for clinical decision making. However, its superiority has not been proven in real-life conditions. It is possible that additional uncontrollable factors might diminish the between-generation improvement and prevent replacement of SMBG with FGM.

Materials & Methods

During two summer camps for youth with T1DM in 2016 and 2019 participants were equipped with FGM devices –FreeStyleLibreA and B respectively (FSL-A, FSL-B).Subsequently, 8-point glucose profiles were recorded on the chosen days, with measurements being performed both by SMBG and FSL (within 1 minute). All measurements were overseen by medical staff. The accuracy of FSL versus comparator glucose meter was assessed in terms of mean absolute relative difference (MARD) and clinical surveillance error grid (SEG). Additional clinical factors during measurements (physical activity, glucose change trend, pre- and post-meal conditions) were recorded.

Results

We analyzed 1655 FSL-A/SMBG pairs and 1796 FSL-B/SMBG pairsfrom 78 and 58 usersrespectively (mean age – FSL-A: 13 +/-2.3 y.o., FSL-B: 13.8 +/-2.3 y.o., $p=0.0549$; mean HbA1c – FSL-A: 7.6 +/- 0.8%, FSL-B: 7.5 +/- 1.1%, $p=0.6371$).12 children participated in both camps. FSL-B sensors exhibited similar bias to FSL-A (-7.6+/- 11.8 mg/dl vs -6.5 +/- 8mg/dl, $p=0.5240$) but lower MARD (11.3 +/- 3.1% vs 13.7 +/- 4.6%, $p=0.0003$) and standard deviation of errors (20.2 +/- 6.7 mg/dl vs 24.1 +/- 9/6 mg/dl, $p=0.0090$).They also provided significantly more results in class A or B risk categories of SEG (97.6% vs 86.4%, $p=0.0012$). However, FSL-B demonstrated significantly worse accuracy when glucose concentration was falling rapidly (> 2mg/dl/min).

Conclusion

New FGM system provides better accuracy than the previous generation when used by children and adolescents with T1D in real-life conditions. However, in specific clinical scenarios the FGM measurements should still be verified with SMBG.

Can probiotic supplements improve complications in diabetic nephropathy? a systematic review and meta-analysis

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Introduction

Diabetes is the epidemic of the era due to its growing prevalence globally. One of its most prevalent complications and the leading cause of end-stage renal failure is diabetic nephropathy. Several studies investigate lifestyle interventions as therapeutic strategies to enhance the renal performance in diabetic patients. Probiotic supplements consumption is one of these strategies. The aim of this meta-analysis is to evaluate the effect of probiotic supplementations as soy protein consumption on the kidney function in diabetic patient with renal impairment.

Materials & Methods

We searched four databases (PubMed, Scopus, Web of science (WOS) and Cochrane Central Register of Controlled Trials (CENTRAL)) from inception till 11 July 2019. We included studies reporting safety and efficacy of probiotic or synbiotic supplementations on the kidney function in diabetic patients with renal disorders.

Results

Our search strategy identified 16 eligible studies (n = 263) comparing the use of probiotic proteins or soy protein to conventional proteins or placebo. Noticing that after qualitative synthesis some of these studies weren't included in the meta-analysis. We used either fixed- or random-effects models in quantitative synthesis of the eligible studies accounting for clinical heterogeneity. Pooled data revealed that probiotic supplements or soy protein consumption significantly improved the renal profile represented in BUN (MD= -1.23; 95% CI: -2.75,0.29; P =0.11), Creatinine levels (MD= -0.17; 95% CI: -0.39, 0.04; P =0.12) and GFR (MD=1.67; 95% CI: -1.63, 4.97; P =0.32). In addition, Serum CRP levels (MD= -1.55; 95% CI: -2.19, -0.92; P < 0.00001) and MDA changes (MD= -0.78; 95% CI: -0.98, -0.59; P < 0.00001) has decreased which reflects enhancement in the oxidative profile. Insulin serum level has markedly decreased (MD= -3.87; 95% CI: -7.51, -0.22; P =0.04) compared with the control group. Lipid profile was also affected with increased HDL levels (MD=2.86; 95% CI: -0.04, 5.75; P =0.05) and decreased total cholesterol (MD= -6.32; 95% CI: -13.16, 0.53; P =0.07).

Conclusion

The results demonstrate the significant role of probiotic supplements or soy protein consumption in improving the renal function and cardiovascular risks in diabetic patients with nephropathy. Further studies are needed to assess the management of probiotic supplementations in those patients.

Genetics
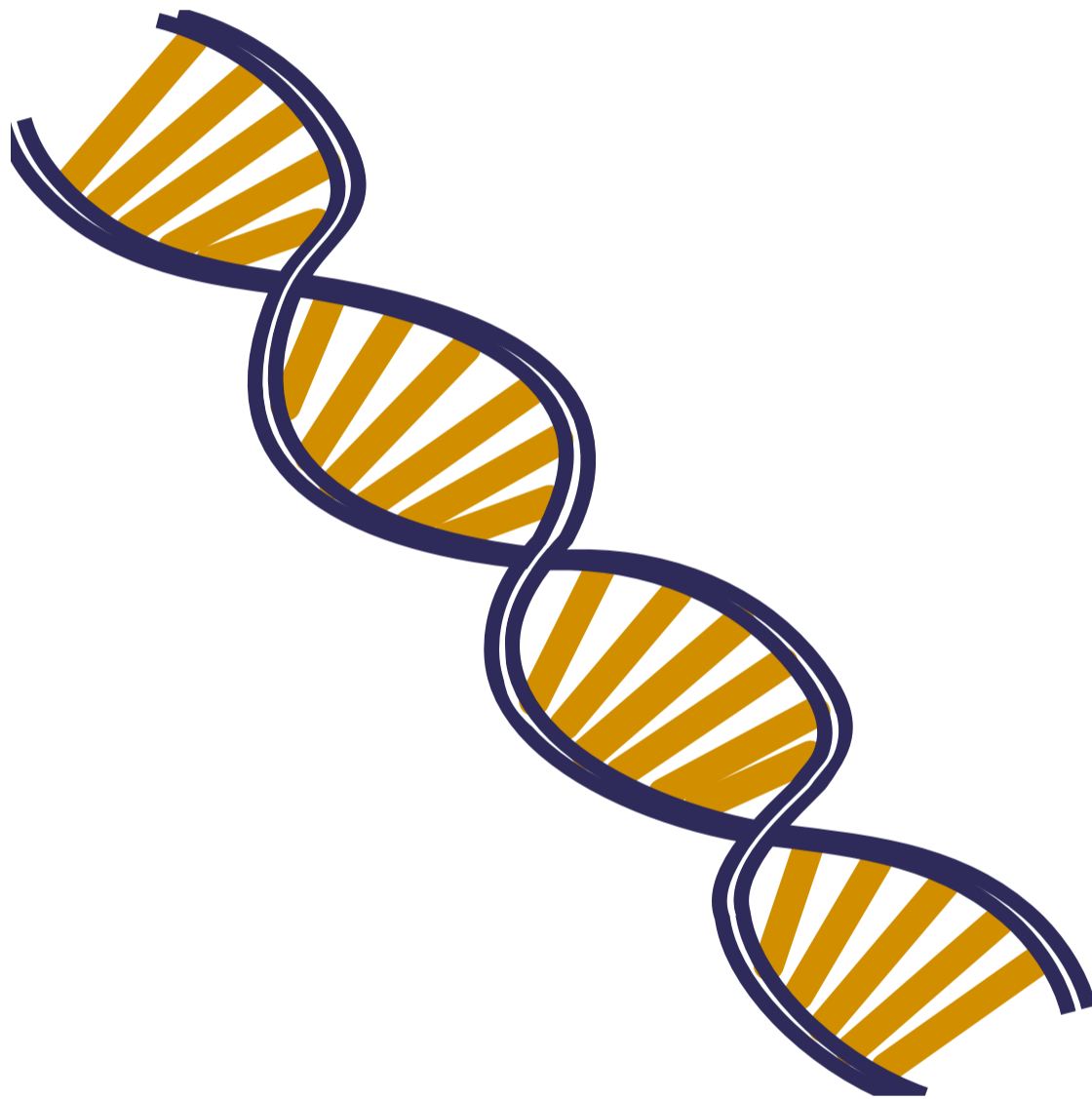
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Hepatitis B virus X protein induce apoptosis in human embryonic stem cells but not in the stem cell-derived hepatocytes

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Introduction

Hepatitis B virus (HBV) were detected in early human embryos from in vitro fertilization couples with HBV. We do not know whether HBV will affect cell fate of early human embryos or not. Hepatitis B virus X protein (HBx) played an important role in HBV replication and was reported as an apoptosis effector. Therefore, we studied the effect of HBx in human embryonic stem cell (hESCs) and stem cell-derived hepatocytes. Unexpectedly, we found HBx induced apoptosis in hESCs but not in stem cell-derived hepatocytes, indicating a novel mechanism of self-protection of human embryo against HBV.

Materials & Methods

Inducible expression of HBx was labeled with EGFP protein. The effects of HBx on hESCs and hepatocyte-like cells were detected by WB, IF, RNA-seq, crystal violet staining and living cell imaging.

Results

After HBx expression for 20 h, hESCs showed significant apoptotic bodies. All HBx-expressed hESCs died after 5 Days. The toxicity of HBx to hESCs was significantly reduced by knocking out DDB1 or inhibiting Caspase. In addition, we also found that this is also related to the GSK3β and p38 pathway. However, HBx expression did not kill cells while hESCs differentiated into hepatic progenitors, fetal hepatocytes or more matured hepatocytes. HBx was observed no cytotoxic effect in hepatoma cell line HepG2, renal epithelial cell line 293T, and cervical cancer cell line Hela.

Conclusion

HBx has significant toxicity in hESCs, but not in hepatocytes like cells and hepatoma cell lines. The embryonic toxicity caused by HBx is related to DDB1, GSK3β and p38 pathway. This finding provided the first proof that HBx would mediate human embryonic lethality.

Robust and Efficient Endoderm Induction from Human Pluripotent Stem Cells by Exclusion of Mesoderm Fates

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Introduction

Embryonic stem cells (ESCs)-derived hepatocyte-like cells (HLCs) are promising in disease modeling, drug screening and cell-based therapy. Although different methods have been established to differentiate ESCs to HLCs, there are still drawbacks of these methods in early Definitive Endoderm (DE) formation. Therefore, the aim of our study is to optimize the method for DE and HLCs differentiation.

Materials & Methods

We examined various combinations of small molecules and established an optimized method for DE induction. The improvement of DE formation was verified by detecting stage-specific markers using qRT-PCR, IF, WB and FACS. The improvement of HLCs were confirmed by examination of cytochrome P450 activity, glycogen storage, indocyanine green staining, drug metabolism and Hepatitis B Virus infection.

Results

Compare with previous methods, our method produces more pure definitive endoderm (DE), with higher endoderm, lower mesoderm and less pluripotency expression. This tendency still shows in later differentiation stages (DAY8/14/18). HLCs derived from our new method presented more matured characters, sensitive innate immune response and permission of HBV infection.

Conclusion

In summary, we found a novel method for DE formation, and the HLCs derived from this method can be served as model for further study such as viral infection, host-virus interaction, and drug screening.

Study of the tridimensional structure of DNA aptamers using to detect prostate cancer biomarkers

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Introduction

Since the discovery of riboswitches DNA or RNA sequences have been used to structural recognition of a different kind of complexes biomolecules. Nucleotide sequences can acquire 3d spatial conformation without losing its capacity to hybridize to a complementary sequence. Selecting and producing of single strain DNA sequence (aptamer) requires an appropriate design to a DNA library that depends on the kind of molecular target. We study aptamers to prostate cancer biomarkers due to the increase of the incidence of this disease in the world and the need for rapid and cheap detection systems that could adapt to new promising kinds of molecular targets. Initially, we choose PSA and PCA3 (protein and LnRNA respectively) biomarkers to design library of random ssDNA sequences for selection and posterior attach in modified serigraphy electrodes.

Materials & Methods

Reported ssDNA sequences for PSA were aligned using the Clustal W algorithm to identify conserved sequences and compared number of base pairs and 3D structure. This information will permit create a DNA library for SELEX selection. PSA aptamer and PCA3 complementary DNA will be attached to gold nanoparticles electrodeposited on carbon-based screen-printed electrodes. After, we evaluated specificity, Kd and detection limits to fix parameters and then transfer this methodology to portable devices.

Results

We found a central region composed of 23 nucleotides in different aptamers. However, a change of three or more nucleotides in 3' or 5' induce a 3D reorganization of aptamer (RSM > 11.88). This condition could affect sensitivity and selected recognition of PSA. These results added to DNA-Protein docking analyses will help to improve the specificity and sensitivity of PSA aptamer what will be used in screen printed electro sensors.

Conclusion

Studies of tridimensional organizations of aptamer help to understand the influence of nucleotide sequences in 3D aptamer conformations and will use to improve sensibility and specificity to detect assays.

Diagnostic Exome Sequencing Identifies 5 Novel Mutations Associated with Autism Spectrum Disorder: Implications for Genetic Counseling and Clinical Diagnosis

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Introduction

Autism Spectrum Disorder (ASD) includes a wide range of complex neurodevelopmental disorders with continuum phenotypic spectrum characterized by deficits in three domains: social skills, communication, and repetitive behaviors or restricted interests. For the time being, ASD is a term commonly designates to this group of highly heterogeneous and multifactorial diseases. The present study aimed to describe a case series of children with autism spectrum disorders (ASD) that have also the presence of other problems. They have been assessed by Whole Exome Sequencing (WES) in consanguineous families.

Materials & Methods

Before 15 families met our Clinical, laboratory, and primary imaging investigation filtering criteria, 30 families suspected to autism referred to Clinic of Medical Genetic at The Genomic Research Center (GRC), Shahid Beheshti University of Medical Sciences (SBMU) recruited. To find the genetic causes of disease Whole Exome sequencing was employed.

Results

Whole exome sequencing identifies the novel homozygous missense variants in the IQSEC2 (c. 1637G > A/ p.W546X), CHKB (c. 382G > T/ p. E128X), SETD2 (c.2096A >G/ p.D699G), FOXG1 (c.563C > A/ p.A188E, and DMD (c.631T>A/ p.L211M) gene in the proband. Segregation analysis depicted that parents carried these mutations in the heterozygote state. Therefore, the overall diagnostic yield of WES in our study was at least 33%. In silico analysis of the variant like DANN, FATHMM, SIFT, Mutation taster and things of that nature supported its pathogenicity and disease causing. 10 other families did not find any suspected variant (2 of them), did not confirm (5 of them) or is on the confirmation Process. FOXG1 and IQSEC2 get High Confidence score in Simons Foundation Autism Research Initiative (SFARI) and related to Rett and Rett like syndrome. CHKB and DMD, both associated autism as long as muscular dystrophy. SETD2 reach high confident score in SFARI for autism and causes luscan-lumish syndrome.

Conclusion

According to heterogeneity of this complex spectrum of disorders, the current study reports five new novel homozygous missense variants. Our experience with our first 15 WES cases in ASD may suggest proband-only WES testing as a first tier test and help to improve directed production for targeted panel sequencing for this genetically heterogeneous disorder.

The role of different DNA repair pathways in healthy ageing

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Introduction

Aging is the primary risk factor for most chronic degenerative diseases, and so the aging population presents a massive global healthcare challenge. Age related pathology is driven by the loss of effective DNA repair. However, it is likely that not all repair pathways contribute equally to this effect. Therefore, this study aimed to define which DNA repair pathways are most important to healthy aging.

Materials & Methods

C.elegans was used as an animal model, with wild-type (N2) and deletion mutants for brc-1, xpf-1 and fcd-2 maintained. Healthspan was measured by performing thrashing, thermorecovery, and oxidative stress tolerance assays on synchronised WT and mutant C. elegans populations at young (D1), middle (D7) and old (D11) age. For thrashing, worms were randomly selected and transferred to a Petri dish containing S buffer, where their movements were scored for 30 seconds and adjusted to counts per minute for analysis. For thermorecovery, animals were incubated at 37°C for 2 hours, then allowed to recover overnight before recording survival. For oxidative stress tolerance, survival of C.elegans in H_2O_2 was recorded at hourly intervals. Lifespan was measured by placing 100 young adults on plates supplemented with FUDR to sterilise them, scoring them every other day, and measuring survival. Statistical analysis included one-way ANOVA for most healthspan analyses, and log-rank test for oxidative stress and lifespan analysis.

Results

Thermorecovery was not significantly affected in DNA repair mutants with age compared to wild-type, while thrashing declined significantly more in xpf-1 and fcd-2, and oxidative stress tolerance was significantly lower in all DNA repair mutants with age. Lifespan was only significantly reduced in xpf-1 compared to the wild-type, but not in the other DNA repair mutants.

Conclusion

This study suggests that all 3 DNA repair pathways are required for maintenance of healthspan, but that loss of any one repair pathway is not sufficient to affect longevity. In addition, the study suggests that the loss of different DNA repair processes leads to susceptibility to different environmental stressors. If these findings are confirmed by others, it could have implications for pharmaceutical research aimed at extending lifespan and healthspan in humans.

Phenotype genotype analysis in a large cohort of 90 individuals with a terminal 6q deletion

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Introduction

Many chromosome aberrations are rare and parents of children with such an aberration often search the internet for more information and peer support. In this process, parents may unite in international social media platforms. Here we present our data on individuals with a terminal 6q deletion collected in a successful collaboration with such a social media platform: the Chromosome 6 Facebook group.

Materials & Methods

Families signed up for the study via the secured project's website by uploading the proband's genetic report. Phenotype data was collected directly from the individuals or parents via the online Chromosome 6 Questionnaire, that was available in seven different languages. Data from literature case reports were added to the database using the same questionnaire, completed by the researcher.

The terminal 6q region encompasses chromosome bands q26 and q27 with 39 protein coding genes of which seven are predicted to exhibit a haploinsufficiency effect, i.e. a clinical effect when one copy is missing (MAP3K4, PARK2, QKI, PDE10A, MLLT4, DLL1, TBP). We analysed the clinical data of the total group of individuals and of seven subgroups based on the number of deleted haploinsufficiency genes.

Results

We collected data on 37 and 53 individuals with a terminal 6q deletion via social media and literature, respectively.

The overall phenotype includes microcephaly, hypotonia, hypermobility of the joints, balance problems, vision problems, strabismus, feeding problems, sleeping problems, developmental delay, seizures and brain abnormalities, including cerebellum abnormalities, corpus callosum abnormalities and ventriculomegaly. In one third of the individuals short stature, respiratory problems, cardiac and kidney abnormalities were seen.

Subgroup analysis showed that umbilical hernia, spina bifida and hearing impairment were only seen in individuals with a deletion including the PARK2 gene. Developmental delay was also more severe in children with deletions including PARK2. Anal abnormalities were only seen in individuals with deletions including the QKI gene.

Conclusion

Social media helps in collecting large numbers of detailed genotype-phenotype data on individuals with rare chromosome aberrations, enabling a more precise description of their phenotypic spectrum.

A novel variant c.516G > C (p.W172C) in the GJB2 gene is the main cause for recessive hearing loss in indigenous peoples of Southern Siberia (Russia)

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Introduction

Assessment of pathogenicity of novel variants in genes involved in the pathogenesis of monogenic diseases plays a crucial role for medical genetics. The most common cause for hearing loss in human populations is mutations in gene GJB2, which encodes a gap junction protein connexin 26 (Cx26). Cx26 molecules form intercellular channels for ion transport between neighboring cells of the inner ear tissue. Disruption of Cx26-channels leads to irreversible deafness.

This study presents a complex assessment of pathogenicity of novel non-synonymous variant c.516G > C (p.W172C) in GJB2 gene which was found with high frequency in deaf patients belonging to indigenous peoples of Southern Siberia (Tuvinians and Altaians).

Materials & Methods

Genetic analysis was performed in the group of deaf patients (182 Tuvinians, 74 Altaians) and ethnically matched control samples (157 Tuvinians, 218 Altanians). Several prediction tools (PolyPhen2, SIFT, MutationTaster etc.) were applied for in silico analysis. HeLa cell line was used for ex vivo studies. CRISPR/Cas9 genome editing system was used to knockout endogenous GJB2 in HeLa cells. Different variants of the GJB2 coding region (exon 2): c.516G > C (p.W172C), c.[79G > A;341A > G] (p.[V27I;E114G]), c.224G > A (p.R75Q), and wild type (wt) were cloned into plasmid vector and then expressed in knockout HeLa cell line. Cellular localization of Cx26 was investigated by immunocytochemistry (ICC).

Results

Segregation of homozygous or compound heterozygous variant c.516G > C with hearing loss was established in the analysis of pedigrees of deaf patients. Frequency of c.516G > C was significantly higher in patient's group than in controls. In silico analysis showed a likely damaging effect of c.516G > C (p.W172C). To study the functional consequences of p.W172C, the genetic constructs with elements of CRISPR/Cas9 system were assembled. To avoid endogenous GJB2 expression, knockout HeLa cell line was obtained. The ICC-analysis revealed predominantly cytoplasmic localization of mutant protein Cx26-p.W172C, while Cx26-wt and mutant proteins (Cx26-p.R75Q, Cx26-p.[V27I;E114G]) present distinct conglomerates on cell membranes as previously described in literature.

Conclusion

Several lines of evidences: significantly higher frequency of c.516G > C (p.W172C) in patients compared to controls, predictive damaging effect and aberrant cellular localization of mutant protein Cx26-p.W172C support pathogenicity of this novel variant in gene GJB2 and its involving in hearing loss.

Medical Microbiology
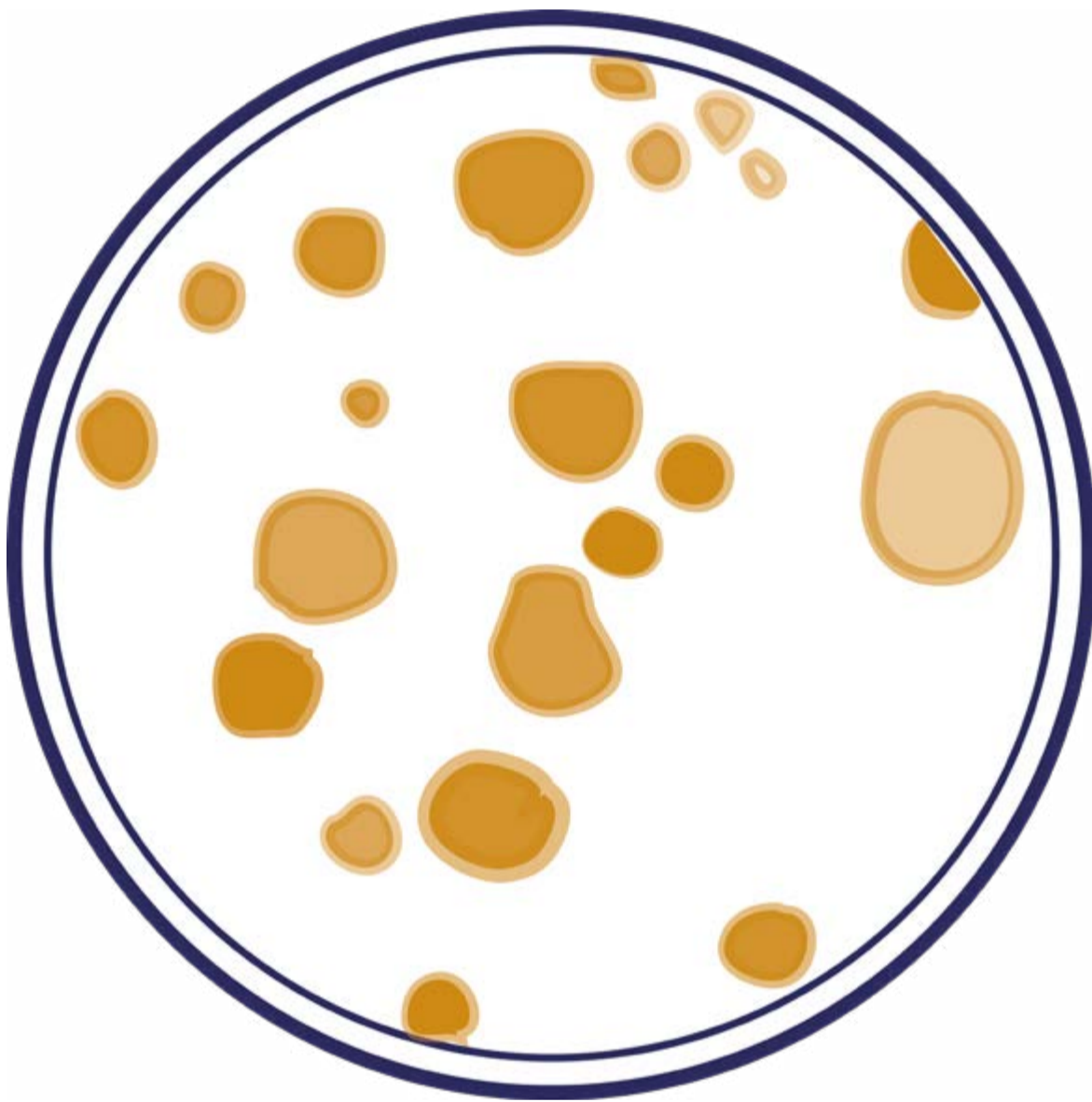
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Juneja, V (Vandya)
Hashemi, F (Farshad)
Menshikh, K. (Ksenia)
Yaghoubi, A (Atieh)
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Antimicrobial Resistance patterns of Salmonella species Isolated from Chicken Eggs in Ilorin, Nigeria

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Introduction

Salmonella is zoonotic bacteria which causes serious economic loss in poultry production and infections in human population. The use of antibiotics for prevention and treatment of diseases has become commonplace in intensive Poultry farming. However, there is a growing concern regarding the development of drug-resistant bacteria. This study was conducted to evaluate the prevalence and antimicrobial resistance of Salmonella spp isolated from eggs sold for human consumption in Ilorin, Nigeria.

Materials & Methods

A randomized design was used to collect 480 eggs from 6 collection points (5 poultry farms and 1 market). Ten samples were collected per week from each point. Descriptive statistics was used to analyse the data Place and Duration of Study: Poultry farms and a market in Ilorin, Nigeria were randomly sampled for eggs over 8 weeks. Egg samples were collected to avoid cross contamination using sterile bags to transport the eggs from the collection points weekly to the Agricultural Laboratory, Kwara State University. The eggs were stored under sterile conditions at 40C until analysed. Standardized microbiological methods were used to isolate Salmonella spp, and identify the serotypes. Disc diffusion technique was used to carry out antimicrobial sensitivity test. Descriptive statistics was utilized in data analysis.

Results

An average Salmonella prevalence of 67% was discovered with a multi-drug resistance to all the antimicrobials used except gentamicin. There were 40%, 60%, 80% and 100% resistance to Ceftriaxone, Ofloxacin, Cloxacillin and Cefuroxime respectively. Also Salmonella enteriditis which is important in human health was the most prevalent serotype (47%) in chicken eggs.

Conclusion

The prevalence of Salmonella isolated from chicken eggs sold in Ilorin metropolis was very high and multi-drug resistance found along this important human food chain require urgent regulation on the use of antibiotics in poultry.

Antimicrobial Resistance in Syria

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Introduction

Antimicrobial resistance is one of the important and serious public health problems worldwide. It is important to know the nature and magnitude of this problem, with periodic updates. However, Syria has a severe lack of data regarding this problem, especially after war. We aimed from this study to provide a unique snapshot on antimicrobial resistance in Syria.

Materials & Methods

This is a multi-centric cross-sectional in-vitro study. The results of routine antimicrobial susceptibility tests were collected and analyzes from five major central hospitals around Syria, during the period from 1st March 2018 through 31th October 2018.

Results

Final analysis included 2861 isolates. We noticed extremely high rates of antimicrobial resistance among all the species studied. Gram negatives have high resistance rates for cephalosporins. 77% of E.coli, 73% of Klebsiella and 82% of pseudomonas are resistant for ceftriaxone. We also noticed minimal effect of macrolides on gram negatives. 25% of Salmonella typhi strains were resistant to ciprofloxacin. High resistance rates to nitrofurantoin is seen among uropathogenic bacteria. Most gram positive bacteria still have a low resistance rate to vancomycin and linezolid. 54% of staphylococcus aureus and 38% of streptococcus pyogens are resistant to amoxicillin-clavulanate. Resistance rates to Colistin are minimal. The comparison with resistance rates before war reveals the great impact of war on antimicrobial resistance problem.

Conclusion

Antimicrobial resistance rates in Syria are worrying. We recommend that the Syrian health authorities apply a policy to restrict the irrational use of antibiotics, and to increase awareness toward antimicrobials use.

Material-induced intracellular macromolecular crowding

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Introduction

Macromolecular crowding is the process of crowding and folding of macromolecules in a cell, essential for folding, association, conformation and diffusion of proteins and poly-nucleic acids. The macromolecular crowding behavior is thought to be highly important within the field of regenerative medicine. An additional phenomenon within regenerative medicine is "Materiobiology" where physicochemical properties of materials direct cellular behavior such as adhesion, differentiation and migration. Therefore, we hypothesize that the macromolecular crowding and materiobiological behavior are strongly correlated.

Materials & Methods

For a spatiotemporal readout of crowding and to determine the impact of excluded volume on protein function in living cells, genetically encodable sensors based on FRET technology are transfected into HEK293T cells. The cells are maintained and seeded on PDMS substrates, that are made with required double and/or triple orthogonal gradients of wettability, topography and stiffness. Different permutations of the substrates are recorded. Live cell imaging of cell spreading, focal adhesion distribution and cell alignment is done.

Cell analysis using ImageJ is done to investigate nucleus and cell size, as well as statistical methods to study the force distribution from FRET data.

Results

The response of cells on substrates with different gradients were recorded; a log of the cell's macromolecular crowding and mechanotransductive properties were derived from this, wherein it was found that macromolecular crowding increased with increasing topography gradient. The level of cell spread on different topogrpahies also changed, increasing with increased topography gradient. The effect on the nucleus was derived, in terms of its size and shape.

Conclusion

Identifying the responses of cells to different substrate properties can give insights into the nature of substrate required for cell proliferation and differentiation. Discovering the response of cells to various material properties can influence the nature of materials that could be studied for use as implants in the body, for bioprinting and other areas of regenerative medicine where cells are grown in vitro.

Identification and Evaluation of Drug Susceptibility of Visceral Candida albicans Isolated from Patients, a multi centered study

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Introduction

In recent years, the ubiquity of Candida infections by isolates resistant to common drugs and lack of proper diagnosis leads to failure in treatment. Considering the existence of the sensitivity pattern determinable for Candida isolates, to select the appropriate drug, it is essential to use the methods of determining the drug sensitivities of the fungal agents. Therefore we decided to study several anti-fungal drugs by using the disk diffusion and microdilution method against Candida species to consider.

Materials & Methods

In this study the 184 clinical isolates of Candida we identified using various different tests such as gram tube, culture on CHROM agar Candida, cornmeal agar-Tween 80 and PCR. The susceptibility test on Amphotericin B, Miconazole, Econazole, Fluconazole, and Caspofungin was undertaken according to the standard Disk Diffusion CLSI-M44A and CLSIM27A3 for microdilution.

Results

The survey found that 98% of Candida studied were sensitive to Amphotericin B, 85% were sensitive to Miconazole, 85% to Econazole, 69% were sensitive to Fluconazole and 100% of isolates were susceptible to Caspofungin. No resistance to Amphotericin B and Caspofungin was observed and a few isolated were resistant to Miconazole, Econazole, and Fluconazole respectively and some isolated show dose-dependent susceptibility.

Conclusion

We observed that the Candida studied had the highest rates of sensitivity to Caspofungin and Amphotericin B. Among Azoles the highest sensitivity respectively are to Miconazole, Econazole and then to Fluconazole. Candida albicans has the highest sensitivity to Caspofungin and Amphotericin B and also has a high sensitivity to Fluconazole, Miconazole, and Econazole.

The experimental model of 3D tumor cell growth using poly(3-hydroxybutyrate) microspheres

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Introduction

Three-dimensional cell culture systems are considered as a link between two ways of anticancer drug testing: in vitro screening models and in vivo drug testing on laboratory animals. The aim of this work was to create 3D cell spheroids on microspheres made from poly(3-hydroxybutyrate) (PHB).

Materials & Methods

To obtain porous microspheres with various diameters, the water phase/oil phase/water phase (W/O/W) method was used, followed by washing out the porogen. An aqueous solution of ammonium carbonate was used as a porogen because of its ability of thermal decomposition to ammonia and carbon dioxide.

To obtain stable spheroids, HEp-2 cells (human laryngeal cancer) were cultured together with porous PHB microspheres in wells coated with 1% agarose gel under constant stirring at a temperature of 37°C and 5% CO_2 content. The dynamics of cell division and growth in spheroids was monitored by MTT analysis, the morphology of spheroids was assessed visually by histological methods, as well as by scanning electron (SEM) and confocal microscopy.

Results

The growth of spheroids peaked on the 7th day of cultivation, after which the number of living cells decreased both in the control (cell spheroids) and in the experiment (cell spheroids with microspheres). Moreover, during cultivation with microspheres with a diameter of 50-100 μm, more active proliferation of cells was observed compared to the control and spheroids with microspheres over 100 μm. SEM studies also showed better cell attachment and aggregation with microspheres with smaller diameters.

Conclusion

The described approach to creating 3D cell models from tumor cells using PHB is promising for obtaining systems for testing antitumor drugs. A more complete understanding of the mechanisms will be achieved through analysis of the expression of various transcription factors and during the scaling of the process via cultivation in a larger volume with a constant circulation of the growth media.

Evaluation of rifampicin and isoniazid resistance in Mycobacterium Tuberculosis isolates by High Resolution Melting (HRM) Real-Time PCR Technique to set-up this method in Regional Tuberculosis Reference Laboratory of Mashhad

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Introduction

Drug resistance to isoniazid and rifampin as two main drugs of the first line of TB treatment in Mycobacterium tuberculosis isolates is increasing nowadays due to inadequate TB control programs and irregular use of these drugs. In this study evaluation of antibiotic susceptibility of rifampin and isoniazid, in Mycobacterium tuberculosis isolates is fulfilled using High Resolution Melting Cruve Analysis (HRMA) as a simple and cost-effective method compared to the phenotypic methods, Allel Specific multiplex PCR, and gene sequencing.

Materials & Methods

PCR was performed to investigate the rpoB, katG and promoter region of the inhA gene and mutations in these genes that are involved in rifampicin and isoniazid resistance. These genes were also amplified by real-time PCR. Then, the presence of mutations in these genes was investigated by the HRMA method and after sequencing the amplified fragments, modified codons were studied throughout the gene.

Results

HRMA assay identified katG gene mutations and the mabA-inhA promoter region in 15 of 18 isoniazid-resistant samples and rpoB gene mutations were successfully evaluated in 11 out of 13 rifampin-resistant samples. The sensitivity and specificity of the HRMA method were 87.71% and 90.9% for isoniazid and 86.66% and 86.95% for isoniazid, respectively. In this study, 85% of rifampin-resistant samples had mutations in the rifampin resistance determining region. The most common mutation in this region occurred at codon 531 (GCT-->GTT) at 78% and then at codon 513 (CAA-->CTA), which resulted in the amino acid change. Also, 83% of isoniazid-resistant samples had mutations in the katG gene and the mabA-inhA promoter region, of which the highest mutation occurred at codon 315 (AGC-->ACC) of the katG gene.

Conclusion

The incidence of drug resistance among Mycobacterium tuberculosis strains is of particular clinical importance. According to the results of this study, HRMA method, despite being able to detect most of the mutations in rpoB, katG and mabA-inhA genes, did not detect some phenotypically resistant isolates. Therefore, it can be concluded that in order to confirm the efficacy of the HRM method, the population under study should be expanded and also examined less frequent gene mutations.

Prevalence and identification of mecC and PVL gene of S aureus isolated from burn wound infection

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Introduction

Staphylococcus aureus is among the most commonly isolated pathogenic bacteria in burn wounds. It is common to identify methicillin-resistant Staphylococcus aureus (MRSA) using PCR technique to detect mecA, but recently described homologue, mecC (mecALGA251), have gained attention due to it being misdiagnosed as methicillin-resistant Staphylococcus aureus (MSSA) in most labs. PVL gene shows high prevalence among community-acquired MRSA isolates. The aim of this research was to determine the prevalence and provide genetic data profile of S. aureus isolated from burn wound infection in a trauma hospital in Tripoli, Libya.

Materials & Methods

We isolated Staphylococcus spp form non-duplicated burn wound swaps in Abo-Salem Trauma Hospital between June 2013 and June 2014. Isolates were identified using standard laboratory procedures and differentiated using Menthol salt agar and coagulase test. All S. aureus positive cultures DNA were extracted using the heating methods, and test for purity then stored. A sample of 12 Staphylococcus aureus isolates was selected initially to test the validity of the method. We used conventional PCR analysis and gel-electrophoresis to identify mecA, mecC, PVL genes using validated DNA primers, and were compared to previously identified controls for each one of the genes from previous study.

Results

Form the 93 specimens, 67 isolates of Staphylococci were obtained, 10 (14.9%) were coagulase-negative staphylococci, and 57(85.1%) were Staphylococcus aureus. 12 Staphylococcus aureus isolates five exhibited mecA genes, and two expressed mecC. Meanwhile, one isolate harboured both mecA and mecC. PVL was positive in the three samples with the mecC gene. The control was positive for each indicated gene.

Conclusion

Preliminary results showed that Staphylococcus aureus isolated from burn wounds exhibit the mecC gene. Although more testing is needed, there is an association between mecC and community-acquired infection indicated by the PVL gene. Further analysis for the rest of the sample is being carried out.

Helicobacter pylori urease: production of the fluorescent-labeled protein and study of biodistribution by in vivo multispectral imaging

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Introduction

Alzheimer's Disease, the most common mental disorder in patients above 60 years old, is a dementia that has the presence of brain neurofibrillary tangles – deposits of hyperphosphorylated tau protein – among its histopathological hallmarks. It has been reported that a filtrate of Helicobacter pylori has induced tau hyperphosphorylation both in vitro and in vivo. This study suggested that H. pylori's contribution to tauopathies is mediated by bacterial exotoxins. H. pylori, responsible for chronic gastritis, ulcers and gastric cancer, infects about half of the world's population. Its survival in the human stomach is only viable because it produces urease, a metalloenzyme that hydrolyzes urea, producing a neutral microenvironment. The aim of this work is to investigate HPU's biodistribution using in vivo multispectral imaging, which consists of injecting a subject with a fluorescent-labeled biomolecule, exposing it to light of the label's excitation frequency and capturing the light it emits back.

Materials & Methods

Wistar rats and Swiss mice use and care were approved by the local animal care committee. Recombinant HPU obtained by heterologous expression in Escherichia coli was purified and verified by SDS-PAGE and Western blotting. Enzymatic activity was quantified by a colorimetric assay. Texas-Red labeled HPU (TR-HPU) was prepared for fluorescence assays. Mice will be submitted to a longitudinal study with TR-HPU, given either on an acute or chronic scheme, and scanned throughout the treatment in a multispectral scanner.

Results

HPU was successfully expressed, purified, and found enzymatically active. Preliminary results have shown that rats injected i.p. with HPU during 7 days had a considerable increase in tau phosphorylation in the hippocampus. TR-HPU displayed stability and fluorescence in sodium phosphate buffer. TR-HPU's emission frequencies were found suitable for in vivo experimenting, taking into account the interference of intrinsic fluorescence from animal tissues.

Conclusion

Increased hippocampal levels of hyperphosphorylated tau in rats treated with HPU suggested that it might be an exotoxin contributing to tauopathies. The assays performed with TR-HPU indicated that in vivo imaging is feasible. Next step will be evaluating protein biodistribution with longitudinal multispectral imaging of mice treated with TR-HPU.

Movement Sciences and Medical Physiology

Presenters:
Vollenbroek, N.J.M. (Nicky)
Danko, D.
Sansgiri, S (Sailee)
Wacka, E. (Eryk)
Sedelkova, V. (Valentina)
Sukhostavtseva, T. (Tatiana)
Hohlstamm, A.H.
Vuelvas-Olmos, C. (Cesar)

Classification of electromyography (EMG) signals of the distal upper extremities to identify different muscle synergies with the aim of giving functional electrical stimulation (FES) feedback

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Introduction

One major consequence of a stroke is motor paralysis and spasticity of the upper extremity, which is a problem that has to be solved. To overcome a small part of this problem, the aim of current research is to read surface electromyography (sEMG) signals of the distal upper extremity, with the objective of giving functional electrical stimulation (FES) feedback according to the EMG. To do so, different muscle synergies for different handgrips will be identified. It is expected that different muscle synergies for grasping can be classified.

Materials & Methods

5 right-handed healthy participants ($\mu = 22.29$ years; median = 24 years), both men (n = 3) and women (n = 2) living in Spain, from different nationalities were included. Grasping tasks with (n = 5) and without (n = 3) objects were carried out and measured, using 1) the NeurOne Tesla neuroscience measurement system (Bittium Biosignals Ltd, Kuopio, Finland), 2) 8 EMG electrodes which were placed on different lower arm muscles, and 3) an obtained Python script. The 3 grasping tasks with the aim of grasping the object from on top were utilised for data analysis, using the 2-class and 4-class support vector machine (SVM) for calculations.

Results

The 4-class Fine Gaussian SVM (Orange vs. Coffee Cup II vs. Phone vs. Rest) showed 37% (Orange), 54% (Coffee Cup II), 41% (Phone) and 60% (Rest) of correctly predicted classes. Furthermore, the 2-class Fine Gaussian SVM showed 51% (Orange vs. Rest), 65% (Coffee Cup II vs. Rest) and 54% (Phone vs. Rest) of correctly predicted classes.

Conclusion

Different grasping tasks can be identified by measuring sEMG signals of the distal upper extremity. However, comparable movements are difficult to distinguish. Furthermore, because of the remaining noise in some of the recorded signals, not all the files could be used in this research. Therefore, it is important for future research that less noise is present in the recorded signals.

Sex differences of physiological adaptation to simulated microgravity in mice

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Introduction

Microgravity causes most of the adverse consequences of spaceflight for human health, including "space anemia", muscle and bone loss. While initially cosmonauts and astronauts were predominantly men, the number of women flying to space is increasing. However gravitational physiology has been largely focused on male individuals, and sex differences in reactions to spaceflight are poorly understood. The study was aimed to evaluate sex differences in reaction of muscle, bone and red blood to microgravity using the hindlimb unloading model in mice.

Materials & Methods

Male and female mice were exposed to hindlimb unloading (HLU) or kept "attached" (ATT) without unloading for 28 days. Animals either had intact gonads (INT), were gonadectomized (GnX) or were gonadectomized and received hormonal replacement (GnX+Horm; 10 mg/kg testosterone propionate or 200 mkg/kg estradiol benzoate in males and females, correspondingly). Thus, a total of 12 experimental groups were studied. After the exposure fore- and hindlimb muscles, femur and blood were harvested for analysis.

Results

Typically for the unloading model, m. soleus and m. gastrocnemius weight were reduced in the HLU mice, gonadectomy with or without hormonal replacement did not affect muscle loss in either sex. Bone mineral density in the femur was reduced in HLU individuals and bone loss was more pronounced in females. Gonadectomy exacerbated microgravity induced bone loss and hormonal replacement ameliorated the gonadectomy effect in both males and females. Loss of red blood cells after HLU was found in intact males only, while RBC in intact HLU females was similar to GnX-HLU females. Inhibition of ovarian function was found in HLU females, but not in the males, as evidenced by the weights of the primary sex steroid target organs and serum sex steroids levels. Thus, the differences in RBC reaction to HLU might be governed by contrasting hormonal changes in males and females.

Conclusion

Sex steroid-governed differences were found for simulated microgravity-induced bone loss and anemia, but not the muscle loss. Moreover, the inhibition of the gonadal function was found female, but not the male mice. Generally, the deteriorative effects of microgravity were more pronounced in female individuals as compared to males.

Automated gait event detection in Crouch and Equinus gait

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Introduction

In clinical gait analysis, detection of gait events (Foot-Strike (FS) and Foot-Off (FO)) allows the standardization of ensemble averaging of spatio-temporal metrics across individuals. Currently, gait events are identified by force-plates or trained experts, which both suffer from limitations on validity and subjectivity.

Hence, in this study, we compared approaches that automatically identify events from kinematic data in two types of walking behaviors- crouch and equinus gait. We focused on FO detection due to inaccuracies limiting its use in clinics.

Materials & Methods

3-D kinematic and kinetic data was collected from 60 participants (20 each for crouch, equinus and non-symptomatic gait) at a local hospital.

Five kinematic algorithms were implemented in MATLAB with two marker configurations for FO: a) as described by the original publication, and b) using a hallux marker, as it was recommended to improve accuracy. One algorithm was modified to estimate events using the participant's walking speed.

To validate our approach against the clinically accepted standard, kinematically estimated events were compared against kinetically detected events (threshold: 15N), with the difference between the two defined as an error. Accuracy was defined as the percentage of subjects for which the absolute error was below 33.3 ms, a standard used by previous comparison studies.

Results

In crouch gait, horizontal position of markers is the most accurate approach for FO detection (Median: 0 ms). Sagittal velocity works best for non-symptomatic (1.667 ms) and equinus gait (6.667 ms), with the speed-dependent threshold improving accuracy for the latter (-5 ms). Using the hallux marker improved detection for the sagittal velocity approach, but was ineffective in other cases. The speed-dependent sagittal velocity approach was the most robust to all walking patterns (Accuracy: 95.83%) and the horizontal velocity approach demonstrated the lowest accuracy across all walking patterns (47.50%).

Conclusion

Therefore, no single algorithm efficiently detects gait events across all walking patterns. Hence, we recommend identifying the most suitable kinematic algorithms for clusters of walking patterns or using deep learning techniques which are robust to these variabilities.

We further propose investigating whether the difference between kinematic and kinetic event detection leads to clinically important differences in the calculation of spatio-temporal parameters.

Intermittent hypoxic exposure reduces a risk of aseptic vascular inflammation

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Introduction

Intermittent exposure to hypoxia (IHE) increases the production of reactive of oxygen and nitrogen species (RONS) as well as erythropoietin, which stimulates the adaptation to intense physical activity. Therefore, IHE is one of the methods has used in professional sports. However, several studies suggest a protective effect of moderate hypoxia for cardiovascular disease (CVD) events. We examined the effects of IHE with sports activity on RONS and inflammatory mediators and their interaction with conventional CVD risk factors.

Materials & Methods

Blood samples were collected from elite/olimpic athletes (control n=6, IHE n=6) during 6-day IHE cycle using hypoxicator GO2Altitude. In serum, hydrogen peroxide (H_2O_2), nitric oxide (NO), 3-nitrotyrosine (3NT), pro-inflammatory cytokines (IL-1β and TNFα) and C-reactive protein (CRP) were determined by enzyme immunoassay methods (ELISA kits). The levels of triglycerides (TG), total cholesterol (TC) and lipoproteins (HDL, non-HDL, LDL and oxLDL) as well as hematological markers were determined by professional laboratory company Diagnostyka (Poland, ISO 15189). Serum erythropoietin (EPO) level was measured every day of IHE by ELISA kit. Statistical analyses were performed by means of statistical software Statistica 13.1 (StatSoft Inc., Tulsa, USA).

Results

IHE significantly increased in serum H_2O_2 and NO but decreased in 3NT concentrations. This indicates higher NO bioavailability following hypoxia. The inflammatory mediators IL-1β, TNFα and CRP tended to increase in IHE group. The serum EPO level increased at 3rd day of IHE, and then decreased at 5th day of IHE, and correlated with NO (rs= 0.486, P<0.05). There were no changes in hematological markers Ret, RBC, Hb and Htc on the contrary to lipoproteins i.e. LDL, HDL and non-HDL showed decreasing trend in response to IHE.

Conclusion

The study demonstrate that intermittent hypoxic exposure combined with sport activity increases nitro-oxidative and inflammatory state. Nevertheless, an enhancement of NO generation and its bioavailability reduce levels of conventional CVD factors. Therefore, intermittent hypoxic exposure seems to be the potential therapeutic and non-pharmacological method to reduce a risk of atherosclerotic diseases.

Research of human operator performance under simulated lunar gravity

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Introduction

The long-term perspective plans for space-manned flights to the Moon include the construction of a lunar base and use of lunar rovers by astronauts for studying moving on the lunar surface to gather information about nature of soil, and performing other scientific and practical tasks. The aim of this study was to evaluate the parameters of operator performance and physiological indicators under conditions of modeling physiological effects of lunar gravity.

Materials & Methods

There was analyzed the data from 4 healthy subjects aged 19-33 years. 14-day head-up bed rest + 9.6° (HUBR) was used to simulate the physiological effects of lunar gravity. The operator performance was in tight time controlling of lunar rover on the lunar surface by virtual reality method using a VR-helmet and joystick.

The parameters of operator performance were the following: expended time (sec) which consists of time of controlling (sec) and downtime (sec); average speed (m/sec); expended energy (conv. unit); trace length (m). Parameters of heart rate (HR, beats/min), respiratory rate (RR, cycle/min), blood pressure (BP, mmHg) were recorded during the operator performance. The data was analyzed by Wilcoxon signed-rank in the statistical program SPSS Statistics v.17.0 and Excel 2010.

Results

Significant changes in the indicators of operator performance was revealed in HUBR in comparison with the initial data recorded before HUBR: a decrease in total time for controlling the lunar rover by 9.6% ($p \leq 0.05$) and an average speed by 4.2% ($p \leq 0.05$). The remaining parameters showed multidirectional changes in the group.
Analysis of physiological data showed an increase in HR by 10.8% ($p < 0.01$).

Conclusion

A significant increase in heart rate was obtained during performing the task of controlling a lunar rover under the tight time conditions. Operator performance under simulated lunar gravity was realized in the conditions of increased cardiovascular system loading, which did not lead to deterioration of work quality.

The assessment of orthostatic tolerance in humans after prolonged stay under simulated microgravity and lunar gravity

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Introduction

The orthostatic intolerance after space flights is an actual problem of space medicine. At the present stage the development of manned space exploration is characterized by the transition from orbital flights to the preparation for missions to the Moon. The purpose of this paper was to assess the orthostatic tolerance in humans after prolonged stay under simulated microgravity and lunar gravity.

Materials & Methods

28 male-volunteers were separated in 2 groups. HDBR-group (n=16) was stayed for 3-day head-down bed rest –6° (HDBR) as a model of microgravity. HUBR-group (n=12) spent 7 days under head-up bed rest +9.6° (HUBR) as model of lunar gravity. The orthostatic tolerance was carried out during 20-minutes passive tilt-test at +70° before and after bed rest. Heart rate (HR), systolic (sBP) and diastolic (dBP) blood pressure were registered. The indicators for early tilt-test termination were the developing signs of precollaptoid state. The data was analysed by Wilcoxon signed-rank and Mann-Whitney U tests (SPSS v23.0).

Results

HBDR-group. Tilt-test was completed successfully by 13 subjects and prematurely by 3 subjects before HDBR. Tilt-test was completed successfully by 7 subjects and prematurely by 9 subjects after HDBR. The average tolerance time decreased from 18.6 ± 0.8 to 13.8 ± 1.6 minute ($p<0.05$). The precollapse time also decreased from 12.7 ± 1.6 to 9 ± 1.4 minute ($p< 0.05$). HR was higher (~25%), sBP was lower (~2.6%) during tilt-test after HDBR than before ($p < 0.05$). HUDR-group. Tilt-test was finished successfully by 9 subjects and prematurely by 3 subjects before HUBR, successfully by 7 subjects and prematurely by 5 subjects after HUBR. The average tolerance time decreased from 19.1 ± 0.5 to 15.9 ± 1.7 minute ($p < 0.05$). The precollapse time decreased from 16.3 ± 1.1 to 10.2 ± 2.3 minute ($p < 0.05$). HR was higher (~18.4%) during tilt-test after HUBR than before ($p < 0.05$).

Conclusion

Prolonged HDBR and HUBR decreased the orthostatic tolerance of subjects significantly. The orthostatic intolerance in subjects was observed more frequently after HDBR than after HUBR. The negative impact of simulated lunar gravity on orthostatic tolerance requires the development of countermeasures against these disorders in future lunar missions.

Quantifying dynamics of cell migration in confluent endothelial cells and after regional injury

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Introduction

Wound healing with a coordinated migration of individual cells is a complex and important response to small and large traumata. The efficiency of this process, for example regarding the duration of wound closure, influences the outcome and determines the occurrence of possible complications. Thus, it is the aim of this work to quantify and characterize the dynamics of individual vascular cells within a confluent layer and relate it to the closure dynamics of a wound.

Materials & Methods

Human umbilical vein endothelial cells (HUVEC) were seeded either in a confluent manner or in 2-well-culture inserts generating a well-defined endothelial gap with a width of 500 μm. The HUVECs were then observed for 24 hours via time-lapse microscopy (sampling interval = 10 min) and cell positions were obtained using image segmentation and tracking of the cell nuclei, stained with Hoechst 33342 beforehand. The resulting several 10000 individual cell trajectories were analysed regarding their movements as a single cell and as part of the cell collective.

Results

Even in the confluent cell layer the cells showed lively proliferation causing a non-equilibrium situation. This process can be characterized by an exponential velocity distribution of the cells where their mean squared velocity slows down over time. In addition, the spatial velocity correlation function showed exponentially decaying correlations over about 3 cell diameters. The strength of cell spreading is quantified by the mean squared displacement (msd). Under confluent conditions, the msd indicated normal cell diffusion, which changed towards sub-diffusion representing the process of ongoing cell localization. In comparison, the msd in the wound set-up was enhanced by factor five. This data elucidates that cells are moving more persistently. This is further supported by an enlarged velocity autocorrelation time of up to 4 hours.

Conclusion

By examining migration with measures like the mean squared displacement or different cell-cell correlations we quantified the dynamics of confluent cells. This enables us to compare and understand the effect of conditions like wounds or to differentiate the influence of external pharmaceutical stimuli on these quantities.

Contact sport practice leads poor performance in cognitive functions in athletes of Mexican population

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Introduction

Contact sports are those sports in which physical contact occurs among contestants during a competition. Nowadays sports are becoming an over growing industry worldwide however the contact sports practice too could lead injuries and adverse effects. In addition, there are substantial costs of sports-related injuries, making these injuries also a societal problem. Support by previous studies, repeated head impacts in sports may leads to a variety of worrisome outcomes, even, when the player is not outward signs of brain injury. In Mexico, there are no previous studies on the effects of contact sports and cognitive effects in athletes. The aim of the study was to determine the effects of repeated head impacts contact sport practice on cognitive performance in athletes of Mexican population.

Materials & Methods

The sample was 45 contact sports athletes 45 noncontacts sport athletes, without record of TBI. All athletes were assessed with CogState Battery for assess cognitive tasks as control motor visual, associated peer learning, psychomotor function, attention, working memory and executive function. To evaluate the score of CogState tasks descriptive statistics were used. To compare the performance of contact sports athletes and non-contact athletes, student T test was used. To test the hypotheses, the level of significance was set at 0.05. SPSS v.26 was used for statistical analysis.

Results

There no found significant differences between contact sport group compared to noncontact sport group; according to age, sex, years of education. There contact sports group showed more expose to time of practice sports and hours by week, difference significant statistics was found in in comparison to non-contact sports group. The contact sport athletes performed more poorly at three cognitive domains with lower score than noncontact sport athletes: Executive function (t=7.313, p=0.001, 95% CI), Working memory (t=8.897, p < 0.001, 95% CI) and Psychomotor speed (t=7.232, p < 0.001, 95% CI). There not found significant differences in others task.

Conclusion

The contact sport athletes were perform more poorly at three cognitive domains with lower score than non-contact sport athletes, a possible explain it that by repetitive head impacts during sport practice may negatively impact cognitive functions, even when there are no outward signs of brain injury.

Neurology I
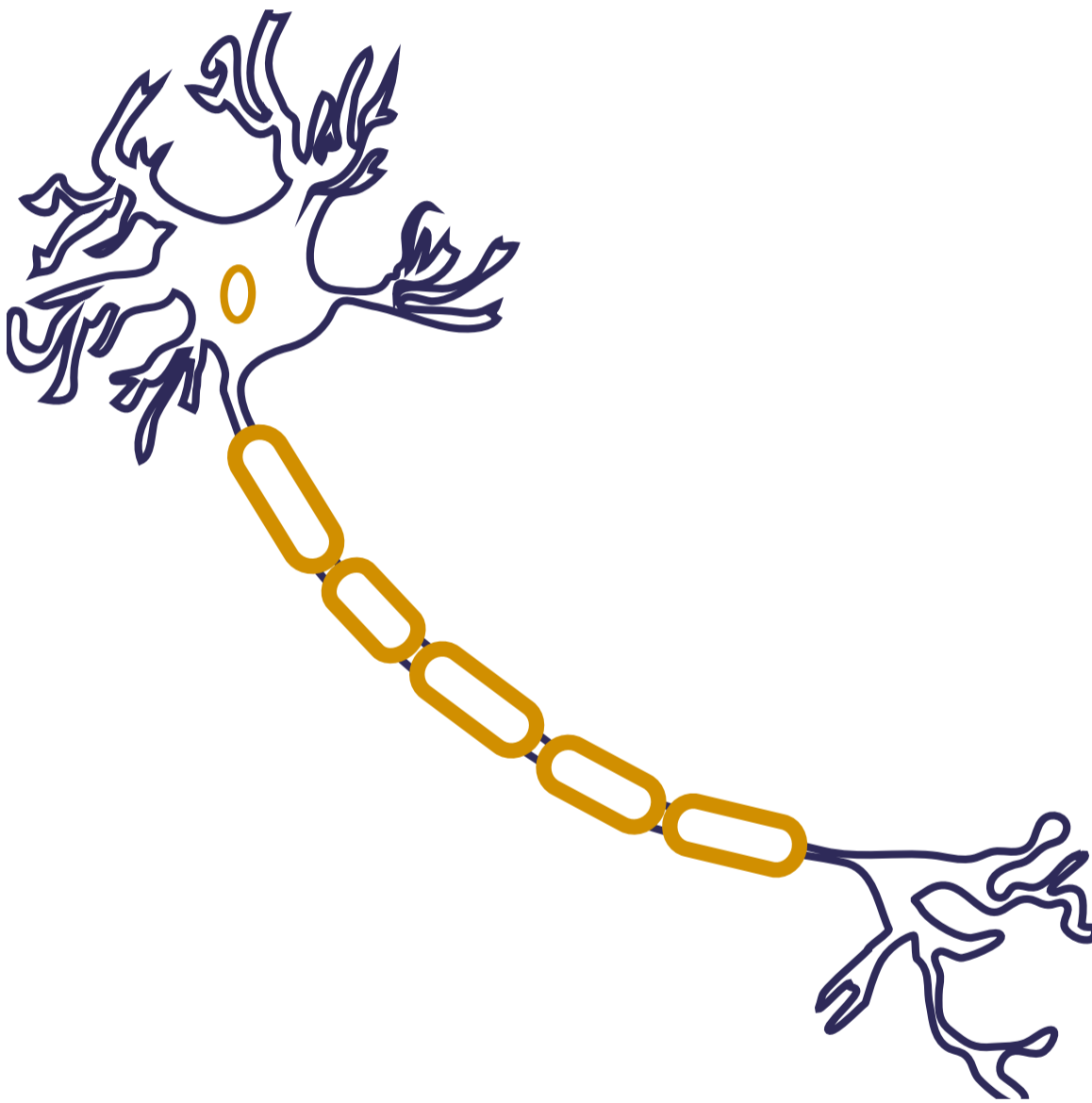
Presenters:
Ren, S.Y.R (Shuyu)
Velázquez Delgado, C.V.D (Cintia)
Cai, H. (Huimin)
Fedotova, A. (Anna)
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Age-Related Cognitive Deficits are a Result of Myelin Degeneration and Diminished Renewal.

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Introduction

As human lifespan increases, age-related cognitive decline emerges as a major obstacle for the elderly. Multiple lines of MRI evidence have identified abnormalities in the white matter (WM) of aged human brains, suggesting that myelin remodeling may participate in the ageing process. we demonstrate significant myelin loss and diminished myelinogenesis in aged mice, along with a prolonged deficit in the spatial learning and memory.

Materials & Methods

MT/mG (The Jackson Laboratory, Catalog # 007676) and tau-mGFP (Catalog # 021162) reporter gene mice were crossed with NG2-CreERt line (The Jackson Laboratory, Catalog # 008538) and PLP-CreERT line (The Jackson Laboratory, Catalog # 005795). Fluorescent images were captured using confocal laser-scanning microscope. Data was analyzed by two-way ANOVA, unpaired Student's t-test or one-way ANOVA.

Results

1. Pre-existing and newly formed myelin were decreased during aging; A deficit in learning and memory was detected in the aged mice in water maze test; 2. Conditional deletion of Olig2 in adult OPCs resulted in a significant decrease in mGFP positive OLs and myelin sheaths; In the water maze, the Olig2 cKO mice exhibited a significant lower frequency of crossing the target sector ($p=0.029$); 3.The M1R deletion in OPCs resulted in a ~5-fold increase in mGFP-myelin expression ($p<0.001$); The M1R cKO mice displayed significant improvement in the performance of water maze task.

Conclusion

Dynamic remodeling during ageing and myelin loss are prominent. Active myelinogenesis is required for maintaining learning and memory, while enhancing myelinogenesis in aged mice reverses this cognitive decline.

Novelty has a protective effect against amyloid-beta toxicity

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Introduction

Alzheimer's disease (AD) is a neurodegenerative disease and leads to an overproduction of amyloid-beta (Aβ). Administration of Aβ affects the catecholaminergic system causing memory impairments (Moreno-Castilla, 2016). Thus, stimulation of the catecholaminergic system, with a dopamine agonist, ameliorate of Aβ toxic effects (Himeno et al., 2011).

Furthermore, novel stimuli augment the release of catecholamines (Moreno-Castilla, 2017). Therefore, in this work, we analyze whether the repeated exposure to novel objects has a protective effect against Aβ1-42 oligomers administration in the hippocampus. For this purpose, we measured the release of catecholamines by in vivo microdialysis, the length of the TH+ terminals in the hippocampus by stereology, and we related them to the behavior of the animals in a spatial memory task.

Materials & Methods

Mice were exposed to a novelty environment (Nov) and were compared to a control group in vivarium conditions (Cage). At the end of the protocol, we administered Aβ1-42 oligomers in the hippocampus. We measured the release of catecholamines by in vivo microdialysis, evaluated the performance in the spatial memory task, and measured the length of hippocampal terminal fibers of tyrosine hydroxylase (TH+) by stereology. The data were analyzed with the one-way ANOVA and Bonferroni's post hoc analysis was used, and $p<0.05$ was considered statistically significant, using GradphPad software.

Results

The novelty protocol maintains the release of dopamine compared with the control group ($P=0.1035$ $F3,15=2.452$), the performance in the memory task between the Cage and Nov group was not statistically different ($P=0.1634$ $F3,24=1.860$) and the length of the fibers was not affected in the Nov group ($P=0.6$ $F3,13=0.6446$), after Aβ administration.

Conclusion

Novelty protocol maintains the levels of dopamine release, the length of the fibers, and a good performance in a spatial memory task, even after the hippocampal Aβ administration. The stimulation of the dopaminergic system through repetitive novelty has a protective effect against amyloid-beta.

Domain-specific characterization of cognitive impairment in Parkinson's disease patients with depression

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Introduction

Both cognitive impairment and depression are common non-motor symptoms in Parkinson's disease (PD). Previous studies demonstrated that these disorders may share similar pathophysiology and depression is negatively correlated with cognitive performance in PD. However, there is inconsistency regarding cognitive domains influenced by depression. Therefore, the purpose of the study is to determine the relationship between domain-specific cognitive impairment and depression in PD.

Materials & Methods

102 PD patients completed a comprehensive neuropsychological assessment that included measures of overall cognitive level, attention, memory, language, visuospatial ability, executive function, and depressive symptoms. Patients were divided into depressed (DPD, N=56) and non-depressed (NDPD, N=46) groups according to DSM-IV criteria.

Results

DPD had significantly more severe motor symptoms (Hoehn-Yahr stage: 2.3±0.6 vs. 2.0±0.6, MDS-UPDRS: 41.7±15.8 vs. 32.9 ±14.1), longer disease duration (5.4 ±4.6 vs. 3.1 ± 3.6) and higher depression score (Hamilton Depression: 19.78±4.8 vs. 5.9±4.2) than NDPD. NDPD had better performance in symbol digit modalities test (31.6 ±11.6 vs. 23.7 ±10.2). There was no significant difference in scores of Mini Mental State Examination (MMSE), Montreal Cognitive Assessment (MoCA), Digit Span Test (DST), Rey Auditory Verbal Learning Test (RAVLT), Animal Fluency Test (AFT), Boston Naming Test, Rey–Osterrieth Complex Figure Test (CFT), the Block Design Test in the Wechsler Adult Intelligence Scale (WAIS-R), the Similarities Test and Picture Arrangement Test in the WAIS-R between two groups.

Conclusion

Both DPD and NDPD share similar cognitive profiles in overall cognitive level, memory, language, visuospatial ability, executive function domains. Depression is associated with worse attention in PD.

The COMT Val158Met polymorphism affects the N100 auditory evoked potential and the oddball task performance in schizophrenia patients

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Introduction

Schizophrenia is a severe, chronic brain disorder that occurs because of physical, genetic, psychological and environmental factors. However, the exact causes of schizophrenia remain unknown. The COMT gene is one of the most investigated candidate genes for schizophrenia. The COMT Val158Met polymorphism leads to alterations in dopamine levels in several brain regions and may contribute to the risk for schizophrenia. We aimed to analyze the effects of the Val158Met polymorphism on the N100 auditory evoked potential and parameters of the oddball task in healthy adults and schizophrenia patients.

Materials & Methods

The study included 47 healthy subjects and 48 schizophrenia patients. The standard active "oddball" paradigm was used. Two types of auditory stimuli, target and standard, were randomly presented to subjects. The N100 negative auditory evoked potential was elicited by stimuli. EEG was recorded during the experiment. To determine the genotype, DNA extraction from saliva samples and the real-time PCR were performed. Based on this input, all participants were divided into three groups: Met/Met, Val/Met, and Val/Val carriers. The amplitude of the N100 and the task performance were then analyzed in different subgroups with a repeated measure ANOVA and t-test.

Results

We found different effects of the COMT Val158Met polymorphism in healthy subjects and schizophrenia patients. The group of healthy subjects with the Val/Val genotype demonstrated increased N100 amplitude and the minimum number of incorrect responses ($p < 0.05$). In schizophrenia patients with the Val/Val genotype, in contrast, decreased N100 amplitude and worse task performance were observed ($p < 0.05$).

Conclusion

The data suggest that the COMT Val158Met polymorphism can modulate N100 amplitude and oddball task performance in healthy people and schizophrenia patients. Our findings might be utilized in medical practice to develop appropriate instrumental methods to diagnose schizophrenia.

Radial glia-like stem cells in the hippocampus cease to respond to memantine with age

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Introduction

Neurogenesis in hippocampus continues throughout the whole life of most mammals. It is supported by radial glia-like stem cells (RGLs) which inhabit hippocampal dentate gyrus. RGLs exist primarily in a quiescent state. After activation they give rise to granule neurons and differentiate into mature astrocytes incapable of division. This process depletes the neural stem cell pool and leads to decrease of adult neurogenesis. It may underlie age-related cognitive impairment. Memantine, a non-competitive inhibitor of the NMDA receptors, is known to enhance neurogenesis. This research demonstrates cellular mechanism of memantine action on RGLs in the adult hippocampus using the novel labeling paradigm for identification of de novo dividing cells and studies the effect of memantine on RGLs in the senescent brain.

Materials & Methods

This study was done on heterozygous nestin-GFP expressing male mice. Two age groups were formed: 3-month and 11-month old. BrdU was applied with osmotic pump over a period of 7 days. During the last 3 days of BrdU application, experimental animals were treated with memantine (50 mg/(kg*d)). Saline solution was used for the control animals. Both groups were injected with EdU 19 h after osmotic pump removal. Labelled cells were manually counted on brain sections.

Results

Labelled cells were distributed in three groups, some were labelled with one of the markers, while others were labelled with both. EdU+ and BrdU- cells did not divide during 7 days of BrdU application, and thus were de novo activated by memantine. In younger mice, the number of dividing cells in general as well as de novo activated stem cells increased by a factor of 4 and 3, respectively, after memantine treatment. This stands in strong contrast to the results obtained from senescent mice, where no significant difference between experimental and control groups has been found.

Conclusion

Memantine induces recruitment of the quiescent radial glia-like stem cells into division, thus enhances neurogenesis in the adult brain. However, the quiescent RGLs cease to respond to memantine in the aged brain. It indicates age-related changes in the signaling pathways involved in regulation of the quiescent state of RGLs. The reported study was funded by RFBR, grant No. 19-29-04016.

Amyloid beta disruption of contextual memory can be reversed by catecholaminergic stimulation

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Introduction

Alzheimer's disease (AD) is a neurodegenerative condition characterized by synaptic dysfunction, amyloid beta (Aβ) aggregates, and neurofibrillary tangles of hyperphosphorylated tau that lead to cognitive impairment like recognition memory loss. Increased production of Aβ has been linked to a reduction in catecholaminergic neurotransmission, recognition memory impairments, and synaptic plasticity alterations in both patients and animal models of AD. We have previously shown that the inability to recognize novel stimuli coincides with alterations in the catecholaminergic system of a 3xTg-AD. Moreover, recently we have shown that catecholaminergic release in the hippocampus is essential for the codification of contextual novelty.

In this regard, it is reported that different treatments with catecholaminergic precursors or agonists have a beneficial effect on cognitive deficits generated by Aβ accumulation.

Therefore, our main goal is to evaluate the effect Aβ administration has on long-term contextual memory evocation and the induced changes in the catecholaminergic system, and if we can attenuate memory impairments with a catecholaminergic reuptake blocker.

Materials & Methods

In a location memory task (OLM) we measured the preference of a novel object location with a two-tailed Student's t-test. To evaluate the length of tyrosine hydroxylase (TH+) and microtubule-associated protein 2 (MAP2+) fibers, stereology analyses were evaluated using a two-way ANOVA test with Bonferroni post hoc test.

Results

We found that intrahipocampal administration of Aβ after memory acquisition and before evocation impairs codification of novel contextual information ($t9= 1.446$, $p= 1.822$), and treatment with nomifensine during evocation of the memory rescues cognitive deficits ($t5=2.679$, $p= 0.0439$) in OLM. Also Aβ adminstration decreases TH + axons, ($F2,7 = 14.25$, $P = 0.0034$) but no MAP2 + axons after 24 h ($F2,7 = 1.152$, $P = 0.3693$).

Conclusion

Our results suggest that improvement of catecholaminergic neurotransmission can attenuate the memory deficits generated by Aβ intrahippocampal administration. These findings highlight that catecholamines may constitute a target for the development of new therapeutic approaches for AD treatment.

Distorted astrocyte GABA homeostasis is correlated with enhanced tonic inhibition and upregulated cannabinoid-type 1 receptors in Alzheimer's disease

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Introduction

Cognitive decline is a major symptom in Alzheimer's disease (AD), which is closely associated with synaptic excitatory-inhibitory imbalance that correlates with excess dysfunctional neurotransmitter GABA mechanisms in reactive astrocytes. Here, we investigated whether presynaptic mechanisms involving cannabinoid type-1 (CB1) receptors, important for regulating excess GABA, were associated with the aberrant astrocyte homeostasis in the hippocampal formation, important for learning and memory and severely degenerated in AD.

Materials & Methods

Using the AppNL-F/NL-F knock in mouse model of AD that closely resembles the human condition in a time-dependent manner, aged-matched to wild-type mice, we performed in vitro electrophysiological whole-cell recordings combined with immuno-histochemistry in the CA1 and dentate gyrus regions of the hippocampus. Furthermore, comparative neuroanatomy experiments were performed in post-mortem brain of human AD patients age-matched to healthy controls.

Results

Using confocal microscope analysis, our data show significantly higher expression of GAD67 (the enzyme responsible for synthesis of GABA), and also the GABA Transporter 3 (GAT3), co-localised with reactive astrocytes in CA1 and dentate gyrus of AppNL-F/NL-F mice in comparison to the age-matched to wild-type mice. These results were mirrored in human tissue with higher levels of GAT3 and GAD67 co-localised with reactive astrocytes in AD patient brain compared to healthy patients. Furthermore, in aged AppNL-F/NL-F mice, in the presence of amyloid beta plaques and increased astrocytosis, there was an up-regulation of CB1 receptors which was consistent with an observed elevated tonic inhibition in both CA1 and dentate gyrus of AppNL-F/NL-F mice compared to the wild-type control mice.

Conclusion

In conclusion, our data is consistent with the hypothesis that AD pathogenesis in the hippocampus is associated with an elevated GABA content in reactive astrocytes, which together with an increased expression of GAT3 may lead to an augmented tonic inhibition resulting in to further changes in compensatory presynaptic mechanisms.

Nutrition
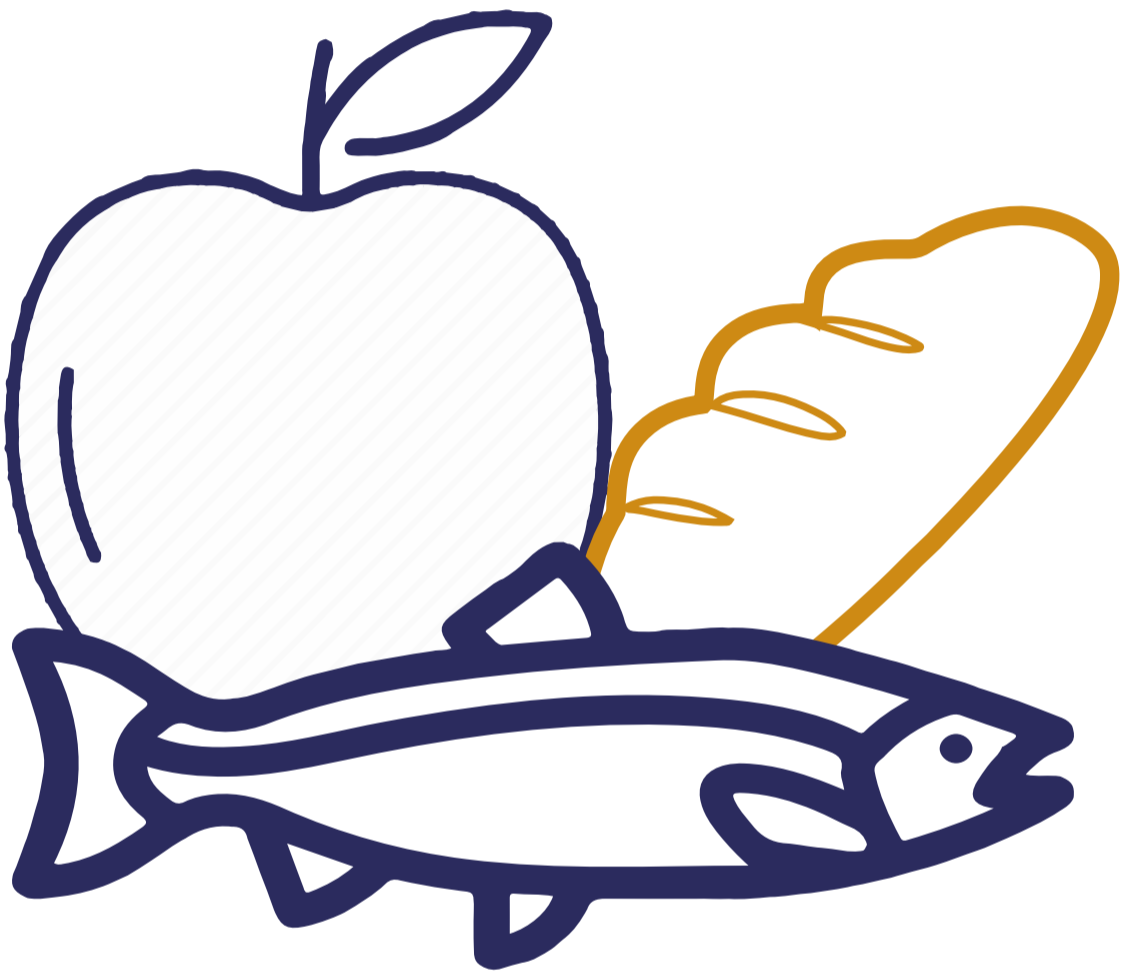
Presenters:
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Mirimoghaddam, M.M. (Mohammad Mobin)
Kramberger, K. (Katja)
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Consumption of animal source protein improves height for age z scores of rural Malawian children aged 12-36 months

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Introduction

In Malawi, complementary feeding is dominated by monotonous, low-quality protein and micronutrient poor foods such as maize, rice and cassava which is liked to malnutrition. Provision of high quality protein has been shown to reduce the rates of malnutrition. The aim of this analysis was to assess the association of the type and protein quality of food consumed with stunting, EED and acute malnutrition in children aged 6–36 months in Limera and Masenjere, two rural Southern Malawian communities

Materials & Methods

We used data from two randomized controlled trials that tested the effects of legume flour addition to the complementary food of 6-36 month old children on stunting. Dietary intake was collected using two interactive 24-h dietary recalls conducted 12 weeks after enrolment into the trials. Food intakes were compared between the regions of Masenjere and Limera villages using Chi-square and Student's t-test.

Results

355 children participated in the dietary recalls. The overall diet of the children was poor in both regions; however, children from Limera consumed more fish (54% vs, 35%, p=0.009) and more bioavailable protein (26.0 (10.3) g/day vs. 23.1(8.1) g/day, p = 0.018, respectively) than children from Masenjere. Protein quality and food type were not associated with with wasting and EED but consumption of animal protein improved height-for-age z score in children 12-36 months of age (p=0.047).

Conclusion

Consumption of animal source food improves height-for-age z scores compared to plant based diets. Animal-source food (ASF) is superior to plant-source food due to a rich protein and micronutrient profile, and we conclude that interventions that promote higher intakes of ASF in populations like this have the potential to reduce the incidence of stunting

Dietary antioxidants and fiber intake and depressive symptoms in Iranian adolescent girls

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Introduction

Depression is a serious mental problem round the world as it was on the top list of world health organization trends. One of the populations who are at the most risk of depression is adolescent girls. Oxidative pathways also may play a role in developing depression thus we urged to assess dietary antioxidants and fiber intake in Iranian adolescent girls and compare it with depressive symptoms.

Materials & Methods

A total of 988 adolescent school girls aged 12-18 years were included using random cluster sampling method. Subjects with a history of autoimmune diseases, cancer, metabolic bone disease, hepatic or renal failure, cardiovascular disorders, malabsorption or thyroid, parathyroid or adrenal diseases were not included in our study. Patients' demographic including age, supplement use, chronic diseases, smoking status, menstruation status, psychological treatment, medical history weight, height and waist circumference were recorded. Dietary antioxidants and dietary fiber intakes were assessed via a validated food frequency questionnaire (FFQ). Depressive symptoms were assessed using the Beck Depression Inventory (BDI-II). All analyses were conducted using SPSS version 20. p value under 0.05 were considered significant.

Results

Subjects with no or minimal depression symptoms had significantly higher dietary intakes of α-carotene (588.9±633 mcg/d vs. 479.1±507.7 mcg/d), β-carotene (3558±2876 mcg/d vs. 3024±2321 mcg/d), lutein (2031±1837 mcg/d vs. 1763±1507 mcg/d), and vitamin C (99.1±65.9 mcg/d vs. 90±53.7 mcg/d) when compared with subjects with mild-to-severe depression symptoms. Soluble dietary fiber (0.42±0.36 g/d vs. 0.34±0.25 g/d) and insoluble dietary fiber (2.17±1.62 g/d vs. 1.79±1.19 g/d) intakes were also significantly higher in healthy adolescents compared to those with depression symptoms. In multivariate-adjusted model 2, the odds ratios of depressive symptoms were 0.61, 0.42, 0.50, 0.71, 0.51 and 0.42 for the highest versus lowest quartile of vitamin C, β-carotene, α-carotene, lutein, soluble dietary fiber, and insoluble dietary fiber cereal intakes, respectively.

Conclusion

Our results indicate that dietary intake of some antioxidants and dietary fiber intake were inversely associated with depression symptoms among Iranian adolescent girls.

In vitro studies of H. italicum traditional extracts state its great potential in phytomedicine

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Introduction

Helichrysum italicum (Roth.) G. Don. is an iconic plant of the Mediterranean area, with versatile biological activities. Extensive scientific research of H. italicum has proven many biological properties of its isolated substances. However, traditional whole plant aqueous extracts have not been examined so far. Our aim was to support ethnopharmacological reports on the use of H. italicum preparations with scientific data.

Materials & Methods

The plant material was collected in the plantation located near coastal town of Ankaran, Slovenia. Dried plant material was milled and used for hydroalcoholic maceration or water infusion. Extracts were subjected to phytochemical screening with UHPLC-ESI-QTOF/MS and further tested for bioactivity. Radical scavenging potential was determined by DPPH test. Cytotoxicity and protective effect against oxidative stress were carried out on mammalian enteric cells – Caco-2 and CCD112CoN.

Results

Phytochemical composition of the infusion was comparable with the hydroalcoholic extracts. H. italicum infusion contained all major bioactive substances: arzanol, pinocembrin and chlorogenic acid. Total polyphenolic content, expressed as pinocembrin equivalents µmol per g of dry mass was 47,63 and 25,24 for hydroalcoholic and water extract, respectively. Maximal DPPH radical scavenging activity of the hydroalcoholic extract was 87 and 83 % for the infusion, whereas for ascorbic acid it was 94 %, with corresponding IC50 values of 31, and 45 and 3,17 µg/mL, respectively. 1000x dilution (approx. 6 µg/mL) of the infusion was non-cytotoxic for Caco-2 cells (p=0,148) but was toxic for CCD112CoN cells (p=0,00254). Lastly, the infusion proved to be protective against oxidative stress induced by t-BOOH. Compared to untreated cells the oxidation of cells pre-treated with H. italicum infusion was lower for 20,7 %.

Conclusion

Oxidative stress is an underlying cause for several degenerative diseases, that can be prevented with the use of antioxidants. In this context, H. italicum can be viewed as the Mediterranean panacea, and its extracts have the potential to be developed as dietary supplement ingredients. The research is ongoing and clinical study on healthy volunteers is planned in the near future.

Low selenium serum levels are associated with poor clinical outcomes in critically ill children

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Introduction

Major gastrointestinal surgeries in childhood era may lead to Pediatric Intensive Care Unit (PICU) admission due to the oxidative stress and inflammation following surgeries, acute stress response that may be associated with poor clinical outcomes. Previous studies reported selenium as a key component of antioxidant defense system which serum selenium levels are directly correlated with the severity of oxidative stress. In this study, we investigated the possible relation between serum selenium concentrations and clinical outcomes following major gastrointestinal surgeries.

Materials & Methods

In this cross-sectional study that was carried out at Akbar Children's Hospital in Mashhad, Iran, gastrointestinal surgical PICU patients with ICU length of stay>24 hours were enrolled. Patients' ages, weight, height, and and weight for height z-score were recorded. Patients' serum selenium level was assessed by atomic absorption. Clinical outcomes including infection, ICU and hospital staying tome and duration of ventilator dependency were recorded prospectively.

Results

Totally, 66 critically ill children were enrolled which their mean age, weight, and height were 13.2±25.6 months, 6.1 Kg (SD= 4.4), and 63.7 cm (SD= 19.5), respectively. The mean of serum selenium concentration upon the ICU admission time was 38.9 ng/mL (SD= 9.8) and only 7 patients (10.6 %) had optimal serum selenium concentration (> 50ng/mL). Eighty percent of the studied patients (N=53) were at normal nutritional status at the admission time (according to WH z scores) and this index was not correlated to serum selenium concentration which was measured upon the ICU admission time. Low concentration of serum selenium was associated with infection and hospital staying time in the studied population (P= 0.01, and 0.04, respectively). However, serum selenium levels upon the ICU admission time was not associated with other clinical outcomes including length of ventilator dependency and ICU staying time, and 28-day mortality.

Conclusion

Low serum selenium levels were associated with higher infection rate and longer hospital staying time in post major gastrointestinal critically ill children; however, furthere studies especially randomized clinical trials are requiered to assess the exact interrelation between oxidative stress, inflammation, and selenium status in pediatrics critically illnesses.

The effect of the ketogenic diet on mitochondrial function in porcine precision-cut kidney slices

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Introduction

Kidneys derived from Donation after Circulatory Death (DCD) donors suffer more ischemic injury compared to Donation after Brain Deatch (DBD) donors. When after transplantation reperfusion occurs, the formation of Reactive Oxygen Species (ROS) contributes to the development of ischemia reperfusion injury (IRI). The major site of production and the major target of ROS are the mitochondria. Preoperative fasting is known to be protective against renal IRI. During fasting or a ketogenic diet, the metabolic substrate switches from glucose to fatty acids, which then becomes the main source for energy production. Precision-cut kidney slices (PCKS) is an ex vivo model to evaluate intra- and extracellular mechanisms. Here, the aim is to evaluate the effect of a ketogenic diet on mitochondrial function using PCKS.

Materials & Methods

Porcine kidneys were obtained at a local abattoir. After 30 min of warm ischemic time (WIT), kidneys were placed on hypothermic machine perfusion (HMP) and preserved for 3 hours with University of Wisconsin Cold Storage (UW-CS) solution. Thereafter PCKS were made and incubated at 37ºC with 80% oxygen. The incubation medium consisted Roswell Park Memorial Institute (RPMI) 1640 medium without glucose. To this 2mg/mL glucose (control) (n=5), 2 mg/mL (±)-sodium 3-hydroxybutyrate (BHB) (n=5) or 1,5 mg/mL SMOFlipids® (SMOF) (n=5) was supplemented. Directly after slicing and after 24, 48 or 72 hours of incubation, tissue and medium samples were taken to analyse for different mitochondrial, oxidative stress and injury markers.

Results

No differences were found in mitochondrial respiratory control rates. After 72 hours ATP levels were significantly higher in the control group compared to the BHB group. In the first 48 hours a significant increase in thiobarbituric acid reactive substances (TBARS) levels was seen in the SMOF group. Over time significantly less lactate dehydrogenase (LDH) was seen in the SMOF group compared to the BHB group. No significant differences in aspartate aminotransferase (ASAT) levels were seen.

Conclusion

A ketogenic diet has no beneficial effect on mitochondrial function in the PCKS model. Dietary modifications as a preconditioning strategy are promising, but more in-depth research must be performed.

The Effect of Quail Egg Yolk Intervention on Rattus novergicus Lipid Profile and Superoxide Dismutase Activity of Pancreatic Tissue

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Introduction

Consumption of high cholesterol have a correlation with high inflammation activity which lead to organ injury, including pancreas. Pancreatitis characterized by low level of antioxidant which marked by superoxide dismutase (SOD) activity. Quail egg yolk is the foodstuff which have a higher cholesterol level than the other birds. The aim of this research is to determine the effect of quail egg yolk intervention on lipid profile and SOD activity of pancreatic tissue.

Materials & Methods

The method of this study is quasi-experimental with post-test only control group design and was conducted in the biochemistry and physiology laboratory, Islamic University of Indonesia. This research used 12 male Rattus novergicus aged 1-2 month which divided into 2 groups. The group I were given the quail egg yolk with dose 5 ml/200 gram body weight/day for 4 weeks. The group II were given by standard feed without quail egg yolk intervention. At the end of study, rats were terminated. The lipid serum i.e. triglyceride, cholesterol total (CT), LDL, HDL, and SOD level of pancreatic organ were examined. The data analyzed by using SPSS 2.5 and expressed in mean group±standard deviasion to know the difference of lipid profile by independent t-test and correlation between lipid profile and SOD activity of pancreatic tissue by Pearson correlation test.

Results

Mean of lipid profile group I was 119.03±3.64 mg/dL (Triglyceride), 189.19±4.98 mg/dL (CT), 89.63±1.16 mg/dL (LDL), and 24.07±1.56 mg/dL (HDL). Mean of lipid profile group II was 72.54±44.46 mg/dL (Triglyceride), 88.05±3.14 mg/dL (CT), 26.24±1.7 mg/dL (LDL), and 89.4±2.21 mg/dL (HDL). Mean of SOD of group I and group II were 43.68±5.07% and 92.24±4.04%, respectively. The result of Independent t-test analysis for lipid profile show significant difference with p=0.00 and SOD activity have also significant difference with p=0.00. The Pearson analysis between lipid profile and SOD activity showed significant correlation with p=0.00.

Conclusion

Quail egg yolk increase lipid profile and decrease SOD activity significantly. High lipid profile have a significant correlation with low SOD activity of pancreatic tissue. This research finding show that the consumption of quail egg yolk can increase the lipid profile and may lead to pacreatitis.

High fat diet induce cognitive impairment and increase of amyloid-β in mouse

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Introduction

The high fat diet (HFD) is associated with numerous risk factors as obesity, inflammation, insulin resistance and hypercholesterolemia. Previous studies have reported that fat dietary exacerbates cognitive decline in animal models of Alzheimer's Disease (AD), however It remains unclear whether obesity is a risk factor or induces the cognitive impairment. Here we show the effect of HFD on cognitive decline and the expression of amyloid-β peptide and its association with development of AD in a mouse model of obesity.

Materials & Methods

We used mouse C57BL/6J of six months, (control native and HFD groups, that was feed with HFD for 20 weeks previously). To evaluate short- and long-term memory hippocampal-depend, which involved exploration two identical objects (A and B) in the first session and a second test session, the animals were presented with the object A in the same position and object B in different position. The time between session 1 and 2 is 1 h for short-term memory, while to log-term memory test is 72 h. All sessions were video recorded and analyzed using a MatLab routine. After the task, we measured wieght, glycemia and the hippocampus was dissected for immunofluorescent detection of amyloid-β.

Results

Compared to control, the HFD group exhibited a 23% increment in body weight and the glycemia incresed 3 times compared to control animals. The HFD group show a decrease performance in memory tasks of short and long-term memory and displayed increase of amyloid-β peptide in the region CA1, CA3 and DG hippocampal regions. In all cases, $p < 0.05$, evaluated by Mann Whitney test.

Conclusion

The HFD induce an increase body weight and glycemia clinically associated with pro-oxidative state, that is a big problem around the world. Also, we demostrated that HFD impairment the hippocampal function and increase the expression of amyloid-β peptide. This results show the relevant role of diet in the development of cognitive decline and progression of neurodegenerative diseases such as AD. To our knowlegde, this results have not been demonstrated in previous research.

Oncology I

Presenters:
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Fala, Y., S. (Salma)
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The association between anemia and the stage of colorectal cancer patients in Vietnam

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Introduction

Amenia is a common syndromes in colorectal cancer (CRC) patients but the knowledge in relationship between amenia and stages at the diagnosis with colorectal cancer is unclear in Vietnam. Therefore, this study amed to describe the anemia and explore the association between anemia and the stage of colorectal cancer patients in Hue Central Hospital.

Materials & Methods

This retrospective cohort study was performed in a total 145 new diagnosis with colorectal cancer patients from january 2013 to December 2015 in Hue Central Hospital. The information were extracted from medical records, classified by ICD-10. The stages of CRC was classifield according to AJCC 7th. Anemia syndrome was determined by Blood hemoglobin level and classified according to WHO standards in 2011. Multivariate logistic regression model used to identify the associated factors with anemia in CRC patients.

Results

82% of CRC patients were diagnosed at late-stages (stage III and IV). Nearly 2 in 3 CRC patients experienced with overall anemia (95% CI: 62-70%). The distribution of mild, moderate and severe anemia accounted for 44.2%; 35.8% and 20.0% in respectively. The rate of anemia in stage I, II, III and IV were 25.0%; 77.8%; 66.7% and 65.9% respectively. In multiple logistic regression the patients who dianosed at stage II were 8.86 times (95% CI: 1.24-63.42) higher risk with anemia compare to stage I. Late stage (III and Iv) were also found the higher with the risk with anemia however there was not statistically significant.

Conclusion

The study confirm again that anemia is a common condition in colorectal cancer in Vietnam. The patients who diagnosed at late-stages were more likely to have the higher risk with anemia.

Brain Tumor Survival prediction using machine learning algorithms: a SEER-based study from 2003 to 2014

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Introduction

Brain tumors are well known for their aggressive and heterogenic nature making it difficult to determine the patients' overall survival accurately. Reliable prediction will help in personalizing treatment and subsequent care. Here we test the ability of machine learning to predict patients' OS.

Materials & Methods

We obtained our data from SEER database. Patient characteristics were extracted including: age at diagnosis, sex, race, marital status, tumor site, histology, tumor size in millimeters, grade, WHO stage, tumor extension, metastasis at diagnosis, number of primary tumors and treatment including surgery, radiation and chemotherapy. Data were randomly divided into training set (80%) and validation set (20%). Algorithms were used to predict the survival rate, using scikit-learn, different machine learning algorithms were trained on the data. After preprocessing, we used trained models to make predictions and then we evaluated their performance under a binary classification at different time periods. Tested algorithms include: K-Nearest Neighbors, Logistic Regression, Support Vector Machine, Random Forest, Light Gradient Boosting and Multi-Layer Perceptron.

Results

In the included 52004 patients, the median survival was 13 months. The most common primary tumor sites were: Glioblastoma (52.8%), Astrocytoma (19.2%), and Glioma (9.4%). Multi-Layer Perceptron algorithm achieved better results compared to other tested models. For evaluating model performance, the Area Under the Receiver Operating Characteristic Curve (AUC) was calculated. Multi-Layer Perceptron achieved AUCs of 88.1 at 6 months, 87.5 at 12 months and 89.2 at 24 months. Sensitivity of the trained model was 90.7, 83.1 and 71.1% at 6, 12 and 24 months, respectively. The model achieved an average accuracy of 82.7 %, 79% and 82.5 % at 6, 12 and 24 months, respectively. The most important characteristics which influenced our model performance were: tumor histology, surgery, age, and tumor size.

Conclusion

Our model has a good performance in predicting patients' survival with much higher sensitivity and accuracy than other traditional used methods as TNM staging. This may help physicians to personalize the treatment and subsequent management plan.

Taste and smell disturbances in patients with gastrointestinal stromal tumors treated with tyrosine-kinase inhibitors

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Introduction

Taste and smell disturbances are an underrated and underreported, but important side-effect of anti-cancer medication and are associated with a lower quality of life (QoL). The prevalence of these disturbances and its impact on daily life in patients with gastrointestinal stromal tumor (GIST) treated with a tyrosine-kinase inhibitor (TKI) are not known. This exploratory study assesses the prevalence and type of taste and smell disturbances in GIST patients using TKIs. Associations between taste and smell disturbances, treatment duration and impact on daily life and QoL are studied.

Materials & Methods

Patients currently treated with TKIs for GIST in three Dutch medical centers were send a letter that explained study design and mentioned that they would receive a telephone call. In this call, a standardized questionnaire regarding taste and smell disturbances was completed. Information about patients characteristics was collected from electronic medical files. Statistics were descriptive. Correlations were investigated with cross tables.

Results

These are preliminary results from one GIST expertise center. A total of 22 GIST patients on active TKI treatment completed the questionnaire. Of these patients, 10 (45%) reported taste disturbances and four (18%) reported smell disturbances. Sweet and salty taste were mostly affected, respectively in five and six of the patients with taste disturbances. Two of the four patients with smell disturbances avoided the smells they reported to be stronger. Furthermore, a dry mouth was reported in nine (41%) patients. In most patients, disturbances had little impact on daily life. QoL was lower compared to before treatment in five (50%) and two (50%) of the patients reporting respectively taste and smell disturbances. Data of at least another 40 patients from two other GIST expertise centers are collected in January and February 2020.

Conclusion

Taste and smell disturbances are a frequent side-effect of TKIs in GIST patients. Although QoL is affected, most patients report a low impact on daily life. Healthcare professionals should be more aware of this side-effect, so patients can be informed beforehand and supported mentally when necessary, for interventions on taste and smell disturbances are yet scarce.

Ex vivo vascular reactivity and structural changes in arteries induced by cancer, aging and diverse models: some experiences from Medellin, Colombia

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Introduction

Cancer is a public health problem and the tumor depends on its vasculature. We are studying vascular mechanisms and eventual druggable targets, evaluating ex vivo vascular reactivity (VR) of human colonic cancer vs. non tumoral arteries. This study led us to measure vascular function additionally in diverse models and different ages, with multiple agonists that could promote tumor development through similar mechanisms.

Materials & Methods

Samples: mesenteric arteries from 25 cancer and 12 non-cancer human patients, aortic arteries from 8 young (1.5±0.5 months) and 8 adult (6±1 months) rabbits, mesenteric arteries from 8 humans with non-tumoral pathology (46±9 years), 8 healthy male rabbits (6±1 months) and 8 wistar healthy male rats (3.5±0.5 months).

Arterial rings were held in organ bath, exposed to sodium chloride (KCl), phenylephrine (FE), a thromboxane analog (U46619), endothelin (ET-1), carbachol (CCH), vascular endothelial growth factor (VEGF) or bradykinin (BK). Histological analysis were performed on cross sections of the arteries with hematoxylin-eosin staining, receptor expression was measured by fluorescent microscopy, and gene expression was measured by RTqPCR. Differences among subgroups were determined by ANOVA, being $p < 0.05$ significant.

Results

Preliminary results show statistical differences between tumoral (TU) and extratumoral (ET) vs non-tumoral (NT) arteries to FE, U-46619 and VEGF; arteries that supply colonic tumors have an increased sensitivity to vasoconstrictors. We also found an increase of ECE-1 expression in TU and decrease in ET, with a decreased expression of VEGF in TU and increase in ET. Also, histological analysis revealed hyperplasia of the tunica intima in TU compared with NT. In the other models, we found that arteries of rat and rabbit show more contractile force than human, and aortic rings from older rabbits show more sensitivity and contraction to FE than youngsters.

Conclusion

We show preliminary results in ex vivo VR and structural changes in the artery modulated by cancer and aging, as well as the comparability of arterial physiology in different models. With this information, we show some mechanisms affected by colon cancer in the arteries that irrigate it, and eventual druggable targets that could be implemented in the future.

Consolidative intensity-modulated radiation therapy (IMRT) following first-line chemotherapy is efficacious and safe for de novo metastatic (M1) nasopharyngeal carcinoma (NPC): A Phase II clinical trial

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Introduction

Platinum-based doublet chemotherapy is the standard first-line systemic treatment for M1 NPC. The role of consolidative IMRT to the primary tumour and the neck following chemotherapy in M1 NPC remains poorly defined. In this study, we reported the feasibility, efficacy and safety of our phase II single-arm study first-line cisplatin and gemcitabine (GP) followed by consolidative IMRT in de novo previously untreated M1 NPC patients whose disease did not progress after 6 cycle of first-line GP.

Materials & Methods

Consolidative IMRT was given in prospectively recruited patients whose previously untreated M1 NPC did not progress after 6 cycles of first-line chemotherapy with GP. The primary study objective was overall survival (OS). Secondary objectives included progression-free survival (PFS), local relapse-free survival (LRFS), regional relapse-free survival (RRFS), response and toxicity.

Results

Sixty-nine patients were enrolled. Sixty-four (92.8%) patients received first-line GP, of which 8 (12.5%) developed progressive disease and another 8 (12.5%) did not receive IMRT despite non-progression to GP. The remaining 48 patients whose disease controlled after GP received consolidative IMRT. After a median follow-up of 3.40 years, the median OS, PFS, LRFS and RRFS of the whole study population were 26.02 months, 9.76 months, not reached and 62.92 months, respectively. OS was significantly better in those who received consolidative IMRT (35.1 versus 14.2 months; P < 0.001), compared to those who did not. PFS, LRFS, and RRFS were also significantly longer with IMRT. Multivariable analyses revealed that only IMRT was prognostic of all survival endpoints. Grade 3 adverse events were observed in 10 (20.8%) patients.

Conclusion

Our study demonstrated the efficacy and safety of consolidative IMRT following non-progressive disease to first-line chemotherapy with GP for previously untreated M1 NPC.

Oncoplastic repair in breast conservation: a comprehensive evaluation of the techniques, and oncologic outcomes of 937 patients

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Introduction

Breast-conserving surgery (BCS), especially with Oncoplastic Breast Surgery (OBS), is becoming the standard of care in the surgical management of breast cancer. In the present study, we investigate the applied technique of OBS and oncologic outcomes in a large series of patients in two centers in Iran.

Materials & Methods

This study was conducted between January 2008 and June 2018 in two centers in Iran. All the breast cancer patients, in whom different techniques of oncoplastic breast surgery were applied, are included in this prospective study. A single breast surgeon performed all the operations in two different centers, Imam and Laleh hospitals (Tehran, Iran). Early and late postoperative complications, as well as oncologic outcomes, and the follow-up data of the patients were documented.

Results

Nine hundred thirty-seven patients with a mean age of 48.1±11.3 underwent Oncoplastic Breast Surgery (OBS). Most of the patients were diagnosed with early-stage disease, of which the most common pathology was invasive ductal carcinoma (83.3%). Lateral Oncoplasty was the most commonly used OBS technique (324 cases, 34.6%). The most common complication was seroma formation. Reduction type OBS technique had the highest rate of complications (13.1 %). Thirty-four patients (5.4%) recurred locally with a median recurrence time of 26.4 months. Thirty-seven (5.4%) patients were diagnosed with distant metastasis with a median follow-up time of 30.5 (1st and 3rd IQR: 20.7 and 46.2) months. Nine patients (1.3%) died from cancer recurrence.

Conclusion

"OBS" is a safe procedure with minor complications and good oncologic outcomes. The risk of recurrence was acceptable. These techniques can be applied for the vast majority of the patients who are candidates for BCS.

Pharmacology I
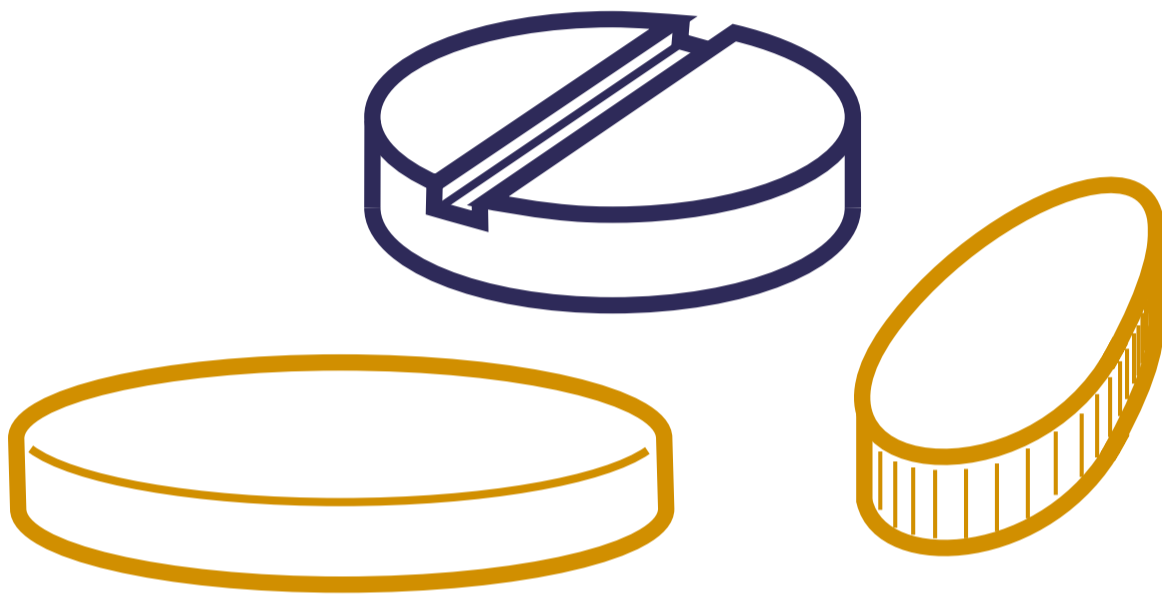
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Prednisolone as Adjunctive Treatment to Risperidone in Children with Regressive Type of Autism Spectrum Disorder: A Randomized, Placebo-Controlled Trial

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Introduction

This study aimed to evaluate efficacy and safety of prednisolone as an adjunctive treatment to risperidone, in children with regressive autism spectrum disorder (ASD).

Materials & Methods

The current 12-week, randomized, single-blinded, placebo-controlled trial recruited 37 patients with regressive ASD. The participants were allocated to receive either 1 mg/kg/day prednisolone or matched placebo in addition to risperidone. The Aberrant Behavior Checklist-Community Edition (ABC-C) scale and Childhood Autism Rating Scale (CARS) were used to measure behavioral outcomes at weeks 0, 4, 8, and 12 of the study course. The primary outcome was the change in ABC-irritability subscale score while the secondary outcomes were the change in scores of other ABC-C subscales, in CARS score, and in the level of inflammatory biomarkers.

Results

Twenty-six patients completed the 12 weeks of study period. Repeated-measures analysis demonstrated significant effect for time-treatment interaction in the CARS [$F_{(1, 2.23)} = 13.22$, $p < 0.001$], as well as four subscales of the ABC-C including: irritability [$F_{(1, 2.12)} = 3.84$, $p = 0.026$], hyperactivity [$F_{(1, 2.09)} = 3.56$, $p = 0.039$], lethargy [$F_{(1, 2.18)} = 31.50$, $p < 0.001$], and stereotypy [$F_{(1, 1.89)} = 4.04$, $p = 0.026$]. However, no significant time-treatment interaction was identified for inappropriate speech subscale [$F_{(1, 2.03)} = 1.71$, $p = 0.191$]. Additionally, inflammatory biomarkers were significantly decreased after 3 months of prednisolone add-on. No significant adverse event was detected during the trial.

Conclusion

Prednisolone, as an add-on to risperidone could remarkably improve core features in children with regressive ASD.

Inhibition of Phosphodiesterase IV Enzyme Attenuates Locomotor and Sensory Complications of Spinal Cord Injury via Altering Microglial Activity

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Introduction

Roflumilast is a selective inhibitor of phosphodiesterase 4 (PDE4) with potent anti-inflammatory properties. In the present experiment, we aimed to assess the efficacy of Roflumilast therapy for improving the locomotor and sensory deficits of spinal cord injury (SCI) as well as its mediating mechanisms.

Materials & Methods

Fifty rodents were randomly allocated to five groups: an SCI group receiving Placebo, three SCI groups receiving different doses of Roflumilast prior to induction of the lesion at the level of T9 vertebra, and a sham-operated group. Locomotor, mechanical and thermal activities were evaluated for 28-days. At the end of the study, spinal cord samples were collected to assess microglial activity, histopathological changes, inflammatory biomarkers, as well as intracellular cAMP.

Results

Repeated measure analysis revealed significant effect for time-treatment interaction in locomotion [$F_{(24, 270)} = 280.7$, $p < 0.001$], thermal sensitivity [$F_{(16, 180)} = 4.35$, $p < 0.001$], and mechanical sensitivity [$F_{(16, 180)} = 7.96$, $p < 0.001$]. H&E staining was suggestive for lesser histopathological disruptions in Roflumilast-treated rodents. Moreover, immunohistochemical (IHC) analysis represented a significantly lower M1/M2 ratio following Roflumilast administration for spinal cord injured rats, which was accompanied by significant reductions in inflammatory biomarkers. Finally, Roflumilast administration leaded to increased expression of spinal cAMP.

Conclusion

Roflumilast, as a selective PDE4 inhibitor, can improve locomotor and sensory dysfunctions caused by SCI via increasing intracellular cAMP level, altering microglial activity, and decreasing inflammatory biomarkers.

Efficacy and safety of nicorandil in acute coronary syndrome: a meta analysis

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Introduction

Nicorandil acts as a potassium channel opener, however its cardioprotective benfit is still uncertain. This meta-analysis was conducted with the objective of evaluating the efficacy of nicorandil in improving cardiovascular outcomes in acute coronary syndrome.

Materials & Methods

A total of 24 RCTs with 1640 patients in the nicorandil group and 1592 patients in the control group were identified following PRISMA guidelines till November 2019 andwere matched for inclusion and exclusion criteria. The following search strings and MESH terms were used: "nicorandil", "ACS", "MACE". Following this, nicorandil was evaluated for its efficacy and safety outcomes.RevMan 5.3 was used for appropriate statistical tests. Fixed and Random Effect Model Test were used and $p<0.05$ was considered statistically significant.

Results

Administration of nicorandil was found to be associated with a significant decrease in MACE ($RR = 0.6$, 95% CI = 0.473-0.761, $p < 0.001$), no-reflow phenomenon($RR =0.418$, 95% CI = 0.305-0.575, $p < 0.001$) and worsening of HF($RR =0.407$, 95% CI = 0.237-0.699, $p=0.001$). It was also associated with significant improvement in LVEF (SMD= 0.303, 95% CI= 0.187 to 0.419, $p < 0.001$) and significant lowering of cTFC (SMD= -0.478, 95% CI= -0.747 to -0.280, $p < 0.001$)

Conclusion

Nicorandil does indeed exert a cardioprotective effect by improving cardiovascular outcomes. There is a significant decrease in occurrences of MACE and worsening of HF. There is also significant improvement in LVEF.

Nitrido-osmium(VI) Schiff-base Complex Induces Caspase-mediated Apoptosis and Anticancer Activity

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Introduction

Cancer is a leading cause of death worldwide for which chemotherapy remains the most effective treatment to prolong survival rates. Central to chemotherapy regimes used to treat a broad range of cancers is cisplatin, the most important platinum-based component. Interest in the third-row transition metal osmium and its compounds as potential anticancer drugs is also growing. The nitridoosmium(VI) complex [OsVI(N)(sap)(OH2)Cl] (H2sap=N-salicylidene-2-aminophenol) bearing a tridenate Schiff base ligand was designed and found to have good anticancer activity in vitro and in vivo. In this paper, we have modified [OsVI(N)(sap)(OH2)Cl] (1) to be [OsVI(N)(sap)(py)Cl] (2) in order to change the substitution reaction rate between "leaving group" and nucleic acid.

Materials & Methods

Physical measurements and characterizations methods including X-ray Crystallography, IR, 1H NMR, MADLI-TOF-MS and CHN. The biological assays involve MTT, colony formation assay, DNA binding assay, DNA extraction, agarose gel electrophoresis, cell cycle and apoptosis by flow cytometry, western blotting and laser confocal microscopic

Results

DNA binding assay including UV-visible absorption spectroscopy, Circular Dichroism spectra and pBR322 plasmid DNA agarose gel electrophoresis revealed that [OsVI(N)(sap)(py)Cl] targets the DNA causing its conformation change through the insertion mode. The IC50 of [OsVI(N)(sap)(py)Cl] is 2.8-8.4µM and it can inhibit the colony formation. [OsVI(N)(sap)(py)Cl] also displays well antitumor efficacy in vivo and without weight loss of nude mice compared with cisplatin. The flow cytometric, laser scanning confocal microscope and western blot analysis indicated that [OsVI(N)(sap)(py)Cl] can induce the G2/M phase arrest, the depolarization of the mitochondrial membrane potential and caspase-mediated apoptosis.

Conclusion

The osmium(VI) nitrido complex, [OsVI(N)(sap)(py)Cl] (2) is a potential anti-cancer drug, based on both in vitro and in vivo results. It exhibits good antiproliferative activities toward a panel of cancer cell lines and inhibits colony formation in HepG2 cells. DNA binding assays reveal that complex 2 targets the DNA, causing its conformation change through the covalent binding and insertion. Mechanistic studies indicate 2 induces HepG2 cells G2/M phase arrest, disrupts the mitochondrial membrane potential and caspase-mediated apoptosis through the activation. In vivo antitumor efficacy study using HepG2-bearing nude mice result good efficacy of 2 in inhibiting tumor growth without weight loss side effect compared to cisplatin.

Integration of co-grinding method and floating systems to enhance the dissolution rate and bioavailability of carvedilol

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Introduction

The floating drug delivery systems have a bulk density lower than gastric fluids; therefore, they remain buoyant in the stomach without affecting the gastric emptying rate, and in this way, the drug is released from the drug-delivery system at the controlled rate. Due to the weak alkyl property of carvedilol and low dissolution rate in the intestine, the longer is the drug residence time in the gastric, the more likely it is to increase the drug bioavailability. The aim of the study is providing the floating system to increase the residence time of the system in the stomach and its integration with the co-grinding method to improve the dissolution rate and drug bioavailability.

Materials & Methods

The floating tablets were prepared by direct compression method using polymers (such as HPMC, carbopol, and psyllium), calcium carbonate, fillers, magnesium stearate, and different ratios of lactose drug. In order to the preparation of solid dispersion by co-grinding method, first, different ratios of drug/carrier were charged into the chamber of a vibration ball mill. Then the tablet was pressed and tested in terms of floating properties. The DSC spectra were taken.

Results

The results show that the selected formulations are capable of floating for 3 hours, which causes increasing the drug- residence time in the stomach and probably increasing drug absorption and drug dissolution rate. Increasing lactose as a water-soluble filler alters drug release mainly by modifying the permeability of drug into the gel layer. Also, using the co-grinding method along with the particle size reduction mechanism increases the drug release rate significantly, thereby causes increasing the rate of drug dissolution.

Conclusion

Because carvedilol has a hepatic first pass, if the drug is slow release, the hepatic enzymes will have the needed time to convert the drug to their metabolites. Therefore, if the drug is rapid release, a saturation of the hepatic enzymes occurs during the hepatic pass, and less inactive metabolites are produced, and as a result, the effectiveness of the drug increases. Moreover, using the floating form and its integration with the co-grinding method increases the dissolution rate and thereby increased drug absorption.

Cardio Protective Effects of Hydroalcholic Citrus Aurantium Extract on Myocardial Infarction Induced by Isoproterenol in Male Rats

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Introduction

The citrus aurantium has traditionally been used by the people of Iran. The aim of this study was to evaluate the protective effects of hydroalcholic citrus aurantium extract on electrocardiographic, biochemical and pathological changes after myocardial infarction induced by isoproterenol in rats.

Materials & Methods

24 male Wistar rats were divided randomly into 4 groups: Control, extract, isoproterenol, and isoproterenol + pre-treatment with extract for two weeks. At the end of the experiment, ECG was recorded in lead II. Finally, blood samples were taken and cardiac marker enzymes such as creatine kinase, lactate dehydrogenase, aspartate aminotransferase, alanine aminotransferase, and alkaline phosphatase, along with oxidative stress markers such as malondialdehyde, superoxide dismutase, catalase, glutathione reductase, glutathione peroxidase, and lipid profile were determined.comparison of the data among groups was done using one-way analysis of variance followed by Tukey`s post hoc test, and non-parametric analysis (Kruskal-Wallis and Mann-Whitney U test) for histopathological examination

Results

Myocardial infarction induced by isoproterenol produced a significant increase in the heart rate, ST-segment elevation, decrease in R amplitude, and a significant increase in the level of cardiac marker enzymes: LDH, CK-MB, AST, ALT and ALP in serum. Also, isoproterenol significantly reduced SOD, CAT, GSH, GPX and increased MDA activity, disturbance in lipid profile, and inflammatory process in cardiac myocytes. Pretreatment with citrus aurantium extract for two weeks significantly reduced the effect of isoproterenol on electrocardiographic parameters, cardiac biomarkers, oxidative stress indices, lipid profile and cardiac myocytes injuries.

Conclusion

Results indicated that citrus aurantium extract ameliorates the cardio-toxic effects of isoproterenol through reinforcement of antioxidant defense system and may be of value in treatment of myocardial infarction. Further studies are required to determine the precise mechanism of the therapeutic effect of the extract.

Efficacy and safety of Preladenant as an adjunctive therapy with Levodopa for Parkinson's Disease and motor fluctuations: A pooled analysis of randomized controlled trials of 1759 patients

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Introduction

Parkinson's disease (PD) comes at the second place for the most common neurodegenerative disorders after Alzheimer's disease. Preladenant, which acts as a potent and selective adenosine A2A receptor antagonist, has been investigated as a potential adjunctive treatment for PD.

In this study, we aim to build a concrete evidence regarding the safety and efficacy of preladenant as an adjunctive therapy to levodopa among patients with idiopathic primary PD.

Materials & Methods

We systemically searched PubMed, Cochrane library, Scopus, and Web of science for all relevant randomized controlled trials (RCTs) that met the inclusion criteria on April 3rd, 2019. Efficacy primary outcomes included change in off-time from baseline to week 12 and on-time with non-troublesome dyskinesia. Efficacy secondary outcomes included change in on-time without dyskinesia, on-time with troublesome dyskinesia and Unified Parkinson's disease Rating Scale (UPDRS- Part 1, 2 & 3). Safety and tolerability included adverse events results.

Results

Four RCTs (n=1720) included in the efficacy meta-analysis each of which included at least one of three subgroup Preladenant doses 2 mg, 5 mg, and 10 mg. Collective efficacy was significantly enhanced with the use of Preladenant compared to placebo, as change in mean off-time from baseline across latter subgroups (P value = 0.033, 0.028, 0.040 respectively). Moreover, change in on-time with non-troublesome dyskinesia across latter subgroups (P value = 0.006, 0.032, 0.040 respectively). Additionally, UPDRS – Part 3 across last two subgroups (P value = 0.002, 0.002 respectively). As for safety, five RCTs (n= 1144) were included in the meta-analysis, adverse effects were insignificantly increased with preladenant except for the 10 mg subgroup (P value = 0.026), and none of the subgroups showed a significant drug related adverse effects compared to placebo, supported by a fact that none of the adverse effects across all dose subgroups lead to significant discontinuation of treatment compared to placebo.

Conclusion

Use of Preladenant as an adjunctive therapy to levodopa in patients with idiopathic primary PD shows promising efficacy and acceptable safety profile compared to placebo, further extensive study to assess clinical significance of Preladenant is warranted to be considered as a treatment modality for idiopathic primary PD.

Public Health
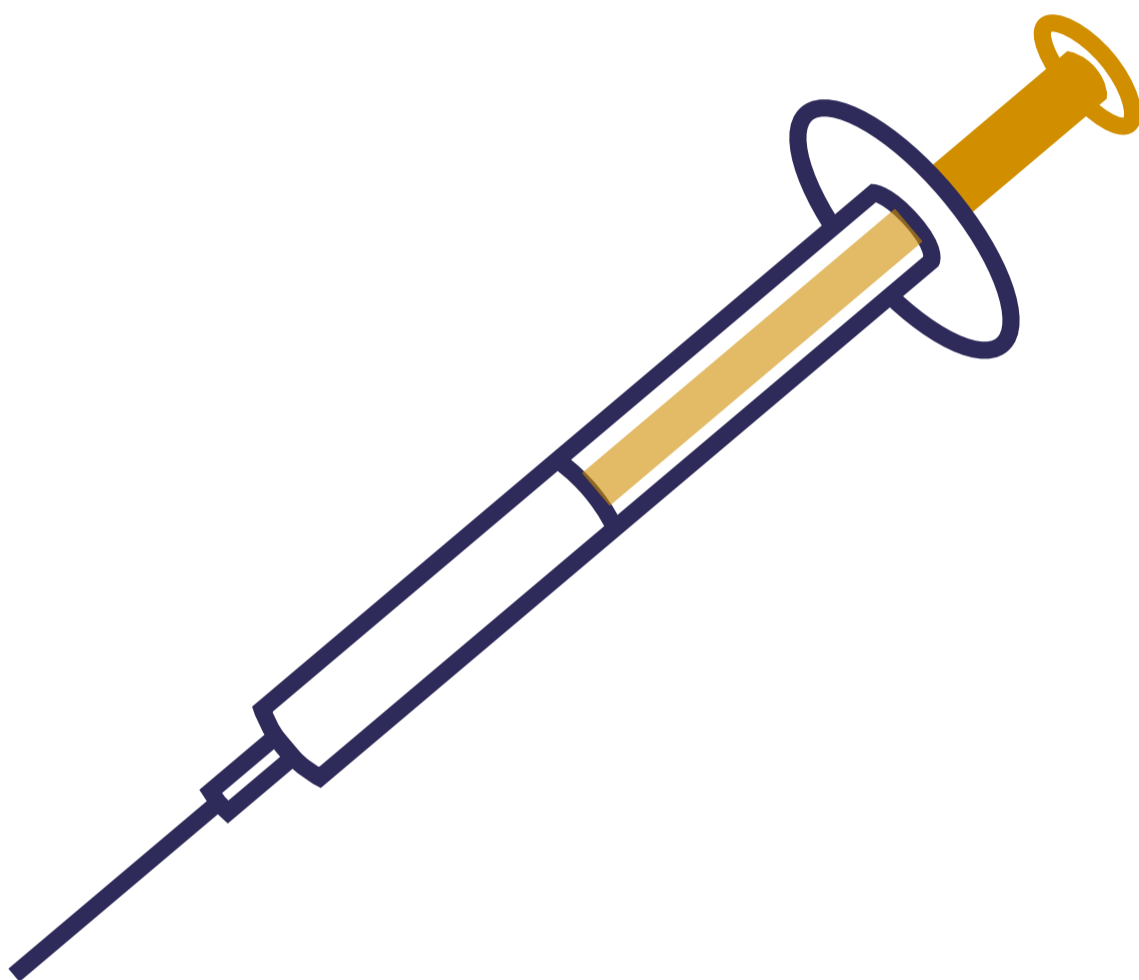
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Impact of the first year of medical school in the growth and personal development of students

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Introduction

Entering medical school represents important changes for students in their abilities to confront academic challenges. This is associated with situations such as the need to adapt to new environments, and their age among other factors, when they experience more intensely this transition. The challenge of adapting are not only to new situations but also to the need for redefining decisions that can influence the rest of their life, since many students before unfavorable abandon the studies.

Materials & Methods

It is a comparative study with 891 students, applying a 10-scale instrument with reliability coefficients between 0.617 and 0.786, at the beginning and at the end of the first year of medical school, to study the differences in their development. This study brings together the following 10 scales: self-esteem, self-knowledge and emotional expression, commitment, creativity, resilience and coping, positive out look on life, self-confidence, assertiveness and leadership, empathy and teamwork, social and interpersonal skills. The Wilcoxon test for paired samples was applied.

Results

Based on the scores obtained in each scale, and by grouping them in levels of low, medium, and high, we observed that around 47% of the students at the beginning of the school year had a general high score in self-esteem, commitment, positive outlook of life, self-confidence, work team and social skills, however, most of them declined at the end of the first year. The exceptions were resilience, assertiveness, leadership, and empathy; which presented a low or medium level at the beginning and increased at the end of the year.

Conclusion

The first year affects students and many of their abilities to confront the academic difficulties tends to diminish, but on the other hand we can see an increase in their intentions to adapt through believing in themselves and if teachers would collaborate in this endeavor students could have a better chance for completing their first year adequately.

Why non-urgent patients visit the ER and is there an alternative?

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Introduction

The demand for urgent care is increasing, and the pressure on emergency departments is of significant concern. Mixture of non-urgent walk-in patients and acute emergencies in the same emergency department can inevitably make it more difficult to provide genuine emergencies with rapid treatment, leading to deterioration in the quality of emergency services. The variety in reasons given can be attributed to this phenomenon to the different heath care systems, cultures, and income. The aim of this research project was to identify profiles in non-urgent presentations and gain insight into; why the ED was chosen by attendees with non-urgent complaints and the presenting health complaint of attendees.

Materials & Methods

A cross-sectional descriptive survey study with patients who were triaged with a 'minor illness' or 'green' on arrival to an urgent care centre (n:613).

Results

Among the 613 patients we have interviewed, we have noticed that the most common reasons behind attending to the ER were perceived emergency (38.6% n:237), and difficulty in obtain a regular appointment (21.3% n:130). The vast majority described their experience in the ER as unpleasant (86% n:527) and comparing the ER experience with other health care experience it was mostly worst (78.4% n:479). Surprisingly, only third of the patients would prefer to go to a family physician instead of visiting the ER (32.4% n:199) if available, more than half would still prefer visiting ER (53.8% n:330). Not having a regular family physician was the main barrier for the patients to visit a PCP (43.8% n:269), cost was rarely mentioned (2.6% n:16). Females were more open to the idea that their cases could be handled using an online medical service (video or audio) (62.3% n:186), than males did (41.7% n:130).

Conclusion

The diversion of nonurgent patients away from the ER would be a difficult mission as it requires changing different misleading perceptions that are deep and common among the population. Providing a variety of alternative such as: open walk-in GP clinics and online medical services could help alleviate the problem

Universal Health Coverage in India– Ayushman Bharat: An Indian experience

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Introduction

To fulfil the vision of Universal Health Coverage, Government of India conceived 'Ayushman Bharat' (Healthy India), for the entire Country, in an attempt to move to a comprehensive need-based health care service. There is paucity of information related to the awareness and utilization of this scheme in the citizens of India.

Materials & Methods

This Hospital based cross sectional study was conducted among 423 outpatient attendees aged 18 years and above in the Tertiary care hospitals attached to Kasturba Medical College, Mangalore, Manipal Academy of Higher Education, Mangalore, India between May and August 2019. Data were collected using a semi structured proforma via digital hand held device. After obtaining approval of the IEC, hospitals were visited for data collection. Awareness and utilization levels towards Ayushman Bharat were assessed and analyzed using IBM SPSS Statistics for Windows, Version 25.0 Armonk, NY:IBM Corp. Comparison across the groups were done using Chi-square test and a p-value < 0.05 was considered as statistically significant.

Results

Out of total 423 participants with mean age 40.01 years (SD:19.9), 240 (56.7%) were males, 108 (25.5%) were in upper socio-economic class, 10 (2.4%) in lower class. Overall, 236 (55.8%) had heard about the word Ayushman Bharat and 213 (50.4%) were aware about its features. Among them, 30 (7.1%) had actually utilized the facilities under Ayushman Bharat for any health ailments. Not having felt need (95) and card not being made available on time (67) were the factors inhibiting them from using Ayushman Bharat scheme. Males had higher level of awareness (62.5% versus 47%; p=0.001). The awareness across the socio-economic strata increased 40% in lower class to 82.4% in upper class (p < 0.0001). Awareness and utilization did not vary across other demographic characteristics.

Conclusion

Nearly half of the participants were aware about the Ayushman Bharat schemes; level of utilization was low. Males and those from upper socio-economic class had higher level of awareness. Other demographic factors did not influence the awareness and utilization.

Is it possible to accurately predict overweight at age 10-12 years based on information at birth and during the first year of life?

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Introduction

Childhood obesity is a worldwide public health problem. Tools for youth health care professionals to predict childhood overweight/obesity from early age onwards are therefore urgently needed. This might facilitate early risk group detection and adequate follow-up from early age onwards. In this study, we have developed a prediction model which uses easily assessable predictors during pregnancy and the first year of life to predict overweight status age 10-12 years.

Materials & Methods

Data from the Amsterdam Born Children and their Development (ABCD) cohort study were used. Overweight status at age 10-12 years was defined according to WHO reference (> 85th percentile, age and sex specific). Seventeen predictors were identified from the literature and collected during pregnancy or during the first year of life. The prediction model was developed using multiple logistic regression analyses, with a backward selection procedure (p-value>0.10). Quality of the model was determined by Area Under the Curve (AUC), pseudo R2 and the Hosmer and Lemeshow tests. Internal validation was done by resampling techniques. Missing data was imputed, resulting in a total sample size of 7810.

Results

Prevalence of overweight was 27.9% at age 10-12. The final model included 12 significant predictors, (ethnicity, educational level of the mother, maternal age, maternal pre-pregnancy BMI, paternal BMI, diabetic status of mother, smoking during pregnancy, gender, birthweight, attending daycare, smoking in house during infancy and Δ weight-for-length during the first 6 months) with an AUC of 0.75 and a pseudo R2 of 0.22. The quality of the model was sufficient.

Conclusion

Prediction of overweight at age 10-12 years, based on easy obtainable information at birth and during the first year of life, is possible with sufficient accuracy. The prediction tool might facilitate early overweight prevention through detection of children at high risk and through for example communication of the risk of overweight of their child to parents.

Understanding Determinants of Health Care Seeking Behavior in Rural Areas. A Qualitative Study in Mangochi District, Malawi

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Introduction

The third Sustainable Development Goal ensures healthy lives and promotes the well being for all through universal health coverage. There is a growing concern, especially in developing countries, regarding the delay of rural residents in seeking timely and appropriate medical care. In Malawi, rural residents still delay in seeking health care services despite the fact that more than 75% of the population is estimated to have access to primary health services. Understanding the underlying factors to such behavior is critical in designing interventions aimed at improving access to health care service. This study was conducted to understand the factors that contribute to delays in seeking health care in a rural Malawian community.

Materials & Methods

A qualitative cross-sectional study was carried out. 34 participants (17 males, 17 females) were recruited using purposive sampling until saturation point. Focus group discussions and in-depth interviews using a semi-structured open-ended interview guide were conducted. Recorded interviews were transcribed, translated and analyzed following thematic analysis approach.

Results

Dissatisfaction of care by hospital personnel, drug stock out and long distances to the health facilities were the main factors associated with delays in seeking appropriate medical care. Most participants preferred going to traditional healers and seeking hospital care only when the condition had worsened. In addition, preference to over-the-counter drugs was depicted and gender was also reported to be a key factor, as some households would wait for the husband to make a decision of seeking hospital care.

Conclusion

This study found a number of factors at personal, family, community and health system level which contribute to the majority of rural residents presenting late with a health condition despite having access to primary health care facilities. Interventions aimed at improving access to health care services should be implemented quickly in order to reduce remarkable adverse effects.

Primary Health Care in the Age of Advanced Technology and Modern Medicine: Perspectives from Future Filipino Doctors

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Introduction

With the recent signing of the Universal Health Care (UHC) Act in 2019, primary health care in the Philippines was re-affirmed as the main strategy to attain "health for all," which would lead to better health outcomes through more efficient utilization of resources.   In a healthcare system that had been accustomed to be specialty-centric, the UHC Act refocuses on primary care in the grassroots levels and improves navigation of the healthcare delivery system.   This paper determined the perception of clinical clerks on the relevance of UHC during their Community Medicine rotation in impacting the practice of the medicine in the Philippines, whether directly or indirectly.

Materials & Methods

247 clinical clerks were surveyed and focus group discussions were conducted to elicit the respondents' viewpoints after their Community Medicine engagements in a semi-rural locality in Taytay, Rizal. With approval from the institutional ethics review committee, thematic analysis of responses was subsequently performed.

Results

Though the majority of respondents viewed UHC and primary care as relevant, some did not fully comprehend the need to shift focus from a specialty-centric orientation to that of a primary health care approach.   Students were still fixated on becoming clinical specialists, and the idea of general medicine practice (e.g., Preventive, Family, and Community Medicine; Public Health and Social Medicine) was not very popular among the subjects. There were negative perceptions on essential healthcare at the community setting, given the inadequacy of medical facilities and technology, medications, and healthcare services. Some even opined that sociopolitical factors remained important determinants of health, which often resulted in inequities in healthcare delivery services, making access to health a bit more difficult for the marginalized and indigent.

Conclusion

In this age of advanced technology and modern medicine, primary health care in the grassroots and resource-limited community levels would need to overcome a lot of sociopolitical and cultural barriers in the entire Philippine healthcare system, if indeed UHC was to be achieved for every Filipino family in coming years.   Champions of patient-centered, family-focused, community-oriented healthcare ought to be born among the roster of medical students and future Filipino primary care providers, in order to truly realize UHC.

Professional communication between the doctors and the nurses: looking from the nurses' side of the fence." An observational study in a tertiary care teaching hospital

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Introduction

Good professional communication is the strength of an efficient team. Efficient team-work is the key to the success of a healthcare team. Doctors and nurses are at the center of healthcare and their roles are complementary. Understanding the importance of communication with mutual trust and respect is important. It is perceived that absence of formal training, egoistic attitude and hierarchic culture are the barriers for communication in India. This evaluated and analysed the factors from the viewpoint of nursing staff and students.

Materials & Methods

An observational cross-sectional study conducted on 215 participants (118 nursing students and 97 nursing staff) using validated questionnaire. Likert scale analysis and other descriptive statistical methods were applied.

Results

All the respondents appreciated the importance of proper doctor-nurse communication in patient care. 97.92% of the staff nurses expressed the need for active involvement in the clinical discussion. Although, 62.36% of them felt uninvited by the doctors. Quite alarmingly, 42.39% of nurses don't feel respected by the doctors. The study identified all the factors acting as barriers of communication as the responders didn't mention about any other specific barrier. The results identified that lack of team-working environment and the perceived indifference/rudeness/ lack of interest of doctors while seeking information are the major barriers of communication. Analysis of the questions assessing general perception about communication revealed a positive attitude in both nursing staff and students towards professional collaboration with doctors (Mean ± SD on 4 point scale for nursing students and staff being 3.50±0.027 and 3.07± 0.041 respectively).. Another notable observation a statistically significant difference in mean score among nursing staff and students (p=0.0137) in the question which was reverse scored and was aimed at measuring acceptance of doctors authority.

Conclusion

This study points out the existing flaws in the team-working environment in the healthcare and quantified the avoidable obstacles to the doctor-nurse communication in the given setting. Hence, based on the results of this study an effort can be made to address the issues with a view to their correction or elimination. This will ensure better professional communication to build cohesive healthcare teams to deliver the best possible patient care.

Radiology and Nuclear Medicine
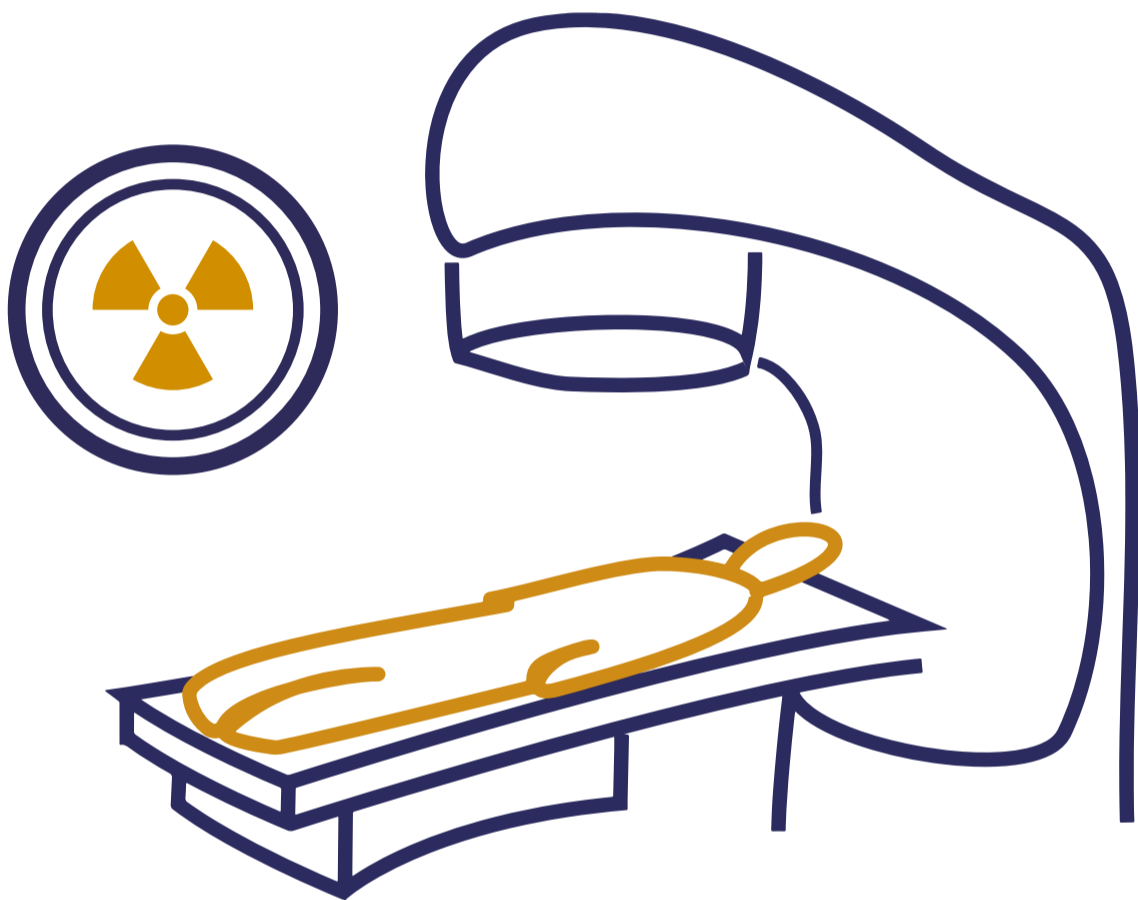
Presenters:
Zhang, J (Jinyu)
Obidov, Sh. (Shokhrukhbek) Student
Willemsen, S (Sam)
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Different effect of optical media opacities on automatic and manual measurement of foveal avascular zone of optical coherence tomography angiographies

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Introduction

Optical coherence tomography angiography (OCTA) provides not only visualization but also quantitative measurement of foveal avascular zone (FAZ). Opacity of optical media is common in elderly subjects with cataract. The purpose of this study is to investigate the impact of optical media opacities on automatic and manual measurement of FAZ on OCTA.

Materials & Methods

Thirty right eyes from 30 healthy subjects were scanned for the macula using 3mm × 3mm mode of Cirrus 5000 and DRI Triton OCTA. Optical opacities were simulated with neutral-density filters (optical density (OD)λ=840nm ranges 0.10 - 0.48 in Cirrus; ODλ=1050nm ranges 0.15 - 0.51 in DRI) placed in front of the eye. Automatic FAZ measurements of superficial capillary plex were analyzed using built-in software and MATLAB respectively. Manual FAZ measurements were also performed. The correlation between the FAZ metrics and optical density was analyzed.

Results

With the increase of optical density, automatic FAZ area decreased in Cirrus 5000 and DRI Triton (rs= -0.344 and -0.766 respectively, both $p<0.001$) but manual FAZ area increased (rs= 0.423 and 0.543 respectively, both $p<0.001$). Similar results were found for FAZ perimeter and circularity. A post-hoc analysis shown that automatic FAZ area of Cirrus 5000 decreased 29.5% ± 7.9% whereas manual measurement increased 12.5% ± 4% as OD increased to 0.38. Automatic FAZ area of DRI Triton decreased 22.0% ± 2.2% whereas manual measurement increased 19% ± 5.5% as OD increased to 0.37.

Conclusion

The effect of optical media opacity on quantitative measurement of FAZ area was different for automatic and manual measurement. Caution must be taken when interpreting OCTA FAZ area measurement in patients with optical media opacity.

Ultrasound of the bone fractures and their reparation: the prospective study

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Introduction

In the European Union, each year more than 355 000 people get bone fractures during the traffic accidents. Convetional radiography is used in the diagnosis of bone fractures and monitoring their repair, neveretheless multiple x-ray examination are accompanied by significant radiation exposure (2,5-3,0 mSv). At the same time, such radiation exposure may be contraindicated for some patients (e.g. pregnant women, newborns, patients with radiation sickness etc.). Our aim was to assess the role of ultrasound performed for the bone fracture diagnosis and future folllow-up.

Materials & Methods

We examined 114 patients with different bone fractures aged 15 to 90 years old. In order to diagnose a bone fracture, there were used conventional radiography and in gray scale ultrasound.

Results

According to our data, the specificity and sensitivity of ultrasound in the diagnosis of bone fractures were 98.7% and 99.5%, in the assessing of soft tissues in the fracture area - 98.5% and 98.3%, in the assessing of primary bone callus - 98.8 and 98.3%. For conventional radiography, the respective parameters were 86.1% and 91.6% - for the diagnosis of bone fracture, 1.5% and 66.7% - for the soft tissue assessment in the fracture area, 3,3% and 75.0% - in the assessing of primary bone callus.

Conclusion

Ultrasound may be the first diagnostic method for long bones and chest bones fractures. In case a comminuted fracture is suspected, a conventional radiography should be performed.

Imaging organoids: a correlative light- and electron microscopy approach

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Introduction

In recent years, correlative approaches in microscopy have allowed for a more complete understanding of complex cellular and molecular events. The emergence of organoids as important pharmacological and disease models requires the revisioning of many protocols as researchers move from 2D to 3D models. The study of organoids would benefit from the advantages of correlative light and electron microscopy but current challenges stand in the way of effective protocols. The current study aims to develop a correlative microscopy approach to organoids.

Materials & Methods

This study used light microscopy z-stack recordings to create 3D models to map locations of bacteria in organoids. The tentative localisation of bacteria within organoid cells was the region of interest. Using focused ion beam scanning electron microscopy (EM), nanoscale resolution volumes were recorded for regions of interests, preselected using 3D models. Near-infrared branding marks were patterned into the specimen using the two-photon system prior to EM. These were used to recover the region of interest during electron microscopy sample preparation and electron microscopy. Finally, different sample mountings and preparations were assessed on compatibility with this workflow.

Results

A protocol of mounting organoids in 1% low melting agarose (LMA) was compatible with epon embedding, cross-sectioning and EM. Key to this sample preparation was suspending the agarose blocks containing organoids in embedding media. Placing sections acquired during EM preparation into the 3D models guided trimming of the organoid for EM. This allowed for approximation of the relative distance to the region of interest. Near-infrared branding was successfully applied to organoids to create marks visible under typical brightfield microscopy. These were instrumental in relocating regions of interests during trimming of the organoid.

Conclusion

The current protocol enables localisation of rare cellular events in organoids and can guide the trimming of organoid samples as preparation for EM. This workflow demonstrates an initial correlative approach to organoid imaging that, when optimised and improved, could open the way for a more comprehensive study of organoids.

Incremental increase in pre-operative grading accuracy of prostate cancer using MRI and MRI-targeted biopsy

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Introduction

Better understanding of prostate cancer (PCa) behaviour and increased interest in quality of life have led to development of active surveillance for low-risk disease. Staging and grading of PCa based on pre-operative assessment and prostate biopsy are essential for the correct treatment selection. Multiparametric prostate MRI (mpMRI) has shown high accuracy for PCa diagnosis, allowing also for a more accurate, targeted biopsy.

The objective of current analysis was to assess the impact of MRI and MRI-guided biopsy implementation upon the accuracy of pre-operative assessment of PCa in our department.

Materials & Methods

Our retrospective analysis compares two cohorts of patients diagnosed with PCa either by systematic biopsy (group 1=342 patients) between 2012-2017, or by MRI-TRUS fusion biopsy (group 2=41 patients) between 2018-2019. We selected an older cohort of patients with systematic biopsy, as the current systematic biopsy performed in association with MRI-targeted cores might be influenced by the knowledge of MRI result. The results of the biopsies were confronted with the pathologic report of the prostatectomy specimen.

Results

The mean age was similar between the two groups: 62.56 (range 46-76) years in group 1 vs 62.78 (range 36-73) years in group 2 (p=0.8) , as well as the mean PSA : 11.3 ng/ml (range 1.3-60ng/ml) in group 1 vs 9.53 ng/ml (range 2.8-70ng/ml) in group 2, p=0.2. We observed a similar upstaging rate (from cT2 to pT3) after radical prostatectomy in both groups: 22.9% (group 1) vs 22% (group 2), p=0.8. The grading accuracy analysis of group 1 showed 28.5% upgrading after surgery, in comparison with 19.5% in group 2, respectively (p=0.3). An overall 3.2% more accurate pre-operative grading was identified for patients in group 2. The rate of positive surgical margins was 23.1% in group 1 vs 22% in group 2 and was significantly correlated with upstaging at radical prostatectomy, p=0.001.

Conclusion

The selection criteria for the patients who undergo radical prostatectomy have not significantly changed in the last years. Active surveillance is underutilized in patients with low-risk disease. The most significant advantage of pre-operative MRI in patients diagnosed with PCa is the increasing of grading accuracy, therefore an improved treatment selection.

Predicting Factors of Echocardiographic Super-Response to Cardiac Resynchronization Therapy

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Introduction

Cardiac resynchronization therapy (CRT) is recommended in patients suffering from symptomatic heart failure with normal sinus rhythm; New York Heart Association (NYHA) class II, III, or IV despite optimal medical treatment; left ventricular ejection fraction (LVEF) ≤35%; and QRS duration ≥120 ms for left bundle branch block (LBBB) and >150 ms for non-LBBB . The aim of this study was to compare the demographic and clinical characteristics and echocardiographic measures of 2 groups of super-responders and non-super-responders to CRT and to determine the predicting factors of super-response.

Materials & Methods

Ninety-seven patients who underwent CRT in Tehran Heart center were successfully followed up for a median time of 19.83 months. All the patients had LVEF ≤35%, NYHA class III/IV, and QRS duration >120 ms. Time-to-peak systolic velocity was measured for each individual left ventricle (LV) segment by tissue Doppler imaging (TDI) prior to CRT. Two-dimensional echocardiography was performed before and at follow-up after CRT. LVEF was assessed via the Simpson method, and ≥12.5% increase in LVEF during the follow-up period was defined as super-response. The Statistical Software Package (SPSS for Windows, version 26, SPSS Inc, Chicago, Illinois, USA) was used for the statistical analyses.

Results

Of the 97 patients, 23 (23.7%) were super-responders. The super-responders were more frequently male than were the none-responders (52.2% vs. 24.3%, respectively; p value=0.012). In the super-responders, the mean of LV end-diastolic and end-systolic volumes were significantly less than those of the non-super-responders. According to dyssynchrony indices, anteroseptal-to-posterior wall delay and standard deviation of all LV segments' timing showed significantly higher values in the super-responders. According to multivariate analysis, LV end-systolic volume and anteroseptal-to-posterior wall delay by TDI remained independently associated with echocardiographic super-response to CRT.

Conclusion

About one-fourth of our patients with CRT were super-responder in that they had ≥12.5% increase in LVEF by echocardiography. Among all the clinical and echocardiographic measures, only a lower LV end-systolic volume and a higher anteroseptal-to-posterior wall delay measured by TDI were able to predict super-response to CRT.

Gadolinium-Loaded Microgel Coatings as MRI Contrast Agents for the Diagnosis of Biomedical Implant Failures

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Introduction

In unforeseen conditions of implant failure, they need to be detected and tracked in the body. In this context, a coating of Gadolinium-loaded microgel particles on the implant surface can be an essential way to increase the efficacy of the MRI examination. Hence, the diagnosis of the failure at the very early stage will be possible without any surgery.

The aim of this project is to synthesize Gadolinium(III) incorporated microgels and prepare coatings with these microgels on clinically relevant substrates like glass, PDMS, PEEK and teflon. Further, study the functionality and efficiency of the Gadolinium(III) incorporated microgel by MRI.

Materials & Methods

Microgels were synthesized by precipitation polymerization and the particles were characterized by dynamic light scattering (DLS) and zeta potential measurements. Using spray coating technique, the synthesized microgels were coated on different substrates and the properties of the coated surfaces were determined by water contact angle and atomic force microscopy (AFM). Further, Gadolinium(III) incorporated microgel coatings will be imaged by MRI.

Results

DLS measurements showed that the average particle size was 731.45 ± 48.15 nm and the Polydispersity Index (PDI) was 0.19 ± 0.01 and the Zeta potential was measured as 19.2 ± 2.9 mV at the scattering angle of $173°$ and wavelength of 633 nm. A homogenous and ordered layer of microgel was observed on the substrates by AFM after coating the substrates. In future studies, the other characterization techniques will be performed and also the modified surfaces incorporated with Gadolinium(III) will be imaged using MRI to check any defect in the implant.

Conclusion

Particles were synthesized successfully. The positive value of the zeta potential indicates the formation of cationic microgel and the value of PDI suggests that the microgel solution was monodisperse, without any aggregations. Moreover, Gadolinium(III) incorporated microgels displayed MRI-detectable signals. At the clinical level, this concept can be used to detect any implant failure in the body, thus increasing their efficacy.

Development and validation of a CT-based margin-related radiomic features to distinguish precancerous lesions from early stage lung adenocarcinoma

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Introduction

The surgical treatment strategies for patients with multiple pulmonary nodules remain a massive challenge since the invasion of pulmonary pericarcinous tissue needs to be confirmed by immunohistochemical study after operation. The purpose of this study was to investigate whether margin-related (5mm) radiomic features combined with machine learning can distinguish precancerous lesions from early stage lung adenocarcinoma.

Materials & Methods

In total, 264 patients with 144 benign and 174 malignant PNs in Guangdong Provincial People's hospital from March 1,2015 to December 31,2019were sorted by three cohorts, who underwent preoperative chest CT(≤3 months) was retrospectively collected. All lesions are pathologically confirmed as precancerous lesions or Stage I lung adenocarcinoma . In training cohort, 145 patients (70%) are selected randomly from the single-nodular patients (N=207). In the validation cohort, the model is validated using the other 62patients(30%) from single-nodular patients and multi-nodular cohort (n =57).Least Absolute Shrinkage and Selector Operation (LASSO) and Support Vector Machine-Recursive Feature Elimination (SVM-RFE) were used for feature selection. ROC analysis and AUC were used to evaluate the performance of the model on distinguishing the precancerous lesions from early stage lung adenocarcinoma.

Results

A total of 861 analyzable radiomic features were extracted from the segmented lesions' margins (5mm) using PyRadiomics by two senior radiologists . After combining 15 radiomic features selected by two algorithms, and developed into the multivariate logistic regression model . It performed well in both training cohort and two independent validation cohorts. The AUC Brock of single-nodular cohort in training cohort was 0.952 (95% CI: 0.913-0.979), while in single-nodular validation cohort was 0.948 (95% CI: 0.886-1.0). Multi-nodular validation cohort (118 lesion) in this model shows an AUC of 0.857 (95% CI = 0.79–0.925).

Conclusion

This study demonstrated the potential of margin-related radiomic features based on preoperative CT scans to distinguish precancerous lesions from early stage lung adenocarcinoma. And it may assist surgeons to predict circumferential margin infiltration of early stage lung cancer more objectively before operation and develop accurate therapeutic strategies for multi-nodular patients in future.

Surgery and Anesthesiology
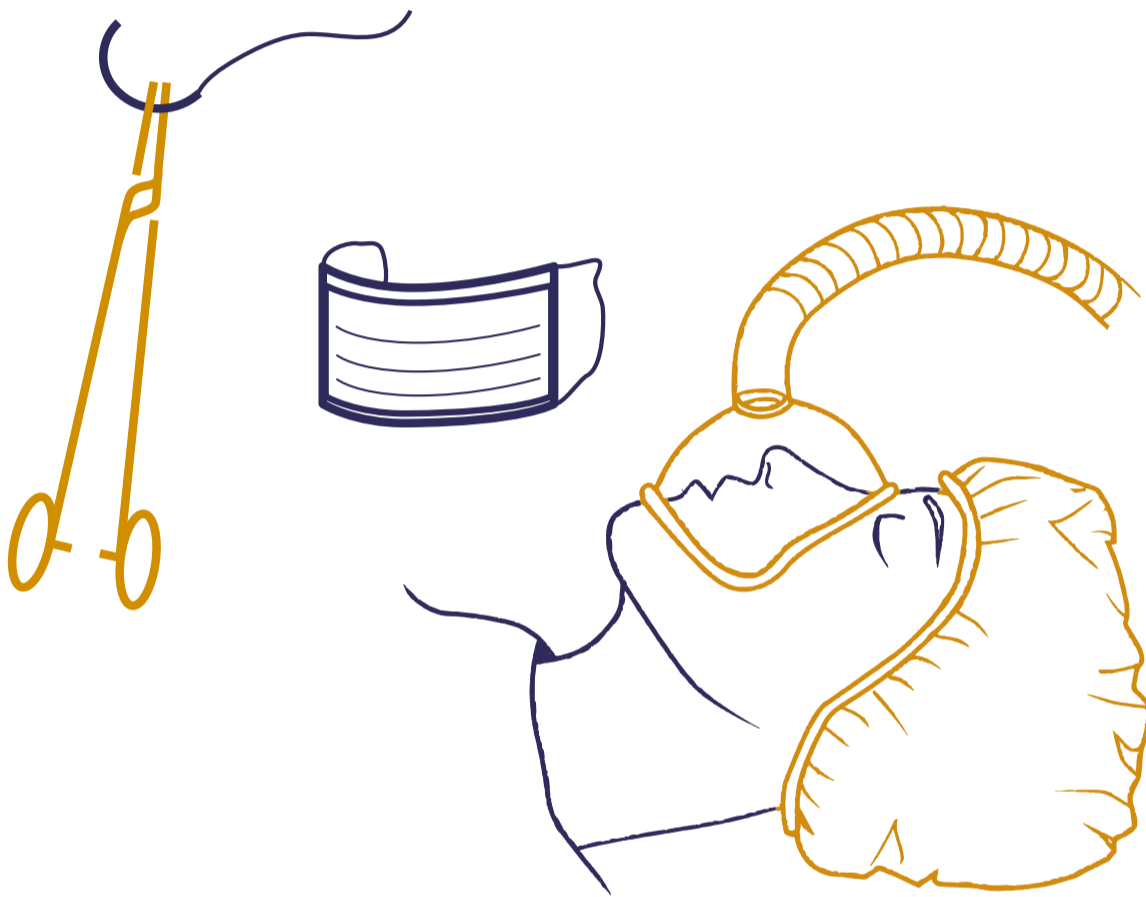
Presenters:
Norouzi, F.N (Fatemeh)
Shahidi, F. (Faezeh)
Raheel, F.S. (Falaq)
Chen, X. (Xin)
Kasmirski, J.A. (Julia)
Parihar, A.S. (Ajitanshu)
Wijesinghe, CI (Channa)

Verifying the association between nitrous oxide added to inspiratory oxygen and postoperative anaesthetic complications: A double blind randomized control study

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Introduction

We performed this study to investigate the effect of Nitrous oxide administration during maintenance phase of general anaesthesia on post-operation pain, cough, laryngospasm, and nausea and vomiting in pediatric patients who underwent elective inguinal hernia surgery.

Materials & Methods

In this double blinded randomized clinical trial, 60 pediatric patients with age 2-8 years, American Society of Anaesthesiologists (ASA) class of I and II, who were candidate for elective inguinal herniorrhaphy, were randomly allocated into two groups; group 1 (30 patients) received Isoflurane 1.5% and nitrous oxide 70% and oxygen 30% during maintenance phase of general anaesthesia while, group 2 (30 patients) received Isoflurane 1.5% and oxygen 30% during maintenance phase of general anaesthesia. Two groups were compared for post-operative pain, cough, laryngospasm and nausea and vomiting.

Results

Post-operative nausea-vomiting (PONV) was observed more in the N2O based group (p= 0.012) when compared with N2O-free group. However; pain, cough and laryngospasm had no significant differences between the groups (p value≥ 0.05).

Conclusion

Isoflurane plus nitrous oxide leads to more Post-operative nausea-vomiting in comparison with Isoflurane plus oxygen. Moreover, they both seem to have a similar effect on post-operative pain, cough and laryngospasm.

Comparison of the Efficacy and safety of Two Doses of Ketamine in Pediatric Eye Examination

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Introduction

Ketamine is extensively used for Peri-operative analgesia, especially in children. It is associated with high incidence of psycho-mimetic symptoms and nystagmus, which complicates some procedures including eye examination. In this study, we compared two doses of Ketamine as premedication for an eye examination in children.

Materials & Methods

This triple-blinded, parallel, 2-group clinical trial included 60 children with American Society of Anesthesiology I and II, aged 3 to 8 years, who were the candidate of eye examination under generalized anesthesia. They were randomized to receive two different doses of oral ketamine (2 or 4mg/kg) as premedication. Sedation level (Ramsay sedation score), nystagmus, hallucination, cardiac rate, and O2 saturation, and the surgeon and nurse satisfaction were evaluated.

Results

The sedation score of ketamine 4 mg/kg group was significantly higher than the ketamine 2 mg/kg group (p=0.01). The occurrence of emesis was positively correlated with the dose of ketamine (r=0.26, p=0.04). However, there was no difference in the presence of nystagmus (p=0.15), heart rate (p=0.7), and O2 saturation (p=0.11) between the groups. There was no report of hallucination. The surgeon satisfaction (p=0.78) and the nurse satisfaction score (p=0.29) showed no significant difference between the two doses of ketamine.

Conclusion

Ketamine at the dose 4 mg/kg has greater sedative effects, whereas it is associated with more emesis. Since there is no difference in the satisfaction of treatment staff with anesthesia or other side effects between the two doses, oral ketamine 2mg/kg is more preferable as pre-medication in children.

Serum biomarker discovery for allograft vasculopathy using murine model of alloantibody-mediated cardiac allograft rejection

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Introduction

Although transplantation is an effective and life-saving treatment for end-stage organ failure, allograft vasculopathy (AV) from chronic alloantibody-mediated rejection precludes long-term graft survival. Current diagnostics in AV (angiography and biopsy), are invasive and expensive. Serum biomarker identification would allow earlier diagnosis and treatment.

Materials & Methods

A murine model of alloantibody-mediated cardiac AV was used, where T cell deficient (Tcrbd−/−) C57BL/6 recipients were challenged with MHC-mismatched BALB/c heart allografts and T cell help provided by reconstituting with TCR75 CD4 T cells that recognise self-restricted allopeptide derived from donor H-2Kd MHC class I alloantigen. Processes for tissue visualisation and laser-capture microdissection were optimised through qualitative assessment and protein estimation. Morphometric analysis determined in-model interindividual variability. Microdissected neointima from explanted allograft arteries with AV underwent mass spectrometry to reveal candidate biomarkers.

Results

In-model morphometric heterogeneity was verified (P=0.0099). Optimal tissue staining (modified haematoxylin) to visualise and prevent protein degradation, and microdissection parameters were established, maximising target tissue harvest. Proteomics revealed candidate biomarkers including vimentin and cardiac-specific actins, amongst others.

Conclusion

Effective methodology for isolating AV tissue has been established. Proteomic analysis has generated candidate proteins, requiring comparison to controls and in-human validation, to aid biomarker development. Such a biomarker will assist AV diagnosis and monitoring.

Laparoscopic versus open distal gastrectomy for advanced gastric cancer: A meta-analysis of randomized controlled trials and high-quality nonrandomized comparative studies

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Introduction

Controversy persists about the effect of laparoscopic distal gastrectomy(LDG) versus open distal gastrectomy (ODG) on short-term surgical outcomes and long-term survival within the field of advanced gastric cancer (AGC). Prospective data is limited to a few RCTs and observational studies.

Materials & Methods

Studies published from January 1994 to September 2019 that compare LDG and ODG for AGC were identified. All RCTs were included. The selection of NRCTs of high quality was based on a validated tool (Methodological Index for Nonrandomized Studies, MINORS). Mortality, intraoperative and postoperative complications, retrieved lymph nodes, surgical time, blood loss, hospital stay, intraoperative blood transfusion, time to first flatus, time to first liquid diet, and time to ambulation were compared using weighted mean differences (WMDs) and odds ratios (ORs).

Results

Overall, fifteen studies were included in this meta-analysis, which comprised 6 RCTs and 9 NRCTs, involving 4898 patients (2411 LDG, 2487 ODG). LDG was associated with a lower postoperative complication rate (OR 0.74; P = 0.0006), a lower postoperative minor surgical complication rate (OR 0.71; P = 0.008), smaller estimated blood loss (WMD -102.58 mL; P < 0.0001), shorter postoperative hospital stay (WMD -1.85 days; P = 0.006), shorter time to first flatus (WMD -0.46 day; P = 0.0001) and time to first liquid diet (WMD -0.70 day; P = 0.009). Mortality, intraoperative complication rate, postoperative major surgical and medical complication rates, intraoperative blood transfusion, and time to ambulation were similar. However, LDG was associated with a lower number of retrieved lymph nodes (WMD -0.90 node; P = 0.03) and longer surgical time (WMD 37.24 min; P < 0.00001).

Conclusion

LDG with D2 lymphadenectomy is a safe and effective technique for patients with AGC when performed by experienced surgeons at high-volume specialized centers.

No social and aesthetic impact of conventional thyroidectomy scar on operated patients

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Introduction

As new techniques of so-called minimally invasive surgery began to be practiced in patients with thyroid affections, upsides were established, such as advances in the aesthetics, since the procedure can have a wound on less visible locations (the axillary region or the areolas). Nevertheless, downsides can also be raised in parallel to conventional thyroidectomies, like increased pain and hospitalization period. This cross-sectional observational study aims to evaluate how relevant the aesthetic and social impact of having a cervical scar is to patients, which contributes to a better knowledge of the patient outcome.

Materials & Methods

The study data were collected from 98 patients, treated at least 6 months before the interview. Patients were requested if their cervical scar impacted them on social aspects, patients who said "yes" were also asked to measure how significant was the impact, choosing between minimal (no issues with scar), moderate(self-conscious about scar) or considerable(wish scar revision). The data of the patient's demographic characteristics were analyzed by intervals of age, a categorization of disease which motivated the surgery and subtype of thyroidectomy procedure. The result from "yes" and "no" answer scale was analyzed using Fisher's exact test by statistics app "R", considering significant P= 0.05 and reliability index (95%).

Results

The mean overall of the age of patients was 47,67 and the standard deviation was 13,7. Participants were composed of 33 men and 65 women, who had a higher level of nonsatisfaction 2/65 (3%). Unsatisfied women claimed moderate impact. The most prevalent pathologies in the study were papillary carcinomas. Part of the thyroidectomies included in the study was more invasive, they had additional neck dissection, which didn't influence patient satisfaction. The categorical variety of data(satisfied/ not satisfied) compared had results of 97,75% of satisfied patients (96/98) and the found P<.001, a statistically significant difference.

Conclusion

The aesthetic and social impact on patients is close to zero. The benefits of lower cost and lesser complications make conventional thyroidectomy an old, yet still effective option for affections of the thyroid gland that need surgical assessment.

Low prevalence of breast reconstruction surgery in breast cancer patients undergoing modified radical mastectomy: an observational retrospective study

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Introduction

2.1 million new cases of breast cancer were reported in 2018. In post-mastectomy patients, the body image may result in negative psychological consequences. Breast Reconstruction (BR) restores the self-image that may be lost as a consequence of mastectomy. It is essential to discuss the various options with the patient before surgery for ensuring patient satisfaction and quality of life. Our study aimed to determine the awareness of BR surgery among patients and also assess the Quality of Life (QoL) of patients in terms of physical and psychosocial well-being and breast satisfaction after undergoing Modified Radical Mastectomy (MRM).

Materials & Methods

Our cohort consisted of 100 breast cancer patients scheduled for MRM in the Surgery ward. We excluded patients with Stage III/IV breast cancer, comorbidities, multifocal tumors, peripheral vascular disease (all relative contraindications to BR surgery) and who could not withstand prolonged anesthesia. We used the BREAST-Q© Questionnaire for assessing QoL. Our variables were age, psychosocial well-being, physical well-being, and breast satisfaction.

Results

Only 2% patients were aware of BR. After we explained the procedure to them, 68% were convinced but needed more time, and 30% were still not convinced. 69% patients were found to be psychosocially ill after undergoing MRM. 74% patients were not satisfied with their breast after MRM. Patients aged 31-40 years formed the majority (26%) in willing to undergo surgery in due time, the proportion decreased as age increased or decreased ($p<0.05$). A significant association was not found between psychosocial well-being, physical well-being, and BR willingness. 42% of patients with low breast satisfaction were willing for BR ($p<0.05$).

Conclusion

98% breast cancer patients are unaware of breast reconstruction. The 68% patients convinced of the benefits of BR show that the low number of BR surgeries done in government setup is not because of the conservative mentality of the people (as previously thought) but because of unawareness. Also, the majority of patients after undergoing MRM are either psychosocially ill or unsatisfied with their breasts. These patterns if confirmed by a larger cohort study demand an urgent need to increase awareness of BR surgery for ensuring breast cancer patients a better QoL.

Knowledge among patients and outcome of flexor tendon repair of the hand following trauma: Multivariate Study in a Tertiary Care Center

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Introduction

Flexor tendon injuries are a common presentation to the Accident and Emergency (A & E) Service. The outcome of flexor tendon repair is important to regain independence of activities of daily living. This study was done to assess the knowledge and factors affecting results of flexor tendon repair among patients who present to the A & E department in a tertiary care center in Sri lanka

Materials & Methods

A multivariate retrospective analysis was done among 117patients with a follow up of 6 months. Knowledge among patients of the injury, treatment and rehabilitation were assessed using an interviewer administered questionnaire. The outcome variables were total active motion (TAM) and grip power at the end of 6, 12 and 24 weeks. The factors assessed were 12 independent variables which included demography, injury pattern, surgical technique and postoperative rehabilitation.

Results

The mean age was 36.5 +/-13.84 years. Ninety-Two percent were male and the rest were females. Fifteen percent of patients knew the injury and 9% knew the surgery that was performed to them. Only 25% of patients knew the importance of regular occupational therapy visits, and 12.5% knew the importance of postoperative controlled active motion. Sixty - seven percent, 78% and 93% of patients achieved fifty percent TAM at 6, 12 and 24 weeks respectively. Fort - five percent , 68% and 81% of patients achieved fifty percent grip power at 6, 12 and 24 weeks respectively. Multinomial regression analysis revealed age less than 50 and early active motion to be significantly associated with better TAM and grip power.

Conclusion

The outcome following flexor tendon repair in this sample is good. Knowledge on the importance of post operative rehabilitation is poor. Therefore, more emphasis should be on educating the patient which will

help improve the results following flexor tendon repair.

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Lateralized differences in relative olfactory bulb volume relate to nasal septal deviation

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Introduction

While previous research confirmed the negative effect of nasal septum deviation on olfactory function and olfactory bulb volume, whether the significance of decrease in both function and olfactory bulb volume has a difference according to the side of deviation remains unclear. Thus, the aim of the current study is to investigate whether the relative volumetric differences of olfactory bulbs between deviated side and nondeviated side are larger when NSD presents on a certain side.

Materials & Methods

In a total of 13 patients (4 female, 9 male) and 9 healthy volunteers (5 male, 4 female), volumetric measurements of the OBs were performed as well as lateralized measurements of odor thresholds, discrimination and identification.

Results

In accordance with previous literature, the majority of patients exhibited an overall decreased olfactory function (as judged for the better side: normosmia in 2 patients, hyposmia in 8 patients, anosmia in 3 patients). OB volumes for patients were significantly smaller when compared to healthy subjects ($22.8\pm10.4mm3$ and $43.3\pm9.5mm3$ respectively). As expected, olfactory function (as assess by Sniffin's Sticks test score) as well as olfactory bulb volume decreased significantly at the narrower side ($p<0.001$). In terms of each test namely Threshold, Discrimination and Identification, scores were significantly lower in patient group ($p<0.01$). In addition, patients with right NSD scored significantly lower in identification ($p=0.032$). When correlating relative volumes (wider minus narrower side) and the side of deviation, subjects presented with a right-sided deviation showed significantly larger differences in volumes than those whose left sides were narrower ($p<0.042$).

Conclusion

Our study clearly highlights that septal deviation leads to decreased olfactory function and OB volume reduction. In addition, lateralized differences in relative volumetric measurements of OB are more significant when the narrower side is the right side.

Physical activity level among Iranian adults aged 18 to 30: A nationwide study

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Introduction

Background and objective: Physical activity plays a significant role in improving and maintaining the health and well-being of individuals while being a modifiable lifestyle-related risk factor for preventing non-communicable diseases including diabetes and cardiovascular diseases. The current status of physical activity among the young adults need to be investigated. Therefore, the objective of this study was to determine the physical activity level among adults aged 18 to 30 in Iran in 2017.

Materials & Methods

Methods: This cross-sectional study was conducted in 2017 in the 31 provinces of Iran. Iranian adults aged 18 to 30 were invited to participate in the study. Multistage cluster sampling method was used for selecting participants. Data were collected through face to face interviews based on Global Physical Activity Questionnaire (GPAQ). The interview sessions were held by trained general practitioners.

Results

Results: As many as 7047, 3780 (53.6%) women and 3267 (46.4%) men, participated in the study. The mean (SD) age of participants was 25.2 (3.4) for women and 25.3 (3.4) for men. As many as 4635 (65.8%) participants did not meet the recommendations of World Health Organization and had low physical activity level. The mean (SD) total MET-min/week among women was lower than men: 254.1 (428.3); 95% CI 240.1-268.1 versus 664.5 (778.8); 95% CI: 634.3-694.7, $p<0.001$. The mean (SD) total MET-min/week in rural areas was significantly higher compared to urban areas: 508.8 (708.2); 95% CI 476.3-541.3 versus 389.1 (594.3); 95% CI 371.4-406.8, $p<0.001$. The educational level was not a predictor of physical activity level.

Conclusion

Conclusion: The level of physical activity among more than 65% of participants was low. Therefore, the necessary measures need to be taken to improve knowledge, proper attitudes, and practices regarding physical activity while also providing the necessary infrastructures to help enhance physical activity.

Different Management Options for Primary Varicose Veins in Females: A Prospective Study

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Introduction

The aim of this study was to evaluate the long term follow up results of different management modalities in treating primary uncomplicated lower limb female varicosities.

Materials & Methods

A prospective study took place within a three-year period from June 2010 until July 2012. Patients were divided into three groups: group I (n=35) included those who underwent open surgical treatment. Group II (n=25) included those who subjected to ultrasound-guided foam sclerotherapy (USGFS). While group III (n=20) included those, who treated with endovenous laser therapy (EVLT). The patients were followed up for six years.

Results

All selected patients were female aged from 35 to 62 years with a mean of 47 ± 7.6 years. Thirty-five patients (43.75%) were treated surgically by saphenofemoral junction disconnection (SFJD), and great saphenous vein (GSV) stripping; 25 patients (31.25%) with USGFS and the remaining 20 patients (25%) were treated with EVLT. A significant success rate for GSV ablation for the EVLT treated group over the USGFS treated patients ($P = 0.023$). There is no significant difference between the surgically treated group and those group treated with EVLT ($P = 0.85$). Recurrence was observed following long-term follow-up after 6 years in 8.5% in group I, 36% in group II, and 10% in group III respectively. Venous clinical severity score (VCSS) and health-related quality of life score (HRQOLS) improved significantly in all treated groups.

Conclusion

ong-term follow-up of patients with primary superficial varicosities among females is mandatory to elucidate the postoperative recurrence, especially those who underwent USGF sclerotherapy. In addition to the observation of the development of newly formed varicosities in susceptible individuals which might develop later following long-term follow-up.

Why did they change? The process behind behavioural change in the home context since the start of the Healthy Primary School of the Future

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Introduction

Dietary and physical activity (PA) habits are formed during early childhood and can track into adult life. Childhood obesity does not only increase the risk of obesity in adult life, but also affects children's physical, mental and social health.

The Healthy Primary School of the Future (HPSF) is a Dutch initiative that improves the health and well-being of all children by sustainably integrating health and well-being within the whole school system through providing healthy school lunches, increased PA and extended school hours.

Materials & Methods

This qualitative study examined the process behind the change in dietary behaviour and PA of children and parents in the home-context since the start of the HPSF. 27 semi-structured interviews were conducted with parents of children enrolled in two HPSF schools. The interviews were recorded and transcribed. The data were coded and interpreted using NVivo software.

Results

Behavioural change (BC) was initiated by both children and parents, and lead to positive changes as well as compensatory behaviour. Children changed their behaviour at home in reaction to the intervention at school, e.g. tasting healthy food items or asking for new items. Parents responded to these changes or implemented changes through direct influence of the HPSF, e.g. by implementing new rules. Awareness of one's behaviour and willingness to change proved to be important barriers towards BC. A broad spectrum was observed in the extent to which BC's were implemented, both between families as well as within one family.

Conclusion

This study shows that school-based lifestyle interventions can lead to BC at home through both children and parents. This suggests that the HPSF is successful in improving the health and well-being in school as well as at home.

Activation of the STAT3/miR-21 pathway participates in angiotensin II-induced angiogenesis

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Introduction

Angiotensin II (AngII) facilitates angiogenesis that is associated with the continuous progression of atherosclerotic plaques, but the underlying mechanisms are not fully understood. Several microRNAs (miRNAs) have been shown to promote angiogenesis; however, whether miRNAs play a role in AngII-induced angiogenesis remains unclear.

Materials & Methods

We evaluated the effects of AngII on angiogenesis both in vivo and in vitro. RT-qPCR was used to detect the expression of miR-21 in HMECs treated with AngII. Bioinformatic analysis was used to explore whether STAT3 could act as a transcription factor initiating miR-21 expression, and which was then verified by ChIP-PCR. A reporter assay was used to identify functional binding sites of STAT3 in the miR-21 promoter region.

Results

HMECs treated with AngII showed a significant increase in cell proliferation, cell migration and tube formation. miR-21 was found to be upregulated in AngII-treated HMECs, and its specific inhibitor potently blocked the proangiogenic effects of AngII. The inhibition of STAT3 phosphorylation by Stattic resulted in a drastic reduction in miR-21 expression induced by AngII exposure. Stattic coadministration subsequently decreased AngII-induced proliferation, migration and tube formation in HMECs. In silico analysis further revealed three putative evolutionarily conserved STAT3-binding sites approximately 5 kb upstream of the transcription start site of the miR-21 gene promoter region. We further demonstrated the role of PTEN as a mediator of the AngII/STAT3/miR-21 signaling pathway manifested as reduced reporter activity for wild type PTEN 3'UTR when transfected with miR-21 mimic. In vivo, the Matrigel plug containing AngII alone presented more extensively distributed neovascularization compared with that of the control group, which could be diminished by the combination with the miR-21 antagomir or specific inhibitor of STAT3.

Conclusion

Our study demonstrated that the STAT3/miR-21 pathway was involved in AngII-induced angiogenic sprouting in HMECs. We further revealed that STAT3-mediated inhibition of PTEN via the induction of miR-21 in HMECs exposed to AngII is a part of the epigenetic switch linking angiogenesis to atherosclerosis.

Long term antibiotic therapy reduced airway remodeling in severe persistent asthma: a double blind randomized clinical trial

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Introduction

More than 10 percent of asthma patients suffer from severe persistent asthma (SPA) which is a type of asthma that remains uncontrolled despite adherence with maximal optimized therapy. It has been shown that macrolides have beneficial effects in asthmatic patients, especially in those with sever persistent asthma. SPA leads to airway remodeling which is the airway structural changes. We designed this study to find the possible effect of Azithromycin on airway remodeling using non-invasive methods in patients with SPA.

Materials & Methods

This was a randomized, double-blind, placebo-controlled clinical trial. Eligible subjects were allocated to Azithromycin (500mg, odd days of week) or Placebo group. Each group received the treatment for 8 months. Airway wall thickness (RB1 bronchus) was measured by HRCT scan before and after the treatment. In addition, TGF-β (cytokine involved in process of remodeling) of the sputum was measured using real-time PCR. Other items consisting of Asthma Control Test (ACT) score, rate of asthma exacerbations, forced expiratory volume in the first second (FEV1) and fraction of exhaled nitric oxide (FENO) were also compared before and after the treatment. SPSS software was used to analyze the data.

Results

50 patients were included in the study (n=25 in each group). Treatment with Azithromycin reduced asthma exacerbations significantly ($p < 0.05$). In addition, there was a significant increase in ACT Score, FENO and FEV 1 ($p < 0.05$) in Azithromycin treated group. More important is that Airway wall thickness was significantly increased in placebo group ($p < 0.05$) but the increase in Azithromycin group was not significant. TGF-β changes in the sputum of the patients were not significant.

Conclusion

This clinical trial revealed that azithromycin may improve airway wall remodeling since the wall thickness did not increase in this group. Due to the fact that TGF-β did not changed significantly, further investigations are recommended to find more about the effect of Azithromycin in SPA.

Long term anti-fungal treatment ameliorate airway wall remodeling in sever persistent asthma: a double blind randomized clinical trial

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Introduction

Severe persistent asthma (SPA) is a type of asthma that remains uncontrolled despite adherence with maximal optimized therapy and treatment of contributory factors. SPA leads to airway remodeling which is the airway structural changes including thickening of the airway wall basement membrane, angiogenesis, increase in airway smooth muscle mass and cartilage. We designed this study to find the possible effect of Itraconazole on airway remodeling using non-invasive methods in patients with SPA.

Materials & Methods

A randomized, double-blind, placebo-controlled clinical trial was designed. Eligible subjects were randomly allocated to Itraconazole (100mg, BID) or Placebo group and were treated for 8 months. To assess the remodeling, airway wall thickness (RB1 bronchus) was measured using HRCT scan before and after the treatment. TGF-β (an important cytokine in the process of remodeling) of the sputum was also measured using real-time PCR. In addition, Asthma Control Test (ACT), rate of asthma exacerbations, forced expiratory volume in the first second (FEV1) and fraction of exhaled nitric oxide (FENO) were also measured before and after the treatment. Results were analyzed using statistical methods by SPSS software.

Results

50 patients were included in the study (n=25 in each group). Treatment with Itraconazole resulted in significant increase in ACT Score and FEV1 ($p < 0.05$). Asthma exacerbation rate was reduced significantly ($p < 0.05$) in Itraconazole group. Although wall thickness was significantly increased in placebo group ($p < 0.05$), it did not increased significantly in Itraconazole group. FENO and TGF-β did not change significantly neither in Itraconazole nor Placebo group.

Conclusion

Based on our results, Itraconazole may ameliorate airway wall remodeling since the wall thickness did not increased significantly in treated patients. In addition, patient's asthma severity was reduced. So, this drug could be a potentially beneficial drug for those patients suffering from SPA. Further investigations are recommended to find more about the effect of Itraconazole in SPA.

Evaluation of anti-inflammatory effects of nAchR-alpha7 in spinal cord injured rats: study of neuro-inflammation

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Introduction

Studying secondary spinal cord injury(SCI) mechanism is still challengeable since there is no definite treatment yet known against neuro-inflammation. NAchR-alpha7 has been known for its role in neuro-inflammation like in Alzheimer's disease, Schizophrenia and Stroke. However, expressing this receptor in Macrophage and microglial could be critical in neuro-inflammatory responses. In this study we have aimed the role of nAchR-alpha7 in neuro-inflammation which interestingly has been inquisitively considered critical due to inflammatory features in SCI. Correspondingly, using M1 and M2 macrophages as a predictive screening after activation of nAchR-alpha7 was a key in our query.

Materials & Methods

In this study, we used various dosage (0.5, 1, 1.5, and 3 mg/kg) of Nicotine as a non-selective agonist and also Methyllycocanitine (MLA, 1.5 mg/kg) as a selective antagonist for nAchR-alpha7 prior to induction of SCI using clips compression model in male rats. Behavioral evaluation including BBB locomotive scoring and Von-Frey mechanical allodynia scoring were performed 1,3,7,14,21,28 days after induction of SCI. Also, spinal cord tissue was sampled for H&E (cavity formation), Immunohistochemistry (IHC, M1/M2 expression), ELISA (TNF-alpha concentration) and real time PCR (alpha7 expression).

Results

Locomotion analysis revealed significant enhancement in Nicotine 1mg/kg group comparing to control group ($p < 0.01$). Also, mechanical allodynia study demonstrated same result for this group comparing to control group ($p < 0.01$). Moreover, administration of Nicotine 1mg/kg could decrease M1/M2 ratio after induction of SCI ($p < 0.01$) while there was no significant change in Nicotine + MLA group and neither in MLA group. Interestingly, expression of alpha7 was increased after SCI ($p < 0.001$) while there was no significant difference between Nicotine + MLA group and control group ($p = 0.967$)

Conclusion

Activation of nAchR-alpha7 could attenuate neuro-inflammation after SCI. Furthermore, expression of this receptor on immune cell can impact macrophages polarization in neuro-inflammation whilst further sub-cellular investigation may be needed in order to clarify effects of Cholinergic Anti-inflammatory Pathway (CAP) on SCI.

Association of mental health and demographics with dietary patterns in medical students

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Introduction

Introduction: Recently, the prevalence of mental health problems in the world has increased, especially in students. During the transition from high school to university, unbalanced lifestyles and inappropriate diets negatively impact mental health, There is a scarcity of research that investigates the association between mental health and dietary patterns in medical students. Therefore, our study aims to assess the health status of medical students at the University of Health Science, Vientiane, Lao DPR.

Materials & Methods

Self-administered questionnaires were used to assess the lifestyles and mental health of third- and fifth-year medical students. The International Physical Activity Questionnaire (IPAQ) was used to evaluate lifestyle. The Patient Health Questionnaire-9 (PHQ-9) was used to evaluate mental health.

Results

Results: A total of 299 medical students, including 176 third-year and 123 fifth-year students, participated. Female and male ratio was 1.32:1. Mean age was 21.9 ± 3.1 years old. Gender is correlated with significant differences regarding self-perceived current health condition (p=0.009), body weight (p=0.032) and weight change (p<0.001), self-reported alcohol consumption (p<0.001), heavy alcohol consumption (p=0.009) and physical activity (p=0.01) and BMI (p=0.018). Regarding dietary pattern, the custom of consuming eating fried or fast food, and the habit of consuming snacks or sweets was proved to be associated with gender and region of hometown . Consuming fruit or vegetable is correlated with the type of living (p=0.001) and gender (p=0.042). Frequency of eating meat last week was related to the type of living (p<0.001) and a region of hometown (p<0.001). People in the province had a habit of adding extra salt into the meal last week, females consumed higher amounts of soft drink. Medical students of high frequency of eating snacks and sweets were more likely to score higher than 10 on the PHQ-9.

Conclusion

Conclusion: Overall, most of medical students perceived the importance of regular medical check-ups. Gender and mental health were strictly associated with the dietary pattern. Health education concomittant with regular medical check-ups needs to be implemented and improved.

Physical Condition and Clinical Parameters in Adults with Moderate to Severe Asthma: A Cross-Sectional Study

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Introduction

Asthma is a chronic airway disease with growing prevalence in Western industrialized countries. This growing prevalence has been suggested to be partly attributable to changes in environmental exposure and lifestyle. Phenotypically, asthma patients may be divided according to eosinophilic and non-eosinophilic type inflammation. Eosinophilic type asthma is one of the most severe and challenging to treat. Cardiorespiratory fitness and physical condition have been suggested to play a significant role in asthma control, therefore we aimed to assess the link between physical condition and clinical parameters in adult moderate to severe asthma patients regarding eosinophilic vs. non-eosinophilic asthma.

Materials & Methods

For this cross-sectional study, 30 moderate to severe asthma patients were recruited at the Medical Centre Leeuwarden pulmonary outpatient clinic. Blood samples were collected to assess eosinophilic inflammation ($\geq 0.15 \times 10E9$ cells/L) and divided accordingly: eosinophilic (N=13) versus non-eosinophilic (N=16). Anthropometrical measurements were conducted, including waist and hip circumference, and bio-impedance analysis. Questionnaires were used to assess quality of life and healthcare utilization regarding asthma. Statistical analyses included Fisher's Exact Test, Chi square, and independent two-sample t-test. Subsequently waist-to-hip ratio (WHpR) and clinical parameters were correlated using the Pearson correlation coefficient.

Results

The study population consisted of 22 (73%) females and 8 (27%) males with a mean age of 50y (Range: 26-77y). WHpR was found to be higher in eosinophilic asthma patients compared to non-eosinophilic asthma patients (Mean ±SD: 0.94 ±0.08 vs. 0.88±0.09, p= 0.046), indicating more abdominal obesity in eosinophilic asthmatics. The number of hospital admissions due to asthma in the last year was positively associated with WHpR (Pearson's r: 0.385, p= 0.043), suggesting more healthcare utilization in asthma patients with central obesity. On the other hand, eosinophilic asthma patients had a better quality of life score compared to patients without eosinophilia (Mean ±SD: 5.86±0.64 versus 5.13±0.82, p=0.017).

Conclusion

Patients with eosinophilic asthma had more abdominal obesity compared to non-eosinophilic asthma, and there indeed exists a positive correlation between healthcare utilization due to asthma and an anthropometrical measure. If our results are mirrored by future studies, these findings may aid clinicians in the early diagnosis of eosinophilic type asthmatics and perhaps the management of overweight asthmatics.

Poster Session II
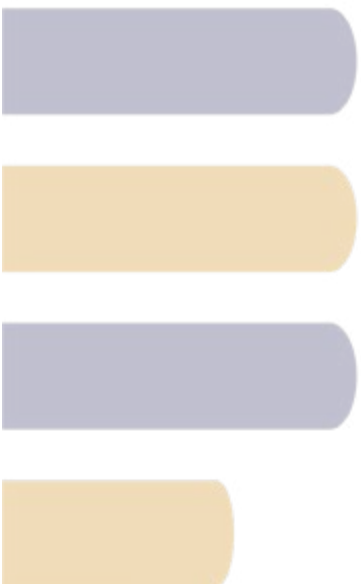
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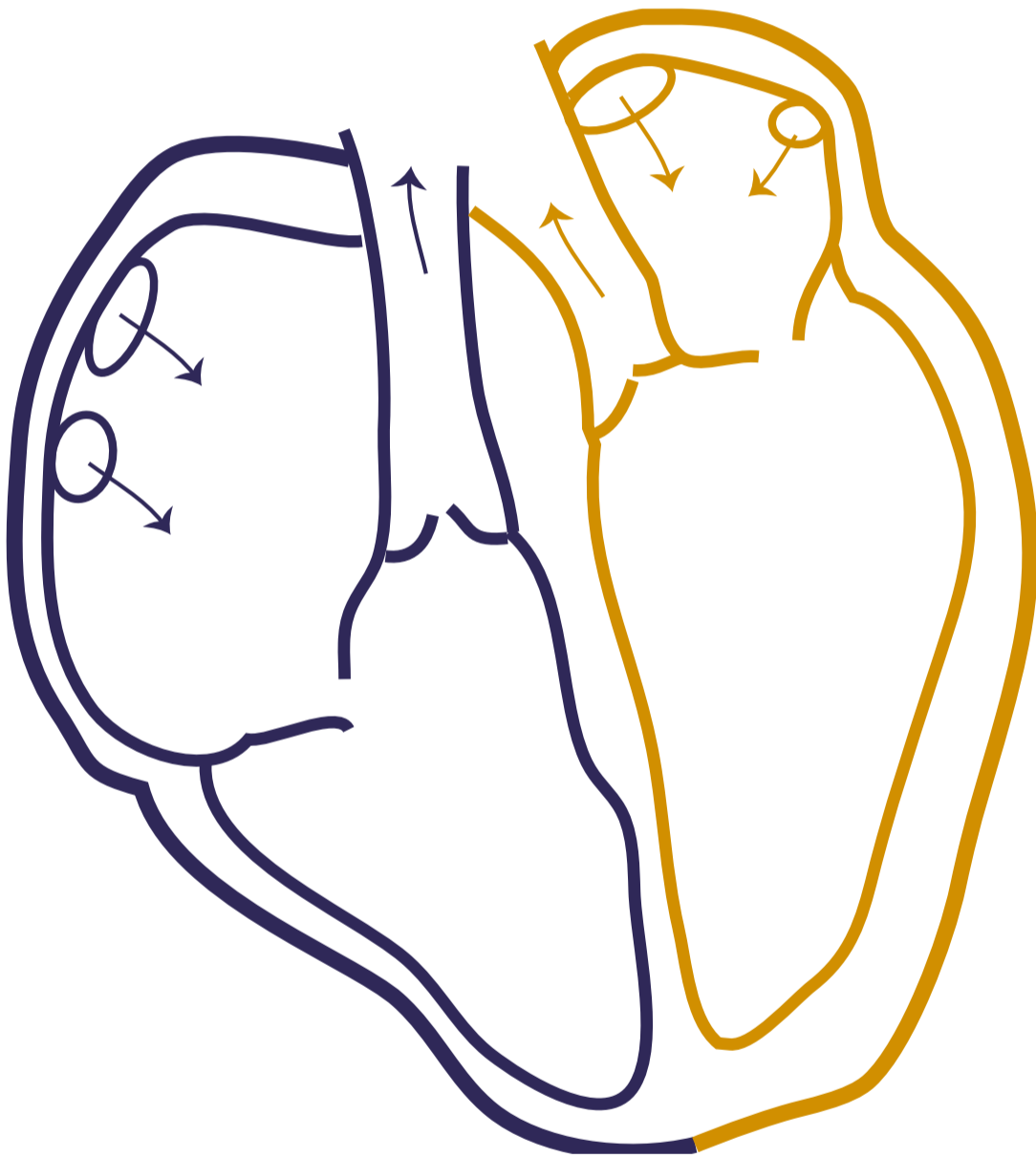
Presenters:
Rajabi, M (Mohammadreza)
Kapomba, S.B (Simbarashe)
Deiman, F.E. Drs. Ing. (Frederik)
Ismail, A.
Laksana, MVRWL (Vico)

Effect of oral MgSo4 administration on serum level of TNFα and CRP as inflammatory markers in patients with coronary artery disease : A randomized, double-blind, controlled trial study

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Introduction

Coronary artery disease is a multifactorial disease, characterized by chronic inflammatory processes that primarily arise in atherosclerotic plaques. Magnesium sulfate has a positive and beneficial effect on cardiovascular function and homeostasis. This study was performed to evaluate the effect of oral magnesium sulfate on serum levels of inflammatory markers in patients with coronary artery disease.

Materials & Methods

This study was a randomized, double-blind, placebo-controlled trial among 60 patients with moderate coronary artery stenosis who were diagnosed based on angiography reports. Participants were randomly divided into two groups that received 300 mg magnesium sulfate (n = 30) or placebo (n = 30) for 6 months. Inflammatory markers including TNFα and CRP were assessed using ELISA kit at baseline, 3 and 6 months after treatment.

Results

After 6 months intervention, compared with the placebo, Mg significantly decreased CRP serum level (1.7 ± 2.6 vs. + 0.1 ± 0.7 mg/L, P = 0.003), but serum level of TNFα showed no significant difference between Mgso4 treated and placebo groups. Clinical trial registration number: http://www.irct.ir: IRCT20151028024756N3.

Conclusion

Our findings demonstrate that Mg administration for 6 months to moderate coronary artery disease patients could not affect serum level of TNFα, but CRP serum level after 6 months decreased in Mgso4 groups compared with placebo groups, Other studies are required to confirm the anti-inflammatory property of Mg in CAD patients.

Development of a new method of aortic valve decellularization using supercritical extraction technology

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Introduction

Pathology of the aortic valve remains one of the most challenging problem for cardiovascular surgery. The limitations of existing prostheses require finding new approaches to help patients who need aortic valve replacement. The tissue-engineered heart valve portends a new era in the field of valve replacement techniques. One of the most promising techniques for tissue and organ regeneration is transplantation of decellularized tissues. We attempted to decellularize ovine aortic valves in the supercritical carbon dioxide medium (scCO2), which can reduce the processing time thereby reducing the risk of contamination.

Materials & Methods

The object of the study was a valve-containing fragment of the organocomplex of sheep (56). The effectiveness of decellularization was evaluated by histochemical staining (hematoxylin-eosin staining). Mechanical tests were carried out at the EZ Test facility. Statistical processing of data was carried out by standard methods. Differences were considered significant at $p<0.05$.

Results

The hybrid treatment with detergent solutions for 24 hours and the subsequent extraction in scCO2 medium for 3 hours (t = 37 C, P = 15-25 MPa) made it possible to extract cells whilst maintaining the extracellular matrix structure. Thus, the combined treatment (detergent + scCO2) makes it possible to obtain cell-free intact matrices.

Conclusion

In the search for the optimal parameters of aortic valve decellularization, it was found that hybrid treatment with a combination of detergent solutions followed by washing in scCO2 medium leads to fast and efficient decellularization with preservation of the structural and mechanical properties of the tissue, which was confirmed by the results of histological examination, as well as during mechanical tests. The data obtained will allow us to proceed to the next stage of testing, in particular, to study biocompatibility, to study the rate of biodegradation and calcification in vitro to develop an effective and safe method for the formation of a new generation of aortic valve bioprosthesis.

Simultaneous analysis of contraction and fluorescent indicators in stem cell-derived cardiomyocyte islands

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Introduction

Human induced pluripotent stem-cell derived cardiomyocytes (hiPSC-CM) are known to be an excellent in vitro tool for the modeling of heart disease and screening of cardiotoxicity. This is due to the relatively low costs to produce these cells and their high accessibility. Contraction is a critical feature of cardiomyocyte fitness, but due to the immature phenotype found in hiPSC-CM, it has been difficult to quantify contraction in these cells.

Materials & Methods

Here, we generate live cell imaging footage of single cell hiPSC-CM and micro patterned hiPSC-CM islands to be used for the validation of the bioinformatic tool Visible. Visible is a novel tool in development that is to be used for the simultaneous quantification of contraction, force and fluorescent indicators in hiPSC-CM.

Results

HiPSC-CM islands can be generated with contraction, action potential and calcium transient curves similar to single hiPSC-CMs. Within these hiPSC-CM islands we are furthermore able to identify changes in contraction before and after pharmacological intervention. We also introduce the bioinformatic tool Visible and several features that can be found therein.

Conclusion

We show that live cell imaging footage to be used for the validation of Visible has been generated. Once a first version of the tool is ready for use, the gathered data will be analyzed. Visible is a user-friendly bioinformatic tool in development that is to be used for the simultaneous quantification of contraction, force and fluorescent indicators. Visible will help in studying the interrelation between parameters of cardiomyocyte fitness, decrease data analysis time and will furthermore induce uniformity and reproducibility in data output amongst laboratories.

Safety and Efficacy of different doses of Bempedoic acid in patients with Hypercholesterolemia: A meta-analysis

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Introduction

Cardiovascular diseases remain the major cause of death globally, despite the advances made in their treatment and prevention. They are mainly caused by atherosclerosis, for which statins are widely used. However, statins are associated with some muscular adverse events that can lead to treatment cessation. Recent clinical trials have proved the effectiveness and tolerability of Bempedoic acid, an ATP Citrate Lyase Inhibitor, that recent clinical trials have proved its effectiveness and tolerability. In our study, we aimed to compare the safety and efficacy of different doses of Bempedoic acid in treating hypercholesterolemia, in addition to its long-term effects.

Materials & Methods

We searched four authentic databases for randomised controlled trials (RCTs) that used Bempedoic acid for patients with hypercholesterolemia. We included studies that compared any dose of Bempedoic acid to placebo. Data were pooled as mean difference (MD) in the Review Manager software, under the random-effects model. Additionally, we compared different doses of Bempedoic acid to each other, when data were available.

Results

We found eight studies that compared Bempedoic acid to placebo, and one study that compared the 120 mg to the 180 mg of Bempedoic acid. The use of a low dose of Bempedoic acid, 40 mg or 60 mg, led to a significant decrease in levels of non-HDLc, LDLc, total cholesterol, and apolipoprotein B ($p < 0.002$), with no significant difference in HDLc level ($p = 0.97$) or in the occurrence of drug-related adverse events. When comparing 120 mg Bempedoic acid to placebo, a similar lipid profile was found, with good compliance to the drug. There was no significant difference between 180 mg of Bempedoic acid or placebo in the level of non-HDLc (MD -20.62, 95% CI [-78.30, 37.05]), with a statistically significant difference in other parameters. There was no significant difference between the 120 mg and the180 mg of Bempedoic acid in terms of efficacy, but the earlier dose had fewer side effects.

Conclusion

Our study showed that different doses of Bempedoic acid were safe and well-tolerated in patients with hypercholesterolemia. However, more studies are required to assess the durability of Bempedoic acid effects on lipid profile and to assess the long-term muscle side effects.

Garcinia mangostana Linn Extract Versus Moderate Intensity Statin for The Treatment of Hypercholesterolemia in High Framingham Risk Patients: A Double Blind Randomized Non Inferiority Trial

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Introduction

Garcinia mangostana Linn extract has been proven to possess beneficial effects on some cardiovascular diseases, including hypertension, ischemic heart disease, atherosclerosis, and thrombosis. In previous trials, Garcinia mangostana Linn extract is demonstrated to exert its cardioprotective properties by significantly attenuating systolic blood pressure, inflammatory mediators, and cholesterol level in high Framingham risk patients compared to placebo. Our study is aimed to analyze the comparability between Garciana mangostana linn extract versus moderate intensity statin in improving cholesterol levels in high Framingham risk patients.

Materials & Methods

A double blind, randomized controlled trial was performed in 40 high risk cardiovascular disease patients determined by the Framingham risk score in Cardiology Outpatient Clinic-Saiful Anwar General Hospital, Malang. The patients were divided into two groups (Garcia and Statin). Within 90 days of treatment Garcia group received 2520 mg/day Garcinia mangostana extract divided into three doses, while Statin group received single dose 20-40 mg/day simvastatin. The primary efficacy outcome was determined by the composite of decreased LDL, increased HDL, and decreased Total Cholesterol levels in addition to the reduction of the Framingham risk score. Efficacy analyses was conducted by modified intention to treat.

Results

Our main findings suggest that Garcinia mangostana Linn extract was non inferior to moderate intensity statin in the primary efficacy analysis, with mean reduction of LDL cholesterol level 18.98% in Garcia group and 20.13% in Statin group (absolute difference -1.14%, 95% CI interval -1.53 to 1.10%; independent t test p=0.409) in addition to 12.28% and 10.32% reduction of total cholesterol level in Garcia and Statin group respectively (1.96%, 0.12 to 2.48%; p=0.24). Framingham risk score was decreased 35.31% and 35.60% in Garcia and Statin group respectively (-0.29%, -1.47 to 1.21%; p=0.536). However, there was no significant improvement in HDL cholesterol level observed both in Garcia and Statin groups (p=0.895).

Conclusion

Administration of Garcinia mangostana Linn extract was as beneficial as moderate intensity statin in improving cholesterol levels and holds a potency to serve as additional treatment option for treating hypercholesterolemia in high Framingham risk patients.

Cell Biology II
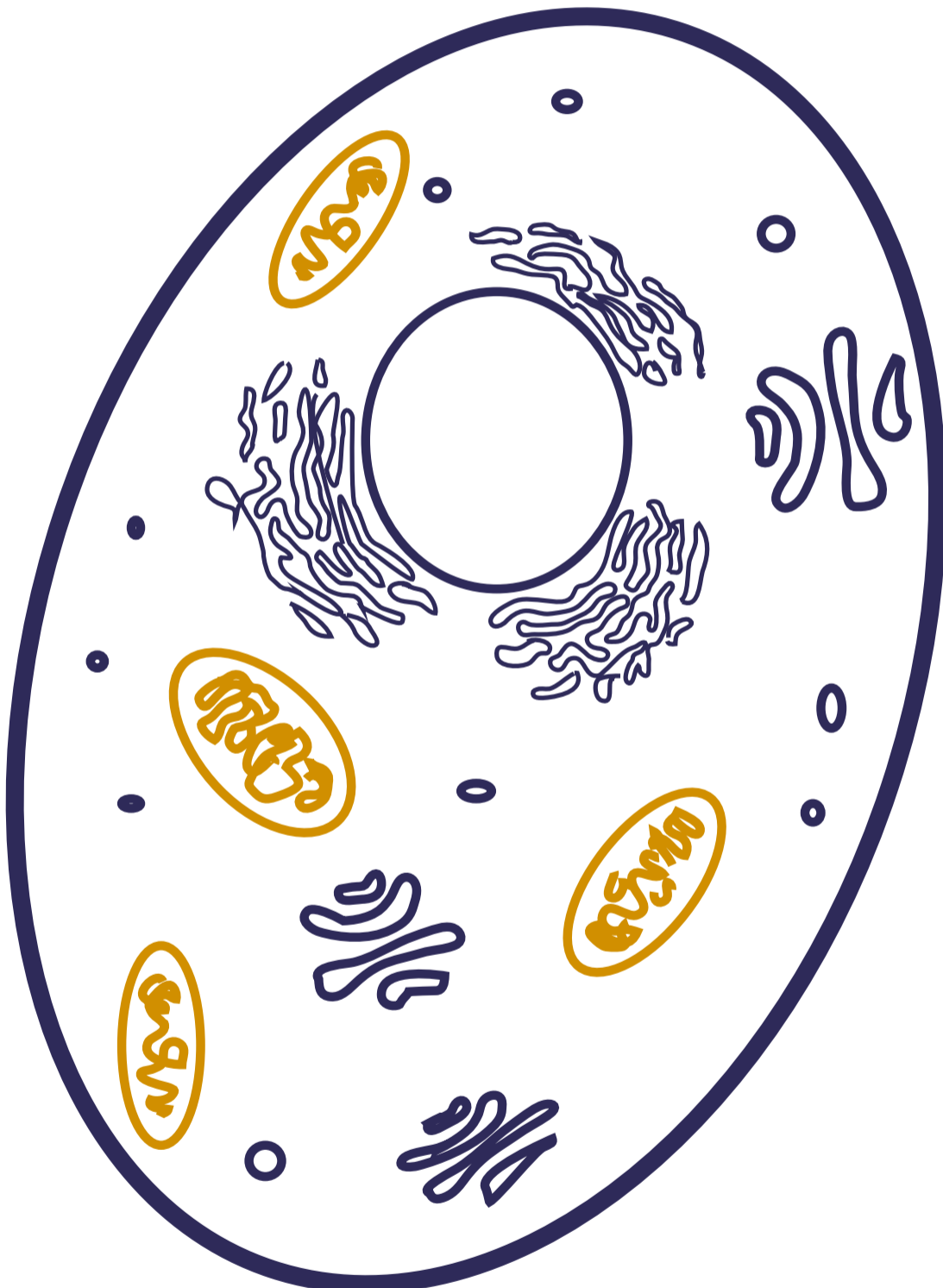
Presenters:
Yildirimsimsek, E. (Ece)
Kamel, F. H. (Fady)
Barna, L. (Lilla)
Alamo, M.A (Martina)
Palm, C. (Constantin)
Quintero-Espinosa, D (Diana)
Oving, N.C.

Investigation the Effects of Phenformin on Fibroblast Growth Factor Receptor-2 in Ovarian Cancer Cells

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Introduction

Ovarian cancer is one of the mostly seen gynecological cancer worldwide. These days cancer research is directed to find alternative compounds that lead cancer cells to apoptosis, although the surgery and chemotherapy combination which is the classical treatment of ovarian cancer. Discovery of the new and effective chemotherapeutics is very important for better treatment of cancers. Phenformin is a hypoglycemic agent in biguanide form and used in diabetes mellitus treatment. Moreover, in literature, it is reported that phenformin causes decreased FGF signaling. It is known that FGF signal inhibition is very effective in ovarian cancer treatment. For this reason, we aimed to investigate the inhibitory effects of phenformin on FGFR2 in human ovarian cancer cells(SKOV-3).

Materials & Methods

Groups are planned as; control group, 0.5 mM phenformin treated group, 1 mM phenformin treated group, 2 mM phenformin treated group, and 4 mM phenformin treated group respectively. 24 hours after the application of phenformin, cell viability is analyzed via WST-1 test, and FGFR2 distribution is analyzed immunocytochemically. Also, using Muse™ Annexin V & Dead Cell Kit, the apoptotic effects of phenformin on SKOV-3 cells are determined.

Results

According to the results of WST-1 analysis, it is determined that the viabil cell number is lowest (%46.57) in 4 mM phenformin treated group. The H-score values of FGFR2 immunoreactivities are calculated as 396.2±1.3, 382±9.38, 307.2±12.04, 245.2±27.44 and 159.2±19.25 respectively. It was seen that between the control group and phenformin treated groups there are statistically significant differences ($p<0.001$). Apoptosis test results showed that early (%2.67) and late (%37.67) apoptotic cell numbers are highest in the 4 mM phenformin treated group.

Conclusion

In this study, it was detected that phenformin treatment on SKOV-3 ovarian cancer cells have an inhibitor effect on FGFR2 expression, which provides survival and proliferation. Moreover, its apoptotic and anti-proliferative effects on ovarian cancer cells are clearly seen. In this study, it is shown that the 4 mM concentration of phenformin treatment is the most effective dose in ovarian cancer cell death. It is expected that this research may lead the in vitro and in vivo researches with different doses of phenformin for different types of cancer.

The Subcellular Localisation of Sorting Nexin 33 in Human Retinal Epithelial Cells

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Introduction

Sorting nexins (SNXs) make up a family of cytoplasmic and membrane-associated proteins involved in the regulation of intracellular trafficking and signalling. SNXs are characterised by the presence of a Phox-homology domain (PX). SNX33 is an incompletely characterised member of the SNX Bin, amphiphysin, Rvs (BAR) subfamily, which contains an N-terminal Src-homology-3 domain (SH3). SNX33 is thought to regulate many crucial processes needed for cell division and endosomal trafficking. This may be due to SNX33's ability to bind to membrane remodelling GTPase, dynamin 2 (dnm2). Dnm2 is a scission protein involved in the pinching-off stage during endocytosis, mitochondrial fission and cytokinesis as well as centrosome cohesion. SNX33 has also been associated with the actin branching Wiskott–Aldrich syndrome protein. Actin polymerisation is vital for cell division and membrane transport. We hypothesise that SNX33 is an important regulator of cell division through recruitment of dnm2 and control of elements of the cytoskeletal system.

Materials & Methods

Human retinal pigmented epithelial cells (RPE-1) were co-immunostained with two independent SNX33 antibodies and markers for the primary cilium, the centrosome, cytoskeletal components and the mitochondria. RPE-1 cells were transfected with yellow fluorescent protein-tagged SNX33 to investigate its overexpression on mitochondrial morphology. Images were acquired using a laser-scanning confocal microscope. Images were then analysed to quantify co-localisation between SNX33 and mitochondrial markers.

Results

We stained SNX33 together with key cytoskeletal networks, which showed minimal co-localisation (intermediate filaments or actin), suggesting an indirect link between SNX33 and cytoskeletal networks. Interestingly, we discovered a novel pattern of co-localisation between SNX33 and mitochondria, which has not been previously described. Furthermore, high-resolution analysis of the images obtained suggested that SNX33 localises in the space between mitochondria. Finally, we discovered that overexpression of SNX33 resulted in significant elongation of the mitochondria.

Conclusion

SNX33 may regulate crucial processes such as cell division and endosomal trafficking through the indirect activation of cytoskeletal networks. Furthermore, our observations shed new light on SNX33's involvement in mitochondrial fission. The pattern of its localisation in the spaces between mitochondria, the changes in mitochondrial morphology upon its overexpression and its localisation to dnm2 suggest a regulatory role in the fission process.

The effects of grape seed proanthocyanidin-rich extract and grape phenolic compounds on an inflammatory blood-brain barrier culture model

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Introduction

The blood-brain barrier (BBB), formed by brain capillaries, is not only involved in inflammatory and other diseases of the central nervous system, but also in many systemic diseases with an inflammatory component. Dietary obesity is a systemic chronic inflammatory condition in which the peripheral and central vascular system is affected. In obesity among the cerebrovascular changes defective leptin transport across the BBB is observed. Our aim was to study the protective effects of grape-seed proanthocyanidin-rich extract (GSPE) and grape phenolic compounds epicatechin (EC), gallic acid (GA) and resveratrol (RSV) on a cytokine-induced vascular endothelial inflammation model and the changes in the expression of leptin receptors and leptin transfer.

Materials & Methods

Primary cultures of rat brain endothelial cells, glial cells and pericytes were used in co-culture as a BBB model. Cells were treated with tumor necrosis factor-α (TNF-α) and interleukin-1 β (IL-1β) to induce inflammatory damages. Cell toxicity was tested by impedance measurement. The expression of leptin receptors was evaluated by RT-qPCR. The production of reactive oxygen species (ROS) and nitric oxide (NO) were detected by fluorescent probes.

Results

GSPE, EC, GA or RSV did not change the viability of brain endothelial cells. The gene expression of Ob-Ra leptin receptor was up-regulated by GSPE, EC and RSV. RSV protected against the cytokine-induced increase in permeability of the BBB model. GSPE and EC exerted an antioxidant effect and GSPE increased NO both alone and in the presence of cytokines. The cytokine-induced nuclear translocation of transcription factor NF-κB was blocked by GSPE, GA and RSV. Cytokines increased the mRNA expression of Lrp2 which was inhibited by EC. RSV increased Ob-Ra and Clu after cytokine treatment. Cytokines elevated leptin transfer across the BBB model, which was not modified by GSPE or RSV.

Conclusion

Our results on a BBB culture models confirm that natural grape compounds protect vascular endothelial cells against inflammatory damage. Grape compounds and GSPE, by exerting a beneficial effect on the BBB, may also be considered in the treatment of obesity after validation in clinical trials.

SNAP23 Regulates antigen extraction and presentation by promoting lysosome secretion at the Immune synapse of B Lymphocytes

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Introduction

Activation of the B cell receptor (BCR) by surface tethered antigens (Ag), leads to the formation of an immune synapse (IS) where lysosomes are locally secreted to facilitate antigen extraction. Antigens uptaken by B cells are further processed within lysosomes and presented to T cells as peptides loaded onto MHCII molecules, allowing B cells to become fully activated. Few studies have focused on the regulatory aspects of membrane trafficking at the IS. We recently showed that B cells rely on the v-SNARE protein Vamp-7 to promote the local exocytosis of lysosomes at the IS and decided to investigate its potential partner, SNAP23 in this process.

Materials & Methods

We used a mouse B cell line activated with antigen immobilized on 3μm-beads or on coverslips to mimic the IS and measured synapse acidification using a pH sensitive probe, as an indication of lysosome exocytosis. We silenced SNAP23 expression with shRNA and evaluated antigen extraction by measuring antigen remaining on beads using immunofluorescence and imaging analysis, while antigen presentation was evaluated in a co-culture assay with an antigen-specific T cell hybridoma.

Results

Our results show that the activation of the BCR induces the recruitment of SNAP23 at the IS, covering the entire area of contact with the antigen (delimited by the bead). We also evaluated how silencing of SNAP23 affected the recruitment and secretion of lysosomes at the IS. The results show that SNAP23 knockdown does not affect the polarization of lysosomes towards the IS, but compromises their docking and local secretion at the IS. Then, we analyzed the functional impact of SNAP23 silencing in B cells, in the context of antigen extraction and presentation. As expected, defect in lysosome secretion compromises the extraction, processing and presentation of the immobilized antigen.

Conclusion

Overall, our results allow as to conclude that SNAP23 is necessary for the extraction of immobilized antigens by mediating lysosome VAMP7+ exocytosis at the IS of B cell.

Unraveling molecular pathways in heart failure: PTPRZ1 and its role in cardiac fibroblast stress response

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Introduction

Heart failure (HF) is defined as a complex end-stage clinical syndrome that can result from cardiac disorders, like among others myocardial infarction, cardiomyopathies, or valvular disease. Over the years, tyrosine phosphorylation by tyrosine kinases has been characterized as an important motif in myocardial remodeling. Kinase signaling pathways have been shown to be involved in the normal myocardial function, recovery and response to oxidative stress, inflammation and fibrosis. Interestingly, despite considerable efforts on the evaluation of the role of protein kinase pathways, the role of protein phosphatase pathways, which are responsible for the dephosphorylation of tyrosine residues, has been under appreciated. The aim of this study was to characterize the role of protein tyrosine phosphatase receptors (PTPRs), a family of protein phosphatases, in HF.

Materials & Methods

PTPRs mRNA expression was determined by qRT-PCR in left ventricular samples from 25 patients with ischemic and dilated cardiomyopathy (ICM and DCM) harvested during left ventricular assist device implantation. Control samples were obtained from five rejected donor hearts (ethical committee MHH approved: Nr 1842-2013). Neonatal murine cardiac fibroblasts and cardiomyocytes were isolated from 1-3 day old pups (project number GT TSG4(3)). RNA and protein were isolated from cardiomyocytes, fibroblasts, and fibroblasts stimulated with TGF-β for 24hrs. Fibroblasts were also exposed to small interfering RNA (siRNA) targeting PTPRZ1, one of the top candidate PTPRs associated with ICM and DCM. Data was analyzed by means of a Student's T-Test.

Results

PTPRZ1, PTPRS and PTPRF were upregulated in both ICM and DCM human samples. In murine cardiac cells, PTPRZ1 was primarily expressed in fibroblasts (2-fold compared to cardiomyocytes, N=4, p<0.05). Fibroblasts stimulated with TGF-β demonstrated a 2-fold increase in PTPRZ1 expression, a 1.5-fold in α-SMA and 4-fold CTGF-increase (N=4, p<0.05). Fibroblasts exposed to siPTPRZ1 had a 90% reduction in PTPRZ1 expression (N=4, p<0.05), linked to a decrease in α-SMA (2-fold, N=3-4, p<0.05) and a trend towards increased apoptosis as determined by the BAX/BCL-2 ratio (1.5-fold, N=3-4, p=0.06).

Conclusion

PTPRZ1 is a novel HF-associated gene primarily expressed in fibroblasts. Our findings suggest PTPRZ1 is involved in fibroblast differentiation and seems to have an anti-apoptotic function.

LRRK2 and PRKN knockout genes by CRISPR/cas9 in HEK 293T cells as a model of Parkinson disease

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Introduction

Mutations in the leucine-rich repeat kinase 2 (LRRK2) and Parkin (PRKN) genes are common causes of familial Parkinson's disease (PD). Indeed, both LRRK2 and PRKN have been linked to OS and DAergic neuronal death. Therefore, research has focused on strategies to model the pathological pathways in these neurons. However, how this proteins participates in PD is not yet fully established. Recently the clustered regularly interspaced short palindromic repeats-CRISPR-associated protein 9 (CRISPR/cas9) has been developed as a simple, low cost and high efficient tool for the genome editing. In this study we use CRISPR/cas9 as a strategy for PRNK and LRRK2 Knocking-out in HEK 293T cell line in order to modeling PD.

Materials & Methods

CRIPSR/Cas9 ribonucleoprotein system was used to knockout the LRRK2 and PRKN genes into HEK293T cell line. Five sgRNAs targeting the first ATG in the Exon 1 of LRRK2 and PRKN were designed using the Vector NTI sofware and nucleofected into HEK293 cells. To assess the efficacy of knockout sgRNAs, a specific PCR was designed to amplify the editing region for each gene. The PCR products were sequenced by Sanger-sequencing method. The sequencing raw data were analyzed by the Inference of CRISPR Editing (ICE) tool provided by Synthego.

Results

The ICE analysis showed a 23% of knockout score for sgRNA at the target site 1 and 12% at the site 2 for PRKN locus. For LRRK2 gene sgRNA targeting site 1 and 2 showed a percentage of efficiency of 11% and 15%, respectively. However gRNA design to target site 3 showed a 51% and 59% at 3 and 5 weeks, respectively.

Conclusion

We create a knockout for PRKN and LRRK2 genes using the CRISPR/cas9 system in HEK 293T cells to model PD. These results can contribute to the study of molecular mechanisms involved in sporadic and familiar PD and the development of gene- and cell- therapy strategies.

Modulation of differential methylation of mitochondrial DNA in cultured skin fibroblast from patients with mitochondrial myopathy

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Introduction

Mitochondria are essential intracellular organelles in maintaining energy homeostasis for cell integrity, function and survival. Mitochondrial disorders, such as myopathy can be caused by mutations in nuclear DNA or mitochondrial DNA (mtDNA). Sometimes, in patients no mutations in nuclear DNA nor mtDNA can be found. They suffer from myopathy in combination with chronic fatigue due to dysfunctional mitochondria. Here, the energy generating capacity of the mitochondria is decreased. In previous research (D. Yildiz ISCOMS 2019) an increased methylation at a specific locus in the D-loop of the mtDNA was found to be the epigenetic cause in these patients. It would be of interest to investigate whether the differential methylation could be modulated by Zebularine, a nucleoside analog of cytidine. While the addition of S-Adenosyl methionine (SAM) would initiate methylation and so reduce energy levels.

Therefore, we hypothesize that reversing the methylation in patients mtDNA by Zebularine may normalize the mitochondrial gene expression and thus, normalize the overall functioning of mitochondria.

Materials & Methods

Skin fibroblasts were obtained from healthy control and myopathy patient whose DNA was negative for nuclear and mitochondrial DNA mutations. Mitoplates were used to measure the mitochondrial function on different mitochondrial substrates. qPCR was used to measure mitochondrial gene expression and mitochondrial copy number indicating the mitochondrial content. From the fibroblasts mtDNA was isolated and bisulfite pyrosequencing was conducted to establish the level of methylation.

Results

Changes in rates of the several substrates were observed in cultured skin fibroblasts from the patient, compared to control after treatment with Zebularine or SAM. The expression of mitochondrial genes was higher in patients compared to control after treatment of the skin fibroblasts with SAM. Normalization was expected after Zebularine treatment. Preliminary data showed increased methylation levels in patients mtDNA when treated with SAM. We expect that Zebularine would normalize these levels.

Conclusion

The observed differential methylation in mtDNA of myopathy patients compared to controls in cultured skin fibroblasts suggest that the energy generating capacity of mitochondria can be modulated by SAM and Zebularine. Although this was a pilot, we would suggest that these modulators might be interesting drug candidates in future therapy for myopathy patients.

Dentistry and Biotechnology
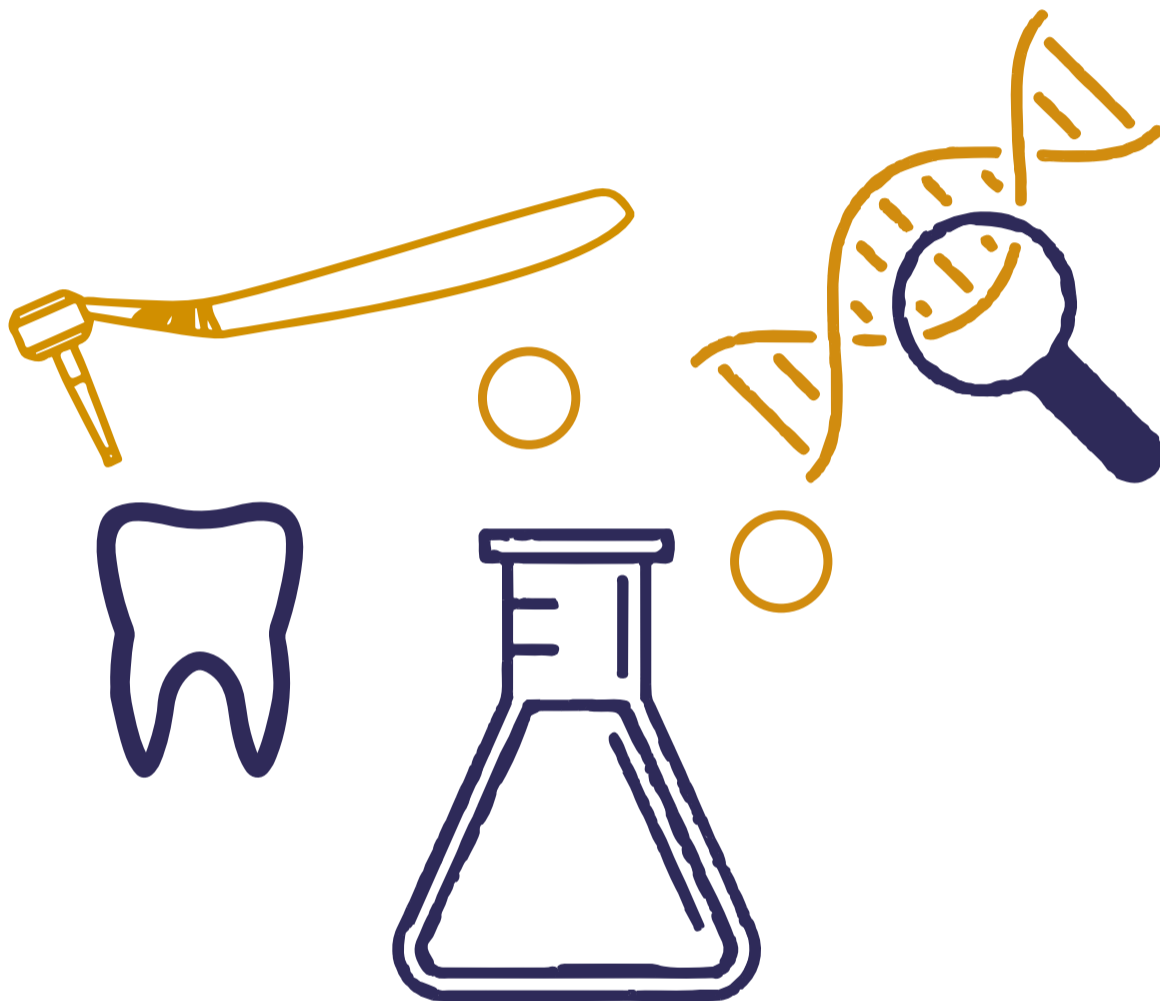
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Up to 12 years clinical evaluation of 197 partial indirect restorations with deep margin elevation in the posterior region

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Introduction

Deep margin elevation (DME) relocates the cervical outline of large-sized cavity dimensions in the posterior area supragingivally, using a resin composite in a direct technique. The aim of this study is to evaluate the clinical performance of partial indirect restorations with DME and compare the effects of selected baseline variables on the (quality of) survival of the restorations.

Materials & Methods

All teeth that were restored in combination with indirect restorations and DME between 2007 and 2016 were eligible for inclusion. Overall cumulative survival rates were calculated (Kaplan–Meier estimates) and compared among subsets of variables. Qualitative evaluation of all surviving restorations was performed using the modified United States Public Health Service (USPHS) criteria using Chi-square tests.

Results

A total of 197 indirect restorations in 120 patients could be included. Restorations or teeth presenting with secondary caries, fracture of the restoration/tooth, debonding of the indirect restoration, root caries, severe periodontal breakdown or pulpal necrosis were considered as absolute failures (n=8) leading to an overall cumulative survival rate of 95.9% (SE 2.9%) up to 12 years, with an average evaluation time of 57.7 months.
Some indication of degradation of the restorations was seen over time. Indirect composite restorations showed more degradation compared to ceramic restorations (p=0.000). More wear of the antagonist was observed when teeth were opposed to ceramic restorations (p=0.04). Endodontic treatment negatively impacted the occurrence of fracture of restorations and teeth (p=0.000).

Conclusion

This long-term study shows the possible clinical applicability of deep margin elevation. Indirect restorations with DME have a good survival rate in this study, however longer follow-up is needed as degradation of the restorations is seen over time.

Non invasive screening tool to detect anemia

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Introduction

Hemoglobin concentration is a vital parameter which can be used to detect anemia and polycythemia. Currently, invasive techniques are used for hemoglobin measurement despite their many disadvantages including discomfort and potential complications for the pregnant, elderly and pediatric patients. This project proposes a method for the non invasive measurement of Hemoglobin level.

Materials & Methods

The non-invasive measurement based on the absorption of light by oxyhemoglobin and deoxyhemoglobin and the analysis of the resulting photoplethysmograph (PPG) signals. PPG wave is analysed using the modulation ratio (R) which is defined as the ratio of AC to DC components of the PPG signal obtained from two different wavelengths of 660nm and 940nm. A linear relationship (Hb = -3.626*R + 15.84) was obtained between hemoglobin concentrations (Hb) measured using the invasive technique and the modulation ratio (R) calculated by analysing PPG signal using the measurements from 106 patients.

Based on the mathematical model developed, a non-invasive screening tool was developed. A probe is used to transmit and record the IR and red light through the fingertip. The recorded PPG waveform is analysed using a microcontroller based processor built into the device. The device subsequently predicts the risk of anemia in patients. This device operates in three modes. Mode 1 is a standalone device. In mode 2, the device is connected to a desktop application that displays the real-time PPG waveforms and can generate a medical report. In mode 3, the device can be connected to a mobile application that facilitates the continuous monitoring of hemoglobin concentration remotely.

Results

The device was evaluated using 22 subjects using the deviation percentage defined as the percentage difference between the actual and measured hemoglobin concentrations. An average deviation of 4.41%, a maximum deviation of 9.4% and a minimum percentage of 0.36% was observed for the tested patients.

Conclusion

The state of the art hemoglobin measuring techniques do not facilitate continuous and remote monitoring. The proposed device has this main advantage in addition to the benefits of non-invasive measurement including the prevention of infections, physical pain, and the lack of operational or maintenance costs while being portable.

A label-free and sensitive terahertz biosensor for microRNA-21 detection based on strand displacement amplification and gold nanoparticle enhanced metamaterial

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Introduction

MicroRNA-21 (miRNA-21) has become an ideal biomarker for breast cancer diagnosis. Although molecular biology techniques using dye labels have been studied, label-free quantification of miRNA is extremely challenging. Recently, terahertz (THz) spectroscopy has attracted wide attention as a promising tool in nucleic acid analysis due to its rapid, non-destructive and safe manner. However, the sensitivity of direct measurement is not satisfying the miRNA detection in complex biological samples. In order to overcome this shortcoming, strand displacement amplification (SDA) technology has been introduced by providing exponential amplification of a trace of miRNA to enhance the THz signal. In addition, metamaterial, a novel artificial structure consisting of sub-wavelength metallic arrays, is also used for the fabrication of a more sensitive THz assay. It can be coupled with the gold nanoparticles and realize the second THz signal enhancement. Herein, a highly sensitive THz biosensor was developed for miRNA-21 detection.

Materials & Methods

In the presence of miRNA-21, amounts of trigger DNA were firstly produced with SDA reaction. Then, the trigger DNA were further hybridized with DNA probe functionalized gold nanoparticles. After introduction of magnetic separation and de-hybridization technology, the pure complex of trigger DNA and gold nanoparticles were prepared and dropped onto the surface of metamaterial for the THz measurement. Since the level of miRNA-21 is highly correlated to the number of complex, by calculating the relative changes in metamaterial frequency shifts, the concentration of miRNA-21 can thus be determined.

Results

Based on the two efficient signal amplifications, the developed method showed a high sensitivity with low detection limit of 14 aM and a dynamic range from 1 fM to 10 pM. It also possessed excellent specificity and could discriminate differences among three different miRNAs. In addition, this strategy was successfully applied to the determination of miRNA-21 in spiked clinical serum samples with the recoveries between 90.92% and 107.01%.

Conclusion

In this work, a label-free and sensitive THz biosensor was developed for miRNA-21 detection based on SDA and gold nanoparticle enhanced metamaterial. According to the obtained results, the developed THz biosensor might be a promising detection platform for miRNA-21 quantitative analysis in biomedical research and clinical diagnosis.

Fabrication and In Vitro Evaluation of 3D Printed Porous Polyetherimide Scaffolds for Bone Tissue Engineering

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Introduction

Bone tissue engineering is a promising approach to heal the bone defect caused by fractures, infection, or tumor.A key factor in bone tissue engineering for bone regeneration is the scaffold that plays the role of a template for cell adhesion, cell proliferation, and formation of the bone-extracellular matrix to provide structural support to the newly formed bone. 5e scaffolds should mimic the bone structure and function in order to optimize the integration between the scaffold and the surrounding tissue.A porous structure scaffold can improve the mechanical properties to match the bone tissue and provide a cell-friendly structure microenvironment for the growth of osteoblasts and tissues

Materials & Methods

In this work, we fabricated porous polyetherimide (PEI) scaffolds using a three-dimensional (3D) printing system, and the pore size was set as 800 µm.The morphology of 3D PEI scaffolds was characterized by the scanning electron microscope. To investigate the mechanical properties of the 3D PEI scaffold, the compressive mechanical test was performed via an electronic universal testing system. For the in vitro cell experiment, bone marrow stromal cells (BMSCs) were cultured on the surface of the 3D PEI scaffold and PEI slice, and cytotoxicity, cell adhesion, and cell proliferation were detected to verify their biocompatibility. Besides, the alkaline phosphatase staining and Alizarin Red staining were performed on the BMSCs of different samples to evaluate the osteogenic differentiation.

Results

Through these studies, we found that the 3D PEI scaffold showed an interconnected porous structure, which was consistent with the design. 5e elastic modulus of the 3D PEI scaffold (941.33 ± 65.26 MPa) falls in the range of modulus for the native cancellous bone. Moreover, the cell proliferation and morphology on the 3D PEI scaffold were better than those on the PEI slice, which revealed that the porous

scaffold has good biocompatibility and that no toxic substances were produced during the progress of high-temperature 3D printing. 5e osteogenic differentiation level of the 3D PEI scaffold and PEI slice was equal and ordinary

Conclusion

These results suggest the 3D printed PEI scaffold would be a potential strategy for bone tissue engineering

Novel technique for port-site closure using a hemostatic agent (surgicel) in robotic-assisted urological surgeries. Tertiary center experience

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Introduction

There are many techniques and devices have been used to close the surgical ports post minimally invasive procedures, however, it has limitations and may entail complications. Therefore, we introduce this novel plugging technique for port-site closure using a hemostatic agent to overcome the limitations and improve the complications.

Materials & Methods

This retrospective study conducted at King Fahad Medical City in Riyadh-Saudi Arabia and covered a period of 4 years plus a minimum of 5-year follow up. It reviewed all patients who underwent any minimally invasive urological surgery in which the surgical ports were closed using the surgicel plugging technique. The collected variables are age, sex, surgery type and the follow up results. The data was taken from the electronic medical records after receiving the International Review Board (IRB) approval. Patients' data were put in and analyzed using a specific secured SPSS file (version 23). The sum of each type of urological minimally invasive surgery was identified, as well as the rate of associated specific type/types of complication.

Results

A total of 113 patients, 54 are males with a mean age of 41.7 and standard deviation of 18.4, and 63 are females with a mean age of 39.7 and standard deviation of 17.9. The male-female ratio is 1:1.2. Among those patients, two cases (1.8%) developed non-infectious discharge, one case (0.9%) developed port-site hernia, and 97.4% ended up safely with no port-site complications.

Conclusion

This study showed that the plugging technique for port-site closure postoperatively using a hemostatic agent (surgicel) is safe, easy, effective, and has low rate of port-site complications. Additionally, several advantages have been observed in this technique. It does not require direct visualization; therefore, no additional opening and camera are needed to assist, Less financial burden as it does not require special devices, less risk of bowel injury or abdominal wall vessel injury due to the lack of sharp tips unlike the devices of other techniques. Finally, it can be used easily and effectively in morbidly obese patients.

A Rapidly Prototyped Lung-on-a-chip Model Using 3D-Printed Molds

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Introduction

Organ-on-a-chip is a microfluidic cell culture model that replicates key organ-specific microarchitecture and pathophysiology in vitro. The current methods to fabricate these devices rely on soft lithography, which is usually tedious, laborious, and requires adroit users as well as cleanroom facilities. Recently, the use of 3D-printing technologies for the rapid fabrication of molds for polydimethylsiloxane (PDMS) casting is on the rise. However, most of the 3D-printed materials are unsuitable for PDMS casting. To address this issue, we have improved the existing techniques and introduced a modified protocol for surface treatment of 3D-printed molds, making them ideal for repeated long-term PDMS casting.

Materials & Methods

Using this protocol, we have fabricated a simple open well lung-on-a-chip model to simulate the in vivo environment of airway tissue under dynamic conditions. To validate the functionality of the developed chip, Calu-3 cells were cultured in the chip and maintained at an air-liquid interface followed by performing several cell-layer based biological assays. To further validate the suitability of this lung-on-a-chip in vitro model for disease studies, the effects of cigarette smoke extract (CSE) on Interleukin-6 (IL-6) and Interleukin-8 (IL-8) release from cultured Calu-3 cells were examined.

Results

The model demonstrated that the cultured cells replicated the 3D culture specific-morphology, maintained excellent barrier integrity, secreted mucus, and expressed cell surface functional P-glycoprotein; all indicative of a promising in vitro model for permeability assays, toxicological tests, and pulmonary drug delivery studies. Moreover, CSE treated cells showed significantly higher secretion of IL-6 and IL-8 over 24 hours compared to the cells treated with both CSE and Budesonide, an anti-inflammatory drug. Moreover, our results illustrated that CSE reduced the expression of E-cadherin as an adherent junctional protein.

Conclusion

In conclusion, the proposed protocol demonstrated an easy and low-cost fabrication technique which will allow a biologist with minimal technical skills to rapidly prototype molds for different/versatile organ-on-a-chip models.

Retention and remineralization effect of moisture tolerant resin-based sealant and glass ionomer sealant on non-cavitated pit and fissure caries: randomized controlled clinical trial

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Introduction

Pit and fissure sealants are an essential part of preventive dentistry and should be adopted as a crucial part of the minimally invasive dentistry due to their profound benefit to our patients.

Materials & Methods

The study design is a single-blind, split-mouth, randomized controlled clinical trial. Forty patients between age 6-9 were selected. First permanent molars' occlusal surfaces with scores of 1, or 2 according to the International Caries Detection and Assessment System II (ICDAS II) and with scores between 14-30 by using DIAGNOdent device (Kavo®, Biberach, Germany) were selected and readings recorded. One side of the mouth was randomly chosen to have either the moisture tolerant resin sealant or the glass ionomer sealant placed, and then the second material was placed on the other side. The retention of these materials was analyzed at 3 and 6 months. The sealants were then removed and DIAGNOdent readings were subsequently taken.

Results

After three months, full retention was found in 38/40 (95%) teeth in Group A (Embrace™ WetBond™) and 35/40 (87.5%) teeth in Group B (Fuji TRIAGE®). Additionally, no sealant suffered a total loss in group A, whereas, three sealants were totally lost (7.5%) in group B. The difference in sealant retention in two groups in this period was not found to be statistically significant (P > 0.05).

At six months, full retention was found in Group A 34/40 (85%) and 25/40 (62.5%) in Group B. Also, the partial loss in Group A was 2/40 (5%) whereas in Group B 7/40 (17.5%). Also, the total loss was 4/40 (10%) and 8/40 (20%) in Group A and B, respectively. The difference in sealant retention in two groups after six months follow-up was found statistically significant (P < 0.05). The initial mean values of DIAGNOdent readings were 22.42 and 22.8 in Group A and Group B, respectively. After six months, DIAGNOdent mean values revealed a drop in both groups, and this difference was statistically significant. Nevertheless, when Group A was compared to Group B in terms of remineralization effect, the differences were found not to be statistically significant (p > 0.05).

Conclusion

Within the limitation of this study, we affirmed that occlusal caries lesions, which is restrictive to enamel and in need of surgical intervention, can be arrested clinically by sealing the lesion with both a hydrophilic resin sealant and glass ionomer sealant materials. Embrace™ WetBond™ showed superiority over the glass ionomer sealant tested in retention after six months follow up.

Radiographic comparison of bone resorption using two method of manually or machine-driven implant insertion in posterior of mandible

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Introduction

Dental implant placement is a common treatment procedure in current dental practice. For implant placement, full-thickness skin flap are reflected. Implant can be placed manually or with machin driven technique. Stable crestal bone levels have been considered a key factor in implant success because it is paramount for long-term survival, aesthetics as well as peri-implant health. The purpose of the present study is to compare the crestal bone loss (3 month and 6 month after implant surgery and fixture insertion) around implants placed according to manual or machine-driven placement

Materials & Methods

In the present randomized clinical trial, dental implant of Dio Corporation inserted in posterior of mandibles of patients that had conditions to inter the study. 50 implants were placed in 34 patients. 25 of implants were placed by manual ratchet with a torque wrench and 25 implants were placed by machine-driven handpieces. Evaluating bone loss in mesial and distal of each implant from the level of the crest of the bone to the cervical part of the implant, was separately measured by PA parallel radiography, after implant insertion and 3 months after surgery when implants functionally loaded with fixed prosthesis and 3 month after prosthesis installation. Bone loss at the implant abutments was evaluated by using Adobe Photoshop CS5 software with a measuring scale and digital images of implants. The length of implant was constant and was considered as a basis for magnification Bone loss in one-stage and two-stage implant were then compared. The data were analyzed using software SPSS

Results

thirty four (25-67 years) were included in the study. A total of 50 implants were inserted, 25 using a manual insertion protocol (19 patients) and 25 using machine-driven insertion protocol (15 patients). This study resulted mean crestal bone loss of 0.44±0.023 mm and 0.5±0.019 mm around manual and machine-driven after three months and mean crestal bone loss of 0.58±0.026 mm and 0.66±0.022 mm around manual and machine-driven after six months.

Conclusion

No differences were found between manual and machine-driven implant placement in crestal bone loss after 3 and 6 months of follow up.

Epidemiology
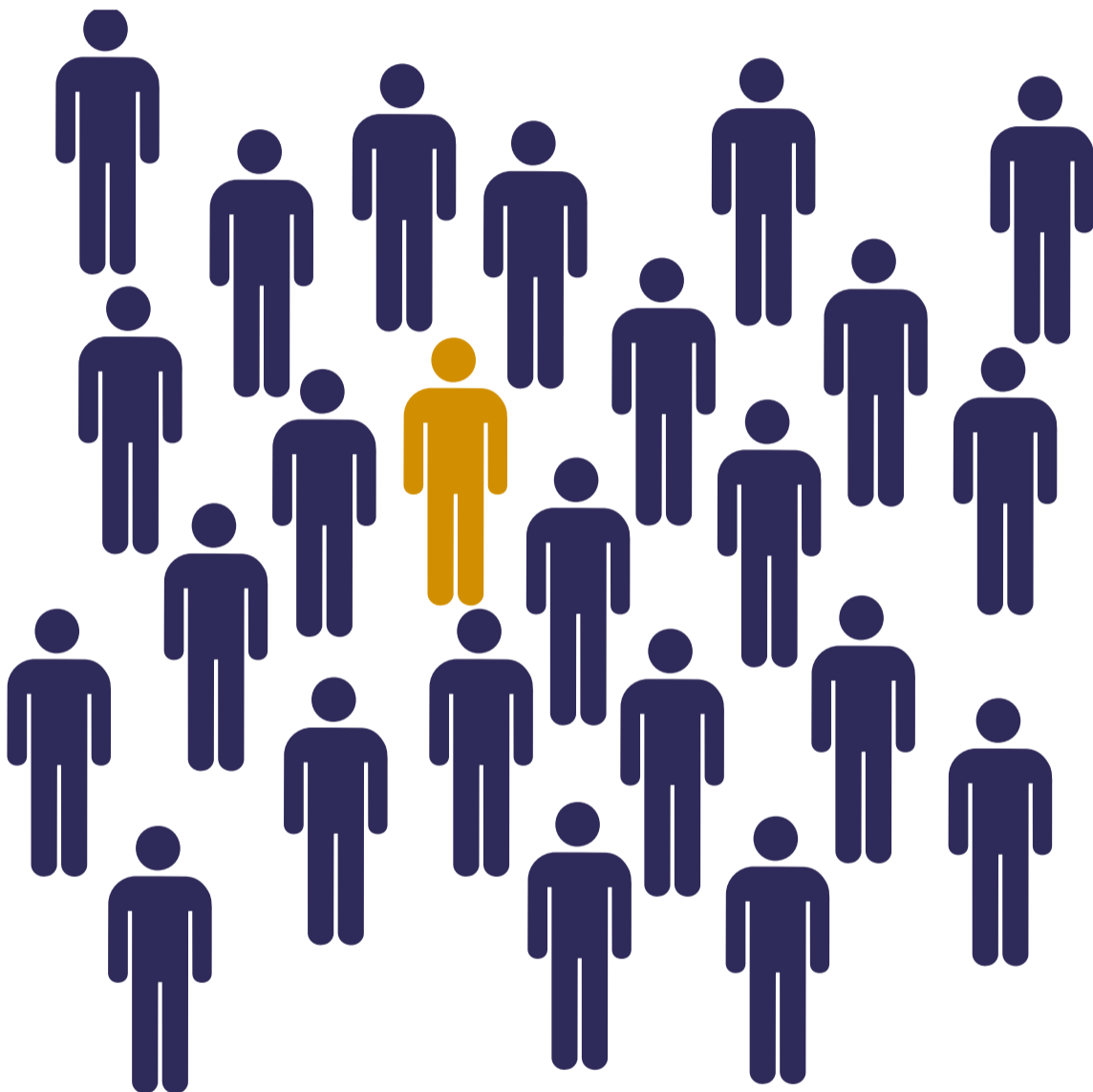
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Monitoring the incidence of clinical malaria before and after the introduction of new interventions in southern Malawi

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Introduction

Use of insecticide-treated nets (ITNs) and indoor residual spraying (IRS) on malaria reduction cannot be understated. In resource limited settings, implementing of both interventions is however not typically done owing to cost mostly. An impending rise in insecticide resistance poses a major threat in malaria control with a surge feared in endemic countries which are mostly developing. The recent development of community-led interventions such as house improvement (HI) and larval source management (LSM), provides a better option for adoption by communities as they are cheaper and easy to implement. This study was designed to determine the clinical malaria incidence and mosquito abundance before and after the addition of house improvement and larval source management, in the context of high ITN usage in Chikhwawa, southern Malawi.

Materials & Methods

We conducted two prospective cohort studies from October 2015 to November 2016 with the follow-up from September 2017 to May 2019, done before and after addition of interventions. Participants were children aged 6-48 months. Children were recruited from a series of cross-sectional surveys called the rolling malaria indicator surveys (rMIS). A total of 282 and 284 children were recruited in the first and second cohorts respectively. Data on household characteristics, health history and use of malaria interventions were collected using a standardized form. Blood samples were taken for measuring parasitemia and anemia. Odor-baited traps were set in selected households for sampling mosquitoes. Follow-up of the participants was done for one year.

Results

Clinical malaria incidence decreased from 1.2 to 0.31 cases per child years at risk after introduction of HI and LSM. A further decrease in anemia cases by 38% was observed. The mosquito density decreased to 0 thus representing a reduction of the sporozoite rate from 9.1% to 0%.

Conclusion

In the context of high ITN usage, addition of community-led HI and LSM contributed to a significant reduction in the clinical malaria incidence and mosquito abundance. Addition of novel community-led interventions to the core ones provides a better option for resource limited settings in preventing malaria transmission.

Assessment of diet quality and adherence to dietary guidelines 1 in gastrointestinal cancer survivors

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Introduction

Gastrointestinal (GI) cancers, including bowel, gastric and oesophagus cancers, are among the most common malignant diseases worldwide, affecting over 3 million new individuals annually. A diagnosis of GI cancer may have a high impact on a person's lifestyle and especially on diet. Difficulties in food ingestion/ digestion following surgical treatment or routine chemo/radio therapies, as well as food restrictions, specifically in patients with oesophagus and gastric cancers, leads to a possible undesired diet quality among GI cancers survivors. This study aimed at investigating diet quality among short- and long-term GI cancers survivors with different tumour sites compared to a cohort of reference population.

Materials & Methods

Diet quality of GI cancers survivors (n=307) was compared to a for age and sex matched reference population with no history of cancer (n=3070). All were selected from Lifelines, a population based cohort. GI cancers were defined as having a history of cancer of bowel,oesophagus or stomach. Diet quality was assessed by a self-administrated food frequency questionnaire (FFQ), in terms of: i) Lifelines Diet (LLD) scores, where higher scores indicate higher diet quality, ii) the adherence to dietary guidelines quantified by percentage of meeting dietary recommendations as given by Dutch dietary guidelines iii) the mean daily intake of food components. All analyses were adjusted for lifestyle.

Results

Diet scores in GI cancer survivors were not different from the reference population (OR=0.97, 95%CI: 0.73-1.23). Stratification for time since diagnosis and tumour site gave similar results. The intake of vegetables, unsweetened dairies, nuts and legumes was almost 50% below the recommended amount, and mean intake of unhealthy food components were at least one serving/day among GI cancers survivors as well as in the reference population.

Conclusion

In the long run, GI cancers survivors do not differ from the reference population in their diet quality. Both groups can improve their diet quality.

Factors contributing to prevalence of mental health disorders in diabetes patients

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Introduction

The initial stress and trauma associated with a diagnosis of diabetes leads to psychological distress in the patient, which if not managed adequately, leads to mental ailments. In India, very few studies have been conducted to analyze the association between diabetes and mental health. Our study aims to find out the proportion of patients affected in this aspect and discover major contributing factors. A major limitation of this study is the inability to distinguish the effects of diabetes from other comorbidities on mental health. Future studies could shed light on specific links between antidiabetic drugs and mental disorders.

Materials & Methods

We recruited 120 patients (60 males and 60 females), having diabetes for at least 6 months, attending the Department of Endocrinology for routine check-up. Patients with other major illnesses like cancer, TB, etc. were excluded. The Patient Health Questionnaire-9 (PHQ-9) and Diabetes Distress Scale-2 (DDS2) were used to assess the mental health status of patients and WHO-5 Screening Instrument for estimating Quality of Life (QoL). Our study variables included age, gender, and residence (rural/urban).

Results

30% of patients were under various degrees of depression, with 21.7% showing moderate to moderately severe characteristics. Male patients (16.6% out of 30%) were more prone to suffer from depression. Of the patients suffering from depression, the rural population formed the majority with 63% affected. A substantial 45% of patients were under diabetic distress with male preponderance of 67% seen in this aspect. Rural patients were again a major contributor with 71% affected under this category. The mean WHO-5 Screening Instrument score was 62.91. No significant correlation was present between age and PHQ-9 and DDS2 scores.

Conclusion

Patients with diabetes are subject to mental ailments like depression and stress disorders. Appropriate medication should be prescribed to manage such cases and improve QoL. Patients coming from rural areas are more likely to suffer from these disorders either due to drug adherence issues or lack of awareness for mental health. Males are more likely to have psychological problems from diabetes compared to females.

Prevalence of overweight and obesity among children with type 1 diabetes treated with a continuous subcutaneous insulin infusion and its clinical impact on diabetic control

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Introduction

It is estimated that c.a.20-25% of children and adolescents in Poland are overweight and obese. Coexistence of T1D and overweight or obesity increases the risk of late chronic complications of diabetes. The aim of the study is to assess the prevalence of overweight and obesity in children with T1D treated with insulin pump and their metabolic control.

Materials & Methods

There were enrolled 270 patients (124 girls) with mean age 13±5.7ys, diabetes duration 5.7±3.3ys and HbA1c 7.2±1.3%. All of them were on insulin pumps for more than 1 year. Overweight was defined as a BMI ≥ 85th pc and <95th pc, obesity as a BMI ≥ 95th pc. We analysed levels of HbA1c, cholesterol, HDL, LDL, triglyceride (TG), vitamin D3 (VD), systolic (SBP) and diastolic (DBP) blood pressure. Total daily insulin (TDD) and basal insulin dose were also analysed. The population was divided into groups depending on body weights: lean (L), overweight (W), obese (O).

Results

ALL n=270 Girls n(%)=124 (45,9%)
OVERWEIGHT&OBESITY n=62 (22,9%) Girls n(%)=33 (53,2%)
OVERWEIGHT n=39 (14,4%) Girls n(%)=17 (43,5%)
OBESE n=23 (8,5%) Girls n(%)=16 (69,5%)
Obese occurs statistically more often in girls than boys (69,6% vs. 30,4%) p=0,04. Group O compared with L had statistically: higher median HbA1c 7.9 [7,4;8,8]% vs. 6.8 [6,3;7,5]%, p<0.0001, lower median VD 20 [15;25] ng/ml vs. 23[18;29] ng/ml, p=0.020, higher median SBP 126 [120;134] vs.119 [110;127] mmHg. Statistically higher median SBP was seen in group W compared to L 126 [120;130] mmHg vs.118 [110;126] mmHg p=0.0008. There were no significant differences between groups in cholesterol, LDL, HDL, TG total and basal insulin dose.

Conclusion

Insulin pump therapy did not cause a significant increase in body weight in children with T1D. The overweight and obesity occurred with a similar frequency as in the general Polish pediatric population.
Insulin requirement in overweight and obese children was not increased, but it was more difficult for them to achieve the recommended metabolic control of diabetes. This was especially expressed in the obesity group. Increased systolic blood pressure was more common in children with obesity and overweight. Obese children had a lower level of vitamin D3 than lean children.

A Cross-sectional Study determining the Association between Family Dynamics and the Length of Screen Time of Preschool Children in Quezon City, Philippines

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Introduction

The American Association of Pediatrics and the Canadian Pediatric Society recommend that children between the ages 2-5 years old should use screen media for no more than one hour per day but despite these guidelines, screen time among preschool aged children continues to rise. Excessive screen time is found to be detrimental to a child's development but in today's fast paced life, screen time babysitting is viewed as acceptable, further emphasizing its role in family dynamics. This study aimed to determine the association between family dynamics and the length of screen time of preschool children in Quezon City.

Materials & Methods

A total of 230 subjects from 115 families with preschool aged children were chosen by convenience sampling and were interviewed using the Family APGAR questionnaire followed by another questionnaire to quantify the average daily screen time use of their child. The total screen time of each child was classified as either adequate (less than or equal to two hours) or excessive (more than two hours) and was associated with their Family APGAR classification using Prevalence Rate Ratio computation (PRR).

Results

Majority of the families interviewed were highly functional and the average screen time of the participating preschool children in the study was 5 hours. Statistical analysis using OpenEpi suggested that preschool children of dysfunctional families are 1.23 times more likely to have an excessive amount of screen time than those of highly functional families. A test for statistical significance using the Chi Square Test, resulted in a p-value of 0.04057, which confirmed the positive association.

Conclusion

In accordance with previous international literature, the results of the study revealed that dysfunctional families are expected to have children with excessive screen time exposure.

Mental health matters: The negative impact of mental health problems in adolescence on employment in young adulthood

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Introduction

Mental health problems (MHPs) cause a considerable burden of disease in adolescents, with potential negative consequences on employment later in life. Earlier, five MHP trajectories (high-stable, moderate-high, decreasing, moderate-low, low-stable) among adolescents (11-19 years) were identified and a significant relationship of the trajectories with employment at age 19 was found. Factors related to this relationship remain unknown. Moreover, at age 19, many participants were still in education. This study aims to 1) identify personal, family and health factors of participants in the five MHP trajectories, and 2) examine associations of trajectory membership with employment at age 26.

Materials & Methods

Fifteen-year follow-up data of the longitudinal TRacking Adolescents' Individual Lives Survey (TRAILS) cohort study (N=1711) were used. Participants in the five MHP trajectories were characterised by personal, family and health factors at age 11 and 13. Logistic regression analyses were used to examine associations of trajectory membership with employment at age 26. Analyses were stepwise adjusted for gender, intelligence, parental education, family composition, physical health, negative life events and MHP comorbidity. Analyses were performed using SPSS version 26.0.

Results

Similar positive family factors were found in the decreasing and low-stable internalising trajectories compared to the other trajectories, e.g. better parental health. Mental health service use was most often reported by parents of adolescents in the high-stable compared to the low-stable trajectories, for internalising (11y: N=25, 24.5% vs. N=27; 7.7%; 13y: N=20, 21.1% vs. N=14, 4.0%) and externalising problems (11y: N=46, 12.6% vs. N=5, 4.7%; 13y: N=40, 16.5% vs. N=2, 2.0%). For internalising problems, high-stable (OR: 2.19; 95% CI: 1.17-4.11) and moderate-high (OR: 1.75; 95% CI: 1.14-2.69) trajectories were strongly associated with not having paid work, compared to the low-stable trajectory.

Conclusion

This study provides new insight into factors related to MHPs in adolescence, and expands current knowledge about the impact of internalising problems on employment of young adults. To understand the development of MHPs and their effect on employment, a life course perspective is needed taking into account predisposing factors in childhood and adolescence. These factors should be addressed at a young age to prevent their negative effect on later life and labour market participation.

Association between daily smartphone usage and smartphone addiction among youth: A cross sectional study

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Introduction

Advancements in smartphone technology are replacing conventional tools like desktops and laptops. Some studies have outlined a relation between smartphone usage and psychological addiction, some even linking psychological effects such as loneliness, anxiety and depression to overt smartphone usage. These effects are particularly pronounced in post pubertal adolescents. However, the evidence linking smartphone usage in adolescence and psychological addiction has been inadequate, particularly in countries like India where access to smartphone and internet technologies has improved. This study aims to assess the relationship between smartphone usage and smartphone addiction among youth in Ahmedabad city.

Materials & Methods

A cross sectional study was conducted among school and college students of Ahmedabad city, of ages 15 to 24 years, with the help of a self-administered online/paper-based questionnaire – a modified version of Smartphone Addiction Scale (SAS), during October to December 2019. The SAS scale score was dichotomized into low addiction potential and high addiction potential based on the sample median as a cut-off. Multiple logistic regression was used to check the association between addiction potential and daily smartphone use and purpose of use.

Results

The study sample comprised of 225 participants, out of which 49.3% (n=111) were males and 50.7% (n=114) were females. 43.6% of the participants used smartphones primarily for social media. The average duration of initiating smartphone use was 46.45 months (SD=36.98 months) and the daily usage was an average of 3.99 hours (SD=2.87 hours). Preliminary results suggest that addiction potential is significantly associated with daily smartphone usage and purpose. It was found that for every 1-hour increase in daily smartphone usage, the odds of having higher addiction potential were higher, controlling for the purpose. (OR=1.364; 95% CI=1.183-1.572; p<0.001).

Conclusion

Higher addiction potential was significantly associated with higher daily smartphone usage, similar to other forms of addiction which show heightened addiction liability with greater exposure to the substance of abuse. Although the results show a quantitative association of smartphone use and addiction, it may be better to explore the relationship in terms of its psycho-social effects. This study merits more research into the causation of smartphone addiction.

Lifestyle intervention reduces oxidative stress in obese women

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Introduction

Oxidative stress (OS) is associated with chronic disease such as cardiovascular disease and obesity. Higher OS can be measured as the depletion of the serum free thiols (FT). Lifestyle intervention based on caloric reduction and increment of physical activities is the first-line treatment of obesity thereby improving the cardiometabolic profile. We aimed to study (i) the effect of OS on cardiometabolic outcomes, (ii) whether the lifestyle intervention could reduce OS, and if so (iii) whether it is due to weight loss, change in physical activities or change in dietary habit in this obese cohort.

Materials & Methods

This is a post hoc analysis of the LIFEstyle study, which is a large randomized controlled trial (RCT) to investigate the effects of a six-month lifestyle intervention among obese women. Serum FT as well as cardiometabolic outcomes were measured at randomisation, three months and six months in the intervention and the control group. Generalized estimating equations (GEE) regression analysis was used to estimate mean differences of serum FT between groups.

Results

In total 487 non-pregnant women had at least one measurement of serum FT at randomisation, three months or six months (243 in the intervention group and 244 in the control group). Triglycerides and total cholesterol were positively correlated with serum FT ($\beta=0.019$, $p=0.017$ and $\beta=0.016$, $p=0.023$, respectively). At three months after randomisation, serum FT in the intervention group was significantly higher than in the control group in both the unadjusted model (1028.9 uM for the intervention group and 997.0 uM for the control group, $p=0.005$) and the adjusted model corrected for age, triglycerides and total cholesterol (1027.6 uM for the intervention group and 994.4 uM for the control group, $p=0.004$) but not at six months in either models. Serum FT increase in the intervention group could not be attributed to weight loss, physical activities or diet habit change.

Conclusion

OS was associated with cardiometabolic outcomes (triglycerides and total cholesterol) and significantly decreased as a consequence of a lifestyle intervention program at three months after randomisation, when on average the biggest weight change occurred in obese women.

GI-Medicine
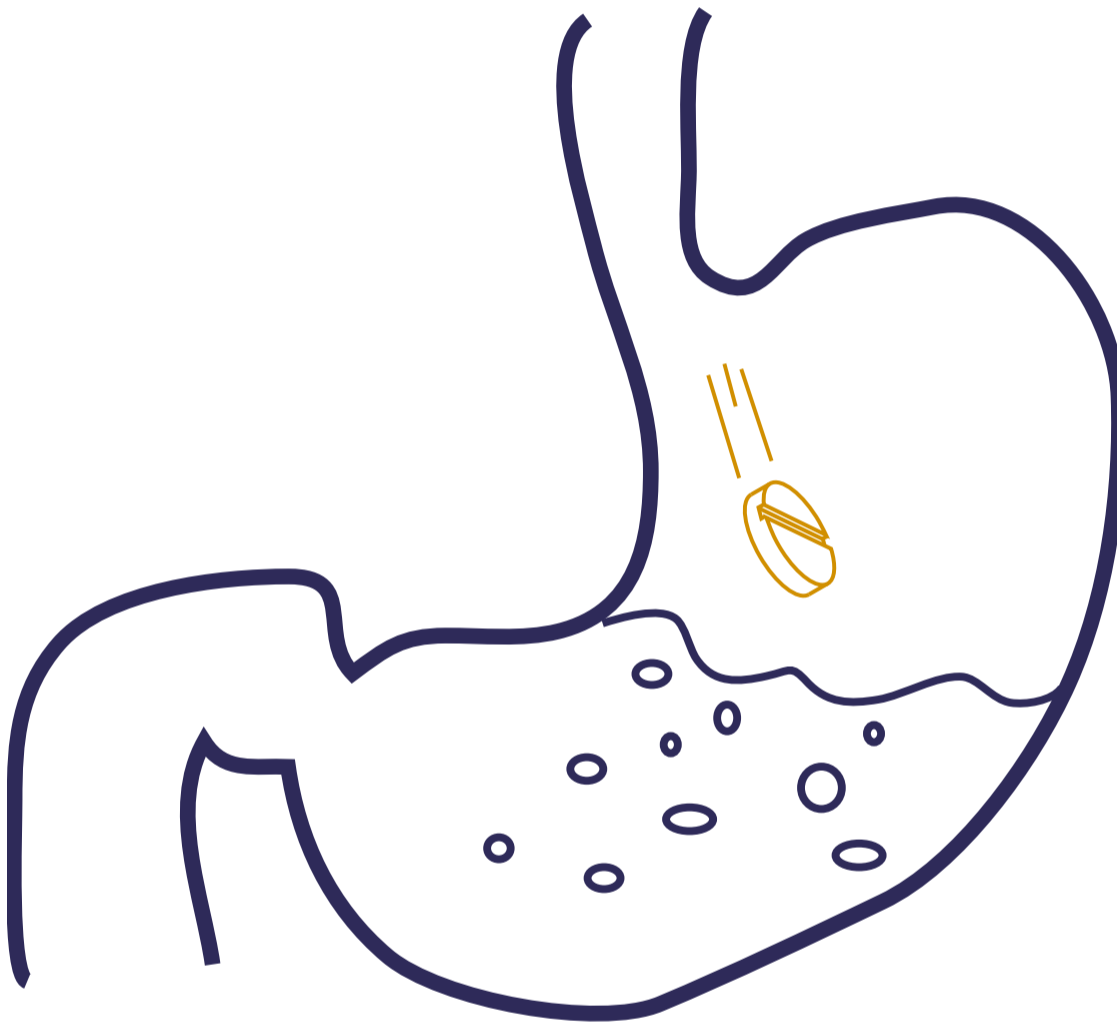
Presenters:
Zuhra, Zakirah B.
Pajouhi, A. (Ali)
Fakhraei, N (Nahid)
Abbasi-Kangevari, M (Mohsen)
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Effectivity Difference of Health Education Using Lecture Method and Discussion Method in Increasing The Diarrhea Prevention Knowledge at Srigading 1 Elementary School, Malang 2019

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Introduction

Diarrhea is global problem with high degree of morbidity and mortality especially for children in developing countries. In Indonesia, the incidence of diarrhea is 2.67%, while in Malang it increased from 2.24% in 2015 to 3.02% in 2017. Diarrhea is also the second highest number of infectious diseases in Srigading Village, Malang. Children in elementary school has a higher risk getting diarrhea than adult. This period is also referred as an intellectual period which is more easily educated than period before and after it. To reduce the incidence of diarrhea, prevention is needed by adding right knowledge about diarrhea especially elementary school children. Currently there are various choices of learning methods that each has a different outcome. This research aimed to compare the effectiveness of health education using lecture and discussion method to increase knowledge of diarrhea prevention in Srigading 1 Elementary School, Lawang, Malang, Indonesia.

Materials & Methods

This research is a pretest-posttest group design. The effect of the the lecture method and the discussion method, was observed on Srigading 1 Elementary School. The effect was observed using the Wilcoxon signed-rank test and Mann Whitney test. A total of 82 students were grouped into two groups with same amount. In the both groups, health education about diarrhea prevention was given in a 15-minute, led by young doctors with the source of material using Diarrhea Pocket Books of the Indonesian Ministry of Health and used leaflets as the media. The discussion group was divided into 5 small groups by simple random sampling.

Results

In the lecture group, the pretest was 38.05($\pm$15.00) and the post-test increased to 48.29($\pm$0.4682). While in discussion group, the pretest was 34.15($\pm$7.1880) and the post-test increased to 83.17($\pm$6.1914). The p value between the pretest and posttest of lecture group was p=0.029, while in the discussion group was p=0,000. The p value between lecture and discussion group was p=0,000.

Conclusion

Health education using discussion methods is more effective than lecture method in efforts to prevent diarrhea in Srigading 1 Elementary School. The recommendation for this study is that health education is better using discussion method to get a more effective increase in knowledge.

The effect of syzygium aromaticum essential oil (SAEO) on oxidative stress and serum cytokines in thioacetamide -induced hepatotoxicity in male rats

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Introduction

Liver disease that changes liver Metabolism, is one of the most important causes of mortality in many countries. Considering that oxidative stress, cause liver diseases, It seems syzygium aromaticum has benefit effect on liver disease, because of its powerful antioxidant effects. In this study, the effect of SAEO against thioacetamide -induced hepatotoxicity in rats was investigated.

Materials & Methods

In this experimental study, 50 adults male Sprug Dwally rats were used. The animals were divided into 5 groups of 10 each: sham group) receiving vehicle only), thioacetamide group (receiving vehicle+ thioacetamide) and 3 experimental groups, receiving SAEO (5, 10 ,15mg/kg) for 21days, before thioacetamide injection in last 3 days. Liver functions and oxidative stress property of liver in all groups were then investigated. serum cytokines in all groups were measured too.

Results

Activity of alanine amino transferase (ALT) in SAEO groups 10 mg/kg (74.2±2.1 IU/L) and 15 mg/kg (69±.24 IU/L) Significantly decreased compared to that in thioacetamide treated group (108.4±3.4) in dose dependent manner. MDA, As a lipid peroxidation index was significantly decreased in groups treated with SAEO 10mg/kg (2.18±0.15nmol/mg protein) and SAEO15mg/kg(2.03±0.11nmol/mg) compare to sham group (4.02±0.21 nmol/mg protein)

Enzymatic activities of superoxide dismutase (SOD) and glutathione peroxidase (GPx) and catalase as enzymatic antioxidants increased in groups treated with SAEO compare to that in sham group. Serum TNFα and IL1b concentrations were lower in the SAEO / thioacetamide groups compared to that in sham group too.

Conclusion

These results show protective effects of SAEO against the thioacetamide induced hepatotoxicity, which may be due to its antioxidant effect and decrease of Serum TNFα and IL1b level, increased in response to thioacetamide.

Effect of sumatriptan on acetic acid-induced ulcerative colitis in rats: A possible role for the 5-HT1B/1D receptors

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Introduction

Inflammatory bowel diseases (IBD) are the most common gastrointestinal (GI) disorders. Role of serotonin (5-HT), an important neurotransmitter in the central nervous system, in the GI tract as a motility stimulant is of great importance. Sumatriptan, a 5-HT1B/1D receptors agonist acts selectively on 5-HT1 receptors and is used generally in the treatment of migraine disorders. This study aims to examine the effect of sumatriptan in an acute animal model of colitis and to clarify the possible role of 5-HT1 receptors.

Materials & Methods

Ulcerative colitis was induced by intrarectal acetic acid (4%) in male rats. Treatments were administered in 3 consecutive days, started from the induction day. Sumatriptan at doses 0.5, 1, 2, and 5 mg/kg were given intraperitoneally (i.p.). Moreover, GR-127935 as 5-HT1B/1D receptors antagonist (0.3 mg/kg, i.p.) was injected, 30 min prior to sumatriptan (1 mg/kg) administration. Following 72 hrs., the colon samples were isolated for macroscopic and microscopic scorings. Furthermore, the gene and protein expressions of tumor necrosis factor-alpha (TNF-α), interleukin-10 (IL-10), and myeloperoxidase (MPO) were determined in the colons using qRT-PCR and ELISA techniques.

Results

The induction of colitis was documented by marked increases in macroscopic and microscopic scorings. Further, significant enhancements of TNF-α, IL-1β, and MPO, as well as pathological damages and weight losses were observed. On the other hand, sumatriptan treatments at doses 0.5 and 1 mg/kg could significantly diminish pathologic increases in the measured biomarkers as well as the pathological damages, and body weight losses. On the other hand, GR127935 could reverse the protective effect of sumatriptan.

Conclusion

Sumatriptan demonstrated a protective impact on the peripherally inflammatory condition and the protective effect of it may be mediated at least in part through 5-HT1B/1D receptors. The current investigation highlighted a crucial role for the brain-gut axis in the control of intestinal inflammation. This study suggests that 5-HT agonists may be efficient in gut inflammatory conditions if they are employed in specific and proper dosages.

Introducing Quality of Care Index for Peptic Ulcer Disease: A Systematic Analysis of the Global Burden of Disease Study Data 1990-2017

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Introduction

Peptic ulcer disease (PUD) affects four million people worldwide annually. Early detection as well as prompt and high-quality treatment could lessen the burden of disease. The absence of a comparison regarding the health-systems approaches towards confronting PUD burden guided us to find methods to examine overall estimates of quality of care for the disease across the globe. Therefore, the objective of this study was to introduce Quality of Care Index (QCI) as a new measure of evaluating the health-system quality of provided care and inequities among various age groups and both sexes in different nations and regions.

Materials & Methods

Data of the study were derived from Global Burden of Disease study 2017. Six indices including incidence, prevalence, mortality, disability adjusted life years (DALY), years of life lost (YLL) and years lived with disability (YLD) were combined and four secondary indices including mortality to incidence ratio, DALY to prevalence ratio, prevalence to incidence ratio, and YLL to YLD ratio were obtained, all of which indicated the quality of care. The four secondary indices were then combined using principal component analysis and to QCI as a single tertiary index which represented the quality of care by health systems and ranged 0-100, with 100 indicating the best quality of care status. Gender Disparity Ratio (GDR) was obtained by dividing QCI of men by that of women, where numbers closer to one indicated a better gender equity.

Results

The global QCI score in 1990 was 65.8 which increased 21.4% to 79.9 in 2017. QCI scores of almost all countries increased during 1990-2017. Although younger age groups had significantly higher QCI scores, the inequities among age groups decreased during 1990-2017. GDR ranged 0.8-1.2 for 162 countries in 1990 and 183 in 2017. The age and gender inequities were less in countries with high socio-demographic index.

Conclusion

The study showed that QCI improved dramatically during 1990-2017 worldwide. The inequities among age groups and both sexes have been reduced. However, there is still room for improvement for QCI score and bridging the equality gaps.

Heart rate variability-based level of stress and gut microbiome composition in adult healthy men

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Introduction

Stress is a multisystem physiological response which has been associated with changes in several physiological variables and has an impact on heart rate variability (HRV) as well as on gut microbiome composition and function through the gut brain axis. This study aims to contribute to the understanding of the modulatory effect that gut microbiome could have in heart and brain function.

Materials & Methods

Stress was measured by a stress index based on physiological, biochemical and anthropometrical variables and a Kmeans analysis of HRV parameters. Individuals were classified as having high or low chronic stress levels (dichotomic phenotype) and were assigned a stress score (continuous phenotype). In addition, gut microbiome characterization was performed amplifying the V3/V4 region of the 16S rRNA gene and through short chain fatty acids (SCFAs) quantification in serum. Operational Taxonomic Units were defined and relative abundances and diversity indexes were calculated. Statistical correlations between chronic stress and gut microbiome measurements were assessed by Pearson's and differences among the groups using Mann-Whitney U test. All statistical analyses were performed by R statistics 3.6.1.

Results

48 healthy men from 21 to 40 years old were included in the analyses. Based on the Kmeans analysis of HRV, 38 subjects were identified in the high stress level group and 10 in the low stress level group. Physiological and anthropometrical variables showed a significant correlation with the continuous and dichotomic HRV based phenotypes. In addition, Prevotella abundance was increased and Bacteroides and Alistipes genus were decreased in the high stress level group. There was no difference in the SCFAs levels and the HRV based phenotypes. The same analyses comparing the stress index and gut microbiota measurements are in progress.

Conclusion

HRV cluster analyses allowed to define a dichotomic and a continuous stress phenotype which were both associated with changes in other variables linked to stress and with genus abundance changes of gut microbiome. These results support the hypothesis that gut microbiome modulates chronic stress and HRV in healthy humans through the gut-brain axis. Colciencias grant 111577757335.

Characterization of patients with chronic hepatitis C treated in a high complexity hospital in Medellin, Colombia

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Introduction

Throughout the world hepatitis C (HepC) is a public health problem, and estimates for its prevalence in Colombia range from 0.5% to 1% but 2.1 % for patients over 50 years of age. The Hepatology Unit at the Hospital Pablo Tobón Uribe (HPTU) has been a benchmark for management of HepC in Medellín and Colombia for years. Our aim was to describe sociodemographic and clinical characteristics together with health outcomes of patients with chronic HepC who were treated at the HPTU between 2013 and 2018

Materials & Methods

This is an observational, descriptive and retrospective study of patients with chronic HepC, treated between January 1st, 2013 and March 31th, 2018, where we included sociodemographic and clinical variables. The statistical analysis of the data was carried out with SPSS 23; for qualitative variables absolute frequencies and specific frequencies were used, and for quantitative variables, means and standard deviation.

Results

One hundred and eight patients were analyzed. The average age was 55.8 years (SD 13.7), 51.9% were men, and 78.7% belonged to the contributory health care scheme. Most frequently, the disease was transmitted by blood, and genotype 1 predominated in the group of patients analyzed. The effectiveness of interferon schemes was 46.9% while that of Direct-Acting Antivirals (DAA) was 94.6%. Adverse drug reactions were found in 68.2% of patients treated with interferon/ribavirin schemes but in only 25.9% of the patients treated with DAA.

Conclusion

The characterization of patients with HepC treated at the HPTU during the study period was performed, in which a similar distribution was found between men and women, with a higher prevalence between 40-70 years, whose most frequent transmission mechanism is the transfusion. The DAA presented greater effectiveness and safety compared to interferon/ribavirin; however, the use of ribavirin is still necessary in cirrhotic patients with previous exposure to treatment, which increases the risk of adverse drug reactions. There is a need to implement comprehensive patient-centered care that seeks access to health services and medications throughout the course of treatment, in addition to the appropriate pharmacotherapeutic follow-up. Likewise, prospective studies evaluating the safety / effectiveness results of DAA in patients with chronic HepC are necessary.

Associated risk of Blastocystis infection in gastrointestinal tract cancer: a case-control study

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Introduction

Blastocystis are intestinal protozoa, showing undetermined pathogenicity and high genetic diversity. According to CDC, 9 subtypes were identified. STs 1, 2, 3 & 4 are the most commonly isolated from human while the rest are thought to be affiliated with zoonosis (CDC, 2019). Blastocystis infection has been postulated to be associated with chronic disease such as, Irritable Bowel Syndrome (El-Badry et al., 2018), and Colorectal Cancer (CRC) (Mohamed et al., 2017). Amongst all gastrointestinal tract cancer (GTC), CRC is the most common (WHO, n.d.). According to a 2011 report released by SEHA, CRC is the second most common cancer and the second highest cause of cancer related deaths in the United Arab Emirates. Hence, it is significantly important to investigate the association of Blastocystis infection in promoting cancer within the Gastrointestinal tract. The aim of the proposed study is to assess the possible association between Blastocystis infection and GTC condition in comparison among cancer patients and healthy population.

Materials & Methods

This study recruits 3 groups of participants: 7 GTC patients, 8 patients with cancers outside the gastrointestinal tract (COGT) and 15 healthy individuals. Participants were consented to provide fresh stool samples. Fecal specimens were analyzed by microscopy for the presence of protozoa and by PCR to detect 7 subtypes of Blastocystis sp.: ST1, 2, 3, 4, 5, 6, & 7.

Results

53.3% (n=8/15) of cancer patients and 33% (n=5/15) of healthy individuals were positive for at least one Blastocystis subtype by PCR. Blastocystis ST1 was the most common (43.3%, n=13/30). Blastocysitis infection was lower in patients with GTC compared to COGT. Microscopic analysis shows that 20% of healthy individuals (n=3/15) and 13.3% of cancer patients (n=2/15) were positive at least for one parasite.

Conclusion

It is hypothesized that the samples of GTC patients will show a higher prevalence of Blastocystis infection compared to the COGT group. However, our current data shows otherwise with a higher Blastocystis prevalence among COGT patients.

Gynaecology and Neonatology
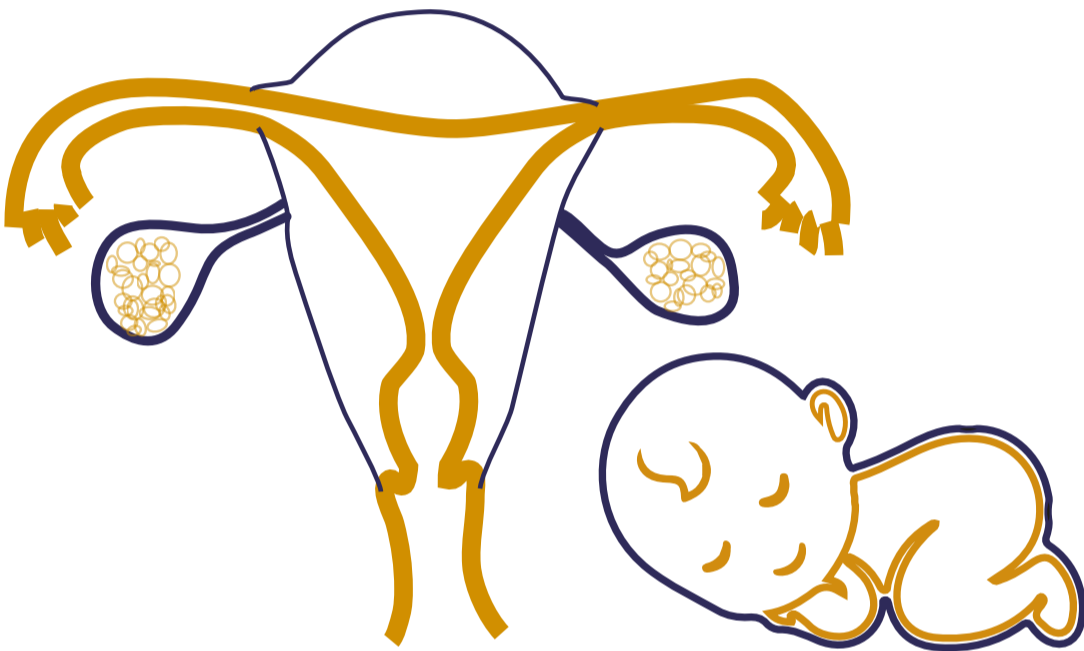
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Platelet indices and CXCL12 levels in patients with intrauterine growth restriction

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Introduction

Intrauterine growth restriction (IUGR) is one of the public worldwide health problems and any factor disturbing the balance of nutrition between the mother and the fetus could be considered as a cause of it. Since chemokine CXCL12 is produced by trophoblasts and mediates a crosstalk between trophoblasts and decoid stromal cells, we aimed to evaluate the relationship between the platelet (PLT) indices and CXC12 in patients with IUGR.

Materials & Methods

In this study, 36 IUGR cases with the gestational age between 24 and 40 weeks were enrolled as case group and the same numbers of healthy pregnant mothers were considered as control. Blood samples were taken and platelet indices were examined by full-diff cell counter and the serum level of CXCL12 were measured employing Elisa. Finally, the data was analyzed using independent t-student test.

Results

In this study, we observed that the mean value of PLT count and plateletcrit (PCT) were significantly higher in control group than the patients with IUGR. In contrast, the amount of PMV and PDW were significantly decreased in patients than the control group. More importantly, we found that the serum levels of CXCL12 were much higher (p =0.02) in the patients compared to the control group.

Conclusion

out data show for the first time that CXCL12 are increased in patients with IUGR and that CXCL12 may play a crucial role in pathophysiology of IUGR. However, further studied employing a higher number of samples is required.

Camparison of maternal serum and umbilical cord blood leptin in IUGR (intrauterine growth restriction) neonates

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Introduction

Gestational weight gain is an impressive factor in the fetal outcome. Intrauterine growth restriction (IUGR) is one of the most important problems during fetal period that may lead to many perinatal and long term complications and growing neonatal morbidities and mortalities. The aim of the study was to ascertain the relationship between umbilical cord blood leptin concentration and fetal growth in neonates born with intrauterine growth restriction.

Materials & Methods

Maternal serum and umbilical cord blood leptin concentration were measured by immune radiometric assay at term gestation. The study was conducted on 22 women with uncomplicated singleton pregnancies as control group (group A) and 22 women with fetal growth restriction in singleton pregnancies as case group (group B). All subjects had normal pregravid body mass index (BMI).

Results

The results of the study showed that maternal serum leptin concentrations were significantly higher in group B comparing to group A (44ng/ml [28.9-58.2] vs. 24.6ng/ml [18.8-33.3]; P<0.001). However, umbilical cord blood leptin levels were significantly lower in group B comparing to group A (8.6 ng/ml [range 4.5-12.7] vs. 14.6 ng/ml [11.7-16.7]; P<0.001). Moreover, umbilical cord blood leptin levels were directly correlated with maternal BMI and neonatal birth weight in both groups.

Conclusion

In growth-restricted fetuses at term, umbilical cord blood leptin concentrations were significantly lower than normal fetuses, suggesting that fetal adipose tissue is a major source for leptin production. Maternal serum leptin concentrations were higher in the presence of a growth restricted fetuses. This increas may be due to early hypoxia or an intrinsic placental mechanism, by which small placenta produces more leptin as a compensatory mechanism. Human recombinant leptin may have some roles in the treatment of IUGR fetuses in future.

Maternal and perinatal outcome of fever in pregnancy with and without dengue - A retrospective observational study

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Introduction

Dengue infection, a mosquito-borne arboviral infection, is endemic to many countries across the world and is a major public health problem in India. Pregnant women in endemic areas are prone for dengue infection. Earlier studies reported an increase in adverse outcomes, while recent studies show no or little increased risk. So, it was aimed to assess and compare the maternal and perinatal outcome in women diagnosed with Dengue infection with those without it.

Materials & Methods

A retrospective observational study was conducted at a tertiary centre in South India, reviewing medical records of 408 pregnant women who underwent Dengue serology testing after admission with fever. For each case with Dengue positive testing, four controls were included from those tested negatives using simple random technique. Outcomes included preterm birth, still birth, low birth weight, maternal mortality and thrombocytopenia. Data analysis was performed using STATA 15.0 (STATA Corp, Texas, USA).

Results

During the study period, 91 women (22.3%) were diagnosed as having Dengue. There were 6 maternal deaths among the cases, with 5 of them due to dengue shock syndrome and one due to dengue haemorrhagic syndrome. Higher rates of thrombocytopenia and need of blood products transfusion were observed among those with dengue infection compared to controls. Relative risk of stillbirth was 2.67 (95% CI 1.09, 6.57) in dengue cases compared with controls, low birth weight RR 1.13 (95% CI 0.87, 1.45) and preterm birth RR.1.33 (95% CI 0.89, 1.97)

Conclusion

Occurrence of adverse maternal and fetal outcomes are increased in pregnant women with Dengue infection compared to febrile controls without Dengue. Hence early diagnosis, close monitoring, and prompt intervention of these antenatal women with Dengue infection is critical in ensuring better pregnancy outcomes.

Effect of early maternal-newborn skin to skin contact in labour room on third stage of labour and success at breastfeeding

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Introduction

Immediate postpartum period and birth pose many challenges for the mother and the newborn. India, though being a fast developing country, still has very high maternal and neonatal mortality rates. It is the need of the hour to find out cost-effective, easy and reliable ways to decrease these rates. In our study, we hence try to prove the statistical significance of giving early skin to skin contact(SSC) in the labour room on 1) the third stage of labor and 2)success at breastfeeding.

Materials & Methods

Randomized control trials conducted over a period of 7 months in a tertiary care center enrolling 400 laboring women.200 in the control group were given routine care. In the 200women in the study group, the newborn was given immediate skin to skin contact by placing him/her on the mother's chest.

Results

The duration of third stage of labor was less than 10 minutes in 95%women of study group compared to 56% women in the control group(p<0.01).Placenta was expulsed as a whole in 98% cases in the study group compared to 81% in the control group. Successful breastfeeding was observed in 88% of women in study group compared to 54%in the control group(p<0.01). Breastfeeding was initiated within 30 minutes of birth in 96%women in the study group compared to 41% in the control group.

Conclusion

The uterus could contract faster with the complete expulsion of the placenta and shortening of the third stage of labor with early skin to skin contact. The newborn showed early initiation and success at breastfeeding and longer first breastfeeding with early skin to skin contact.

Effect of Dexamethasone on reducing pain associated with cesarean section: A systematic review and meta-analysis

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Introduction

Dexamethasone is a glucocorticoid which is known for its strong anti-inflammatory effect, and is widely used in many medical procedures. Cesarean section is one of the most common operations in obstetrics. Many drugs are attempted to decrease the pain associated with the procedure. Here we combine the evidence from published randomized clinical trials about the safety and efficacy of dexamethasone for reducing pain associated with cesarean section

Materials & Methods

We performed this systematic review and meta-analysis including only randomized placebo-controlled clinical trials. Our main population target was women undergoing elective cesarean delivery. Intervention is dexamethasone IV, SC, or IM administration with different doses, compared to placebo. We assessed the quality of included studies using Cochrane's risk of bias tool mentioned in Cochrane's handbook for systematic reviews of interventions.We performed a literature search of available studies and combined them in a meta-analysis.

Results

We found that dexamethasone significantly reduces pain ($p<0.001$), nausea ($p<0.001$), and vomiting ($p<0.001$). The drug also showed significant improvements in other secondary outcomes; post-operative analgesia need ($p<0.001$), post-operative anti-emetic requests ($p<0.001$), and retching ($p<0.001$). However, the drug showed no significant effect in reducing the incidence of headache and pruritus

Conclusion

Dexamethasone decreases pain perception, and protects against nausea and vomiting. However, it is not effective against headache attacks

First Time Fatherhood: Perceptions, role, experiences and their correlation with maternal and newborn health

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Introduction

Stepping into fatherhood leads to fundamental changes in man's identity and lifestyle. Expression

of paternity has undergone major changes over the last few decades. Progressively, fathers have assumed a more active role in supporting a mother during pregnancy, childbirth, and childrearing. Up to now, research has focused mainly on motherhood. The aim of this study is to explore First Time Fathers' (FTFs) perception, role and experiences during pregnancy, childbirth and early infancy of their children, taking into account various stress factors and their impact on maternal and newborn health.

Materials & Methods

The sample size of this study is 100 First Time Fathers. Preliminary results were obtained from 30 First Time Fathers. Consenting participants were asked to fill a pre-validated First Time Fatherhood - 25 (FTF-25) questionnaire and relevant medical data was collected. FTF-25 is divided into 4 domains: physical health, social health, mental health & fatherhood. Data was analyzed using unpaired t-test, Pearson correlation coefficient test and other suitable statistical methods.

Results

An increasing trend of birthweight positively correlated with mental health score of FTFs ($r=+0.5241$, $p<0.05$). The number of antenatal checkup visits significantly increased when husbands accompanied their wives. 63.33% of FTFs agreed that mothers are more important to their children than they are. 76.67% of FTFs were stressed due to changes in their work-life. 50% of FTFs responded to be under economic stress of funding their child's birth. Stress among FTFs living in nuclear families was significantly higher compared to joint families.

Conclusion

The mental health of FTFs increases with the increasing birth weight of newborns. Husband's support during pregnancy increases exposure to healthcare system, which will help in reducing maternal morbidity & mortality. Awareness for work-life stress & money management is of prime importance for every parent trying to conceive baby, which is often ignored. In joint families, household responsibilities are shared which results in reduced stress compared to nuclear families. Since this preliminary result is limited, after complete data collection, appropriate statistical tests will be applied to understand the FTFs impact and draw accurate inferences on newborn & maternal health.

The effect of endometrial scratch injury on women undergoing in vitro fertilization, systematic review and meta analysis for RCTs

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Introduction

In-vitro fertilization (IVF) is considered one of the best techniques to overcome the infertility problem but the main cause of its failure is the inability of the embryo to implant itself in the endometrium, So the solution is to improve the implantation process that may be enhanced by Endometrial scratch injury (ESI).

Materials & Methods

We conducted our meta-analysis according to PRISMA statement guidelines through searching PubMed, Web of Science, SCOPUS, And Cochrane CENTRAL library for randomized clinical trials (RCTs) comparing groups underwent ESI to control ones in terms of the review objectives.

Results

A total of 27 RCTs (no. of women =5113) were included. The overall effect estimate favoured endometrial scratching during the follicular phase over the control group (RR 1.47, 95% CI [1.17, 1.84], p =0.009). In contrary, overall effect estimate did not favour endometrial scratching during the luteal phase (RR 1.14, 95% CI [1.00, 1.30], p =0.05) or during both follicular and luteal (RR 1.30, 95% CI [0.67, 2.50], p =0.43). Likewise, the overall effect estimate favoured endometrial scratching during the follicular phase (RR 1.43, 95% CI [1.10, 1.87], p =0.007); but not during the luteal phase (RR 1 1.19, 95% CI [0.94, 1.49], p =0.14) or during both follicular and luteal (RR 1.25, 95% ci [0.79, 1.97], p =0.34). These findings were more notable in women with previous IVF failure.

Conclusion

In conclusion, endometrial scratching improves the rates of implantation, clinical pregnancy, and live birth, especially in women with previous failed embryo transfer attempts.

To determine the efficiency of the sepsis-risk calculating scoring system in meeting the antibiotic stewardship goals in the NICU

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Introduction

Neonatal septicemia is a clinical syndrome which is characterized by systemic signs of infection and accompanied by bacteremia in the first 28 days of life. Due to the fear of incurring septicemia, neonates are administered antibiotics as soon as they are admitted in the NICU. We aimed to determine the efficiency of the scoring system in reducing the use of antibiotics and the number of blood cultures sent, thereby reducing the duration of stay of the neonate in the NICU of a semi urban hospital. Knowledge of likely risk factors could help in instituting early and effective antibiotic therapy for neonatal sepsis.

Materials & Methods

It is a prospective observational study which included all the neonates suspected of neonatal sepsis admitted during study period of 4 months. They were evaluated using the scoring system before starting antibiotics. Neonates admitted only for phototherapy and observation after delivery were excluded from the study.

Results

In a sample of 60 neonates, blood culture was sent only in 36 neonates (60%) and was positive in 8 (13.33%). This shows reduction in use of blood culture by 40%. Blood cultures were sent only if CRP was positive or if there was a strong clinical suspicion of sepsis as well as in all the babies with score more than 10 in the scoring system.

Using scoring system, we did not use antibiotics at all in 20 neonates (33.33%). Antibiotics were used in 32 neonates (61.53%) with score less than 10. Antibiotics were given for 3 days only in 15(25%) neonates as their CRP tests were negative and they were stable.

Conclusion

Application of the scoring system reduced the use of blood culture in neonates of suspected sepsis. It specifically targets new born infants who are at the highest risk for a serious bacterial infection without exposing those at low risk for infection to antibiotics. This system has also cut down on the usage of blood cultures and unnecessary investigations which can prolong the duration of stay of neonate in the NICU. Total duration of antibiotic course in the neonates was also shortened, thereby decreasing their hospital stay.

Immunology
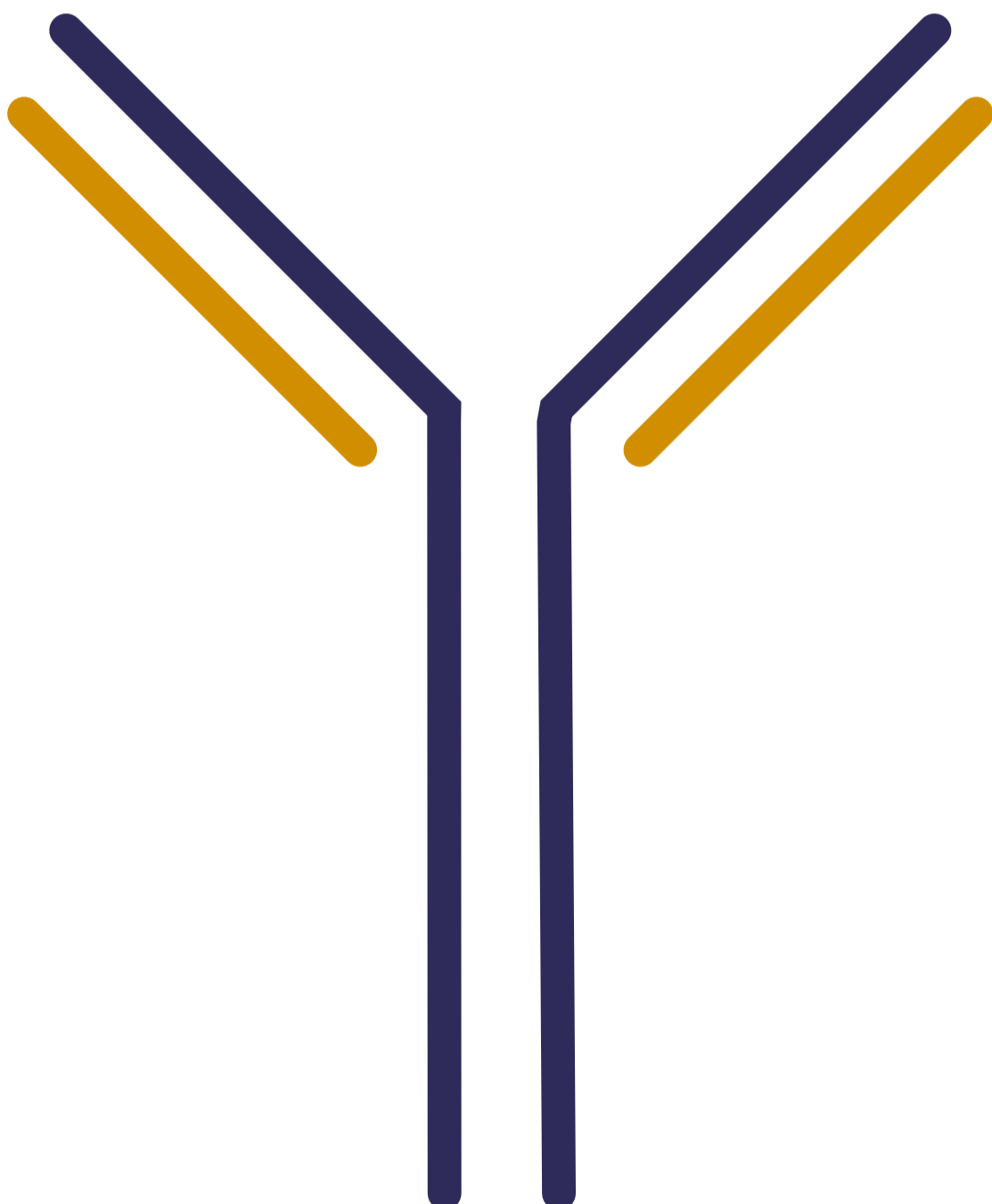
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Krasnova, T.V. (Tayisiya)
Rodriguez, C.A. (Carlos)
Ito-Achoa, J.T. (Juliana)
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Do hematological indices predict prognosis in renal cell carcinoma? - a retrospective study from South India

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Introduction

The systemic inflammatory response plays a significant role in cancer progression and can be assessed using hematological indices to predict disease prognosis. This could serve as a simple and cost effective prognostic tool. We aim at investigating the prognostic role of neutrophil-lymphocyte ratio(NLR), platelet-lymphocyte ratio(PLR), red cell distribution width(RDW) and RDW to platelet ratio(RPR) in renal cell carcinoma(RCC).

Materials & Methods

121 patients diagnosed with RCC treated with partial/radical nephrectomy were retrospectively analysed. Data collection included patient demographics, WHO/ISUP grade,TNM staging, and preoperative NLR,PLR,RDW and RPR. ROC analysis was performed to determine optimal cut off values for these parameters with their WHO/ISUP grade and pT stages. Pearson chi square test was used to determine association. SPSS v11.5 was used.

Results

Out of total 121 patients, the most common age group was 60-69 years (n=42,34.71%, with male preponderance (n=100,82.64%). Majority underwent radical nephrectomies(n=102,84.3%). The most common tumor type was clear cell RCC(n=106,85.48%), followed by papillary cell type(n=7,5.65%). Most common WHO/ISUP grade was G2(n=52,42.98%), and tumors were most commonly diagnosed at pT1 stage(n=59,49.58%).

Preliminary data of hematological investigations was available for 38 patients. The cut off values for NLR and PLR for WHO/ISUP grades were 3.06 and 1.204 and for T stage were 2.95 and 1.25 respectively. There was insufficient data for RDW/RPR analysis.

The association between NLR, PLR and WHO/ISUP grade was not statistically significant (p=0.45 and p=0.29 respectively). The NLR and T-stage association was statistically significant(p=0.002). However there was no statistically association between PLR and T stage (p=0.07).

Conclusion

The study showed that higher NLR was associated with higher T-stage, hence it can be used as a prognostic marker in renal cell carcinoma.

A study of the effects of immunoglobulin G sub-types on T lymphocytes

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Introduction

Both cellular and humoral immunities play important roles in protecting and balancing the normal bodily function and fighting diseases. However, many aspects of the interactions between the two constitutes of the immune system have not been clarified. In this study, we investigated the interactions between IgG sub-types (IgG1,2,3 and 4) which are the major components of humoral immunity, with T lymphocytes which are the major components of cellular immunity. Several interesting phenomena were obtained.

Materials & Methods

We used human peripheral blood mononuclear cells (PBMC) extracted from normal human peripheral blood to further isolate CD3-positive T lymphocytes. We use 1640 culture medium as the basic medium, added 10% human serum with antibiotics to prepare the primary cell culture. Phytohemagglutinin (PHA) was used as cell stimulant in culture. CCK8 cell proliferation kit was used to determine cell proliferation activity. Flowcytometry was used to analyze CD4- and CD8-positive cell numbers. ELISA was used to measure IL-2 content in culture supernatant to reflect the proliferation of cells. Immunocytochemistry was used to analyze the possible reaction between the proteins and T lymphocytes.

Results

At low concentration, IgG sub-types had no effect on the proliferation of T lymphocytes. However, with increased concentration to 500 ug/ml, IgG2 and particularly IgG3 inhibited the proliferation of T lymphocytes. This inhibition was concentration-dependent. The IgG sub-types were significantly different in reacting to T lymphocytes in morphology, and the reaction of IgG3 was the strongest. This reaction can be eliminated after IgG3 was co-incubated with anti-IgG3 antibody indicating the effect was produced by IgG3 protein. Upon stimulation with IgGs, the amount of IL-2 secreted by T lymphocytes was decreased, and this effect was most obvious by IgG3. IgG sub-types can inhibit the proliferation of CD4-positive and CD8-positive T lymphocytes to different degrees. IgG2 and particularly IgG3 had the strongest inhibitory effect. The above effects could be induced with and without PHA stimulation in cell culture.

Conclusion

It is known that the concentration of four sub-types of IgG in healthy human adult serum is 3.2-10.2 (IgG1), 1.2-6.6 (IgG2), 0.2-1.9 (IgG3), and <1.3 (IgG4). Therefore the IgG concentrations used in our experiments are within the range (from 50 ug/ml to 500 ug/ml) and may have physiological and pathological implications in health and diseases. The role of IgG3 in cancer and other diseases is currently unknown. The findings in our study indicate that IgG3 may play a role in regulating T lymphocyte proliferation. The exact mechanism and clinical implications of these original observations await for further investigation.

Specificity of some cytokines' blood profile in schoolchildren with persistent bronchial asthma, born with low birth weight

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Introduction

Published data regarding the particularities of bronchial asthma (BA) in children born with low birth weight (LBW) remains conflicting. The aim of the survey was to study the particularities of some serum immunological markers in schoolchildren with persistent BA depending on their birth body weight.

Materials & Methods

In the Chernivtsi Regional Children's Clinical Hospital detection of the blood serum levels of total immunoglobulin E (IgE) and interleukins (IL) -4, 5 and 8 has been performed in 61 schoolchildren with persistent BA, who was born on term, but either with LBW (I group, 35 children) or with adequate relatively to gestational age body weight (II group, 26 patients). The results were analyzed by parametric (Pt, Student's criteria) and nonparametric (Pφ, Fisher's angular transformation) methods of calculation.

Results

The average concentration of total IgE in serum was 361,7±84,4 IU/ L in children of the I group and 695,6±107,8 IU/ml in patients of the II group (Pt <0,05). At that, the serum level of total IgE below normal value (less than 120 IU/ml) was recorded among 29,4% of children with LBW, and only in 5,9% of cases in the II group (Pφ <0,05). However, the high content of IL-4 (> 7 pg/ml) in serum has been typical for most (53,3% of cases) patients with LBW in comparison to the II group (7,7% of patients; Pφ <0,01). At the same time, in patients, born with LBW, there more often has been registered in a serum low (≤ 4 pg/ml) level of IL-5 (66,7% of cases) and medium range (> 4 pg/ml but less than 7,5 pg/ml) of IL-8 (70% of children) with respect to the results of the II group (44,4% of children; Pφ> 0,05) and 42, 9% of patients (Pφ> 0,05) respectively.

Conclusion

Persistent BA in schoolchildren with LBW is associated with low serum levels of total IgE, IL-5 and IL-8. Such data suggesting nonatopic noneosinophilic asthma phenotype, which, on our opinion, require the necessity of correction of the controlling treatment in this group of patients, namely to use so-called "antineutrophil" drugs (sustained release methylxanthines, long-acting beta-2-agonists, macrolides, etc.).

Bacterial suspension up-regulates peripheral blood regulatory B Lymphocytes in patients with active allergic conjunctivitis and correlates with improved clinical outcome

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Introduction

Regulatory B lymphocytes (Bregs) are not yet fully understood. Fortunately, regardless of their relative novelty and their apparent endless subtypes, a functional definition does exist: a Breg is defined as any B cell from any subtype that produces IL-10. Another novelty in immunology are bacterial suspensions, which are inactivated complete bacteria, these relate to Bregs as they have been found to activate these cells and induce tolerance through IL-10.

The role of Bregs in the induction of tolerance has been proved several times but not in active allergic conjunctivitis. Therefore, we developed this study where we aim to determine the effect of the administration of bacterial suspension (BS) in patients with active allergic conjunctivitis (AC) on relative frequency of regulatory B lymphocytes (Bregs, defined for the study as CD19+IL10+ cells) and its correlation with clinical outcome.

Materials & Methods

This is an experimental, prospective, pilot study where individuals with current active AC were selected to donate blood to evaluate mononuclear cell populations before and after the administration of bacterial suspension. These samples were processed through flow cytometry to determine the relative frequency (%) of Bregs before and after BS administration, and were analyzed statistically though frequency distribution. Also, a validated clinical score was used to determine clinical status of the AC before and after BS administration.

Results

We found that after BS administration, Bregs relative frequency was 29.8+-3.1% compared to 2.8+-0.3% before the BS (CI: 95% and p value of 0.0140). In other words, after BS administration, CD19+IL10+ subpopulation was upregulated in a statistically significant manner and clinical outcome improved as well, proven by the decrease in the clinical score referred by subjects after the BS administration.

Conclusion

These results suggest that BS has a positive regulatory effect on peripheral blood regulatory B lymphocytes in subjects with active allergic conjunctivitis, proven by the increase in CD19+IL10+ populations and it also modified clinical course of the disease positively. Therefore, these first results suggests that BS can induct immunological tolerance, but further research is required to confirm this.

Analysis of the intracellular signaling pathways involved in the Th17/Treg balance in different lung compartments in a CS-induced animal model

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Introduction

Chronic obstructive pulmonary disease is characterized by chronic inflammation in the airways and lung parenchyma, leading to different patterns of inflammatory mediators in the lung compartments. Previously, we showed that a Th17/Treg imbalance leads COPD development and progression. Furthermore, we verified in lung samples from patients that difference in Treg cell distributions in lung compartments and the decrease in TGF-β+ and IL-10+ cells in the airways may lead to the obstruction in smokers. Therefore, we aimed to assess how the intracellular proteins (STAT and SOCS) in different lung compartments (lung tissue and peribronchovascular areas) could interfere in Th17/Treg imbalance in a cigarette smoke (CS) induced model.

Materials & Methods

C57BL/6 mice were exposed to CS (twice a day for 30 minutes, 5 days a week during 3 and 6 months), and control groups were remained under filtered air conditions for the same time periods. In lung tissue, we quantified IL-10 and IL-17 expression by ELISA, and relative expression of pSTAT5/STAT5 ratio, pSTAT3/STAT3 ratio, SOCS1, and SOCS3 by Western Blotting. In peribronchovascular areas, we quantified positive lymphocytes for FOXP3 (Treg), IL-17, pSTAT5/STAT5 ratio, pSTAT3/STAT3 ratio, SOCS1, and SOCS3 by immunohistochemistry.

Results

Lung tissue samples analysis showed a decrease in anti-inflammatory response (IL-10 expression, $P<0.05$; pSTAT5/STAT5, $P<0.01$; and SOCS1, $P<0.02$) since the third month of CS exposure, as well as an increase in pro-inflammatory response (pSTAT3/STAT3, $P<0.04$). However, the increase in IL-17 expression ($P=0.01$) was observed only after six months. Although we observed a similar response in peribronchovascular area analysis, in contrast, there was an increase in SOCS1 ($P<0.04$) and a reduction in SOCS3 ($P<0.05$) in both time points.

Conclusion

Although the Th17/Treg imbalance was observed in both lung compartments assessed, there was a different pattern of the SOCS1 expression between the analyzed compartments. The reduction of SOCS1 expression observed in the lung tissue corresponds to the decrease of IL-10 expression, since SOCS1 plays an important role in Treg cells suppressive activity. In addition, these findings suggest that, in animal models, the inflammatory response is best represented in lung tissue, whereas in humans it is in the small airways.

CD39/CD73 positive dental derived mesenchymal stem cells as a promising cell-based therapy in acute spinal cord injury via anti-inflammatory Adenosine signals

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Introduction

Dental pulp offers an accessible and non-invasive source of potent mesenchymal stem cells (MSCs). Following traumatic spinal cord injury (SCI), acute cell death and damage arouses release Damage associated molecular patterns (DAMPs), as Adenosine triphosphate (ATP). ATP is considered as pro-inflammatory molecules, triggers a complex secondary inflammatory cascade in SCI mainly through receptor P2X7. Ectonucleotidase CD39 & CD73 are two membrane-bounded ecto-enzymes that phosphohydrolyzes ATP & ADP to AMP and then to Adenosine, respectively. Adenosine is considered as an immune-modulator, anti-inflammatory molecule.

Our study aims to localize the co-expression of CD39/CD73 ecto-enzymes in dental stem cells to investigate the immune-modulatory capacity of such subpopulation in SCI inflammatory disease.

Materials & Methods

In vitro experiments were performed to isolate dental derived stem cell lines from human extracted teeth using handheld pulp isolator device a novel method invented by our team patency (WO2016162041A9) by different methods, moreover, we performed characterization using flow cytometry against MSCs surface markers CD 73, CD 105, CD90 and hematopoietic stem cells marker CD34 & CD45 also, CD39. Fluorescent compensation and isotype control were used. Additionally, we sorted subpopulation positive for CD39/CD73 markers and evaluate expression's maintenance on passaging. The co-expression of CD39/CD73 is confirmed by Immunofluorescence analysis.

Results

We successfully isolate Dental pulp stem cells (DPSCs), Stem cells from the human exfoliated deciduous tooth (SHEDs), Stem cells from Apical papilla (SCAPs), and Dental follicle stem cells (DFSCs). We prove for the first time the differentially co-expression of both CD73 & CD39 surface markers on four different dental derived stem cells comparatively, SHEDs showed the highest expression profile with about 85% of the population co-express both marker, while SCAPs had the lowest percentage just 19%. DFSCs & DPSCs are both intermediate with expression of 31% & 42% respectively. Sorted SHEDs maintains CD39/CD73 expression till passage 20.

Conclusion

Our Data introduce stem cells from deciduous teeth co-expressing CD39/CD73 with the highest percentage, which in turn can hydrolyze Pro-inflammatory ATP to anti-inflammatory adenosine at SCI site in the acute stage, and these results provide a more potent tool than the non-selective antagonist of the ATP-sensitive receptor P2X7 to prevent the ATP induced secondary inflammatory cascades.

Luffa operculata extracts negatively regulate the proinflammatory profile of leukocytes in peripheral blood

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Introduction

Luffa operculata is one of the most popular medicinal plants used in South America, where it has been proposed as a low-cost therapeutic alternative to treat rhino-sinusitis. In addition, anti-tumoral, anti-inflammatory and immunosuppressive effects have been reported by unknown mechanisms. The purpose of this study was to evaluate the effects of aqueous and ethanolic infusions of L. operculata on human leukocytes and to discriminate the cytotoxic effects from the anti-inflammatory and the regulatory ones. The effect of both preparations on lymphocyte proliferation induced in response to PHA and cytokines was studied. The effects of the extracts on the respiratory burst in neutrophils and monocytes were also evaluated on patients with rhinosinusitis and controls.

Materials & Methods

In cells from patients with rhinosinusitis and healthy controls, by flow cytometry, the cytotoxic effects of L. operculata. were evaluated with DIOC6 and propidium iodide. The antiproliferative using CFSE-assay in PHA stimulated PBMC and cytokines (TNFα., IL-1β, IL-8, IFN-, IL-12 and IL-10) by CBA. The respiratory burst was evaluated with DHR123. FACS data were analyzed using the Flowjo 10.6.1 and the statistical analysis with the Graphpad prism version 5.0 program.

Results

Both aqueous and ethanolic extracts inhibited PMA-induced respiratory burst in neutrophils and monocytes in a dose-dependent way. And monocytes were more sensitive to the L. operculata effects. Both extracts also inhibited PHA- induced proliferation and activation of lymphocytes and significantly reduce the accumulation of IL-2, IL-4, IL-8 and TNFα. In addition, the comparison of cells from healthy donors and patients with rhinosinusitis showed no differences between both groups in response to the different extracts.

Conclusion

In this study we found that the anti-inflammatory effects of L. operculata extracts are independent of the cytotoxic effects. The results indicate that L. operculata is a negative regulator of processes such as proliferation, the production of pro inflammatory cytokines in lymphocytes and respiratory burst in neutrophils and monocytes.

Infectious Disease
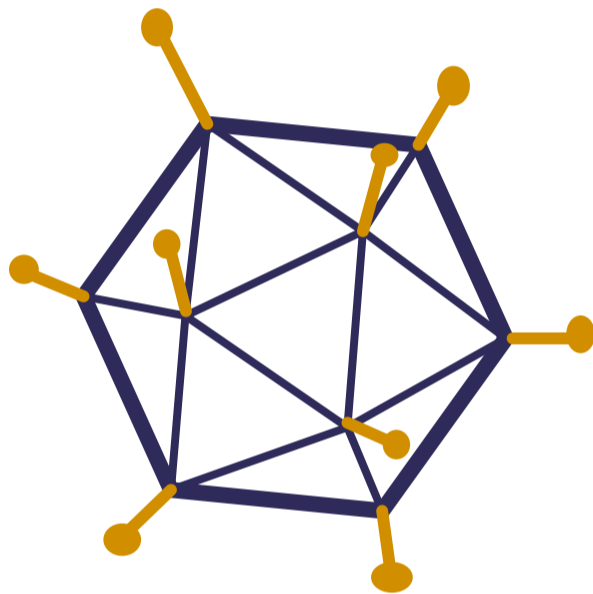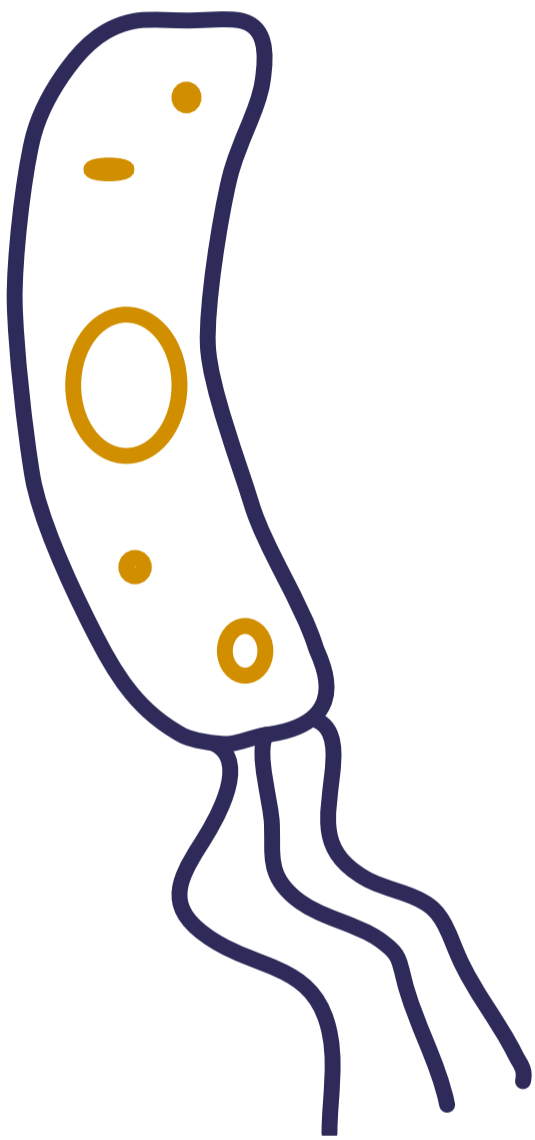
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Psycho-social factors affecting adherence to anti-retroviral therapy among persons living with HIV in Lilongwe, Malawi

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Introduction

HIV is a major public health problem in Malawi. Anti-Retrial Viral Therapy(ART) has allowed people living with HIV(PLHIV) to live longer and healthier lives. In an attempt to manage the disease, Malawi adopted a Test and Treat policy in 2016 that enables patients to begin ART regardless of their clinical stage and viral load. No study has investigated adherence and the psycho-social factors affecting it since the introduction of this policy in the country. This study addressed this gap in knowledge.

Materials & Methods

The study was cross-sectional in design with quantitative and qualitative components conducted on patients attending ART clinic at Lighthouse clinics (Martin Preuss Centre and Lighthouse), Lilongwe, Malawi. Secondary data were extracted from the case notes of 658 and 580 recruited a year before and after the policy respectively. A guide was used to conduct in-depth interviews among 12 purposively selected respondents.

Results

The mean ages of the respondents were 37.3years (±9.7) and 38.6years (±8.0) before and after test and treat policy respectively. Majority were females in both groups (56.5% and 62.1% respectively). The prevalence of poor adherence before and after the policy was 33.9% and 50%(p=< 0.001). Urban residents were more likely to adhere to ART drugs compared to those living in rural areas in both groups. In-depth interviews revealed that the psychosocial factors that caused poor adherence included depression, fear of side effects of the drug, discrimination, fear of stigma, discouragement from the family, pill burden and fear that taking drugs every day may not be healthy for the body.

Conclusion

Poor ART adherence after test and treat policy remains a significant challenge. Educational interventions and introduction of psycho-social counselors are recommended to overcome poor adherence to ART in the country.

The impact of public health policies on the dynamical changes in a measles epidemic: A retrospective study

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Introduction

The 2019 WHO European Immunization Summary declared the elimination of measles a goal yet to be achieved. Countries such as Romania with 18 996 cases and 64 deaths sustain the dangers of new outbreaks in Europe. We propose to give an insight on the impact of the measures taken by the healthcare system and the encountered obstacles. As well as the influences and the changing dynamics of numbers focused on the counties of Romania.

Materials & Methods

We collected data between 2015 until 2019 from the official site of the National Institute of Public Health of Romania. We divided the counties into the 21 most and 21 least affected.

Results

From the start of the measles outbreak in 2016 out of the 42 counties 61.90 % preserved their status either as a low/high affected area during the peak of the epidemics (2017). After 3 years,66.66 % of the counties occupied the same position as in 2016. In the encountered vaccination shortage,7 counties had not had a single MMR dose,10 of the most affected once failed to comply with vaccination schedules. There was no correlation found ($p < 0.05$ Pearson=0.04, Pearson=-0.06) between the vaccination percentage in 2015 and the numbers in 2016 or the total amount of cases. The supplementary vaccination campaigns in 2017 had a minor effect on the dynamics ($p < 0.05$ Pearson=0.184).

Conclusion

Countries failing to achieve the threshold revealed that small raises in immunization do lead to a decrease in cases, but changes are not statistically significant. Awareness campaigns did not considerably improve vaccination, the MMR vaccine having the highest refusal rate. In addition, the inequity in the distribution of vaccines leads to ineffective prevention. To conclude the failing implementation of health policies, the obstacles in vaccination supplies and the misconceptions about immunization sustains the high prevalence of measles. Leaving the challenges of acquiring an acceptable level of immunization open.

Perioperative antibiotic prophylaxis prescribing practice in tertiary care hospital - the impact of educational intervention

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Introduction

The aim of the study is to evaluate the perioperative antimicrobial prophylaxis (PAP) prescribing praxis in three elective procedures (total hip replacement, radical prostatectomy and caesarean delivery) in a single tertiary care hospital in Slovenia and to evaluate the impact of educational intervention on improvement of compliance to recommended local guidelines in Slovenia.

Materials & Methods

We performed an interventional study to evaluate the impact of educational intervention on PAP compliance. The PAP prescribing praxis at three selected surgical departments (A, B, C) was observed for three elective types of surgery. Thirty operative reports for each type of surgical procedure were revised according to: indication, timing of preoperative prophylaxis administration, antibiotic selection and dosage, and total duration of prophylaxis. This was followed by educational intervention where infectious disease specialist that encompasses personal discussion with department leaders, continued with a meeting with surgeons with educational seminar about appropriate PAP and supplemented by PAP recommendations as pocket reminders. In the postinerventional period (3-6 months after the intervention) we evaluated again the compliance with PAP recommendation for same type of procedures performed in postinterventional period.

Results

We observed preinterventional complete compliance with local guidelines in 67%, 70% and 3.3% for procedures type A, B and C, respectively. The major deviation from PAP recommendations was observed in the timing of preoperative PAP administration and in the total duration of PAP. In postinterventional period we observed significant improvement in total compliance with PAP recommendation with 80.0%, 90.0% and 50.0% fully compliance in type A, B and C procedures, respectively. The major improvement was observed in the timing of preoperative PAP administration and in the total duration of PAP.

Conclusion

Our study revealed a significant improvement in adherence to PAP recommendation after educational intervention in selected procedures at our institution. The simple intervention can have an important impact on quality of patient care and should be routinely and regularly performed for further improvement in all surgical departments.

Effect of Calcitriol Supplementation on Infectious Biomarkers in Patients with Positive Systemic Inflammatory Response

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Introduction

sepsis is one of the common causes of hospitalization in the intensive care unit worldwide. A significant role for vitamin D in sepsis has been proposed, which is due to the important effect of its active metabolite, calcitriol, on the host defense system. In the present study, the effect of calcitriol on the markers of infection, including Procalcitonin (PCT) and presepsin, has been studied in these patients.

Materials & Methods

This study was designed as a randomized, open label clinical trial. This study was done in Emam Hossein Hospital during 2018. Patients with positive systemic inflammatory response syndrome who had specific criteria were included and divided into two groups as intervention and control groups. Patients in intervention group received intravenous calcitriol every day for three days. The serum levels of procalcitonin and presepsin were evaluated at baseline, third day and fifth day after injection. SPSS version 23 was used for statistical analysis.

Results

27 patients with positive systemic inflammatory response were included and randomly divided into 2 groups (14 patients in the intervention group and 13 patients in the control group). In terms of basal factors, changes in SOFA score and blood levels of vitamin D were not significantly different between the control and intervention groups. The Procalcitonin levels on day 5 and the differences between day 5 and baseline were significantly different between intervention and control group ($P = 0.02$ and $P = 0.026$). In the intervention group the Presepsin levels on day 3 and 5, was decreased; and in the control group, there was an increasing trend, but there was no significant differences between the two groups on day 3 and 5 after the injection ($P = 0.170$ and $P = 0.069$, respectively). When baseline was compared with day 3 and day 5, the percentage changes in the serum presepsin levels in the two study groups were not statistically significant ($P = 0.933$ and $P = 0.929$ respectively).

Conclusion

Finally, the results of this study showed that administration of intravenous calcitriol can reduce the level of procalcitonin as a diagnostic marker for sepsis but did not have a significant effect on presepsin.

Co-circulation of all four serotypes of Dengue virus in endemic region of Saurashtra, Gujarat in 2019

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Introduction

Dengue is a fast emerging mosquito-borne viral disease endemic in many regions, causing a severe flu-like illness and sometimes potentially lethal complications. Its causative agent-the dengue-virus, belonging to the genus Flavivirus, has four serotypes, namely, DENV-1, DENV-2, DENV-3 and DENV4. These may either mono-infect or co-infect a patient based on their prevalence and predominance in the given region and time; hence conferring the potential to cause global pandemics. The aim is to study epidemiology of dengue, determine the circulating serotypes and patterns of co-infection in Saurashtra region of Gujarat, India.

Materials & Methods

Total 11,181 blood samples of clinically suspected dengue cases were studied over a period of one year, from Jan 2019 to Dec 2019. The serum was tested for Dengue NS1 Antigen using Microlisa test kit (symptoms < 7 days) and for Dengue IgM Antibody using NIV Pune test kit (symptoms >7 days). After serological confirmation, 120 samples from different geographical areas were selected for serotyping by Dengue specific RT-PCR.

Results

Out of the 11,181 samples tested, 3998 (36%) had serologically confirmed dengue. The proportion of male cases (60%) was greater than that of females and majority of confirmed cases belonged to the age group of 21-35years (41%) followed by 6-20years(34%). Seasonal trend showed a gradual increase in positivity starting from June with a peak in October (39%). Circulation of all four serotypes was observed with predominance of DENV-1(44.8%), followed by DENV-4 (22.6%), DENV-2(21.5%) & DENV-3 (6.45%). Co-infection of DENV-1 & DENV-2 (2%), DENV-1 & DENV-3 and DENV-1 & DENV-4 (1%) was observed.

Conclusion

The study concluded that all 4 Serotypes co-circulated (with predominance of DENV-1 serotype) in the Saurashtra region of Gujarat during 2019; since the immunity to one serotype does not protect against a heterotopic serotype. Dengue cases constituted mainly of adult male population (21-35yr) and showed a seasonal peak during monsoon and post-monsoon periods, which coincide with increased vector breeding; hence emphasizing on effective implementation of vector control & personal protective measures during these periods for disease control.

Short-term application of dexamethasone helps dengue fever recover: a clinical study based on 112 patients

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Introduction

Dengue fever is a globally susceptible infectious disease without effective treatments. Using dexamethasone may be beneficial for the treatment, but the efficacy remained unknown. This study aimed to explore the efficacy of short-term application of dexamethasone in the treatments of dengue fever.

Materials & Methods

This study screened 217 cases of dengue patients admitted to the Second Affiliated Hospital of Shantou University Medical College, China, from July 1st to November 30th, 2019. A total of 112 cases met the following admission criteria. Inclusion criteria: Platelet (PLT)<125×10^9/L on the first day of admission; positive result for dengue virus NS1 antigen, dengue virus nucleic acid or IgM antibody. Exclusion criteria: Patient failed to receive dexamethasone treatment for three consecutive days; patient's age≤5 years; patient's data could not be completely collected.
Treatments: On the basis of general treatments and symptomatic treatments, patients were given short-term continuous daily intravenous dexamethasone (5-10 mg, qd or q12h). On the first day of treatment (the recruitment day) and the fifth day, patients were examined for platelet and white blood cell (WBC) values.
Statistical methods: This study used a self-paired t-test to detect differences in WBC or PLT. Statistical analysis was performed using SPSS 24.

Results

After short-term daily application of dexamethasone, all 112 patients with dengue fever recovered, without using platelet or leukocyte-raising drugs, and without giving platelet or plasma transfusion. The WBC of the patients on the fifth day increased 3.02×10^9/L (95%CI 2.42-3.62, P=0.000<0.01) compared with the first day. The PLT on the fifth day increased 14.67×10^9/L (95%CI 0.58-28.76, P=0.041<0.05) compared with the first day.

Conclusion

Short-term daily application of dexamethasone can increase blood PLT and WBC in the treatment of dengue fever patients. All patients recovered and did not progress to severe condition. This study implied that the therapy could reduce the risk of dengue hemorrhage, ameliorate the toxic response, and prevent dengue fever from progressing to severe cases.

Nanocarriers for delivering therapeutic agents against intracellular infections

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Introduction

Infection diseases caused by intracellular microorganisms represent a major challenge in health care due to the appearance of co-infections and drug-resistant pathogens, which limits the existing therapies. This work aims to encapsulate therapeutic agents against intracellular infections into bioreceptor-functionalized nanocarriers for their targeted and controlled release into macrophages.

Materials & Methods

Itraconazole (ITZ) was encapsulated into nanoparticles based on poly(lactic acid-co-glycolic acid) (PLGA) polymers of different compositions, molecular weight and lactic:co-glycolic acid ratio, i.e. PLGA 50:50 of 24-38 KDa and PLGA 75:25 of 4-15 KDa. The nanocarriers were self-assembled by the high-energy nanoemulsion method. I was studied how the polymer: drug ratio affects the formation of nanocarrires, their loading capacity (DLC) and their encapsulation efficiency (EE). pH modifications of the aqueous phase; and type and concentration of the surfactant were assessed in order to improve the DLC and EE. The release kinetics and thermo-stability under physiological conditions were also evaluated.

Results

The nanocarriers were exhaustively characterized by a variety of physicochemical techniques. The results showed that the DLC and EE with both polymers went up to 6.7 and 82.1 %, respectively by lowering the pH to 5.0 and using a mix of Kolliphor with tocopherol surfactants. The concentration and type of surfactant impacted the morphology and colloidal properties of the nanoparticles as demonstrated by Dynamic Light Scattering (DLS), Electrophoretic Light Scattering (ELS) measurements and Transmission Electron Microscopy (TEM) images. The Fourier Transformed Infra-Red spectroscopy (FT-IR) and Differential Scanning Calorimetry (DSC) analysis demonstrated the interaction between ITZ and PLGA in the NPs. Regarding the drug release at optimal conditions, the NPs showed a burst release followed by a prolonged release phase profile, which fit well with an anomalous Fickian diffusion model. They also showed thermo-stability at 4°C in both untreated and sucrose-containing aqueous solutions (after cryopreservation).

Conclusion

In conclusion, ITZ has been encapsulated into biocompatible and monodisperse nanoparticles of two types of PLGA polymers, with adequate particle size and charge, high thermostability, optimal DLC and EE and release kinetic profile that fits with an anomalous Fickian-type model. The current work is directed to functionalize the nanoparticles with specific bioreceptors for their efficient uptake by macrophages.

Characterization of antibiogram fingerprints in Listeria monocytogenes recovered from irrigation water and agricultural soil samples

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Introduction

Listeria monocytogenes is a foodborne pathogen and the etiologic agent of listeriosis, which can be disseminated within the agricultural environment, contaminate farm produce and cause high mortality and morbidity among vulnerable individuals. This study assessed the incidence and antibiogram of Listeria monocytogenes recovered from irrigation water and agricultural soil samples collected from Chris Hani and Amathole District Municipalities (DMs) in Eastern Cape Province, South Africa.

Materials & Methods

The distribution of presumptive Listeria monocytogenes in irrigation water and agricultural soil samples was done using the standard plate count method, while polymerase chain reaction (PCR) was used to identify the isolates. The confirmed isolates were screened for 9 key virulence markers using PCR after which they were subjected to antibiotic susceptibility testing against 18 antibiotics used for the alleviation of listeriosis using the disk diffusion method. Relevant putative antibiotic resistance genes in the resistant variants were screened for using PCR.

Results

The distribution of Listeria monocytogenes in irrigation water samples and agricultural soil samples was statistically significant ($P \leq 0.05$) and ranged from log10 1.00 CFU/100ml to log10 3.75 CFU/100 ml and log10 2.10 CFU/g to log10 3.51 CFU/g respectively. Of the 117 and 183 presumptive Listeria monocytogenes recovered from irrigation water and agricultural soil samples, 8 (6.8%) and 12 (6.6%) isolates were confirmed respectively. Nine virulence genes including inlA, inlB, inlC, inlJ, actA, hlyA, plcA, plcB, and iap were detected in all the isolates. The proportion of the isolates exhibiting phenotypic resistance against the test antimicrobials followed the order: tetracycline (90%), doxycycline (85%), cefotaxime (80%), penicillin (80%), chloramphenicol (70%), linezolid (65%), erythromycin (60%) and trimethoprim/sulfamethoxazole (55%). The isolates exhibited multiple antibiotic resistance against 3 or more antibiotics and the MAR indices of all the multidrug isolates were ≥ 0.2. The isolates harboured antibiotic resistance genes including tetA, tetB, tetC, sulI, sulII, aadA, aac(3)-IIa and ESBLs including blaTEM, blaCTX-M group 9, blaVEB as well as AmpC.

Conclusion

Irrigation water and agricultural soil collected from Chris Hani and Amathole DMs in Eastern Cape Province of South Africa are reservoirs and potential transmission routes of multidrug-resistant Listeria monocytogenes to the food web and consequently threat to public health.

Neurology II
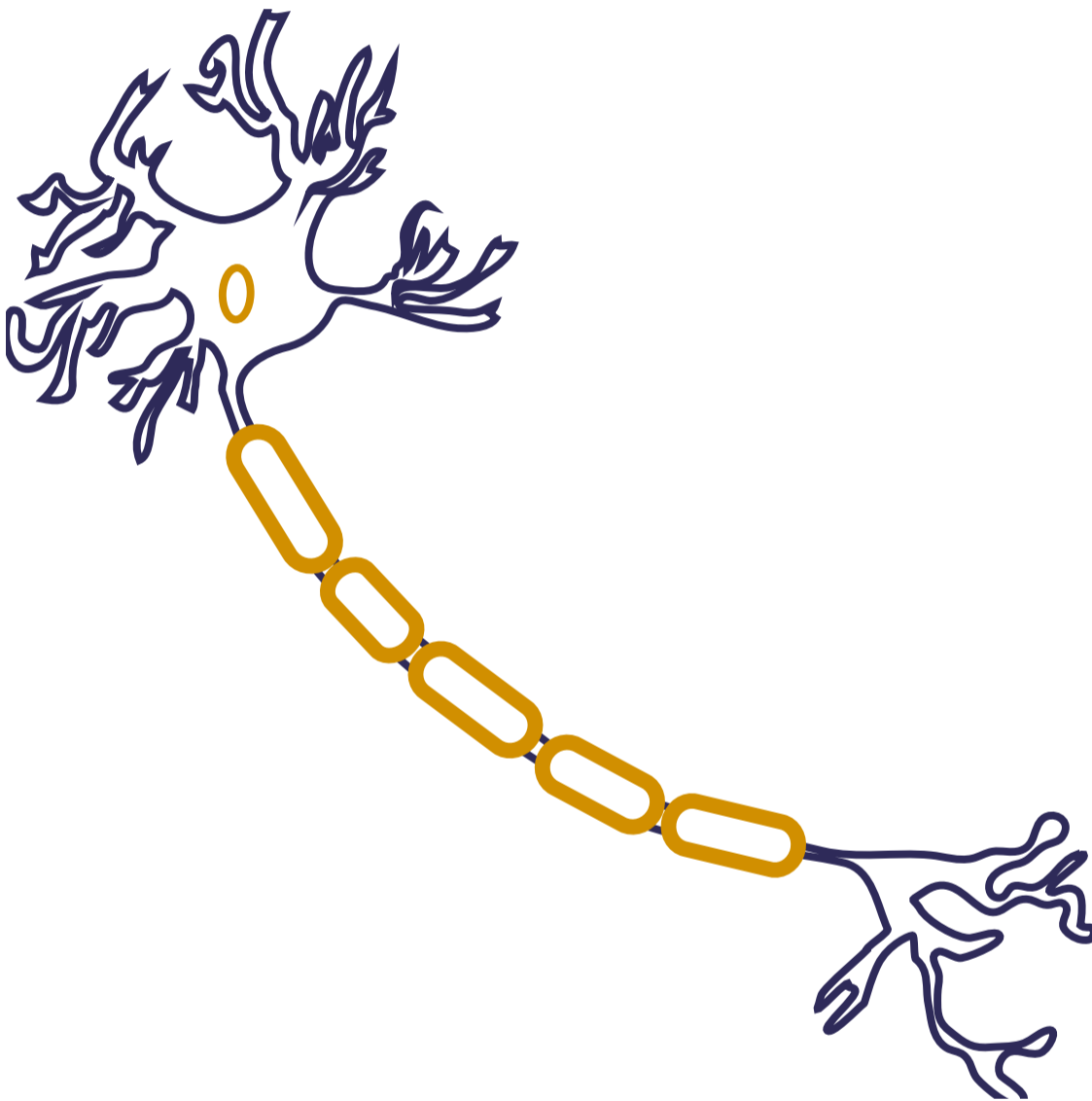
Presenters:
Lule, L.H (Herman)
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Kuśmierczyk, H. (Hanna)
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Delays and Determinants of Traumatic Brain Injury Care Outcome in Low-Income Uganda

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Introduction

Increasing traumatic brain injury (TBI) has paralleled need for decompression surgery for acute subdural (ASDH) and acute extradural haematoma (AEDH). Knowledge of key determinants of clinical outcomes inclusive of delays is mandatory to guide treatment protocols. This study determined the thirty-day clinical outcomes and predictor variables for patients with extra-axial haematoma at Uganda's National Referral Hospital, Mulago.

Materials & Methods

Prospective observational cohort study of 109 consecutive patients with Computed Tomography (CT) confirmed extra-axial haematoma. Ethical Clearance was obtained from School of Medicine Research and Ethics Committee of Makerere University (REC REF. 2018-185). Admitted patients were followed-up for Glasgow Outcome Scale (GOS) and final disposition. Multivariate regression analysis was performed using Stata 14.0 (StataCorp. 2015) at 95% confidence-interval, regarding $p<0.05$ as statistically significant.

Results

No participant received surgery within six hours of decision making. The overall proportion of favourable outcome was 71.7% (n=71), with 42.3% (n=11) and 81.7% (n=58) for ASDH and AEDH respectively (p=0.111). Factors associated with a favourable outcome were: Admission Systolic BP>90mmHg [IRR=0.88 (0.26-0.94) 95%CI, p=0.032), Oxygen saturation>90% [IRR=0.5 (0.26-0.94) 95%CI, p=0.030] and Diagnosis AEDH [IRR=0.53 (0.30-0.92) 95%CI, p= 0.025). Moderate [IRR=4.57 (1.15-18.06) 95%CI, P=0.03] and severe TBI [IRR=6.79 (2.32-19.86) 95%CI, p<0.001] were associated with unfavorable outcomes.

Conclusion

The study revealed that amidst delays, post resuscitation GCS, Systolic BP, Oxygen circulation and diagnosis of AEDH at admission, are the most important determinants of outcome for patients with extra-axial intracranial haematoma. These findings are valuable for triaging teams in resource constrained settings.

How to deal with vertigo patients in the emergency department of a teaching hospital : A clinical audit study

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Introduction

Vertigo, as a common disorder, has symptoms similar to those of many lesions in the central nervous system that can directly affect the patient's life. Considering the high prevalence of vertigo and varying success rates reported for various treatments applied to the patients with vertigo in various studies, this study aimed to evaluate the vertigo assessment procedure for the patients referring to the emergency department.

Materials & Methods

This descriptive-analytic study was conducted during the period from April 2013 to April 2015. In this period, 3279 patients diagnosed with vertigo had referred to the emergency department , out of which 718 had been hospitalized. According to the inclusion criteria, medical records of 402 patients meeting these criteria were investigated in this study. Finally, the collected data were analyzed using SPSS 20.

Results

The results showed that less than 10% of the patients (N=402) with an average age of 58.32±17.07 were suffering from central vertigo. Also, the results showed that 78.35% of these patients had CT scan and 42.78% had MRI and the results of these tests contained no pathologic findings in more than 97% of the cases.

Conclusion

The results of this study showed that vertigo experienced by most of the patients referring to the hospital with vertigo symptoms was peripheral and there was no need for additional diagnostic and therapeutic procedures and imposing heavy costs on the patients. It seems that lack of enough human resources and emergency crowding are the reasons of over-ordering imaging in vertigo patients in ordering not to missing the central type. Therefore, the costs and risks of radiation can be reduced with correct diagnosis using clinical tests and other procedures.

Neurological comorbidities in children with T1D

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Introduction

Type 1 diabetes (T1D) is an autoimmune disease of unknown and possibly very heterogeneous pathogenesis. Some children suffer from additional neurological (ND) conditions such as epilepsy or autism spectrum disorders (ASD),that can affect the metabolic control of diabetes. The coexistence of T1D and ND suggests their common genetic background. The aim of the study was to evaluate the prevalence and type of neurological disorders in children with T1D and to compare the course of diabetes between those patients and control group of children without neurological comorbidities.

Materials & Methods

The study included children with both T1D and ND identified by a retrospective chart review of all children with T1D (n= 815) treated in Pediatric Diabetes Outpatient Department of Medical University of Lodz. T1D was confirmed by the presence of anti-islet autoantibodies in all included patients. The data collected included age, age of diagnosis of both T1D and neurological conditions, glycated haemoglobin (HbA1c) level, presence of autoimmune and non-autoimmune comorbidities and a detailed family history. Control group included children with T1D without neurological disorders.

Results

The coexistence of both T1D and additional neurological disorders was identified in 35 children (4.3%). The most common was epilepsy (n=16; 2%), followed by autism spectrum disorders (n=10; 1.2%). In 2 children both conditions coexisted. In 22 patients (63%) diagnosis of ND were made before the onset of T1D, in 10 (28.6%) after and in 3(%) of them simultaneously with T1D. Interestingly, 24 of 35 patients with ND were boys(68.5%), with 10 of them suffering from ASD. 43 % (n=15) of T1D plus ND children had positive family history for autoimmune disease. Mean HbA1c in the study group was 7.85±1.45 [SD=1.45] which was slightly worse than in controls 7.41±1.42, but it did not reach statistical significance (p=0.06).

Conclusion

Neurological conditions are common among children with T1D.The metabolic control in patients with neurological disorders is statistically not different from the group of children with T1D only. It is important to take a closer look at children with T1D and neurological disorders in order to find possible common pathogenesis of these disorders.

Nutritive Status Screening in Patients with Acute Cerebrovascular Accident

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Introduction

Acute cerebrovascular accident is the most relevant medical and social problem. Patients who suffered a stroke are in the malnutrition syndrome risk group.

Materials & Methods

The study group consisted of 63 inpatients in the medical rehabilitation department, Ufa. Nutritional deficiency screening and assessment was performed on admission to hospital using the following scales: Subjective Global Assessment (SGA), Nutritional Risk Screening 2002 (NRS-2002), Malnutrition Universal Screening Tool (MUST) and Short Nutrition Assessment Questionnaire (SNAQ). Elderly patients (over 65) were additionally examined using the Mini Nutritional Assessment (MNA) scale. The growth, weight, BMI and skin-fold thickness (TFT), mid-arm muscle circumference (MAMC) was calculated for the entire group of examined patients. The amount of glucose and cholesterol were measured using laboratory methods

Results

Among all patients, 16% (10 people) had an increased risk of malnutrition on all scales. According to the SNAQ scale, 9.5% (6 people) had moderate malnutrition and 29% (18 people) had severe malnutrition. According to the MUST scale, 32% (20 people) had an average risk of malnutrition and 14% (9 people) had a high risk of malnutrition. On the SGA scale, 27% (17 people) had moderate malnutrition and 5% (3 people) had severe malnutrition. According to the NRS-2002 scale, 54% of patients (25 people) had a high risk of malnutrition. According to the MNA scale, 33% (9 people) had malnutrition, 59% (16 people) had an increased risk of malnutrition.

Average glucose values - 5.34 mmol / L and average cholesterol - 5.03 mmol / L did not change according to the results of the scales. The average MAMC was 25.39 cm, which was significantly lower in malnutrition group. According to the MUST scale, in malnutrition group, the average MAMC was 23.3 cm, and in malnutrition group, it was 25.1. The TFT median value of 10.0 cm and the BMI median of 26.1 kg / m^2 did not have significant differences in malnutrition group.

Conclusion

In the group of patients who suffered cerebrovascular accident, there is moderate to severe nutritional deficiency. Anthropometric and laboratory data do not have predictive value.

Zoledronic acid prevents bone loss in patients suffering from spinal cord injury: A systematic review and meta-analysis

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Introduction

Spinal cord injury (SCI) reaps life-threatening complications and debilitating life-enduring sequelae. A well-established complication of SCI is osteoporosis as SCI patients exhibit a regional form of osteoporosis that is localized to skeletal regions below the level of injury. Therefore, early precautions with anti-osteoporotic agents could be of value. Bisphosphonates has been the mainstay of osteoporosis management for many years, and Zoledronic acid is a new generation bisphosphonate. We aim at appraising recently provided evidence on the medical prevention of bone loss in patients suffering from spinal cord injury using the osteoclast inhibitor Zoledronic Acid.

Materials & Methods

We searched four electronic databases; PubMed, Scopus, Web of Science and Cochrane Central for relevant randomized controlled trials (RCTs). Data were extracted from eligible studies and pooled as risk ratios (RR) or mean difference (MD), using RevMan software. We performed a subgroup analysis to stratify the timing endpoint at which the outcome was assessed.

Results

Pooling data from four RCTs (n = 105 patients) showed that Zoledronic Acid significantly reduced the bone mineral density (BMD) loss compared with placebo, from baseline to 3 months (at femoral neck (MD = 4.18, 95% CI [0.56, 7.80], p = 0.02), and hip (MD = 5.15, 95% CI [2.82, 7.49], p<0.0001)), 6 months (at femoral neck (MD = 10.02, 95% CI [5.90, 14.14], p<0.00001), hip (MD = 10.28, 95% CI [3.32, 17.23], p = 0.004), and spine (MD = 4.79, 95% CI [2.87, 6.71], p<0.00001)), and 12 months (at the femoral neck (MD = 0.14, 95% CI [0.10, 0.18], p<0.00001). Regarding changes in BMD from baseline to 3 months at the spine and to 12 months at the hip, heterogeneity could not be solved as only two studies were included in each analysis.

Conclusion

IV Zoledronic Acid given once yearly is an effective treatment to prevent osteoporosis post-SCI, thus decreasing the risk of fractures in such patients. Therefore, it should be considered of great importance in SCI treatment regimens.

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Inadequate in-hospital screening and insufficient oral anticoagulation on admission in acute ischaemic stroke patients with atrial fibrillation

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Introduction

Atrial fibrillation (AF) is one of the most common types of arrhythmias. The presence of AF is associated with an increased risk of thromboembolic stroke. Therefore, adequate screening and antithrombotic prophylactic treatment is required to reduce the incidence of acute ischaemic stroke (AIS). It is recommended to perform a 24-hour ECG screening (Holter monitoring) for AIS patients after admission to detect subclinical AF. We aimed to assess whether the quality of diagnostic practices and adequate prophylaxis is provided to patients with AIS admitted to Vilnius University Hospital (VUH).

Materials & Methods

A retrospective cohort study was done for four nonconsecutive months between December 2018 and July 2019. AIS patients' medical records were checked for a previous diagnosis of AF, usage of prophylactic antithrombotic treatment prior to admission and in-hospital screening for AF.

Results

237 AIS patients were included. The mean age was 71.3 years and 44.8% were female. 90 (38.0%) patients were diagnosed with AF, 61 (25.7%) of whom had been diagnosed with AF prior arrival and 29 (12.2%) diagnosed after admission. CT Angiography was performed in 159 AIS patients (67.1%). Large vessel occlusions (LVO defined as occlusion in the Internal Carotid, Vertebral, Basilar Arteries, Middle Cerebral Artery (MCA), M1 MCA) were found in 37.1% cases. Patients with AF were at a significantly higher risk for LVO (RR=1.58, CI 1.02 to 2.43) compared to patients without AF. Information about antithrombotic prophylactic treatment prior to admission in patients with previously known AF was available for 60 patients: 18.3% were using non-vitamin K antagonists, 38.3% vitamin K antagonists, 11.7% antiplatelets, and 31.7% with no treatment. All patients received a 12-lead ECG, however, during the hospital stay Holter monitoring was only performed in 3.4% AIS patients without previously known AF.

Conclusion

As expected, patients with AF were at a higher risk for large vessel occlusions. Antithrombotic prophylaxis was inadequate prior to hospital admission and diagnostic tools for subclinical AF were greatly underutilized. The reasons for lack of prophylactic antithrombotic treatment in AF patients need further investigation. Screening for AF in VUH could be significantly improved.

Acupuncture in the treatment of HTLV-I-Associated Myelopathy / Tropical Spastic Paraparesis

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Introduction

HTLV-I-associated myelopathy/tropical spastic paraparesis (HAM/TSP) is a neurological disorder characterized by a myelopathic syndrome of progressive spastic paraparesis. Currently, there is no proven curative treatment for HAM/TSP. In this clinical trial, we investigate the possible effects of acupuncture on the improvement of neurological problems in HAM/TSP disease.

Materials & Methods

Twenty patients with HAM/TSP were studied in this pilot pre- and post-test clinical trial. HAM/TSP was diagnosed based on the WHO diagnostic criteria. Patients underwent 12 sessions of general body acupuncture. International consultation on incontinence questionnaire - short form (ICIQ-SF), Osame's motor disability score (OMDS), and modified Ashworth scale (MAS) were used to evaluate urinary incontinence, global motor disability, and spasticity respectively, before, one month, and three-month after the intervention.). Our trial was registered in the Iranian Registry of Clinical Trials (IRCT) website (www.irct.ir; IRCT code: IRCT2016031327036N1).

Results

Statistical analyses of ICIQ-SF demonstrated a significant reduction of urinary symptoms one month after acupuncture (P=0.023). Friedman's test showed that the mean rank of MAS at the upper extremity joints was significantly decreased from the baseline, three-month after the intervention ($X2$=10.33, P=0.006). In the lower extremity, the mean value of MAS of the soleus muscle was significantly decreased from 2.3 at baseline to 1.9 at three-month after treatment ($X2$=7.75, P=0.021). The reduction of pain (based on VAS scale) was also a significant one and three months after acupuncture (P=0.012 and 0.018, respectively).

Conclusion

This study suggests that body acupuncture can be used as a complementary treatment to improve neurological symptoms of HAM/TSP. Further trials with a longer period of acupuncture and a more extensive follow up period are needed to confirm these potential effects.

Oncology II

Presenters:
Calvo-Alvarez, J.C (Jazmin)
Tong, S. (Shanlin)
Farrokhi, P. (Pegah)
Baltussen, J. C. (Joosje)
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D-α-Tocopherol polyethyle glycol 1000 succinate (TPGS) induces cell death in an in vitro model of myeloid leukemia

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Introduction

Chronic myeloid leukemia (CML) is hematology disorders that showed resistance to conventional treatment. The idea of treating CML with drugs that either directly or indirectly generates oxidative stress (OS) as effective therapeutic strategy has ultimately gained scientific momentum. Therefore, the repositioning of promissory molecules such as TPGS, a vitamin E derivate compound, is relevant. Interestingly, TPGS has been found to induce apoptosis in Jurkat cells (a model of acute lymphoblastic leukemia) through OS. The aim of this investigation was to determine whether TPGS might cause cell death in K562 (a model of CML) by a similar mechanism of OS.

Materials & Methods

K562 cell suspension (1 x 10^6/ well in 1 mL final volume) was exposed to increasing TPGS concentrations (10, 20, 40, 60, 80, 100 µM) for 24 h at 37 ºC. Then after, K562 cells were evaluated in terms of cell death markers and mitochondrial damage by flow cytometry, cell/ nuclei morphology and mitochondrial membrane potential were assessed by fluorescence microscopy, and overexpression of proteins involved in the cell death by Western blot technique.

Results

Treatment of K562 cells with TPGS at 40, 60 and 80 µM concentrations affected the viability, proliferation, nuclear morphology and mitochondrial membrane potential of cells. These effects were observed simultaneously with oxidation of DJ1 protein, an indicator of OS generation. Additionally, it was detected a significant increase in the expression levels of PUMA, and cleaved caspase-3 proteins compared to untreated cells.

Conclusion

We demonstrate that TPGS induce apoptosis in K562 cell via OS. Although further ex vivo and in vivo investigation is required, our data suggest that TPGS might be used in the treatment of CML.

Characterization of Bidirectional Cellular Reprogramming of Tumour Cells and Stromal Cells in Rhabdomyosarcoma(RMS)

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Introduction

Tumour microenvironment plays an important role in controlling tumour growth, metastasis and response to therapy. These aspects are well studied in epithelial tumour biology, but less described in mesenchymal lineage derived soft tissue sarcomas (STS). This lack of understanding the sarcoma biology has limited the field to develop effective therapies. One significantly under researched STS type is rhabdomyosarcoma (RMS), which is the most common STS in children. The preliminary results showed RMS tumour cells have the ability to reprogram naive tumour suppressive stromal cells in order to gain tumour cell properties. It provided a new direction to investigate the role of stromal cells gained with this "pseudo-tumour like" phenotype in contribution to the development of RMS. This study focuses on how paediatric RMS regulate the behaviour of its adjacent stromal cells as well as how the sarcoma associated stromal cells affect the behaviour of cancer cells.

Materials & Methods

We aimed to investigate the crosstalk between RMS and stromal cells to understand the mechanisms of potential therapeutic relevance, including the use of a combination of indirect co-culture system of RMS cells with RMS associated stromal cells. Other methods will include the use of immunotaining to identify candidate biomarkers in patient material and testing potential drug candidates targeting RMS associated stromal cells with"pseudo-tumour like" phenotype.

Results

The indirect co-culture system had shown naive BJ fibroblasts were activated by RD tumour cells suggested by a higher proliferation in BJ fibroblast. And RD tumour cells became more migrative after exposing to activated BJ fibroblast. CTGF gene is down regulated by tumour suppressive stromal cells in RMS. We identified CTGF induced a higher proliferation in tumour cells, suggesting its oncogenic contribution to RMS development. PDGFRa blockage showed inhibition in the proliferation of co-cultured RMS associated stromal cells and mono-cultured RUCH2 tumour cells and FUCH fibroblasts, suggesting its therapeutic potential in blocking paracrine fibroblast activation and autocrine activation in both sarcoma associated fibroblast and tumour proliferation.

Conclusion

In summary, the study demonstrated the "pseudo-tumour like" response in activated sarcoma associated fibroblast might play a significant role in promoting tumour growth and metastasis.

Comparative study of Survival and Toxicity of the FLOT, DCF, FOLFOX and ECF Perioparative Chemotherapy Regimens for Resectable Gastric Cancer Patients

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Introduction

The best chemotherapy regimen for managing gastric cancer is still a matter of debate. The aim of this study was to evaluate the efficacy and toxicity of common regimen used as perioperative chemotherapy including ECF, DCF, FOLFOX, and FLOT to identify the most effective chemotherapy regimen with less toxicity.

Materials & Methods

This retrospective cohort study was based on 152 eligible gastric cancer patients recruited in a tertiary oncology hospital in Isfahan, Iran (2014-2019). All resectable gastric cancer patients who had received one of the four chemotherapy regimens including ECF, DCF, FOLFOX or FLOT and followed for at least one year (up to five years) were included. The primary endpoint of this study was Overall Survival (OS), Progression-Free Survival (PFS), Overall Response Rate (ORR). We also considered toxicity according to CTCAE (v.4.0) criteria as a secondary endpoint. Cox-regression was used to estimate OS and PFS time, controlling for relevant covariates.

Results

Of included patients, 32(21%), 57(37.5%), 37(24.3%), 32(21%) had received ECF, DCF, FOLFOX and FLOT, respectively. Overall survival was enhanced in the FLOT regimen in comparison with other groups (hazard ratio [HR] = 0.052). Median OS was 28, 26 and 23 months for DCF, FOLOFX, and ECF regimens, respectively. On the other hand, median PFS of 25, 17, 15 and 14 months was observed for FLOT, DCF, FOLFOX, and ECF regimens, respectively (Log-rank = 0.021). FLOT regimen showed 84.4% ORR which was remarkably higher than other groups (p-value <0.01). The number of patients with related serious adverse events including grade III-IV neutropenia was significantly (p-value=0.03) higher in the DCF regimen (51%) in comparison to other groups.

Conclusion

FLOT regimen seemed to ascertain significant improvement in patients' OS and PFS in comparison with ECF, DCF, and FOLFOX regimens. At the same time, FLOT regimen toxicity seems to be manageable and well-tolerated in the patients. Our findings suggest that FLOT regiment could be considered as the optimal option for managing gastric cancer patients.

The CARG tool can predict chemotherapy-related toxicity in Dutch older patients with cancer: A validation study

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Introduction

Older adults are vulnerable to chemotherapy-related toxicity. However, since older adults are underrepresented in cancer research, limited data to guide oncology practice is available. In order to identify older adults at risk for severe chemotherapy toxicity, the Cancer and Aging Research Group (CARG) developed a prediction tool for toxicity that uses various geriatric variables as well as tumor, patient and treatment characteristics. This tool was validated in the distinct USA oncology practice (Area under the Receiver Operating Characteristic curve (AU-ROC) 0.65, 95% CI 0.58 to 0.71). We aimed to validate the CARG tool in Dutch older patients treated with chemotherapy.

Materials & Methods

In this prospective cohort study, patients ≥ 70 years with cancer and scheduled to receive chemotherapy in the LUMC or Hagaziekenhuis, underwent pretreatment geriatric frailty screening plus five additional questions that are incorporated in the CARG tool. Grade 3-5 chemotherapy toxicity according to NCI Common Terminology Criteria for Adverse Events (CTCAE) V5.0 was observed during the first two months of treatment. Discriminatory accuracy of the tool was determined by calculating the AU-ROC. Calibration was assessed by composing calibration plots of predicted and observed toxicity. We stratified patients by concurrent radiotherapy treatment or not, to compare performance of the CARG tool in both groups.

Results

We included 144 patients ≥70 years. Median age was 75 years (range 70-87). The majority (57%) of patients was treated with concurrent radiotherapy. Severe chemotherapy-related toxicity was observed in 54% of all patients. Stratified by radiation therapy, the AU-ROC for patients receiving chemotherapy only was better than the AU-ROC for patients receiving combined chemoradiation treatment (AU-ROC 0.64, 95% CI 0.51 ; 0.78 and AU-ROC 0.53, 95% CI 0.40; 0.66 respectively). Observed toxicity in risk groups for patients treated with chemotherapy only non-significantly increased (20%, 46% and 67% respectively, P=.057).

Conclusion

The CARG tool was predictive for severe chemotherapy-related toxicity in Dutch older adults treated with chemotherapy only. The non-significant increase in toxicity might be related to our small sample size, therefore we will continue to include patients. In contrast, we found a poor performance of the tool in patients receiving chemoradiation.

Evaluation the status of p53-ki67 in epithelial ovarian tumors and its relation with prognosis in patients referred to the Shahid Sadoughi hospital of Yazd in 2008-2013

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Introduction

Ovarian cancers are the fifth most common cancer in the united states. These tumors are also the fifth cause of cancer deaths in women. Fifty percent of the malignant human cancers appear with a mutation in p53, which Is the most common tumor suppressor gene. The ki67 gene also indicates cell proliferation. Considering the epithelial ovarian tumors of patients of different ages and the importance of prognosis in this study, we examined the frequency of p53 and ki67 markers by IHC in benign and malignant ovarian epithelial tumors.

Materials & Methods

in this study, 80 samples of ovary serous and mucinous tumors and 10 ovarian borderline tumors were extracted from the pathology 8264080 archives of Shahid Sadouhgi hospital in Yazd, Iran from 1387-1392. IHC tests were performed to determine the prevalence of p53 and ki67 in these tumors. The patient's demographic information included age, type of tumor, duration of disease and the rate of relapse of mortality that was obtained by telephone and all the information extracted analyzed by spss version 22. P-value less than 0.05 was considered statistically significant.

Results

in this study, the mean age of patients was 44.9 ± 16.91 with a range of 15-79 years. The results showed that there was a significant relationship between the type of tumor with both p53 an ki67 markers ($p<0.05$). However, there was no significant relationship between the tumor grade and these two markers. In undifferentiated cases, the color intensity of ki67 marker was significantly positive, which was not significantly correlated with p53. The mean survival rate in this study was 40.67 months, with a significant association with age, ki67, p53 markers and tumor type($p<0.05$).

Conclusion

the results of this study showed that there is a significant relationship between the type of tumor with two markers p53 and ki67 is significant. Therefore, p53 and ki67 markers are a predictor of overall survival, tumor type, disease grade and prognosis in patients

Circular RNA ZNF800 drives stemness in colorectal cancer stem cell population: A novel cancer epigenetic biomarker

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Introduction

The challenges surrounding colorectal cancer (CRC) treatment remain focused on the existence of chemoresistant population known as cancer stem cells (CSCs). Eradication of CSCs, where the conventional chemotherapy has failed, has been postulated as an effective treatment strategy. On the other hand, recent evidence has shown that circular RNAs (circRNAs), a novel epigenetic member of the long non-coding RNA family, could control major biological processes, including chemoresistance and tumorigenesis. Owing to high stability and long half-life coupled with existence in blood and other bodily fluid, circRNAs have been hypothesized to be promising candidates of molecular markers in disease progression. However, the involvement of circRNAs in CRC-CSCs remains unexplored. This study attempted to explore the role of circRNA in maintenance of CR-CSCs.

Materials & Methods

We generated a prolonged 3D anchorage-independent spheroidal culture model to enrich CR-CSC from CRC cell lines, HCT-15 and WiDr. The spheroidal cells were characterized for stemness properties and circRNA expression profile was established by RNA-sequencing.

Results

The 3D culture model yielded a population of cancer cells with higher stemness properties, evident by the up-regulated CSC markers and pluripotency transcriptional factors with enhanced multi-lineage differentiation potential, resembling CSCs-like population. Genome-wide circRNA sequencing of the 3D cultured cells revealed 1,503 and 1,076 circRNAs were up-regulated and down-regulated, respectively, from a total of 62,321. Bioinformatics analysis uncovered a core epigenetic network of circRNA-microRNA-mRNA, where circZNF800 and circDCBLD2 drives stemness properties by sponging microRNAs targeting WNT5A, SMAD2, IL6ST, FZD3, ACVR1C and SKIL, which are collectively involved in pluripotency regulation. Further analysis showed that circZNF800 was significantly up-regulated in passage-dependent manner in the 3D spheroidal culture, but not circDCBLD2. Chemoresistant CRC cells showed an increased expression of circZNF800 when treated with 5-flourouracil. To investigate the potential function of circZNF800 as a blood biomarker for detection of chemoresistant cells, blood samples of CR C patients were subjected to digital-droplet PCR for detection of circZNF800. Compared to the healthy group, CRC patients exhibited higher levels of circZNF800 in the blood.

Conclusion

Collectively, we have identified a core epigenetic network regulating stemness properties in CR-CSC population with a potent candidate, circZNF800 as a biomarker for CSC and chemoresistance detection.

Inhibiting mitochondrial ribosomal biogenesis as a novel approach of targeting cancer cells

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Introduction

Mitochondria-encoded proteins are vital for the assembly and function of OXPHOS complexes, which in turn are vital for cell proliferation. Cancerous, rapidly dividing cells, are in special need of rapid mitochondrial biogenesis for energy and metabolite supply. NSUN4 and TFB1M are mitochondrial rRNA methyltransferases essential for the mitoribosomal biogenesis. This project focuses on characterisation and optimization of three drug leads, referred to as T21, T82 and N1, for targeting NSUN4 and TFB1M in an effort to intercept the mitoribosomal assembly and to block cancer cell proliferation.

Materials & Methods

Colon carcinoma (RKO) cell lines were treated in order to determine the compounds' LD50 and their effect on colony formation and cell viability. Linear sucrose gradient assay was used to establish the compounds' effect on mitoribosomal assembly, and biochemical analysis of cell content was performed to examine mitochondrial translation. Screening of new leads was done by comparison of cell growth on glucose- versus galactose-based media, and similar methods as described were used to characterise analogue lead compounds.

Results

First, we determined the compounds' LD50 at 10 µM for T21 and T82 and 25 µM for N1, and showed a concentration-dependent decrease in cell proliferation both in planar and 3D cultures for all three compounds. Inhibition of mitochondrial translation was established by showing a selective concentration-dependent decrease of the mitochondria-encoded protein MTCO2. T21- and T82-treated cells showed a significant decrease in mitoribosomal monosome assembly, whilst N1 treatment was not effective at tested concentrations. Screening of 80 new analogues for their selective inhibition of mitochondrial translation and cell growth suppression in galactose-based medium revealed five promising analogues. Following further biochemical characterisation, two of them demonstrated concentration-dependent inhibition of mitochondrial protein synthesis.

Conclusion

This project is a part of a drug discovery project, targeting the mitochondrial methyltransferases TFB1M and NSUN4. Three established leads were characterised and two new leads were selected for further analysis. Based on the acquired knowledge, the structure-activity relationship (SAR) of the compounds will be characterised, aiming to achieve better potency and specificity.

Development of a promising cellular model to study human brain metastasis

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Introduction

Approximately 10-30% of patients with metastatic breast cancer develop brain metastases (BMs).

Although efforts have been made to characterize metastasis-initiating cells (MICs), known to be able to disseminate and colonize the brain relying on migratory/invasive properties and on stem-like behavior, still the metastatization process remains unclear. Based on this, our purpose was to isolate MIC subpopulation to shed light on the molecular mechanisms regulating their dissemination and tumorigenic properties.

Materials & Methods

We isolated MIC subpopulations from a patient affected by breast cancer BMs, and we cultured them in selective medium supplemented with growth factors. We assessed their clonogenic capability performing methylcellulose assay in vitro and their tumorigenic potential through in vivo orthotopic injections in nude mice at decreasing concentrations, determining the MICs frequency by ELDA algorithm. Intracardiac injections were also performed and the derived xenografts were stained with haematoxylin/eosin to analyze their morphological architecture. RT-qPCR and time-lapse microscopy were exploited for the molecular characterization and migration analysis, respectively.

Results

We found MICs to be endowed with great self-renewal ability in vitro and intracerebral transplantation resulted in high MICs frequency. Intracardiac injections demonstrated the capability of these cells to return to the brain and generated metastases in the bone recapitulating the morphology of the original patient tumor and displaying a biomarker expression similar to the original BM. In conclusion, we demonstrated the presence of a stem-like population in BMs secondary to breast cancer, able to trigger tumor growth and to be serially transplanted in mice recapitulating the original patient tumor.

Preliminary results from migration assays highlighted the presence of subclones more prone to migrate than others within the MIC population. Furthermore, ongoing experiments including RNA-sequencing will define specific molecular signatures associated to the brain/bone recurrence.

Conclusion

We managed to obtain for the first time a promising cellular model for human BMs. This, together with our preliminary results on their migratory capabilities and the global transcriptomic profiling, may pave the way to novel therapeutic strategies targeting the cellular compartment responsible for the metastasis progression.

Opthalmology
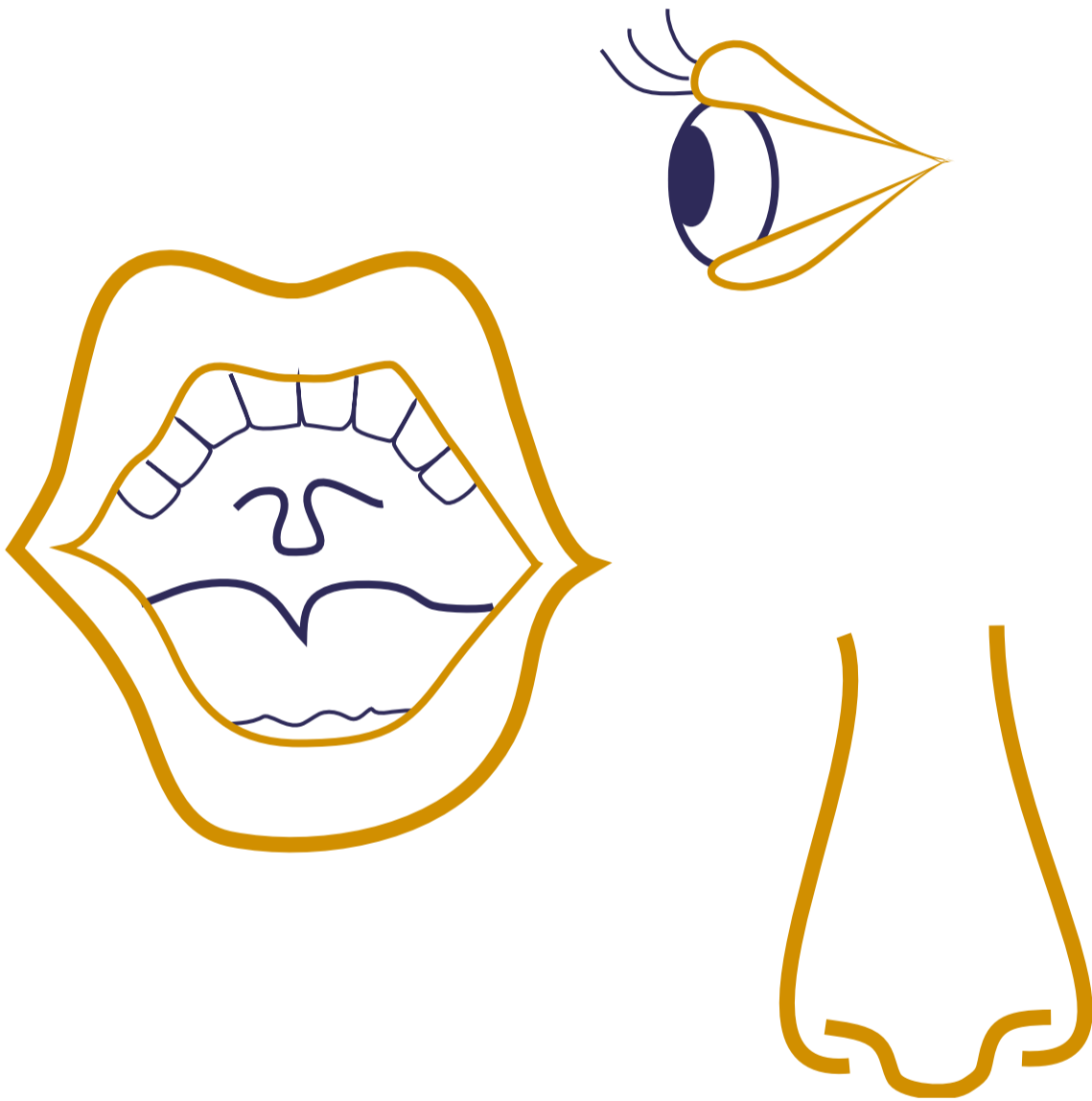
Presenters:
Zhang, J (Jinyu)
Shkarupa, A. (Anastasiia)
Bian, B (Bai Shi Jiao)
Susanna, FNS (Fernanda)
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Different effect of optical media opacities on vessel density measured by different optical coherence tomography angiography

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Introduction

Optical coherence tomography angiography (OCTA) is a vital imaging innovation in ophthalmology, which demonstrates the high-resolution retinal microvasculature noninvasively, safely and quickly. It has been shown that opacity of optical media can reduce retinal vessel density (VD) measured by some models of OCTA. However, different models of OCTA used different algorithms and may have different effect. This study is aimed to investigate the impact of optical media opacities on quantitative measurement of Cirrus 5000 and DRI Triton OCTA.

Materials & Methods

Cirrus 5000 and DRI Triton OCTA were used to image retinal microvasculature from 22 right eyes at the macula using 3mm×3mm scanning protocol. The VD of superficial capillary plexus was measured using the built-in software. Optical opacities were simulated with neutral-density filters (optical density (OD)λ=840nm ranges 0.10 - 0.48 in Cirrus; ODλ=1050nm ranges 0.15 - 0.51 in DRI) placed in front of each eye, signal strength (SS) or signal strength intensity (SSI), and parafoveal VD were then recorded and measured. The correlation between the parameters and OD was analyzed.

Results

With the increase of OD, SS and SSI decreased (rs= -0.576 and -0.922 respectively, both p 0.001), parafoveal VD decreased in Cirrus 5000 (rs= -0.539, p 0.001). Parafoveal VD increased as SS increased in Cirrus 5000 (rs= 0.471, p 0.001). There was no correlation between parafoveal VD and OD or SSI in DRI Triton (rs= -0.143, p= 0.137 and rs= -0.009, p= 0.924 respectively).

Conclusion

The effect of optical media opacity on quantitative measurement of VD is different for Cirrus 5000 and DRI Triton OCTA, depending on the algorithm of OCTA used. Caution must be taken when interpreting OCTA VD measurement in patients with optical media opacities.

The association of TGF-β1 (rs1800469) polymorphisms with high myopia in Ukranian population

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Introduction

Disorganization in the processes of scleral matrix remodeling can cause increased eye growth, leading to myopia and increased risk of ophthalmologic pathologic complications. TGF-β is a key intrascleral mediator of extracellular matrix (ECM) remodeling. TGF-β1 stimulates the production of ECM proteins and reduces the secretion of ECM degradation enzymes, stimulates the production of proteins that inhibit their activity. Association of SNP TGF-β1 gene with the risk of myopia development is controversial and non studied in European populations. We aimed study was to investigate the allele frequency and genotypes distribution SNP rs1800469 TGF-β1 among the Ukrainian pediatric population with different degrees of myopia.

Materials & Methods

Genotyping of TGF-β1 rs1800469 polymorphism was performed in 105 children with myopia (–0.50D –14.88D) aged 4–18 years (11.3±3.4) and in 107 children of the control group with emmetropy (–0.25D–+0.37D) aged 4–13 years (7.7±1.3), by PCR-RT method.

Results

Polymorphism rs1800469 TGF-β1 not association with common myopia. Compared to controls, significant differences in allele and genotype frequencies for the SNP under investigation were found only in the high myopia group. The presence of the C allele of TGF-β1 (rs1800469) was found to increase the risk for developing high myopia (OR = 2.44, 95% CI, 1.17–5.08; p = 0.02). The presence of a variant T allele was found to have an additive protective effect against developing high myopia in the CT genotype carriers (OR = 0.85, 95% CI, 0.34–2.16; p = 0.02) and TT genotype carriers (OR = 0.16; 95% CI, 0.02–1.29; p = 0.02).

Conclusion

To our best knowledge, this study is the first to demonstrate that the CC genotype of rs1800469 TGF-β1 is associated with the risk of the development of high myopia in a European population.

Exosomes derived from neural progenitor cells preserve photoreceptors during retinal degeneration by inactivating microglia

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Introduction

Retinal degeneration (RD), characterized by progressive degeneration of photoreceptors, is one of the most common causes of visual impairment and blindness. Transplantation of neural stem/progenitor cells (NPCs), is a promising treatment for RD. Paracrine effect of NPCs is more efficient to rescue the degeneration. NPC derived exosomes (NPC-exos) have been reported to carry functional molecules to mediate neuroprotective effects in Alzheimer's disease (AD) and stroke. However, little is known about its effects on RD.

Materials & Methods

NPCs were harvest from C57BL/6 mice and were isolated via differential centrifugation and sucrose gradient density centrifugation. NPC-exos were transplanted into the subretinal space of RCS rats. Optokinetic response test and scotopic electroretinogram test were performed to determine their treatment outcomes. TUNEL staining of retina and the outer nuclear layer (ONL) thickness analysis were used to estimate the apoptosis of photoreceptor cells. Immunofluorescence staining, confocal scanning and PKH26 labeling were used to estimate the target cell of grafted NPC-exos. In vitro co-culture of BV2 cells and 661W cells were used for further confirmation. The inflammatory responses of BV2 cells were estimate by RT-qPCR and Enzyme-linked immunosorbent assay.

Results

In RCS rats, implantation of NPC-exos delayed photoreceptor degeneration, preserved visual function, prevented thinning of the ONL, and decreased apoptosis of photoreceptors. Mechanistically, mNPC-exos were specifically internalized by retinal microglia and suppressed their activation in vitro and in vivo. Functional inhibition of microglial activation by NPC-exos protects photoreceptors from apoptosis in vitro.

Conclusion

We demonstrated that grafted NPC-exos efficiently suppress the activation of retinal microglia to mediate protection against apoptosis of photoreceptors by NPC in RD model. This study indicates that transplantation of NPC-exos may potentially be an alternative therapeutic strategy for treating RD.

Awareness of diabetes' ophthalmologic complications among patients treated in a students' academic organization

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Introduction

Diabetes has become a global epidemic. Diabetic retinopathy (DR) is a serious cause of irreversible blindness and is the most common complication of diabetes, early detection and treatment can prevent irreversible blindness. We aim to evaluate the current knowledge and awareness of diabetes and DR among patients of a students' academic organization.

Materials & Methods

We conducted a study with patients who attended a DR screening program for patients from the Diabetic League, a students' academic organization that provides clinical management for patients with diabetes in a tertiary center. Two self-administered questionnaires validated in previous studies from other groups were applied. The questionnaires contained multiple-choice questions on knowledge related to diabetes and ophthalmology complications. The questionnaires included questions to assess awareness about diabetic retinopathy, sources of knowledge about the disease, and patients' knowledge and compliance with available treatments and routine eye examinations.

Results

A total of 60 patients completed the questionnaire, 33 women and 27 men. Mean age was 61.5 (± 15.07). 43 patients (78.18%) had diabetes for more than 10 years. Of the study population 100% were aware that diabetes could affect the eye and mentioned especially retina alterations (71.67%), glaucoma (35%) and cataract (33.33%) and 93.10% thought these alterations had treatment. Most patients associated the acquisition of these information to physicians (66.67%) and 56.67% of patients had undergone ophthalmology screening in one year or less. 41.03% of patients presented some degree of DR and of these only one had proliferative DR. Presence of disease wasn't associated with higher level of awareness (P=0.86).

Conclusion

Awareness of the nature and consequences of diabetic retinopathy in our study group was satisfactory. A relatively high percentage of patients also showed an adequate screening interval period; however, this was still below optimal. This corroborates that patients treated in students' academic organizations receive an attentive care which translates to a better knowledge degree.

Effect of combination of tDCS and visual occlusion therapy on vision in adult patients with amblyopia

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Introduction

Ocular occlusion is the gold standard treatment in amblyopia and depends on the high neuroplasticity levels found in children under 14 years, leaving little to do in adult patients with later diagnoses and thus lower neuroplasticity. Transcranial Direct Current Stimulation therapy (tDCS) is a fairly new technique used in other neurological diseases to increase neuroplasticity, by changing the resting potential of neurons. We propose that the combined treatment of ocular occlusion with tDCS should increase neuroplasticity levels, leading to an increase in visual acuity (VA), contrast sensitivity, and depth perception in adults over 18.

Materials & Methods

A double blind, randomized and controlled clinical trial is proposed. The intervention consists of the application of ocular occlusion therapy and bilateral tDCS (2mA, 20min) on the scalp of the primary visual cortex. Subjects (Proposed N=40) are randomly assigned to an active or "sham" stimulation group (only 30s of stimulation). During the 20min, subjects have to read using only their amblyopic eye. Assessment before and after the stimulation consists of measurements of VA (LogMar-Test), contrast sensitivity (Pelli-Robson-Test), depth perception (Titmus-Test), and visual evoked potentials (Checkerboard-Reversal).

Results

At the time of writing, only 10 subjects have been intervened and measured, 5 underwent bilateral stimulation, and 5 underwent sham-stimulation. Increases in VA were 0.14±0.02 for the active-stimulation group, and 0.04±0.02 for the sham-stimulation group (Shapiro-Wilks test p=0.07). Increases in contrast sensitivity were 2%±1.2% for the active-stimulation group, and 3%±1.2% for the sham-stimulation group (Shapiro-Wilks test p=0.99). Increases in depth perception were 84"±55.6" for the active-stimulation group, and 40"±24.5" (Shapiro-Wilks test p=0.84). Visual evoked potentials results are still being processed.

Conclusion

The number of subjects at the time is too low to draw any conclusions, but these preliminary results show a trend of increase in VA in the active-stimulation group compared to the sham-stimulation. No trends were clearly observed in the other secondary results. It is important to note that only one fourth of the proposed N was intervened and measured.

Orthopeadics
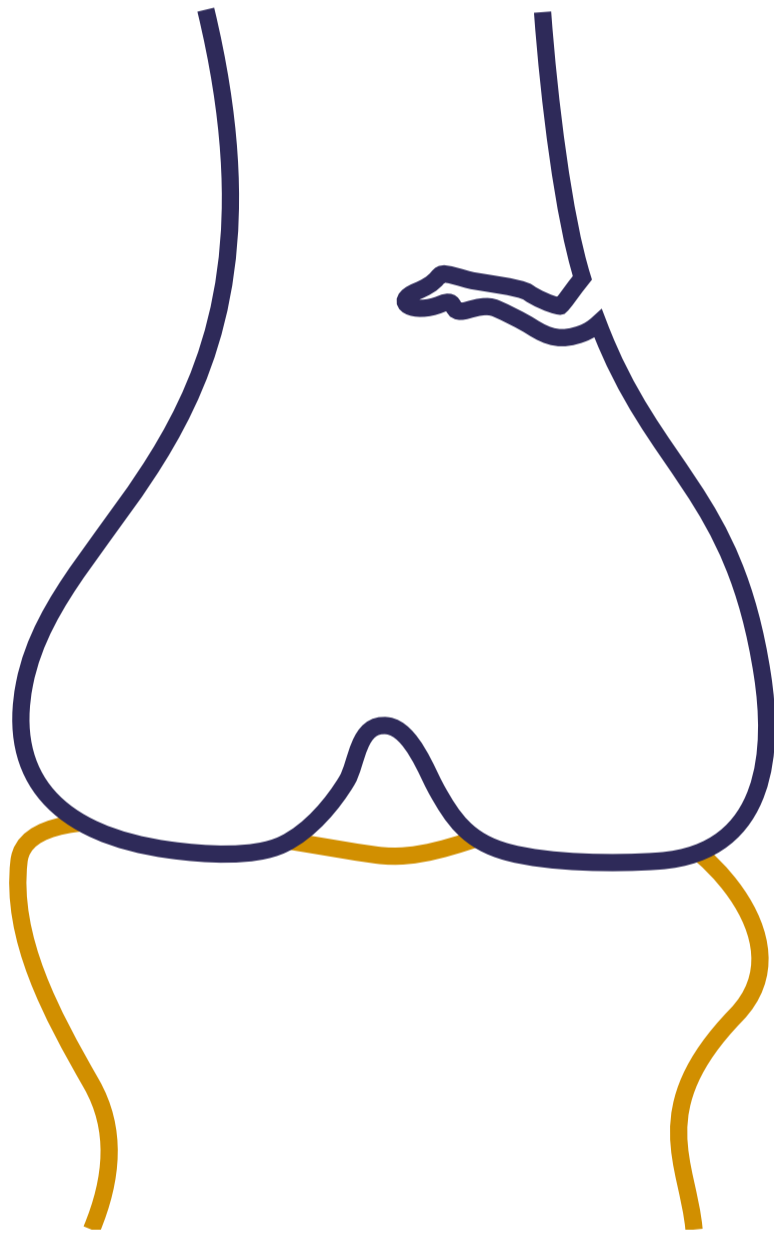
Presenters:
Wales, E.H.E (Emily)
Beraldo, R.A.B. (Rodrigo)
Gunn, F (Finn)
Arias Pérez, R.D. (Rubén)
Jhaveri, S.S. (Sharan)
Majd, A.M. (Alireza)
Filiak, Y. (Yuliia)

Clinical and radiological outcomes of sacroiliac stabilisation using Hydroxyapatite coated fully threaded screws

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Introduction

The clinical and radiological outcomes of sacroiliac screw fixation as a treatment of sacroiliac joint pain using hydroxyapatite (HA) coated fully threaded screws. The study was a single surgeon series to evaluate how successful sacro-Iliac joint fusion (SIJ) using HA coated fully threaded screws is in patients with a diagnosis of SIJ instability.

Materials & Methods

Commencing January 2016, a total number of 75 patients underwent SIJ fusion by a single surgeon at Llandough University Hospital between the ages of 33-86. They underwent minimally invasive SIJ fusion and stabilisation using HA coated fully threaded screws. Patients were reviewed at the start of the study and with a 12 month follow up. Pre- and post-operative outcomes in patients were evaluated utilising validated questionnaries; health-related quality-of-life scales EuroQol-5D (EQ-5D), Short Form (SF)-36, Majeed Pelvic Scores, Oswetry Disability Index and EQ-5D.

Results

35 patients (7 male and 28 female) out of the 75 patients completed follow-up. The mean physical health SF-36 score was 24.44 and 28.85 for preoperative and postoperative respectively (not Sig). The mean mental health SF-36 score was 37.83 and 42.03 preoperative and postoperative respectively ($p<0.05$). The mean preoperative and postoperative Majeed score was 23.14 and 18.17 respectively ($p<0.01$). The mean preoperative and postoperative Oswestry score was 29.83 and 24.29 respectively ($p<0.01$). The mean EQ-5D score preoperative and postoperative was 11.26 and 9.71 respectively (not Sig).

Conclusion

In our cohort of patients, we had mixed results for our validates questionnaires. We believe more work is required to improve patient selection.

Treatment of irreparable rotator cuff tears: superior capsular reconstruction with fascia lata allograft

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Introduction

Rotator cuff tear is the most common shoulder injury. However, an ideal procedure to treat irreparable tears does not exist. Superior capsular reconstruction (SCR) is one of the procedures for irreparable supraspinatus tears. The objective of this study was to evaluate the efficacy and safety of SCR using a fascia lata allograft

Materials & Methods

A prospective case series of 15 patients with irreparable supraspinatus tear who underwent SCR fascia lata allograft. The American Shoulder and Elbow Surgeons (ASES) scale at 12 months after surgery was the primary outcome. The University of California Los Angeles (UCLA), Constant-Murley, and Single Assessment Numeric Evaluation (SANE) scales, in addition to the range of motion, were secondary outcomes. Radiological parameters were also evaluated by simple radiographs and magnetic resonance imaging (MRI)

Results

Fifteen patients completed 12 months of postoperative follow-up. The ASES score increased from 34.0 to 73.0 (p=0.005). The UCLA, Constant-Murley, and SANE scales also showed statistically significant differences (p=0.001, p=0.005, and p=0.046). In the range of motion evaluation, there was improvement in elevation and external rotation (95º to 140º, p=0.003 / 30º to 60º, p=0.007). Six patients (40%) had complete graft healing. The clinical scales were significantly higher in the patients who presented graft healing

Conclusion

Superior capsular reconstruction using a fascia lata allograft is a safe and effective procedure.

The Attune™ Knee Prosthesis: A 3-Year Review

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Introduction

Without treatment, knee osteoarthritis can lead to major disability and an increased risk of cardiovascular disease, metabolic syndrome and depression. 96% of total knee arthroplasties are carried out for osteoarthritis. In 2013, the Attune™ knee implant system was released as an updated prosthesis design, to supersede the previous PFC Sigma™. Limited data exists regarding the early-to-midterm survival, functional and clinical benefits over other models of knee prosthesis. The primary aim of this study was to compare functional outcome between the Attune™ and the PFC Sigma™, primarily using preoperative and 3-year American Knee Society Score and Oxford Knee Score.

Materials & Methods

A prospective cohort study of 110 patients, selected by propensity score matching was conducted. All patients underwent a cemented, fixed bearing, cruciate retaining total knee arthroscopy by one of two senior consultant surgeons in the same district general hospital. Data reporting on patient demographics, perioperative care, clinical outcomes and functional scores were investigated by Pearson chi-squared tests, non-parametric tests, independent student's t-test, Cox- regression and Kaplan-Meier analyses.

Results

Median and mean increases in American Knee Society Score for the Attune™ and Sigma™ knees were 53 (26.9) and 43.6 ($\pm$ 15.4) respectively (p =0.307). Mean increase in Oxford Knee Scores were 21.8 ($\pm$ 8.8) and 18.7 ($\pm$ 8.8) for the Attune™ and Sigma™ respectively (p= 0.27, 95% CI -2.56 to 8.7). Mean and median increased range of movement was 11.8° ($\pm$ 28) and 1.7° ($\pm$ 13.5) for the Attune™ and Sigma™ respectively (p= 0.05, 95% CI -0.015 to 20.2).

Conclusion

The Attune™ knee system displays a significantly improved range of motion and a trend towards higher knee scores over a conventional implant at 3 years post-surgery, which may support use in future clinical practice. However, future studies, such as a high quality RCT, are needed to verify these findings.

Satisfactory results using a novel arthroscopic technique for fixation of tibial spine avulsion fractures

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Introduction

Displaced tibial spine avulsion fractures cause instability of the knee, due to the secondary lesion of the anterior cruciate ligament. the spine avulsion fractures are infrequent lesions and there are several surgical techniques described for its fixation, although none have demonstrated superiority. However, performing the fixation of these fractures arthroscopically with double-row suture anchor technique could guarantee a stable fixation, while avoiding the need for a second surgery to remove the intra-articular osteosynthesis material. Therefore, this research aims to present a novel arthroscopic fixation technique using double-row suture anchor for tibial spine avulsion and evaluate the clinical results.

Materials & Methods

Retrospective case series. Patients with tibial spine avulsion fracture were included, who presented type III and IV fractures, according to the Meyers and McKeever classification, and received this new surgical treatment from 2013 to 2018 in two specialized hospitals in Medellín city (Colombia). To determine the knee function, Lysholm and objective and subjective International Knee Documentation Committee (IKDC) scores were performed, before and after surgery. The data were analyzed in GraphPad software version 7.02.

Results

24 patients were followed with a mean age of 31 years; 12 patients were female. The time between trauma and surgical fixation was an average of 16 days and the follow-up period of 22 months. When comparing the initial state of the patients and the postoperative period, statistically differences were found in all the scores analyzed (p<0.005). Likewise, there were no complications and no reinterventions were performed during the follow-up period and all patients were satisfied with the outcomes of the procedure.

Conclusion

The fixation of tibial spine avulsion fractures using a double-row suture anchor technique, provides an improvement in the function, pain and activity level of the patients and it is an anatomical and minimal access technique that leads to a satisfactory clinical evolution of the patients.

Surgical Outcomes In Patients Operated For Cervical Myelopathy Using Modified Japanese Orthopaedic Association Cervical Myelopathy Evaluation Questionnaire

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Introduction

Cervical Spondylotic Myelopathy (CSM) is a leading cause of morbidity. Patients present with spasticity, gait imbalance and loss of fine motor function. Most patients present early; however, few manage with disability for years; and present late. This study aims to assess the surgical outcomes of patients with cervical myelopathy, using the modified Japanese Orthopaedic Association Cervical Myelopathy Evaluation Questionnaire (JOACMEQ).

Materials & Methods

52 consecutive patients, undergoing surgery for cervical myelopathy from 2008 to 2013 were included. 46 patients were ambulatory, while 6 were non-ambulatory at the outset. 23 patients underwent anterior surgery, and 29 patients underwent posterior surgery. Frankel, Nurick grades, Neck Disability Index (NDI) and Modified JOACMEQ scores were recorded at time of admission, 6, 12, 24, 52 weeks, and then annually. Outcomes at final follow-up were included for statistical analysis.

Results

34(81%) patients improved, 4(9.5%) patients remained static and 4(9.5%) patients worsened. Nurick grades improved from 3.52 to 1.64. Mean NDI scores improved from 42.28 to 20.28. Analysing the JOACMEQ scores, Cervical spine function improved/unchanged in 34(80.9%) of 42 patients, Upper extremity (UE) function improved in 33(78.6%) patients, while Lower extremity (LE) function improved in 32(76.2%) patients. Bladder function improved/static in 40(95.2%). Quality of life improved in 37(88.1%) patients. LE improved more than UE, in the younger (<45 years) group, and those with sub-axial myelopathy. Pre-operative symptoms greater than twelve months had a negative impact on the outcome. Pre-operative neurology, approach & instrumentation did not impact outcomes. 5(9.8%) patients developed major neurological deficit, 7(13.7%) patients had laryngeal palsy/Horner's syndrome.

Conclusion

Surgical results of CSM are highly satisfactory, even in late cases. LE improved more than UE in sub-axial cases and younger individuals. Surgical intervention within twelve months of symptoms affects outcome positively.

A comparison between relationship of lower limb deformities with two types of idiopathic and congenital scoliosis in scoliotic patients undergoing deformity correction surgery in Sina Hospital in the years 2011-19

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Introduction

Scoliosis is defined as the lateral bending of the spinal column from its original place. Based on its etiology, scoliosis can be categorized into congenital and idiopathic scoliosis, as of former being due to vertebral malformation and segmentation problems while the latter is when no pathology can be attributed to vertebrae. It has been shown that scoliosis has concordance with other organ systems malformations, i.e., urologic, and orthopedic disorders. Many underlying spinal cord anomalies are present in the scoliotic cords while they might be asymptomatic; among which Tethered Cord Syndrome (TCS), a group of tethering conditions can be named. These occult pathologies interfere with the reconstructive realignment surgeries. There is a body of literature claiming scoliosis, and probably underlying tethered cord syndrome, has an association with lower limb orthopedic malformations.

Materials & Methods

We recruited patients suffering from scoliosis who attended Sina Hospital Neurosurgery Clinics between 2011 and 2019. Based on medical history, physical examinations and radiographic findings, they allocated to idiopathic or congenital groups. With the help of MRI, each group was then divided based on the presence of TCS. The prevalence of different lower limb malformations between the groups was checked if they are statistically different. Also, to put more light on the TCS role in this relation, we analyzed the prevalence of deformities between TCS positive and negative subgroups within two forms of the disease.

Results

In total, 119 subjects met the inclusion criteria consisting of 79 subjects with idiopathic, and 40 patients with congenital scoliosis. The prevalence of Clubfoot appeared to be significantly higher ($P<0.019$) in congenital scoliosis than idiopathic form. Also, Genu Valgum found to be more prevalent ($P<0.011$) in TCS positive subgroup among idiopathic forms. No statistical significance was observed for the other deformities investigated (Limb length asymmetry, Genu Varus, Claw toe).

Conclusion

The presenting data traced a positive relationship between Clubfoot and congenital scoliosis. Also, we report a significant correlation between Genu Valgum and TCS in idiopathic scoliosis. This result suggests conducting more studies on possible etiologies between named morbidities to produce preventing strategies to improve scoliotic patient's quality of life.

Intertrochanteric fractures: a retrospective analysis of the FRAX tool and radiographic measurements in patients with osteoporosis

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Introduction

Intertrochanteric fracture match with one of the most common hip fractures. Specifically for the elderly with osteoporotic bones, these fractures along with other hip fractures are associated with high mortality. 280,000 fractures occur annually. As the osteoporosis became a worldwide disease, it's no longer could be neglect in operation prognosis. The FRAX tool was designed to evaluate fracture risk in osteoporosis patients. The tendency shows an increased fracture rate in the future. Assuming that this study was made to determine the relationship Radiographic measurements indices in patients with complications after surgery.

Materials & Methods

A retrospective analysis of 193 patients (164-female and 29-male) with an average age of 76.2 ± 10.3 years and intertrochanteric fractures (A1-A3 by AO/OTA) of the femur was performed. Osteosynthesis by nail PFNA from 2009 to 2019. Exclusion criteria considered patients with: 1) pathological fractures; 2) polyfocal fractures; 3) coxarthrosis 3-4 stage; 4) pronounced impairment of cognitive functions. Radiographic measurements: Tip-Apex Distance (TAD), Parker's Ratio (PR) Software: universal pixel-based measurement, Microsoft Excel 2010, FRAX tool

Results

Patients' treatment analysis shown complications in 9 patients (76.2 ± 10.3 years old). 3 patients (1.5%) had a "cut-out", and 6 patients (3.1%) - anti-rotation screw migration. The average TAD score was - $18,5\pm6,0$ among all 9 patients with complications. TAD score of 2 patients with the "cut-out" effect was 18.4 mm and 17.3 mm, which is 6.1 mm and 5 mm higher than in the patients without complications; 1 patient, TAD -12.5 mm (patients without complications -12.3). PR in the anteroposterior line (after surgery-46.1 ± 6.0; after 6 months-48.2 ± 7.8) and axial lateral planes (after surgery-54 ± 6.4; through 6 months - 55 ± 2.3) without statistically significant changes. In patients with "cut-out" $n = 3$ (1.5%), the FRAX index was 22.12 ± 1.76, when in remaining patients -18.6 ± 0.45.

Conclusion

In 83.5% of cases were achieved successful anatomical repositions. All patients with "cut out" complications have a high FRAX index (22.12 ± 1.76): 1.03 % of patients with deficient anatomic reposition and 0.4% adequate anatomic reposition. This may indicate the FRAX intends to predict complications.

Pharmacollogy II
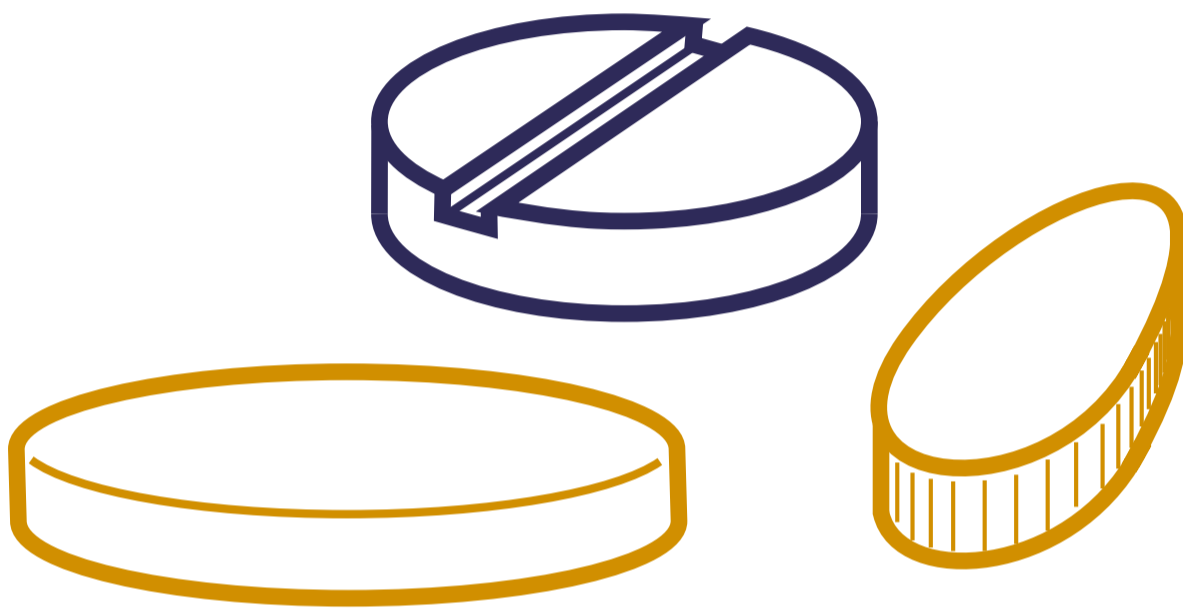
Presenters:
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Effects of Mellisa Officinalis Extract on Streptozotocin-Induced Diabetes in Rat Models; a Stereological Study on Pancreas

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Introduction

The prevalence of Diabetes Mellitus (DM) is increasing as it has been asserted the number of people with diabetes will approximately be doubled between 2000 and 2030. Proper nutritional use of antioxidant agents could prevent the disease by inhibiting peroxidation chain reactions. Melissa Officinalis (MO) is consisted of phenolic and flavonoid materials which have antioxidant and anti-inflammatory properties.

Materials & Methods

Stereptozotocin was injected intraperitoneally to rats in order to mimic DM in animal models. The rats divided in four groups as control 1 (non-diabetics), control 2 (diabetics without treatment) and experimental groups which received treatment by different dosages for 14 days. After sacrificing the models, their pancreases were extracted, weighed and the primary volume of the pancreases were estimated. Volume density and absolute volume of the islets, besides numerical density of the beta cells and total number of the beta cells were measured by stereological methods.

Results

Significant differences (P-value<0.001) were presented in the volume density and total volume of pancreases' islets in treatment groups, comparing to control 1 group. Moreover, treatment groups showed significantly higher rates of numerical density and population of beta cells compared to control 2 group (P-value<0.001). Treatment groups also had significantly lower blood glucose than the untreated diabetic rats (P=0.008).

Conclusion

According to stereological analysis, MO can have anti-diabetic potential, which can be used as an alternative treatment for DM. However, clinical trials are needed to examine the beneficial effects of MO on human diabetic patients.

Transcriptomics and behavioral changes reveal the effect of 2,2',4,4'-tetrabromodiphenyl ether exposure to zebrafish embryos (Danio rerio)

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Introduction

Polybrominated diphenyl ethers (PBDEs) are a class of widely used flame retardants, but their residue in environment may threaten ecosystem and human health. However, though some studies have proved the effect of PBDEs in vivo and vitro experiment, the mechanisms of them are less known.

Materials & Methods

We used transcriptomics and behavioral analysis to assess the effect of zebrafish embryo and larvae. The embryos were collected after fertilization and exposed to control (0.05% DMSO), 10, 50, 100(ug/L) BDE-47 for 7 dpf (day post fertilization). Enrichment of functions and signaling pathways of differentially expressed genes (DEGs) were analyzed by GO and DAVID database.

Results

The comparison with the control group showed an adverse development such as low hatching rate and high mortality rate, high spontaneous tail movements (48hpf) of the embryos.For the zebrafish larvae, behavioral analysis results suggested an anxiety reaction in exploration trail, also a decreased activity and movement in the light-dark flash period.The affected functions included steroid hormone regulation, neuro regulation, circadian regulation, cardioblast differentiation, immune-related regulation. At the same time, two KEGG pathways, sonic hedgehog and toll-like receptor signaling pathway were enriched.

Conclusion

In summary, PBDEs could influence development and behavior of zebrafish embryos and larvae by altered the hormone regulation, neuron regulation and immune-related regulation. The results help us to explore the toxicity of PBEDs and support us to use zebrafish model as a high-throughput tool to screen the potential target genes for the better understanding the complex toxicology mechanisms of environmental pollutants.

The effect of low dose aspirin on estrogen levels in postmenopausal women

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Introduction

Breast cancer is one of the most common cancers among women throughout the world.

Some studies revealed that using aspirin, a nonsteroidal anti-inflammatory drug (NSAID), has been associated with decreasing risk of some cancers such as breast cancer.

NSAIDs block both isoforms of cyclooxygenase (COX 1-2) enzyme, leading to inhibit prostaglandins E2 (PGE2) biosynthesis, as a result inhibit up-regulation of aromatase enzyme activity. The aromatase enzyme changes androgens into estrogens and increase estrogen levels which may have an effect on breast cancer recurrence.

Although, numerous studies have demonstrated the effect of Nonsteroidal anti-inflammatory drugs (NSAIDs) on reducing the risk of breast cancer, there are some other surveys declare the opposite effect. Therefor the aim of this survey is to study the effect of low-dose aspirin on serum estradiol level in postmenopausal women.

Materials & Methods

55 postmenopausal women were randomly divided into two groups. Twenty-seven of participants received low-dose aspirin (100 mg/day), and 28 received placebo once daily for six weeks. Serum level of estradiol (pg/ml), testosterone (ng/dl), and SHBG (nmol/ml), were measured using ELIZA assay before and after this intervention.

Results

The estradiol level in the intervention group (receiving aspirin) was less than the placebo group and this reduction was statistically significant (P= 0.02). According to the difference testosterone and SHBG levels were not significantly different between two groups during the study (respectively P= 0.58, P=0.32), indicates that the changes in the estradiol level are not influenced by these two other factors.

Conclusion

Data analysis showed that low-dose aspirin can effectively reduce the level of estradiol in postmenopausal women, which can decrease the risk of breast cancer.

Protective effect of epigallocatechin-3-gallate against paracetamol nephrotoxicity in rats

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Introduction

Background: Paracetamol is the commonest globally used analgesic-antipyretic. In high concentrations, paracetamol may damage the kidney and liver tissues by causing an oxidative stress. N-Acetylcysteine has long been the preferred antidote for paracetamol overdose through its antioxidant effects. Epigallocatechin-3-gallate (EGCG) is the main active component of green tea which showed antioxidant properties in many previous studies.

Aim: To investigate the potential protective effect of epigallocatechin-3-gallate against paracetamol nephrotoxicity in rats.

Materials & Methods

Fifteen male Sprague-Dawley rats weighing 200-250 grams were randomly divided into 3 equal groups (n = 5, each). First group (control) received nothing but water, food and libitum. Second group received a single intraperitoneal (i.p.) injection of paracetamol (350mg/kg). Third group received paracetamol and epigallocatechin-3-gallate treatment for two days (10 mg/kg/day, i.p.).

Results

A significant increase of serum creatinine and kidney tissue levels of malondialdehyde (MDA) and nitric oxide (NO) were found in the group that received paracetamol in comparison to the control group. On the other hand, epigallocatechin-3-gallate significantly decreased serum creatinine and kidney tissue levels of MDA and NO in comparison to the paracetamol-challenged rats. Also, the histopathological kidney tissue damage induced by paracetamol was markedly minimized by epigallocatechin-3-gallate.

Conclusion

Epigallocatechin-3-gallate may significantly protected against paracetamol nephrotoxicity in rats through its antioxidant effect.

Therapeutic Activity and Chromatographic Analysis of the Extracts of Gnetum africanum Leaves

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Introduction

The use of plants in treatment of diseases is as old as medicine itself and since there has been progressive resistance of microorganisms to drugs conventionally designed to kill them or stop their activities, it is only appropriate to retrieve the use of plants. This study is ongoing to discovery of the anti-micriobial activites of the extracts of Gnetum africanum, as well as identification of the bioactive compounds contained in the leaves of G. africanum.

Materials & Methods

The fresh leaves of G. africanum were collected from Eke market, Awka Nigeria. After being air-dried under laboratory condition, the leaves were milled into powdery form from which 10g is measured and added to 100mL of each of the solvents: methane, hexane, choloform, obtaining the respective extracts. Under the nitrogen stream, the extract was allowed to evaporate, and the residue was filtered using nylon membrane filter. 1mL of the residue of the corresponding organic solvent was prepared for GC-MS analysis.

Results

Methane extract exhibited IR of 3 mm on S. aureus and E. aerogenes, while an IR of 2 mm on B. cereus and Klebsiella sp. at the same conc. of 25.50 mg/mL and 31.85 mg/mL. Hexane extract intermediately inhibited B. cereus, with IR of 2 mm - 4 mm, whereas S. aureus was inhibited only at 132.75 mg/mL conc. Chloroform extract failed to show any significant anti-microbial activity. Volatile compounds obtained by extraction of Gnetum africanum with different solvents based on gas chromatography-mass spectrometry (GC-MS), using a 450-GC coupled with 240-ion trap MS. With retention time in minutes and area in %, chloroform extract presented palmitic acid trimethylsilyl ester (16.04%), heptadecanoic acid trimethylsilyl ester (7.69%), stearic acid trimethylsilyl ester (19.11%). Hexane extract: trifluoromethyl-bis-(trimethylsilyl)-methyl ketone (14.70%), 2-phenylindolizine (11.74%), cis-10-nonadecenoic acid trimethylsilyl ester (17%). Methane extract: 2,5-bis-(1,1,3,3-tetramethylbutyl) thiophene (13.09%), 5,7-dimethyl-1,3-diazaadamantan-6-one hydrazine (20.84%), 1,8-dimethyl-3,6-diazahomoadamantan-9-spiro-2'-oxirane (20.95%).

Conclusion

Extracts of Gnetum africanum have an antibacterial effect, which is depending on the type of solvent used for the extraction, the concentration tested and the bacterial strain of concern and Gas-chromatographic results evidenced the presence of various bio-active compounds and the extracts applied on human pathogenic bacteria presented antibacterial effect.

Protective effect of Sinapis alba against Isoniazid and Rifampicin induced hepatotoxicity in experimental rats

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Introduction

Sinapis alba (white mustard) seeds are a rich source of polyphenolic compounds with documented antioxidant property protecting against oxidative stress, which is implicated in the pathophysiology of drug-induced hepatotoxicity. Hence with this view, the present study evaluates the effects of Sinapis alba seeds in a murine model of antitubercular drug-induced hepatic damage.

Materials & Methods

Adult wistar rats were divided into seven groups; Group 1(normal control), group 2(hepatotoxic control), group 3(standard control) receiving silymarin at a dose of 50mg/kg orally, groups 4, 5 and 6, the test groups treated orally with ethanol extract of Sinapis alba seeds at doses 250,500 and 1000 mg/kg per day respectively and group 7 received silymarin in addition to ethanol extract of Sinapis alba seed at a dose of 1000 mg/kg. Hepatotoxicity was induced by administering isoniazid with rifampicin at a dose of 50 mg/kg each intraperitoneal. Following the administration of drugs for a period of 21 days, the blood samples were collected and evaluated for estimation of liver function parameters like aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), total protein, albumin and total bilirubin. The animals were sacrificed, liver dissected and processed for histopathological evaluation. One way ANOVA followed by Tukey's test was used for analysis. p value <0.05 was considered significant.

Results

Pre-treatment with Sinapis alba seed extract at doses 250, 500, and 1000 mg/kg and standard drug silymarin showed a significant decrease in AST, ALT, ALP and total bilirubin when compared to hepatotoxic group signifying hepatoprotection afforded by Sinapis alba. The decrease in biochemical markers was more significant in the group treated with Sinapis alba 1000 mg/kg in addition to silymarin However, there was no significant difference in protein and albumin between groups. Histopathological assessment according to the criteria of Knodell et al.of the liver sections from the extract and silymarin treated group showed a reduction in pathological features compared to hepatotoxic group suggesting marked hepatoprotective potential of the seeds of Sinapis alba.

Conclusion

Sinapis alba seeds protect against drug-induced liver injury in a murine model and the underlying mechanism can be accorded to its antioxidant activity.

Assessment of Awareness of Deprescribing amongst Doctors of a Tertiary Care Hospital

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Introduction

Deprescribing, the basic component of good prescribing practices is the systematic review and reduction of dose or complete cessation of drugs intended for chronic use following a risk-benefit analysis whilst remaining in congruence with the patient's quality of life and economic circumstances. Deprescribing is a crucial pillar in matters of growing concern about polypharmacy and drug cascading. This study was planned with the aim to explore the knowledge of prescribers about deprescribing and their willingness to adopt the concept.

Materials & Methods

A validated PACPD-12 Questinnaire on Deprescribing was filled by the doctors working in a Departments of a tertiarry care hospital. Data was collected and recorded on Microsoft Excel 2019 spread sheet and assessed by conversion into percentages.

Results

Out of the surveyed doctors, 55% were previously unaware of the term 'deprescribing' and a 100% believed there existed a lack of awareness on the topic in the medical community. Most agreed that deprescribing was beneficial in the current clinical scenario whilst 25% expressed a neutral stance in the same. Steroids, Benzodiazepines, antibiotics and Proton pump inhibitors were the most preferred drugs for deprescription and the most prevalent reason cited was to protect the patient from adverse drug reactions. 65% doctors did not use any specific criteria for deprescription however 90% of them expressed being amenable to following set guidelines on the same. The biggest barrier to deprescribing was reported to be the current doctor being unsure of the rationale behind previously prescribed medications by other doctors. Lack of experience (25%) and resistance from the patient (30%) was also outlined. A resounding 75% agreed that advanced age and comorbidities affecting drug metabolism made the physician more likely to deprescribe.

Conclusion

It is the first time that the prevalence of deprescription was assessed at a government tertiary healthcare centre. This study concludes that there exists a lack of awareness of the concept stemming from a lack of representation in the degree curriculum and absence of department set criteria for deprescribing. The biggest hurdle was identified as a lack of information on the rationale behind previously prescribed medicines.

Ecdysten treatment decreases hypercholesterolemia and hyperglycemia in an alloxan-diabetic rat model

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Introduction

Diabetes mellitus is a chronic condition characterized by insulin resistance, accompanied by hyperglycemia and metabolic disorders affecting about 2.8% of the global population. Artificially synthesized anti-diabetic drugs like Metformin and Nandrolone along with insulin administration are widely used for the treatment of diabetes type II. However, current therapy is associated with high costs and many side effects. Thus, alternative antidiabetic agents from natural sources have received great attention. Ecdysten is a phytohydroxylate steroid commonly occurring in plants and invertebrates have been shown to reduce hyperglycemia and hypercholesterolemia in mammals and demonstrated no off-target effects. In this study, we investigate the therapeutic potential of ecdysten in the treatment of diabetes type 2 and compare its efficacy with Metformin and Nandrolone therapy.

Materials & Methods

Diabetes was induced in albino rats with alloxan monohydrate injection (150mg/kg). A total of 45 diabetic and 10 intact, not diabetic rats were used. Rats were divided into five groups. Group I of not diabetic rats served as the untreated control. Group II was diabetic control. Group III and Group IV were diabetic rats received standard drugs Metformin or Nandrolone (20 mg/kg) respectively. Group V was diabetic rats treated with Ecdysten (20mg/kg). The experimental groups were treated for 21 days. Blood samples were collected on days 1, 7, 14, 21 and glycemic, lipid parameters and hemostatic profile were measured. Data were expressed as mean ± SD of three parallel measurements.

Results

Ecdysten reduced blood glucose(27%), free fatty acids (18%), cholesterol (10%), increased insulin levels in diabetic animals compared to the control diabetic group. It decreased activated partial thromboplastin time, thrombin time and prothrombin time. Ecdysten treated animals had physiological parameters more similar to those of healthy controls than in Metformin and Nandrolone treated groups.

Conclusion

Our data showed a marked improvement in glycemic, lipid parameters and hemostatic profile of alloxan-diabetic rats treated with Ecdysten. These results demonstrate anti-diabetic effects of Ecdysten comparable and even superior to the existing antidiabetic drugs Metformin and Nandrolone while no adverse side effects were observed. That identifies ecdysten as a promising therapeutic agent for diabetes type 2 treatment.

Psychiatry
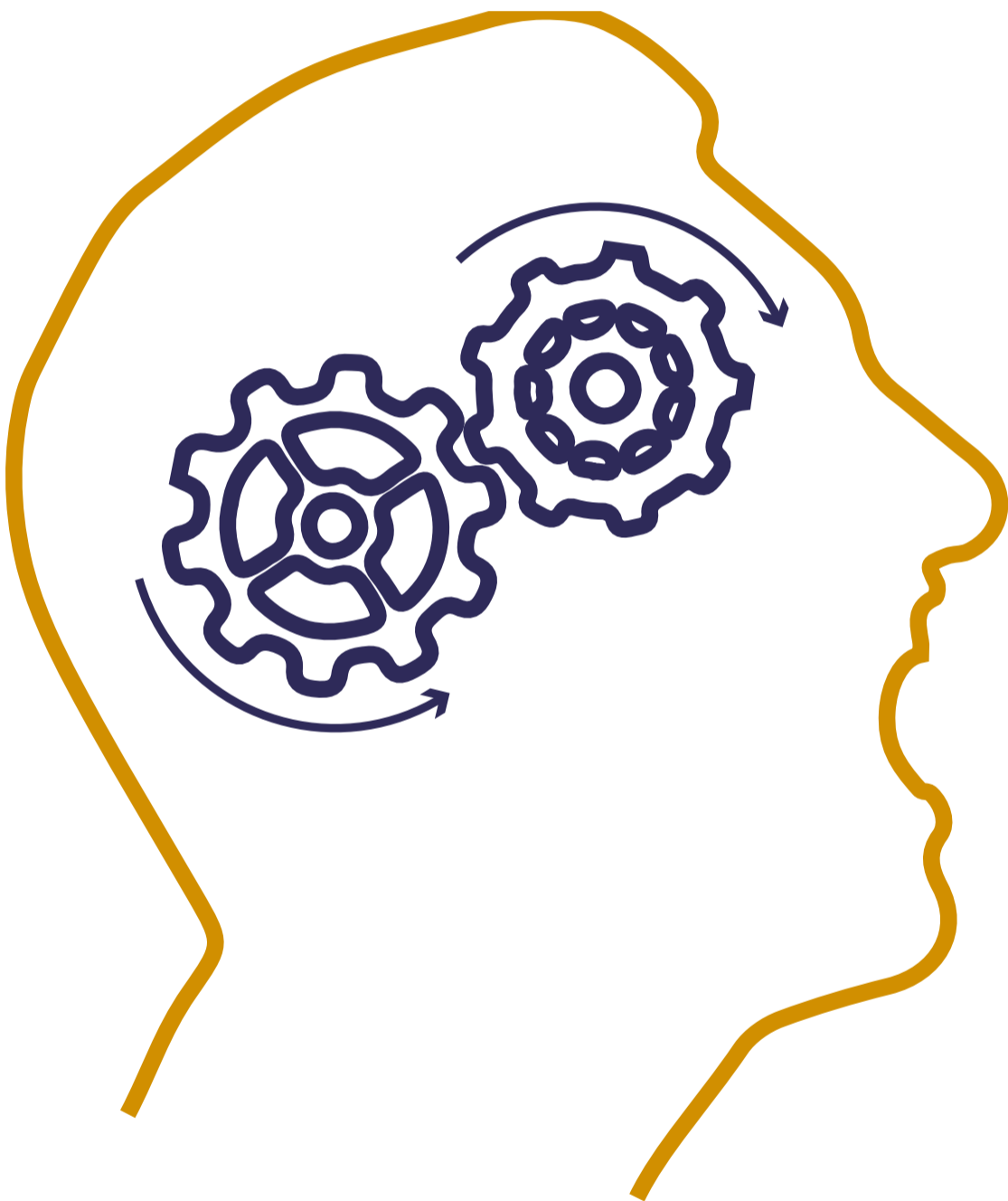
Presenters:
Bagheri, S (Sayna)
Chirwa, S.D (Salomé)
Ghozy, S.A.A. (Sherief)
Chen, M. (Molei) M.M.
Mutume, MNVB (Nzanzu)
Waqas, A. (Ahmed)
Trepl, J (Julia)
Tieks, A (Alieke)

Resveratrol Adjunct to Ritalin Attenuates Core Symptoms of Attention-Deficit/Hyperactivity Disorder: A Randomized, Double-Blind, Placebo-Controlled Clinical Trial

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Introduction

Current pharmacological approaches have failed to provide complete remission for patients with Attention-Deficit /Hyperactivity Disorder (ADHD). This study aimed to evaluate the efficacy and safety of Resveratrol as an adjunct to methylphenidate in pharmacologic treatment of ADHD.

Materials & Methods

This 8-week, double-blinded, placebo-controlled trial randomized 66 participants to receive either Resveratrol or matched placebo in addition to methylphenidate. Core symptoms of ADHD were evaluated in the patients using the Parent and Teacher versions of ADHD Rating Scale (ADHD-RS) at three measurement points with time intervals of 4 weeks. Furthermore, the safety of the treatment strategies were systematically compared.

Results

Repeated measures analysis demonstrated a significant effect for time-treatment interaction on all three subscales of the Parent ADHD-RS during the trial period (total: $F = 5.08$, $df = 1.50$, $p = 0.015$; inattention: $F = 3.88$, $df = 1.61$, $p = 0.032$; hyperactivity/impulsivity: $F = 3.99$, $df = 1.38$, $p = 0.036$). Nevertheless, the effect for time-treatment interaction was not significant on the Teacher version of ADHD-RS (total: $F = 0.81$, $df = 1.33$, $p = 0.401$; inattention: $F = 0.57$, $df = 1.37$, $p = 0.507$; hyperactivity/impulsivity: $F = 0.65$, $df = 1.34$, $p = 0.466$). The frequencies of complications in the treatment groups were similar.

Conclusion

Resveratrol administration for a duration of 8 weeks improved characteristic symptoms in patients with ADHD, according to their parents. Further investigations containing larger sample sizes, longer supplementation periods, and dose-response evaluations are required to replicate these findings in ADHD children more confidently.

Anxiety and depression among adolescents living with HIV in Blantyre Malawi

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Introduction

Globally, adolescents bear the greatest burden of HIV/AIDS. Mental health disorders such as anxiety and depression are common among people living with HIV/AIDS in general. There is a dearth of literature, in particular the prevalence of mental disorders among adolescents living with HIV (ALHIV) in low and middle income countries.

This study was conducted to investigate anxiety and depression among ALHIV attending antiretroviral clinic at Queen Elizabeth Central Hospital in Blantyre Malawi.

Materials & Methods

This was a cross-sectional study that utilized mixed methods apprpach. A total of 123 adolescents participated in the study. The General Anxiety Disorder Scale-7 (GAD-7) was used to assess anxiety while depression was assessed using the Patient Health Questionnaire (PHQ). Data was entered and analysed using SPSS.

Results

A total of 40 (32.5%) of the participants had anxiety. Among them, 22 (18%) of females had anxiety; in comparison to 18 (15%) of males. 32 (26%) of the participants had depression. 19 (16%) of males had depression; compared to 13 (10%) of females. 22 (18%) had both anxiety and depression. When an individual has anxiety, it is 24 times more likely that they will have depression (p value ≤0.05). We examined variables such as age and sex; against depression and anxiety; and there were no significant association (p value≤0.05).

Conclusion

Our study shows high levels of anxiety and depression among adolescents living with HIV in Blantyre, Malawi. This emphasises the need of extensive mental health care services for adolescents living with HIV in order to ensure that mental health does not interfere with their medication adherence among other elements.

Association of breastfeeding status with risk of autism spectrum disorder: A systematic review, dose-response analysis and meta-analysis

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Introduction

Current evidence indicates that nutritional status in newborns, especially the duration of breastfeeding, plays a key role in the pathogenesis of autism spectrum disorder. We aimed to systematically review and meta-analyze relevant studies with findings of an association between autism spectrum disorder and breastfeeding patterns, and undertook an extensive dose-response analysis to interpret the results more accurately.

Materials & Methods

Ten electronic databases and manual search of reference lists were used to identify relevant studies in September 2018. Dose-response and conventional meta-analysis were conducted by the random-effects model. The study protocol was registered in PROSPERO with CRD42016043128.

Results

Seven case-control studies were found in which the association between ever breastfeeding and risk of autism spectrum disorder was investigated. We found a 58 % decrease in the risk of autism spectrum disorder with ever breastfeeding and a 76 % decrease in the risk with exclusive breastfeeding. According to our dose-response meta-analysis, breastfeeding for 6 months was associated with a 54 % reduction in the risk. In the conventional meta-analysis, breastfeeding for 12–24 months was associated with the most significant reduction in the risk of autism spectrum disorder.

Conclusion

Our results highlight the importance of breastfeeding to decrease the risk of autism spectrum disorder.

Parvalbumin interneuron injury and cognitive impairments in adolescent mice treated with rotenone: effects of n-acetylcysteine

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Introduction

Parvalbumin interneurons (PVIs) are a group of neurons with long-term development tracks and vulnerable to risk environmental factors. Damage to PVIs may cause abnormal connections within local cerebral regions and lead to cognitive, emotional and social dysfunctions. The aim of this study was to explore the oxidative stress mechanism of PVI damage in mice treated with rotenone (ROT), a typical inhibitor of the complex I on the mitochondrial respiratory chain.

Materials & Methods

Male C57BL/6 mice (3 weeks old) were divided into 4 groups and given vehicle (VEH), ROT, n-acetylcysteine (NAC, an FDA approved antioxidant), and ROT plus NAC (ROT+NAC), respectively. NAC was dissolved in saline and given intraperitoneally at a dose of 400 mg/kg/day while ROT was dissolved in 0.5% sodium carmellose and given by gavage at 20 mg/kg/day for consecutive 14 days. Twenty-four hrs after the last vehicle/drug administration, Y-maze, puzzle box, and novel object recognition (NOR) tests were performed followed by biochemical analyses and immunofluorescent staining.

Results

ROT group, compared with VEH group, showed significantly lower spontaneous alternation in the Y-maze test, longer (time) to complete T8 and T9 in puzzle box tests, but performed in NOR test at a comparatively level. ROT mice showed lower activities in total superoxide dismutase and glutathione peroxidase, but higher levels of ROS in prefrontal cortex, caudate putamen, and hippocampus. Both NAC and ROT+NAC groups did not show these changes. In addition, ROT and ROT+NAC groups showed lower levels of ATP in the above brain regions, compared to VEH group, while NAC group did not show this change. Furthermore, ROT group showed significantly few profiles of PVI and their perineuronal nets (PNN) in these brain regions. But, NAC and ROT+NAC groups did not show these changes.

Conclusion

ROT impaired cognitive function in adolescent mice via adversely affecting the redox capacity in brain tissue thus leading to PVI loss there. NAC, via its antioxidant actions, protected mice against the ROT-induced damage to PVI and the accompanied cognitive deficit.

Mental disorder: a burden in the Eastern part of Democratic Republic of Congo, where Ebola virus disease outbreak appeared in persistent conflict setting

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Introduction

Patients exposed to armed conflict are at high risk of developing

mental health problems. The exposure to recurrent deadly illness in this region also has psychological consequences and complicates management. To date, no psychosocial approaches and clinical/psychiatric interventions have been developed to address the mental health intervention in this doubly exposed group.

We aimed to provide an overview of the burden of mental disorder in a conflict region and also investigate the mental health consequences of recurrent Ebola outbreaks, to that region. We also intend to explore the different mental health interventions in a population doubly exposed to war and recurrent Ebola virus disease outbreaks.

Materials & Methods

A cross-sectional pilot study was conducted for the pilot study which was set at Masereka health district, in a north Kivu, Democratic Republic of Congo, which is of low socioeconomic statues and having limited mental health care services. Patient's files were assessed to collect data according to the questionnaire. Data were analyzed by SPSS 18.0 to determine the prevalence and associated factors of the according to the Diagnostic and statistical manual 5th edition.

Results

38 persons have been admitted at Masereka Hospital at 2015and 159 at 2018 for a population of 180 000 persons for mental health care services. Out of those patients, HIV induced mental disorder was concerned by 23 cases, Acute stress disorder induced by the rape and kidnapping post war, epileptic 45 cases, alcohol use 60 cases, cannabis 43 case, suicide and related disorder 28 case, post traumatic stress disorder 32 patients, Bipolar affective disorder 44. The relapse was seen in 87% of cases.

Conclusion

This study Cleary showed the current mental disorder of a mental disorder in this area. However, patients were treated by general practitioners and nurses; due to the lack of mental health workers in the whole district. Efforts should be done to integrate mental health in primary care and to avoid the occurrence of the consequences and need the government support with its partners. The implementation of mental health services must be a priority of the government and its partners to reduce the morbidity of the war at North-Kivu.

Predicting risk of antenatal depression and anxiety using neural networks & support vector machines

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Introduction

Depression and anxiety during pregnancy, around childbirth and after child delivery is a debilitating mental health condition. Albeit prevalent in developing countries, it can easily go undetected and under-diagnosed due to scarce availability of psychiatric experts. It has been associated with debilitating consequences of perinatal anxiety and depression including poor maternal physical health, compromised child neurodevelopment and impaired child-mother relationship. If left untreated, several women with perinatal anxiety and depression indulge in self-harm and suicidal behaviors. It is difficult to diagnose every pregnant woman for depression and anxiety owing to high costs and scarce psychiatric expertise in low income settings. Therefore, this work proposes use of machine learning techniques to diagnose depression using routine healthcare data.

Materials & Methods

This cross-sectional study was done in obstetric and gynecology departments of four teaching hospitals in Punjab, Pakistan. After obtaining informed consent, a total of 500 pregnant women belonging to lower socioeconomic class were recruited for a detailed interview comprising of four sections: participant characteristics, experience of domestic abuse and harrassment, obstetric and gynecological history, parity, home environment, the Hospital Anxiety and Depression Scale and the Social Provisions Scale. Using R software, this work proposes a multi-layer perceptron based neural network classifier that can predict the risk of depression and anxiety in pregnant women. This can be used as a facilitator for screening women during their routine visits in hospital's gynecology and obstetrics departments. ReliefF was used for feature selection prior to modelling. Performance evaluation metrics such as sensitivity, specificity, precision, F1 score, and area under the curve (AUC-ROC) were utilized for model performance evaluation.

Results

Mean age among respondents was 27.41 years (5.65) where a total of 71% of the women reported borderline or severe anxiety symptoms and 56.4% borderline or severe depression symptoms. Harassment and domestic abuse were reported by 33 (6.6%) repondents. The MLP-NN based classifier achieved 89% specificity and 87% sensitivity for antenatal depression and 93% sensitivity and 77% specificity for antenatal anxiety making it a reasonably better classifier as compared to Support Vector Machine.

Conclusion

Machine learning can be used for screening women during their routine visits in hospital's obstetrics departments.

Antidepressant drugs show common downstream effects on neuronal networks in dissociated hippocampus cultures

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Introduction

Major depressive disorder is one of the most burdensome diseases in the western world with insufficient medical treatment available. To understand this complex psychiatric disease, the focus is shifting from single neurons to neuronal networks. Accordingly, alterations on single synapses through antidepressant drugs can translate to the entire network. We proposed that antidepressant drugs operate through changes on micro-scale neuronal networks.

Materials & Methods

We measured the effects of selective reuptake inhibitors on neuronal networks in vitro. Hippocampal neronal cultures were treated with 1μM sertraline, 50μM venlafaxine, 10μM amitryptiline or 10μM GBR-12783 (dopamine reuptake inhibitor). Cells were recorded using high-speed calcium fluorescence imaging. Effective networks were then reconstructed from synaptic activity on single-cell level and were analyzed by calculating network parameters, such as clustering coefficient, vulnerability, centrality, connectivity degree, modularity degree and global efficiency.

Results

We found that different classes of antidepressants can have diverse effect on network parameters: Only networks treated with sertraline depicted a higher number of clusters and an increased vulnerability to the loss of single synapses. Centrality, describing the reliance on connections that link local neighbors and play a central role in the distribution of information, was only modulated with venlafaxine. Although yielding different detailed topological formation, we found common network alterations on a larger scale: GBR-12783, sertraline and venlafaxine significantly decreased the total number of existing connections in the network, measured by the connectivity degree. Cultures treated with GBR-12783, sertraline, venlafaxine or amitriptyline had more submodules with less connections between the submodules, described by an increased modularity degree. These networks also showed a reduced global efficiency regarding parallel information transfer.

Conclusion

In summary, we found that antidepressant substances, which selectively target the uptake of different neurotransmitters converge on a common pattern of network changes that might be relevant for its antidepressant action in vivo: networks had less connections, more submodules and a reduced efficiency, indicating a sharpening of network structure. These alterations could be the basis for the reorganization of a miswired network in major depressive disorder.

Does one size fit all? Evaluating individual temporal associations between affect and cognitive function in older adults using a single-subject design

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Introduction

Depression and cognitive impairments often co-occur in older adults and account for a high disease burden. Getting more insight into how affect and cognitive function influence one another on a day-to-day basis could be helpful in the diagnostic process and treatment decisions for individual patients. However, little is known about the daily associations between affect and cognitive function in older adults and it is unknown whether the direction and sign of these associations differ per person. Therefore, the objective of this study was to get insight into the temporal associations between affect and cognitive function within individual older adults.

Materials & Methods

For this single-subject study eight older adults with depression and cognitive impairments filled in electronic diaries for 63 consecutive days in their home environment. The diaries included a questionnaire evaluating positive affect (PA), negative affect (NA) and a brief cognitive test battery to evaluate working memory reaction time (WMRT) and visual learning accuracy (VLA). Time-series analyses using Vector Autoregressive (VAR) modelling were conducted for each individual separately. Granger causality tests were used to determine the temporal direction of the individual associations. The contemporaneous associations were derived from the correlation between the residuals in the VAR model.

Results

For one out of 8 participants higher NA was associated with better WMRT the next day (B=0.2567; χ^2=8.9438; p=0.003). For another participant higher NA and lower PA were associated with worse WMRT at the same time (r=-0.3687; p=0.004 and r=0.3524; p=0.005 respectively). For a third participant better VLA was associated with lower NA and higher PA the next day (B=-0.3466; χ^2=9.5581; p=0.002; and B=0.4511; χ^2=10.2814; p=0.001; respectively). The other 5 participants showed no contemporaneous or lagged associations between affect and cognitive function.

Conclusion

For the majority of the individuals there appears to be no contemporaneous or temporal association between affect and cognitive functioning. For the others, the associations differed in direction and sign. This highlights heterogeneity even in a small and relatively homogeneous sample. Future studies should evaluate how such individual data can be used in personalizing diagnoses and treatments.

Miscelleanous II

M I
S C

Presenters:
Chen, CXD (Xiaodong)
Zenardi, G.A. (Gabriel)
Al Khamees, M. M. A Mr. (Mujtaba)
Allert, I. (Isabel)
Almarzooq, W.A.A (Wejdan)
Shreyans, Mr. (Singhvi)
Moghimi, P (Parinaz)
Bianco, M.C.M (Marina)
Wacka, E.W. (Eryk)
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Hosseini Rivandi, M (Maryam)

An analysis of the risk factors of falls among the elderly in urban and rural areas of Shantou City

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Introduction

To investigate the prevalence of falls among the elderly in urban and rural areas of Shantou City, and to explore the risk factors of falls among the elderly, so as to provide theoretical basis for the prevention of falls among the elderly.

Materials & Methods

The elderly aged 60 and above were recruited by cluster random sampling in urban and rural areas of shantou to investigate their social demographic information, living habits, medical history and falls in the past 1 year, and the balance ability and fall risk of the elderly were evaluated by the balance ability test form of the elderly.Chi-square test and binary logistic regression were used to analyze the risk factors of falls in the elderly and significance was set at a=0.05.

Results

The incidence of falls and injuries in the past year among the elderly in urban areas was 27.3% and 18.6% respectively, while that of the elderly in rural areas was 17% and 12.2% respectively. The results of multivariate analysis showed that the risk factors of falls in the elderly in urban areas included: Education level is junior college and above (OR=0.25, 95%CI: 0.099-0.630); taking diabetes drugs (OR=3.807, 95%CI: 1.011-14.328); urinary incontinence (OR=6.479, 95%CI: 1.323-31.721); the balance ability is weakened (OR=3.501, 95%CI: 1.714-7.151).The risk factors for falls of the elderly in rural areas included: the former working condition was farmers (OR=0.401, 95%CI:0.227-0.706);urinary incontinence (OR=11.396, 95%CI: 1.901-68.327); poor living environment (OR=3.457, 95%CI: 1.488-8.033); the balance ability is weakened (OR=4.260, 95%CI: 2.361-7.688).

Conclusion

The risk of falls of the elderly in urban areas of Shantou City is higher than that in rural areas, the emphasis of urban areas is on the intervention of the elderly with low education background and the guidance of taking diabetes drugs,while the rural areas should focus on improving the home environment of the elderly.

Impacts of sexual violence experienced by adolescents and young adults

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Introduction

Sexual violence is a public health problem that affects millions of people worldwide. In Brazil alone, there are an estimated 500,000 new cases each year, of which 70% of the victims are children and adolescents. Depression, anxiety, substance abuse, suicidal ideation are the main short and long terms consequences. Thus, the comprehension of the impact of this violence on the victim's life is necessary to guarantee a comprehensive health care and to create strategies for the prevention of various possible damages.

Materials & Methods

Students, under 25, who agreed to participate in the research, answered validated instruments: Exposure to Traumatizing Events – QUESI (to assess the presence of sexual violence in their lives); World Health Organization's Quality of Life Assessment - WHOQOL; Inventory of Beck's Depression – BDI; Beck's Anxiety Inventory – BAI and Alcohol Smoking and Substance Involvement Screening Test - ASSIST. Statistical analysis was performed using the SPSS software comparing the group that suffered sexual violence with the group that did not.

Results

Of the 858 students who answered the questionnaires, 71 were victims of sexual violence (8.3%). They have higher score for depression ($p < 0.001$) and anxiety ($p < 0.001$), lower score for quality of life ($p < 0.001$) and an abusive use of tobacco ($p = 0.008$), marijuana ($p = 0.025$) and hypnotics/sedatives ($p = 0.048$).

Conclusion

Adolescents and young adults who suffered sexual violence most often have anxiety and depression symptoms, in addition to being more prone to abuse of tobacco, marijuana and hypnotics / sedatives when compared to the group that did not suffer violence. Even years after the event, worse quality of life is perceived in this group. The understanding that the impacts of sexual violence are so diverse and that make the victim more susceptible to different situations of risk is necessary for quality prevention and in accordance with the concept of Comprehensive Health Care, generating a more precise reception and wider attention to this population.

Public awareness of antibiotics in Saudi Arabia, Al Ahsa

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Introduction

Antibiotic resistance is a major problem worldwide. It gives rise to bacteria to could leave patients with nothing but hope. In as recent as the end of 2017 in Saudi Arabia the acquisition of Non-Prescription antibiotics was alarmingly high. Thankfully there were many changes that reduced these practices. In this study, we aim to evaluate the local progress in antibiotic control and study the areas that need improvement when it comes to public awareness.

Materials & Methods

We designed a questionnaire assessing the general knowledge of the public about antibiotics. It was divided into 4 main sections: biographical information, use of antibiotics, knowledge about the effects of antibiotics, and knowledge about antibiotic resistance. We received 537 responses of which 426 are Saudi, Al-Ahsa residences.

Results

(54.8%) reported using antibiotics rarely. Also, there is a significant drop in the amount of non-prescription antibiotics (16.7%). In contrast, general knowledge about antibiotics is lacking. (49.6%) don't know that only Bactria is killed by antibiotics. Furthermore, (51.5%) of the respondents believe that antibiotics treat the flu. Other common conditions like toothaches and general body pain are also thought to be treated by antibiotics by (33.6%) and (23.3%).

Conclusion

The Over-the-counter antibiotics have fallen significantly in comparison to as recent as the end of 2017. However, there is still misunderstanding in the public about antibiotics that must be addressed. Future efforts must be directed to improve the knowledge of the general public about antibiotics as it will help encourage the healthy use of them.

Judgement and Education About vaccinations among Germans

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Introduction

Surveys answered by people everywhere in Germany provide useful insights into the general alacrity of people to get vaccinated nowadays and if vaccination should be mandatory. As only surveys which specialize on specific vaccinations can be found, this survey doesn't specialize but generalizes the question if vaccinations are important and if not, why.

Materials & Methods

This study included over 200 participants, who were chosen by age, gender and education level. The survey includes eleven questions. It is differentiated between vaccine recommendations for children and for travelling abroad to determine whether the essential 95% of vaccinated people and with that extermination of diseases might be reached. Another question includes whether participants would vaccinate their children. This may show how many people in the future might be vaccinated. Other questions involve if participants were vaccinated as a child, if they think vaccinations should be compulsory and they were asked for reasons in case they wouldn't want to vaccinate themselves or their children.

Results

The findings show minor differences regarding gender but surprising differences in age-groups, as under 18-year olds mostly have positive attitudes towards vaccinations.

Mostly against compulsory vaccinations are 30 – 40 years-old. They present the largest group against vaccinating their children. This is interesting as they are next to raise children.

Another finding shows that despite the great education level distances, people who graduated in 10th grade and people with A-levels both answered positively towards vaccinations while participants with secondary education and those with vocational-baccalaureate-diploma answered more negatively. Three-quarters of the participants want vaccinations to be compulsory.

Conclusion

The main discoveries show that the majority think vaccinations are important. This may be due to good education regarding vaccination. Nevertheless, it is insufficient to reach for extermination necessary 95%.

As three-quarters of the participants agree with compulsory vaccinations, the already existing obligation to measles vaccination is likely to only be the first step to overall compulsory vaccinations.

Carpal Tunnel Syndrome and the Use of Keyboard and Mouse among Office Workers

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Introduction

Carpal tunnel syndrome (CTS) is a symptomatic disorder resulting from local compression of the median nerve at the wrist leading to functional impairment and local ischemia of the nerve it has been associated with long weekly hours of using keyboard as a risk factor.

Materials & Methods

384 participants whose ages are between 25 and 59 years old office worker from Eastern province in Saudi Arabia will participate in this study. A questionnaire will be distributed to the participants who are free of any neurological disease and never go to CTS surgery to provide information about the presence and severity of CTS symptoms, body mass index (BMI) and work activities. For those who will have symptoms of CTS would ask to undergo a physical examination and nerve conduction velocity testing to confirm the diagnosis. There will be a comparison between groups of subjects that will differ in their intensity of keyboard use.

Results

Excessive computer use, particularly keyboard and mouse usage, is expected to have a significant association with high prevalence of CTS and would be considered as an occupational risk factor among officers. Also the risk of CTS is expected to be more in female, and subjects who are overweight (BMI > 25)

Conclusion

Significant relationship between using keyboard and mouse and CTS would be expected.

Assessment of factors affecting lung function and oral health amongst workers in a factory

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Introduction

This study is aimed to evaluate the factors affecting Lung Function and Oral Health amongst workers in a factory in Gujarat. The objectives of the study are - To study the socio-demographic profile, general health of workers, pulmonary function and it's abnormality associated with the duration of exposure in the factory and with other personal habits /addiction, to associate the abnormality in lung functions with the specific unit of the factory in which they were working , the association between oral lesions (pre-malignant or malignant lesions) and tobacco use.

Materials & Methods

A cross sectional study of 240 workers employed in a textile industry of Gujarat were undertaken for the study. Workers who gave informed verbal consent and had minimum one year of exposure in the factory were included in the study. A self-administered questionnaire was used for the study which included - Socio-demographic information, addiction history including history of tobacco use (chewing and smoking), alcohol consumption,current and past history and occupational history. Pulmonary function was examined by examining the Peak expiration flow rate(PEFR) by Wright's peak flow meter.The oral cavity was screened for oral lesions and signs of smoking or chewing tobacco. The data was recorded and analysed in Google spreadsheet using statistical methods.

Results

A positive association between type and duration of exposure, age, section of work with lung functions was found with odd's ratio of 7.86, 13.21, 9.654, 6.74 respectively.

Out of the total 240 workers, 20.83% of the workers were found to have some oral pre-malignant lesion while the other 79.17% did not present with any lesion. The oral lesions found were – Submucosal Oral Fibrosis (56%), Leukoplakia (22%) and Ulcer (2%). 20% of the workers presented with stained teeth.

Majority of the workers that presented with oral lesions had a history of tobacco consumption.

Conclusion

The results show that textile workers are highly susceptible to occupational health disorders primarily affecting the lung and oral cavity. This can be reduced by taking appropriate precautionary measures and conducting regular health checkups and health awareness programs for the workers.

No Significant Association between Vitamin D deficiency and body mass index (BMI) in an Iranian population of children

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Introduction

Vitamin D deficiency that is one of the factors which were found to be associated with obesity is increasing in Iranian children. There is an inverse relationship between the serum levels of 25-hydroxy vitamin D and the body mass index (BMI) of children in observational studies. In order to correction and prevention of vitamin D deficiency that can cause many adulthood complications, such as metabolic syndrome and Diabetes mellitus (DM), a precise depiction of the current situation and identification of associated risk factors is required. This study aimed to determine the relationship between serum 25-hydroxy vitamin D and body mass index (BMI) in children over two years old in an Iranian Population of Children.

Materials & Methods

In this cross-sectional observational study, 150 children who were more than two years old, were referred to Javheri Hospital in 2017. Anthropometric values: weight, height was measured and recorded by using identical instruments (Seca digital medical weighing scale and Tape measures, respectively). BMI was also determined as per CDC 2000 criteria. Vitamin-D levels were assayed by LIAISON automated analyzer (The LIAISON 25 OH Vitamin D assay). Vitamin D serum levels less than 10 ng/ml considered as vitamin D deficiency, level which were 10 - 30 ng/ml considered as inadequate vitamin D Level , and those which were equal or greater than 30 ng/ml considered as sufficient. Data were analyzed by SPSS software (version 25).

Results

78 children (52%) were Female and the others were Male. 10 children (6.7%) had vitamin-D deficiency, 82 children (54.7%) had insufficient vitamin D levels and 58 had adequate levels of vitamin-D. Average of height and weight were 105.81 ±13.86 Centimeter and 17819.33±654.82 gram respectively. Moreover, there was no significant relationship between the level of vitamin D in children with BMI, age and gender (P-Value> 0.05).

Conclusion

There was a high prevalence of vitamin D deficiency or insufficiency in children more than 2 years old. Although there was no significant relationship between serum level of 25-hydroxy vitamin D and BMI, more exposure to sunlight and prescription of vitamin supplements was recommended.

Contingency Management in Adolescents with Substance Use Disorders: A Systematic Review

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Introduction

Contingency Management (CM) is a CBT-based psychosocial intervention that has shown good results for promotion of abstinence and retention to treatment in outpatients with substance use disorders (SUDs). We aimed to review the controlled randomized clinical trials (RCTs) that tested the efficacy of CM for any SUD among adolescents.

Materials & Methods

We researched PubMed and Lilacs using the following research strategy: "contingency management" and (adolescent or youth or teenager). We also searched clinicaltrials.gov for study protocols and examined references of the trials included. The articles included in this review met the following inclusion criteria: (i) written in English or Portuguese (according to the authors' fluency); (ii) conducted with humans; (iii) randomized controlled trials (RCTs); (iv) adolescent population (aged 12-21); (v) use of substances; and (vi) contingency management as an intervention. Trials with tobacco, cannabis, and multiple drugs were included. In tobacco trials, we analyzed the following outcomes: (i) point prevalence (PP) abstinence at week 1 of treatment and (ii) PP abstinence at week 4 of treatment. As to cannabis trials, we analyzed: (i) longest cannabis abstinence, (ii) PP abstinence at end of treatment, (iii) 2 weeks sustained abstinence, (iv) 4 weeks sustained abstinence, (v) 6 weeks sustained abstinence, and (vi) 10 weeks sustained abstinence.

Results

Thirteen trials met our inclusion criteria and were included in the review: five trials with tobacco, four with cannabis, and four with multiple drugs. We did not find statistical significance for a beneficial effect of CM compared with control interventions for any of the outcomes assessed. Nevertheless, this should be interpreted with caution. The point estimates of CM outperformed the control interventions for all outcomes, with point estimates that were clinically meaningful despite statistically not-significant. Hence, the lack of statistical significance could have been due to the scarcity of trials available rather than to inefficacy of the intervention.

Conclusion

CM is possibly efficacious intervention for adolescents with SUDs. Further trials with standardized methods are warranted to elucidate this issue.

Neopterin as a diagnostic biomarker of chronic lower limb ischemia

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Introduction

Endothelial dysfunction is an essential factor preceding the development of chronic lower limb ischemia. There have been many attempts to investigate endothelial function including NO metabolism, lipoprotein oxidation, inflammatory mediators etc. Recently, an attention has been focused on neopterin produced by monocytes/macrophages and dendritic cells upon stimulation with IFNγ. Neopterin is a pyrazino-pyrimidine compound that may play an important role in the pathogenesis and progression of cardiovascular diseases (CVD) by regulating NO production and the proliferation and differentiation of hematopoietic stem cells. The study was designed to evaluate the neopterin level and its interaction with conventional and non-conventional CVD risk factors.

Materials & Methods

The study was conducted on 59 patients (women n=17, men n=42) aged 67.0 ± 8.2 years with chronic femoral popliteal ischemia (n=45), aorto-iliac ischemia (n=9), multilevel (n=3) and peripheral ischemia (n=2) from WROVASC Integrated Center for Cardiovascular Medicine. The hemodynamic parameters an ankle-brachial index together with ankle and brachial systolic pressures were measured. Plasma levels of neopterin, C-reactive protein (CRP), homocysteine (Hcy), total cholesterol (TC) and lipoproteins (HDL, non-HDL, LDL and oxLDL), 3-nitrotyrosine (3NT) and the number of CD34 and CD38 hematopoietic cells were determined by enzyme immunoassay methods (ELISA kits). Statistical analyses were performed by means of statistical software Statistica 13.1 (StatSoft Inc., Tulsa, USA).

Results

Neopterin concentration reached values above 10 nmol/L in 25% of patients. High levels of CRP >7 mg/dL, Hcy >15 µmol/L, TC >200 mg/dL, LDL >100 mg/dL and non-HDL >130 mg/dL were found in the same group of patients, indicating the relationship between neopterin and conventional CVD risk factors. The number of CD34 and CD38 cells was signiffanctly correlated (Pearson's coefficient >0.9) with 3NT as an indicator of low NO bioavailability. There was no correlation between the number of CD34 and CD38 cells with the concentration of neopterin.

Conclusion

These findings demonstrated that neopterin exhibits high plasma levels in chronic lower limb ischemia and it can also be a useful and innovative tool for monitoring CVD. However, the role of neopterin in chronic peripheral atherosclerotic diseases has yet to be elucidated.

Burnout among Health Workers in a Tertiary Health Facility in the Central Region of Ghana – An emerging threat

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Introduction

Burnout (BO) among health workers entrusted with patient safety in hospitals, is an increasing worldwide concern; a phenomenon which evolves through a long-overlooked process of chronic stress. It has the potential to progress to overt depression, lowers immunity among other complications thus compromising patient care and safety. Early detection, prevention and the provision of supportive care could potentially contain this phenomenon. The study aimed to assess the prevalence of burnout and interactions between its attributes among health workers in the Cape Coast Teaching Hospital (CCTH), a tertiary health facility in the Central Region of Ghana.

Materials & Methods

This was a cross-sectional study using the Burnout Assessment Tool (BAT). Sampling was multi-stage and randomized.

The cut-off scores for BO was set at the 25th, 75th and the 95th percentiles with 4 categories: Low (<25th), Average (25th to <75th), High (75th to <95th) and Very High (≥95th). Average to Very high was considered BO. The chi-square test was used in determining the sex distribution of selected demographic factors and BO attributes. Pearsons' correlation demonstrated the relationship between BO attributes whiles logistic regression was employed to evaluate the odds of developing BO relative to an intra-group reference category. Significance level was set at 0.05

Results

Valid responses were 335 (88 doctors,233 nurses,14 health assistants). Overall prevalence was 73.4%. Cognitive Impairment was most prominent among the core attributes. Younger age groups with less years of work experience were more at risk of BO. Females and singles similarly had more BO rates. Among the health professionals, doctors had higher BO rates. Junior doctors and Midlevel nurses experienced higher BO rates than their cohorts. There were statistically significant and positive correlations between the BO attributes particularly between Exhaustion and Mental Distance.

Conclusion

Overall prevalence of BO in CCTH was estimated at 73.4% with prominent cognitive impairment. BO was higher among the following groups including, singles, females, younger age; fewer years of work experience; junior doctor and midlevel nurse. There were statistically significant and positive correlations between BO attributes.

Recognizing obstacles, barriers, and potential facilitators in oral health care of young children by their parents

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Introduction

To investigate obstacles, barriers, and potential facilitators which parents were confronted with, in terms of their children's oral health care, in order to design a tailored behavioral intervention.

Materials & Methods

The qualitative study was conducted at a kindergarten in a moderate SES municipality region in Tehran. Data was collected based on focus group method with 8 parents of 12-to-36-month-old children with different levels of education and using semi-structured interview by the investigator who previously attended communication skill workshops. This approach was applied to discuss young children's oral health care. "Adequacy of evidence" (reliability in qualitative studies) and "trustworthiness" (validity) were achieved when similar relationships between issues frequently emerged from the data and constant comparison between items were documented, respectively. Focus group lasted 2 hours. Additionally, they were asked to complete a short questionnaire for their demographics and educational level. The data were analyzed and classified as two major topics: 1) barriers and obstacles in oral health of young children and 2) potential facilitators in oral health care of young children. The investigator fulfilled the main themes of barriers by coding the data for each participant separately. Analyzing data was performed by labeling each paragraph once they were studied for the evident theme and in relation to the issues investigated. With the analysis completed, searching process was initiated to review similar literature and compare the results to those from other studies. The results of the qualitative phase of the study was brought to a panel of experts in the pediatric dentistry department at Shahid Beheshti School of Dentistry.

Results

Four major categories of barriers and obstacles were recognized. Behaviors of children, positioning for brushing teeth, attitude of parents, and accessibility of valid information were four major themes of barriers to care for oral health of young children. In addition, given to the oral health care of young children and barriers discussed, two main potential facilitators are classified as production of valid information and intersectional cooperation.

Conclusion

Behaviors of children, positioning for brushing teeth, attitude of parents, and accessibility of valid information were four major themes of barriers to care for oral health of young children.

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