YES MEETING

9th YOUNG EUROPEAN SCIENTIST MEETING

18-21 SEPTEMBER 2014

FACULTY OF MEDICINE OF PORTO

YES GUIDE '14

YES MEETING

YOUNG EUROPEAN SCIENTIST MEETING

18 - 21 SEPTEMBER 2014

Porto - Portugal

Message from the YES Meeting Organizing Commitee

Dear colleagues,

It is with great pleasure that the YES Meeting Organizing Committee welcomes you to the 9th Young European Science Meeting.

We have been working hard all year long and we are very proud of this year's programme. If you have already been to a previous edition you will find this one full of new and interesting activities.

First, the pre-congress day has evolved from its groundbreaking first edition and this year includes not only talks about public speaking and scientific articles publishing but also a discussion about medical mistakes with the Head of our Faculty, Professor Agostinho Marques and a lecture about Scientific Fraud with the renowned neuroscientist, Professor João Lobo Antunes.

Our social programme was also remodelled and you will have the opportunity to be guided through the Porto city center and seeing Porto from the top of the emblematic Clerigos tower, visit the Discoveries Museum, take a Douro river tour in Rabelos boats and discovering the Port Wine caves or enjoy a Sightseeing Bus Tour around this magnificent city .

The workshops were also renewed, in this year's programme you will enjoy an even more interactive experience thanks to some new sessions and a greater focus on a hands-on approach.

You will also enjoy a number of scientific sessions where you will have the opportunity of listening to world renowned science communicators, ranging subjects from cancer and neurodegenerative diseases to ophthalmologic surgery and even schizophrenia. This edition of YES gathers internationally recognized portuguese lecturers such as Carlos Caldas, Duarte Nuno Vieira and Carlos Fiolhais, alongside fellow researchers John Kheir, Martin Hallbeck and Denis Dufrane, amongst many more.

Once again, the YES Meeting Organizing Committee is very proud to be able to give to all the young scientists a chance to present their own work in an international conference. You should not miss the Parallel Oral Sessions and the Plenary Session. The quality of all the presentations from your colleagues will not disappoint you!

We hope you enjoy this meeting and use this opportunity to make new friends and develop your network with the fellow young scientists in the congress!

Now it's up to you make this an unforgettable scientific experience!

Our best regards,
The 9th YES Meeting Organizing Committee

YES Meeting 2014
Organizing Committee

Sérgio Costa
President

Inês Gonçalves
Vice-President

Beatriz Ferraz
Ana Lídia Rouxinol
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Workshops

Carolina Braz
Social Programme

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Francisco Gonçalves
Marisa Martins
Scientific Programme

José Bernardo
Treasurer

Programme Outline

Pre-Course - 18th September

10.00 am **Opening Session**

10.30 am **Public Speaking**

12.00 pm **How to Make my Article Publishable**

2.00 pm **Weight of Medical Mistakes**

3.30 pm **Science Integrity**

5.00 pm **Communicating bad news**

6.00 pm **High Performance Techniques – DeRose Method**

7.30 pm **Welcome Cocktail (El Corte Inglés)**

19th September

8.00 am **Check-in**

9.00 am **Opening Session - Neurosciences**
- *Neuron-to-neuron transmission neurodegenerative proteins*
Prof. Martin Hallbeck (Linkoping University)
- *Chemical prevention of brain tissue death in Alzheimer's disease*
Prof. Helois Radford-Rose (University of Leicester)

10.30 am **Coffee-break – "Physiology & Immunology" and "Neurosciences" Poster Presentations**

11.30 am **Internal Medicine Session**
- *Haemoglobin/hemerythrin - based blood substitutes (HBOC)*
Prof. Radu Silaghi-Dumitrescu (Babes-Bolyai University)
- *Reversal of life-threatening hypoxemia using intravenous oxygen*
Prof. John Kheir (Boston Children's Hospital)

12.30 pm **International Journal of Medical Students**

12.45 pm **Lunch**

2.00 pm **Parallel Oral Sessions**

3.30 pm **Social Programme**

7.00 pm **Mental Health Session**
- *Listen to The Voices: Moving Beyond 'Schizophrenia'*
Prof. Rachel Waddingham (London Hearing Voices Project)
- *Schizophrenia: an integrated sociodevelopmental-cognitive model*
Prof. Michael Bloomfield (Imperial College London)

20th September

9.30 am **Oncology and Molecular Biology Session**
- *Fighting gastric cancer through biomedical engineering*
  Prof. Inês Gonçalves (INEB)
- *Breast cancer-molecular stratification and molecular monitoring*
  Prof. Carlos Caldas (Cambridge University)

10.30 am **Coffee-break** – "Oncology & Molecular Biology" and "Internal Medicine" Poster Presentations

11.30 am **Surgery Session – Ophtalmic Surgery**
- *A tooth in the eye - the osteo-odonto-keratoprosthesis*
  Prof. Venkata Avadhanam (Sussex University Hospital)

12.30 pm **Lunch**

2.30 pm **Workshops**

4.00 pm **Coffee-break**

4.30 pm **Workshops**

7.00 pm **Ethics Session**
- *Scientific Fraud Throughout History*
  Prof. Carlos Fiolhais (Department of Physics, University of Coimbra)

9.00 pm **Dinner**

21st September

9.30 am **Speed Meeting with Scientists** – an informal talk with our speakers

10.30 am **Regenerative Medicine Session – Technology in Medicine**
- *Is virtual becoming a reality - the use of CAD/CAM technologies to manage facial deformity*
  Prof. Julian Yates (University of Manchester)
- *Bone tissue reconstruction: from tissue to cell transplantation*
  Prof. Denis Dufrane (Saint Luc University Clinic Hospital)

11.30 am **Coffee-break**

12.00 pm **Plenary Session**

1.00 pm **Lunch**

2.30 pm **Keynote Session – Douglas Lucas Medal 2014**
- *"Quidne Mortui Vivos Docent?" - What can the dead teach to the living?*
  Prof. Duarte Nuno Vieira (Faculty of Medicine, University of Coimbra)

6.00 pm **Award Ceremony**

9.00 pm **Farewell Gala Dinner**

Extended Programme

FRIDAY, 19TH SEPTEMBER

Opening Session – 9h00 – Auditorium CIM (Centre of Medical Investigation)

9h00 – Sérgio Costa, President of the 9th YES Meeting Organizing Committee
9h05 – Agostinho Marques, Director of Faculty of Medicine
9h10 – Manuel Fontes de Carvalho, Dean of Porto University representative
9h15 – Miguel Guimarães, Head of the North Section of College of Physicians
9h20 – Maria Amélia Ferreira, Director of the Integrated Master in Medicine Course
9h25 – Francisco Rocha Gonçalves, Vice-Director of Faculty of Medicine
9h30 – Francisco Silva, President of our Students Association

Neuroscience session – 9h40 – Auditorium CIM

- Neuron-to-neuron transmission neurodegenerative proteins
  Martin Hallbeck – Linköping University
- Chemical prevention of brain tissue death in Alzheimer's disease
  Hellois Radford-Rose – University of Leicester

Coffee Breaks – **"Physiology & Immunology" and "Neurosciences" Poster Presentations** – 10h40 - CIM Hall

Internal Medicine Session - 11h40 – Auditorium CIM

- Haemoglobin/ Hemerythrin – based blood substitutes (HBOC)
  Radu Silaghi-Dumitrescu – Babes-Bolyai University
- Reversal of life-threatening hypoxemia using intravenous oxygen
  John Kheir – Boston Children's Hospital

International Journal of Medical Students - 12h40 - Auditorium CIM

Lunch – 12h55 – Students' Hall

Parallel Oral Sessions – 14h00

ONCOLOGY & MOLECULAR BIOLOGY – Library of Health Information and Decision Sciences (CIM)

- PS 220: Ana Isabel Cardoso Soares – Reproductive ageing and antioxidants: effect in uterine function
- PS 167: Agnieszka Sarnecka – Is the process of entosis a way to escape from chemotherapy?
- PS 184: João Carlos Crispim da Costa da Encarnação – Is butyrate and irinotecan combination a new therapeutic approach for colon cancer?
- PS 197: Joana Margarida Verdasca Jorge – Methylation pattern in myelodysplastic syndrome – comparative study between bone marrow and peripheral blood
- PS 202: Nuno Simões Costa - Buparlisib, another step in the quest to cure haematological malignancies.

PHYSIOLOGY & IMMUNOLOGY - Pharmacology and Therapeutics Amphitheatre (CIM)

- PS 146: André Filipe Mendes Leite Moreira – Role of PKG-related Pathways in the Diastolic Response to Acute Myocardial Stretch Under Ischemic Conditions
- PS 206: Rui Miguel da Costa Adão – Neuregulin-1 preserves right ventricular diastolic function in animal model of pulmonary arterial hypertension
- PS 194: Ana Rita da Costa Silva Gomes – Ghrelin's effects in diabetic retinopathy: Inhibition of choroid retinal cells migration and proliferation under a hyperglycemic environment
- PS 125: Margarida Ferreira da Mota Freitas – Effects of aging and cardiovascular risk factors on expression of SIRT1 and SIRT6 in the human corpus cavernosum

• PS 170: Henrique Nuno Nazaré e Silva – Studying the effect of oxygen inhalation on cutaneous microcirculation by the wavelet transform

INTERNAL MEDICINE - Novo A Amphitheatre
• PS 90: Patricia Kovács – Changes of para- meta- and ortho-tyrosine levels in serum and urine of septic and burned patients
• PS 117: Manuel António Gonçalves de Pinho – Legalization of abortion: hospitalizations related to legally induced abortion

• PS 97: Jesús Joaquín Maldonado Ostios – Praxis application, a nexus between clinical units and university.
• PS 135: Lazar Vladimir – Correlations of osteoprotegerin with cardiovascular risk factors in a risk population
• PS 142: Natasa Stankovic – Role of MSCT in treatment plan of patients with chronic total occlusion of coronary blood vessels

NEUROSCIENCES – Room 4 - CIM
• PS 159: Marta Canha – Effect of selective removal of cholinergic afferents in the retrosplenial cortex on the performance of rats in aversively motivated active avoidance test
• PS 95: Sónia Martins – Effects of estrogen receptor agonists in the expression of estrogen receptor alpha in the female medial preoptic nucleus
• PS 96: Ratko Radeta – The role of Akt signalling pathway in the toxic effect of extracellular ASYN, in vitro
• PS 176: Tenk Judit M.D. - Age- related alterations in acute central corticotropin effects regarding the parameters of energy balance
• PS 177: Ildikó Rostás M.D. – Catabolic effects of central leptin infusion during aging

SURGERY – Novo B Amphitheatre
• PS 122: Sárvári Katalin – Role of pre- and postconditioning to avoid noxious oxidative stress induced by pneumoperitoneum
• PS 152: Marcin Piejko – Does implantation of Adipose Stem Cells on the granulation tissue increase chance for healing large tissue damage? A case report of patient with recurrence perianal fistula treated by the cell base therapy.
• PS 66: Maral Namdari – Compersion of astigmatism and visual function before and after refractive surgery by two methods (wavefront-guided ablation PRK and aspheric ablation)

Social Programme – 15h30
Guided tour in Porto
Sightseeing Tour – Porto Castles
World of Discoveries – Interactive Museum and Thematic Park
Douro River by Rebelo Boats and Porto Wine Cellars

Mental Health Session – 19h00 – College of Physicians Noble Hall
• Listen to the Voices – Moving beyond "Schizophrenia"
  Rachel Waddingham – London Hearing Voices Project
• Schizophrenia: an integrated social developmental – cognitive model
  Michael Bloomfield – Imperial College London

SATURDAY, 20TH SEPTEMBER

Oncology and Molecular Biology Session – 9h30 – Auditorium CIM
• Fighting Gastic Cancer Through Biomedical Engineering
  Inês Gonçalves – National Institute of Biomedical Engineering
• Breast Cancer – Molecular stratification and Molecular monitoring.
  Carlos Caldas – Cambridge University

Coffee Break – 10h30 – **"Oncology and Molecular Biology" and "Internal Medicine" Poster Presentation** – CIM Hall

Surgery Session – 11h30 – Ophthalmic surgery – Auditorium CIM
- A tooth in the eye – the osteo-odonto-keratoprosthesis
  Venkata Avadhanam – Sussex University Hospital

Lunch – 12h30 – Students' Hall

Workshops 1st Turn – 14h30

Coffee Break – 16h00 – CIM Hall

Workshops 2nd Turn – 16h30

Ethics Session – 19h00 – Auditorium CIM
- Scientific Fraud Throughout History
  Carlos Fiolhais – Department of Physics, University of Coimbra

Dinner – 21h00 – Students' Hall

SUNDAY, 21ST SEPTEMBER

Speed Meeting with Scientists – 9h30 – Room 2 CIM
An informal talk with our speakers

Regenerative Medicine Session – Technology in Medicine – 10h30 – Auditorium CIM
- Is virtual becoming a reality – the use of CAD/CAM technology to manage facial deformity
  Julian Yates – University of Manchester
- Bone tissue reconstruction: from tissue to cell transplantation
  Denis Dufrane – Saint Luc University Clinic Hospital

Coffee-Break – 11h30 – CIM Hall

Plenary Session – 12h00 – Aula Magna – 3rd Floor

ONCOLOGY & MOLECULAR BIOLOGY
- PS 103: Catarina Alves do Vale – Quality control of mRNA in the nucleus: safeguarding cells from disease-causing proteins

PHYSIOLOGY & IMMUNOLOGY
- PS 195: Glória de Fátima Almeida Conceição - Effects of adipokines in cardiac structure

NEUROSCIENCES
- PS 174: Nora Furedi - Melanocortin system and neuropeptide Y in the dysregulation of energy homeostasis in SHR rats

INTERNAL MEDICINE
- PS 189: Sara Isabel Freitas Ramos - Tuberculosis re-screening in patients under biological therapy

SURGERY
- PS 221: João Vasco Nunes dos Santos - Depression as a predictor of pancreatic resection and in-hospital mortality in patients with pancreatic neoplasms

Lunch – 13h00 – Students' Hall

Keynote Session – Douglas Lucas Medal 2014 – 14h30 – Aula Magna 3rd Floor
- "Quide Mortui Vivus Docent?" – What can the death teach to the living?
  Duarte Nuno Vieira – Faculty of Medicine, University of Coimbra

Award Ceremony – 18h00 – Porto City Hall

Farewell Gala Dinner – 21h00 – "Casa dos Arcos da Boavista"

Useful Information

Admission

Participants are requested to wear their credentials at all times during the congress. Admission to the meeting rooms, social program events, lunches and coffee-breaks is limited to those wearing the YES credentials.

Information board

An information board is located near the Information Desk. All news and changes can be found there.

YES Meeting Staff

You can identify YES Organizing Committee members and YES Task Force members by their coloured identification cards and shirts. May you have any question or problem, please feel free to contact us any time.

Insurance

Congress organizers cannot accept any liability for personal injuries or for loss of or damage to property belongings to congress participants, either during or as a result of the YES Meeting. Participants shall make their own arrangements for health and travel insurance.

Internet Access / Wireless LAN

Free internet stations are available in the YES Meeting exhibition area.

Language

The official language of the event is English. No simultaneous interpretation facilities are provided during the conference.

Mobile phones

Mobile phones must always be switched off inside lecture halls.

Smoking policy

Smoking in the Meeting area will not be allowed. You should go outside to do so.

Coffee-breaks and lunches

From September 19th to the 21st coffee-breaks and lunches will be served free of charge to participants wearing YES credentials.

Electricity

220 volts AC, 50Hz. Round two-pin European plugs are universally used in Portugal.

Useful Information

Currency and sales tax

The Portuguese currency is Euro (€). Major credit cards are accepted virtually everywhere. ATM cards with the "Maestro"-sign are accepted at all ATM machines (Multibanco - MB) for cash withdrawal as well as payment cards at many shops. Sales tax is normally included in quoted prices.

First aid

Please contact a staff member or the Reception desk.

Photography, filming and audio recording

Unless previous permission has been granted by the speakers or poster presenters, photography, video and audio recording is strictly prohibited during the scientific sessions.

Personal property

Please take good care of your personal belongings. Neither the Faculty of Medicine nor the YES Staff will be held responsible for any loss or damage to your personal property.

Lost and Found

If you loose anything, please ask the Information Desk about it. If you find anything in the YES Meeting premises please deliver it at the Information Desk.

Prizes & Awards

Prizes will be announced during in a ceremony held in the afternoon of the 21st September. Each prize will be given for each of the Themes. The prizes are as follows:

Best Plenary Session Award – 1000€

Professor Ernesto Morais Best Oral Presentations Award (per area) – 250€

Best Poster Presentations Award – 150€

ATTENDANCE CERTIFICATES

Attendance certificates will be delivered online to every participant that has done the check-in. If attend the workshops, they will
figure in your certificate. More information will be available online after the meeting is over.

Useful Contacts

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Social Programme

GUIDED TOURS IN OPORTO

Participants will be divided into groups and accompanied by specialized guides who will accompany them to the most emblematic and beautiful places in Oporto.

SIGHTSEEING TOUR – PORTO CASTLES

This is an innovative idea that we are starting this year. It will begin at the historical center of the city, heading towards the Douro River mouth and including tour across some of the beautiful Oporto's beaches and the city of Matosinhos.

WORLD OF DISCOVERIES – INTERATIVE MUSEUM AND THEMATIC PARK

The "WORLD OF DISCOVERIES" is an interactive museum and thematic park that was inaugurated this year. It reenacts the Portuguese navigators' odyssey throughout the immense and unknown world. It is a one of a kind opportunity that you won't want to miss.

DOURO RIVER BY RABELO BOATS & PORTO WINE CELLARS

Rabelo boats are traditional boats that still today transport wine barrels through the Douro River. As you travel around the river in these boats, you will have the opportunity of sight the Oporto city and Vila Nova de Gaia in a privileged perspective. You will also visit the Port Wine Cellars which provides you an unforgettable experience about the port wine, its history and tradition.

THEMATIC DINNERS AND SOCIAL ACTIVITIES

September 21th, 9:00 pm

Dinner at the Faculty of Medicine with the performance of "Tuna Feminina de Medicina do Porto". It will be a great opportunity to get to know a little more about our university's traditions and our culture.

September 22th, 9:00 pm

Closing dinner: semi-formal dinner with the performance of "Grupo de Fados" (Fado Group) from our Faculty of Medicine. This year we chose a different and unique place called "Casa dos Arcos" in Boavista's Avenue (http://www.casadosarcosboavista.com). "The 'Casa dos Arcos' is not just a comfortable and elegant space. It is also a variety of services with the intention of giving you an absolutely unforgettable experience.

Workshops

HEART BEATS Speaker: Joana Pimenta

In order to be a great doctor, our way through knowledge and clinical sense is formed by a series of small steps. Our heart, more than any other organ, is our center, and knowing how to listen to it, and how it works, is one of the most important skills in a doctor. This workshop is about listening, more than earing, and about knowing what is the meaning of each heart beat, about feeling the pulse, and about recognizing signs of cardiac disfunction. This workshop will take place in Serviço de Medicina B,with real patients and that's the reason why it will only accepts inscriptions of FMUP students.

CURIOUS CASES IN HEMATHOLOGY Speaker: Manuel Sobrinho Simões

If you think that hematology is all about monotonous diseases with little semiology, come to this workshop and prove yourself wrong! We invite you to a journey among the most curious clinical presentations in all Medicine. Don't stay behind and bring all your "clinical sense" to diagnose these cases.

HANDS OFF, INFECTION! Speaker: Ana Cláudia Carvalho

Nosocomial infection is one of the most commom problems in clinical pratice with significantly associated morbidity and mortality.
In this workshop it will be demonstrated how to prevent nosocomial infections with simple steps and participants will be given the opportunity to put those skills at test.
Learn how to use personal protective equipment, how to perform correct hands hygiene, how to manipulate cathethers and many other procedures that will help you to deal with your patients. Clinical cases will also be presented to address the importance of an adequate antimicrobial therapy in order to reduce the emergence of multiresistant bacteria.

KEEP IN TOUCH Speaker: Catarina Correia Martins

Alternative medicines are, nowadays, the key to some chronic pathology. Even though, med school does not teach much about this innovative and very interesting area.
Dra Catarina Correia-Martins will show the participants how to examine and discover the origin of the pathology; if it's related with the muscle system, she will show how to treat it. All the treatment is achieved trhough with physical contact, using oour own hands, so she will show us the importance of "keeping in touch".

Workshops

ARTHROSCOPY: HANDS-ON APPROACH Speaker: João Torres

Minimally invasive techniques are no longer the future, they are the present of Orthopedics. Learn the right arthroscopic technique using our models, do not miss this chance to train this valuable technique.

TARGETING THE BRAIN Speaker: Rui Vaz

Deep Brain Stimulation is becoming more and more importante in neurology. Learn the targets, the cerebral pathways involved (thalamus, subthalamic nucleus, globus pallidus) in electrode placement and how to surgically treat the clinical manifestations of movement disorders (Parkinson, Dystonia).

ANTIBIOTICS: A FUTURE FULL OF CHALLENGES Speaker: Daniel Moura

This workshop is about the good old antibacterial therapy. Participants will be presented with clinical cases to choose the initial empiric treatment and to review it later. The reduction in the development of new medicines to solve diseases caused by multiresistant bacteria will also be discussed.

DR. HOUSE: A HIDDEN SURGEON? Speaker: António Taveira Gomes

If you think that surgery is just about beautiful techniques and lots of props, be ready to be amazed! This workshop, led by Surgery Professor António Taveira, will be a collection of appealling clinical cases that will surely get you puzzled.

LAPAROSCIPIC TECHNIQUES Speaker: Hugo Sousa, Tiago Henriques Coelho

Do not miss this unique chance to train your laparocopic skills. Ready, steady hands and GO! Good luck!

CSI: CRIME SCENE INVESTIGATION Speaker: Prof. Teresa Magalhães

Feel a CSI with one of our best doctors in the field figuring out crimes behind dead bodies. Be ready to discover reality behind the scenes.

INTERVENTIONAL RADIOLOGY Speaker: Miguel Madureira

Not everything is black and white in radiology and in life. This workshop will introduce you to the brave new world of interventional radiology in a very practical way. A great chance to train your skills in the surgical radiology field.

Workshops

TECHNIQUES IN GASTROINTESTINAL ENDOSCOPY / NEW ENDOSCOPY APPROACHES Speaker: Pedro Pereira

This session will not only enhance the knowledge about techniques in gastrointestinal endoscopy as well as introduce some new endoscopy approaches.

WHAT'S BEHIND SEX? Speaker: Manuel Esteves

Once a taboo, sexology is rapidly evolving into one of the main topics of research in science. Learn all about the mecanisms behind the sexual attraction in this session.

U, THE ICU TEAM Speaker: Jorge Tavares, Marcos Gouveia, Carla Sá Couto

In this workshop you're encharged: gather your team, get all your knowledge ready and let's simulate an intensive care unit! The Anesthesiology Department prepared this extremely interactive workshop in cooperation with the Medical simulation center in which they will use a very convincing bionic model to simulate a medical emergency that you will handle.

MINOR SURGERY Speaker: José Costa Maia

Surgery in one of the most important areas in medicine, and despite the title of this workshop includs the word "minor", what will be teached in this ws is the major skill of any doctor and surgeon: suture.
It will be monitored by Prof. Dr. José Costa Maia, director of surgery departemente of CHSJ.

SPINE SURGERY Speaker: Paulo Pereira

Be part of this unique experience: in this workshop you will be able to watch a live surgery of the spine with one of the Europe's leading spine neurosurgeons, Dr. Paulo Pereira.

SPLINTS AND CASTS Speaker: João Torres

The orthopedics session is back to show you all about the handling of common fractures. In a very relaxed environment, you will be able to experience and learn the correct techniques of splinting and casting a limb. If you choose this workshop, you are "cast" to have fun!

Workshops

EYE SURGERY Formador: Manuel Falcão

Did you ever wonder what it takes to fix a lazy eye? With the help of Dr. Manuel Falcão, you will be guided step by step troughout a surgery to correct that condition. Don't be lazy, don't miss this workshop!

INTERVENTIONAL RADIOLOGY Formador: Miguel Madureira

Not everything is black and white in radiology and in life. This workshop will introduce you to the brave new world of interventional radiology in a very practical way. A great chance to train your skills in the surgical radiology field.

INVASIVE HEMODYNAMIC EVALUATION Formador: Manuel Pinto

A unique chance of experiencing life in a physiology lab. In this workshop you will be able to learn and execute techniques of hemodynamic evaluation in mice.

Abstract Book - Index

Plenary Session

Parallel Oral Sessions

ONCOLOGY & MOLECULAR BIOLOGY

• PS 167: Agnieszka Sarnecka – Is the process of entosis a way to escape from chemotherapy?

• PS 184: João Carlos Crispim da Costa da Encarnação – Is butyrate and irinotecan combination a new therapeutic approach for colon cancer?

• PS 197: Joana Margarida Verdasca Jorge – Methylation pattern in myelodysplastic syndrome – comparative study between bone marrow and peripheral blood

• PS 202: Nuno Simões Costa - Buparlisib, another step in the quest to cure haematological malignancies.

• PS 220: Ana Isabel Cardoso Soares – Reproductive ageing and antioxidants: effect in uterine function

SURGERY

• PS 66: Maral Namdari – *Compersion of astigmatism and visual function before and after refractive surgery by two methods (wavefront-guided ablation PRK and aspheric ablation)*

• PS 122: Sárvári Katalin – *Role of pre- and postconditioning to avoid noxious oxidative stress induced by pneumoperitoneum*

• PS 152: Marcin Piejko – *Does implantation of Adipose Stem Cells on the granulation tissue increase chance for healing large tissue damage? A case report of patient with recurrence perianal fistula treated by the cell base therapy.*

Poster Presentations

PHYSIOLOGY & IMMUNOLOGY

• PS 121: Marta Krzywon – Critical care after allogeneic hematopoietic stem cells transplantation in pediatric patients: case control study.

• PS 123: Rada Jeremic – Effects of acute high-intensity exercise on plasma IL-17 concentration in elite athletes

• PS 131: Milica Djoric – Analysis of the association between rs3024505 polymorphism and IBD in Serbian population

• PS 132: Daniel Martinho Ferreira Dias – Positive and Negative Regulation of Toll-like receptors signalling pathways in innate immune responses

• PS 181: Ana Filipa Faim Moço – Rat corneal endothelium primary cell cultures

• PS 191: Diana Raquel Santos Ribeiro – Urocortin-2 Improves Right Ventricular Function In Pulmonary Arterial Hypertension

• PS 203: Bárbara Silvana Alves Silva – Right ventricle pressure overload-induced hypertrophy is attenuated by neuregulin-1

• PS 208: Carolina Isabel Maia Rocha – Molecular mechanisms underlying the beneficial effects of neuregulin-1 in pulmonary arterial hypertension

• PS 210: Katarzyna Wzorek – Recombinant human growth hormone (rhGH) in Prader-Willi Syndrome therapy- benefits and adverse events.

• PS 216: Ewa Tobór – The significance of glucokinase inactivating mutations in the regulation of carbohydrate metabolism - clinical characteristic of patients with MODY 2

• PS 222: Gonçalo Sampaio de Almeida – Brain oxymetry and cardiac output during sleep in low FiO2 using an altitude simulator.

NEUROSCIENCES

ONCOLOGY & MOLECULAR BIOLOGY

INTERNAL MEDICINE

PLENARY SESSION

QUALITY CONTROL OF MRNA IN THE NUCLEUS: SAFEGUARDING CELLS FROM DISEASE-CAUSING PROTEINS

Alves-Vale, C., Vaz-Drago, R., Custódio, N., Carmo-Fonseca, M.
Instituto de Medicina Molecular, Faculdade de Medicina da Universidade de Lisboa, Portugal

AIM

Understand the mechanisms of nuclear mRNA quality control operating in human genetic diseases.

INTRODUCTION

Human cells have advanced mechanisms to recognize abnormal mRNA molecules and prevent them from being translated into disease-causing proteins. These control mechanisms modulate the severity of the phenotype of many genetic diseases. Beta-thalassemia, a hematological genetic disease, is caused by mutations along the beta-globin gene and it is one of the best characterized diseases in which the phenotype can be modulated by mechanisms of quality control of gene expression. When compared with healthy cells, there are lower levels of beta-globin mRNA in cells containing mutations similar to those of beta-thalassemia patients. One of the best described mechanisms of quality control of gene expression is the degradation in the cytoplasm of transcripts with premature termination codons, by nonsense-mediated decay. However, there is increasing evidence that the quality of the mRNA is also assessed at the nuclear level to prevent defective mRNAs from reaching the cytoplasm for translation. In this work we studied if reduction of transcription is one of the nuclear mechanisms used by the cell to prevent the expression of mutant genes and we investigated if proteins involved in cytoplasmic mRNA quality control also participate in nuclear mRNA surveillance.

METHODS

As a model system, we used inducible stable HEK-293 cell lines with a single copy of either the wild-type (βWt) or a mutant (βMut) human beta-globin gene. We performed FISH and RT-qPCR to evaluate the levels of beta-globin RNA in these cells. To determine if the mutation affects transcription we performed run-on assays with quantification of newly transcribed RNA molecules by RT-qPCR. To evaluate if the nonsense mediated decay factors UPF1 and SMG6 have a role in the nucleus, we performed knockdown of these proteins by RNA interference and quantified by RT-qPCR the levels of the beta-globin transcripts in the chromatin-associated RNA fraction.

RESULTS

The analysis of the run-on assay revealed that in mutant cells the levels of nascent beta-globin RNA were significantly lower comparing with wild-type cells. This result corroborates the FISH data. Our findings support the existence of a feedback mechanism to the transcription machinery. The knockdown of UPF1 increased the pre-mRNA levels of beta-globin associated with chromatin in both cell lines. However, this effect was not shared by SMG6. Furthermore, we also assessed that UPF1 and SMG6 regulate each other's levels.

CONCLUSION

With our work we found that the transcription of the beta-globin mutated gene is reduced, what supports the existence of a regulatory feedback to the transcription machinery in order to decrease the levels of mutant transcripts and, consequently, try to avoid the production of disease-causing proteins. Furthermore, we also uncovered a novel role for UPF1 in the nucleus, in addition to the well-established role in the cytoplasm. Nevertheless, further work is required to better understand both the feedback mechanism to transcription and the potential of UPF1.

PS195

EFFECTS OF ADIPOKINES IN CARDIAC STRUCTURE

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AIM

This project aimed at investigating the potential role of adipokines in cell proliferation and collagen production by cardiac fibroblasts and evaluating the crosstalk between epicardial adipose tissue and the myocardium.

INTRODUCTION

Heart failure (HF) represents a major and growing problem in the developed countries and several risk factors, such as obesity, are associated with its development. Obesity is defined as a pro-inflammatory state associated with an increased secretion of factors, named adipokines, which regulate the function of several organs and tissues. Epicardial adipose tissue segregates adipokines that can act in a paracrine and vasocrine manner on the myocardium, exerting direct effects in fibroblasts and cardiomyocytes.

METHODS

Experimentally, atria tissue from 25th week old ZSF1 lean (ZSF1 Ln, n=11) and ZSF1 obese (ZSF1 Ob, n=11) rats was used for the isolation of cardiac fibroblasts, as well as for obtaining conditioned medium from pericardial adipose tissue. Fibroblasts were cultured separately with apelin (100 nM) and adiponectin (10µg/ml). After 48h, BrdU assays and Sirius Red staining were performed in order to evaluate the effect of those adipokines in cell proliferation and collagen production, respectively. Moreover, organotypic cultures were obtained from cardiac explants from 7 day-old Wistar rats and incubated with conditioned medium from pericardial adipose tissue of obese and lean groups. After 24h of incubation, fibrosis and cross-section area of hematoxylin-eosin stained cardiomyocytes were assessed.

RESULTS

Incubation with apelin and adiponectin led to a significant increase in fibroblasts' proliferation in both groups ($p=0.0496$). In ZSF1 Ln, apelin induced a significant decrease in collagen secretion, while in ZSF1 Ob it increased collagen secretion and production ($p=0.0054$). Adiponectin significantly reduced collagen synthesis in both groups and decreased collagen secretion in ZSF1 Ln ($p<0.001$). Regarding the organotypic cultures, pericardial adipose tissue secretome from obese rats triggered a significant increase in fibrosis deposition (3.48%±1.51% vs 4.79±1.53%, $p<0.05$) and in the cross-section area of cardiomyocytes (100.7±18.98 µm2 vs 111.25±24.02µm2, ($p<0.05$), compared with the secretome from lean animals.

CONCLUSION

Adipokines produced by adipose tissue depots from obese animals seem to modulate the cardiac structure, through changes in extracellular matrix components and cardiomyocytes, features typically related to the appearance of diastolic dysfunction.

MELANOCORTIN SYSTEM AND NEUROPEPTIDE Y IN THE DYSREGULATION OF ENERGY HOMEOSTASIS IN SHR RATS

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AIM

We aimed to study the potential role of the major anorexigenic or orexigenic hypothalamic neuropeptides in dysregulation of body weight in spontaneously hypertensive rats (SHR).

INTRODUCTION

The SHR strain has been developed for the research of essential hypertension (Okamoto and Aoki, 1963). By the 4-6th week of their life, in these rats develop hypertension, which rises further during the course of aging. The hypertension of this rat strain may be prevented by chronic caloric restriction (Dolinsky et al., 2010). Their sympathetic tone is enhanced, their calorie-intake and body weight (BW) values are lower than those of age- matched controls (Oliveira et al., 2009

METHODS

Food intake (FI) of adult male SHR rats and normotensive Wistar rats (NT) was recorded in an automated FeedScale system upon intracerebroventricular injection of NPY (5 µg) or a MC agonist (5 µg alpha-melanocyte-stimulating hormone, alpha-MSH) or during central infusion of a MC antagonist (HS024, 1 µg/h, 7 days). Using immunofluorescent labeling we determined the number of alpha-MSH producing cells and also performed the quantitation of alpha-MSH and NPY specific signal density (SSD) in the arcuate nucleus of the hypothalamus.

RESULTS

The alpha-MSH-injection reduced spontaneous night-time FI more efficiently in SHR than in NT rats. HS024 started to increase daily FI and consequently BW in the NT group already from the 1st, in SHR animals only from the 3rd day. In contrast, responsiveness of day-time FI to NPY injection was found to be suppressed in SHR. We did not find difference between SHR and NT rats in terms of alpha-MSH-producing cell counts and NPY SSD in the arcuate nucleus, but the SSD of alpha-MSH immunosignal was significantly higher in SHR rats than in NT animals.

CONCLUSION

Our in vivo and also in vitro results suggest higher MC-production and -responsiveness and lower NPY-responsiveness in SHR rats, that may contribute to the explanation of the dysregulation of their BW.

TUBERCULOSIS RE-SCREENING IN PATIENTS UNDER BIOLOGICAL THERAPY

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AIM

Evaluate the rate of active tuberculosis and immunodiagnostic conversions among patients under biological therapy

INTRODUCTION

Biologic therapies are a known risk factor for tuberculosis (TB). Portuguese guidelines recommend that all patients are screened for TB, prior to starting biologic agents (2006 guidelines) and annually thereafter for those with a negative screening (2012 guidelines). TB screening comprises a medical history, chest radiography, tuberculin skin test (TST) and interferon-γ assay (IGRA). Patients with past non-treated TB, recent TB exposure or a positive TST or IGRA are proposed for preventive therapy after exclusion of hepatotoxitcity risk.

METHODS

All patients screened for TB, prior the start of biologic therapy, at a TB reference centre between 2008 and 2012 were identified. Data on the starting of biologic therapy of the screened patients was questioned to the assistant physician. Data from re-screening was collected from the clinical files – if the re-screening was performed and its results. Exclusion criteria: unavailable information regarding the start of biologic therapy.

RESULTS

From the 350 patients that performed the baseline screening, we received information regarding the initiation of biologic therapy on 183 patients – 115 patients started biological therapy (45 had (39,1%) psoriasis, 21 (18,3%) Crohn's Disease, 21 (18,3%) Multiple sclerosis, 12 (10,4%) ankylosing spondylitis, 8 (7%) rheumatoid arthritis and 8 (7%) other pathologies). The baseline screening was positive in 52/115 (45,2%) patients – 50 were proposed for preventive therapy (two had hepatic risk for toxicity). Among those who started preventive therapy, 4 (8%) had hepatotoxicity that rapidly resolved without hospitalization or need to interrupt prophylaxis; 1 (2%) had dermatological toxicity to isoniazid and rifampicin regimens; 1 (2%) abandoned treatment on the first 2 months without any adverse event. Among the cases that screened positive at baseline, no cases of active TB were reported during follow-up. Among the 63 patients with a negative baseline screening, 2 patients developed active TB (one with adalimumab and the other with infliximab) more than one year after the starting of biologic therapy. Re-screening was performed in 26 (41%) – 5 (19,2%) had TST conversion, one of which with indeterminate IGRA. No one had IGRA conversion.

CONCLUSION

The rate of latent TB at the baseline screening was higher than expected, re-enforcing the need for baseline screening. Preventive therapy was well tolerated, with good compliance and no significant adverse events. None of the patients who screened positive developed active TB. Only 41% of the patients with negative baseline screening were re-screened at the reference centre, pointing to a lack of compliance to this recommendation. Larger studies, across the country should be designed in order to evaluate the efficacy of this re-screening strategy for all. We should be able to better understand what risk groups should be re-screened. Both cases of active TB suggest new infection which cannot be avoided by annual re-screening, but only by an increased awareness of the clinicians and patients about exposure to TB along the biologic therapy.

DEPRESSION AS A PREDICTOR OF PANCREATIC RESECTION AND IN-HOSPITAL MORTALITY IN PATIENTS WITH PANCREATIC NEOPLASMS

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AIM

To assess if depression predicts pancreatic resection in patients with pancreatic neoplasm

INTRODUCTION

Pancreatic resection is the elective treatment for pancreatic neoplasm. However, patients who undergo this treatment may represent an in-hospital mortality of 5 to 8%. This mortality can be predicted by demographic factors such as age or sex, clinical factors such as TNM staging, comorbidities, diagnosis or treatment; and hospital factors such as hospital volume. Using administrative data, variables such as TNM staging are not included, but other groups have already studied pancreatectomy mortality using only this data.

METHODS

Records were queried from the National Hospitalisation Database (NHD) provided by the Health System Central Administration (ACSS) for 2003-2010, comprising all Portuguese public hospitals. We included in-patients with a principal diagnosis of pancreatic cancer, using ICD-9-CM codes 157.0, 157.1, 157.2, 157.3, 157.8 and 230.9,. Primary outcome measure was pancreatic resection coded as 52.51, 52.53, 52.6, 52.7, 52.52 or 52.59 as procedural ICD-9-CM codes. Secondary outcome measure was in-hospital mortality. Predictor variables were demographics (sex and age), comorbidities (Charlson index and depression, coded as 296.2, 296.3 300.4 and 311) as secondary diagnoses, hospital type (central or peripheric,) annual hospital volume (<3, 3-8 and >8 per year) and pancreatectomy type (only used to analyse in-hospital mortality as outcome). Descriptive statistics and logistic regression were performed using IBM SPSS Statistics 21.

RESULTS

Among the total 12,001 patient discharges with pancreatic neoplasm, 308 (2.6%) had a comorbid diagnosis of depression. Composite pancreatic resection rate was 10.3% and in-hospital mortality rate in patients, who underwent this surgery, was 14.1%. In depressed patients, these rates were from 21.7% and 1.8%, respectively.

CONCLUSION

Contrarily to other studies, we found that depressed patients with pancreatic neoplasm were more likely to undergo pancreactomy. Moreover, in these surgical and oncologic patients, depression might be a protective factor to predict in-hospital mortality. Low depression prevalence may be due to undercoding or underrecognition, possibly leading to bias. However, these bias might be towards (depression is not a priority; symptoms overlapped) and away from the null hypothesis (selected only more severe cases of depression) at the same time.

PARALLEL ORAL SESSIONS

CHANGES OF PARA- META- AND ORTHO-TYROSINE LEVELS IN SERUM AND URINE OF SEPTIC AND BURNED PATIENTS

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AIM

The aim of the study was to assess if the different tyrosine isoforms can distinguish infective and non-infective SIRS.

INTRODUCTION

Systemic Inflammatory Response Syndrome (SIRS) can develop due to several different conditions (burn, infection). Nowadays it is difficult to determine whether the origin of the condition is infectious or not. Both sepsis and non infectious SIRS is associated with oxidative stress that can result in the production of three tyrosine isoforms, para-, meta- and ortho-tyrosine (p-, m-, o-Tyr) which can be detected in the blood and the urine. Based on our previous data leukocyte antisedimentation rate (LAR) shows reliably the presence of inflammation.

METHODS

12 burned (TBSA>20%) (Group SIRS) and 26 septic patients (Group Sepsis) were involved in our prospective study. Blood samples were taken on admission and in the morning of the next four consecutive days. PCT and creatinine levels were measured at the same time similarly to LAR which was calculated from the one-hour gravity sedimentation of white blood cells. Urine has been collected in each 24 hours. Serum and urinary m-, o-, p-Tyr levels were determined using reverse phase-HPLC. Non-parametric tests were used for statistical analysis since the distribution of values was not normal.

RESULTS

In septic patients serum p-Tyr levels showed a significant day-by-day elevation ($p=0.001$) the difference reached the level of significance on day 5 compared to the SIRS Group ($p<0.05$). Serum o-Tyr and m-Tyr levels did not show significant changes during the study interval. Urinary m-Tyr/creatinine ratios showed a decreasing tendency ($p=0,017$) and the difference was significant on days 1-2 ($p<0.01$) and 3-5 ($p<0.05$), between the two groups. Urinary m-Tyr/creatinine ratios regarding the presence of infection demonstrated a similar predictive value compared to PCT. The elevated LAR ($p<0.001$) confirmed the development of SIRS in both groups.

CONCLUSION

Based on our results, urinary m-Tyr levels may be a useful parameter in establishing the sepsis diagnosis.

PRAXIS APPLICATION, A NEXUS BETWEEN CLINICAL UNITS AND UNIVERSITY.

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AIM

New teaching strategies and implementation of management systems assessment and development.

INTRODUCTION

The transversality of training and his practical component are given much importance in the Medicine degree and the Bologna plan. The need to improve the current system of clinical practice was noted by UGR's teachers responsible, and SAS's clinicians responsible. Improvements in clinical practice are focused on the development of these in the centers by establishing specific learning objectives, and how to evaluate and apply the knowledge acquired by students during clinical practice. The PRAXIS application arises in order to manage and coordinate clinical practice in undergraduate studies satisfying these needs.A complete and individualized learning path map with detailed skills acquired during the studies will be made available to students before they graduate.The accreditation of technical training and preparation for the implementation of certain procedures by students will be integrated into the European Diploma Supplement by this document.

METHODS

Adapting clinical practice to the requirements of the new European Higher Education Area, EHEA is the reason I was born the PRAXIS application. PRAXIS application is a multiplatform computing tool for managing the practice place, acquired competencies, and indicators for achieving each. Assessment of the level of competences acquisition and evaluation of clinical tutors teaching is another option on the PRAXIS application. PRAXIS is available on SAS internal network for health professionals (DRAYA's identified access) and UGR network for students, teachers, and administrative staff and services (UGR network identified access). A practices schedule, with location and competences that are offered for each practice will be provided to students by PRAXIS. Calendar of practice, list of students assigned to each day, the skills associated with the role will be provided to clinical tutors by PRAXIS. First, the assessment of the skills acquired by the student with specific indicators for each end of the practice schedule will be made by clinical tutor. their qualifications and evaluation of clinical tutors teaching then be accessible to students. The degree of clinical training to work in healthcare settings can be credited with the competency assessment.

RESULTS

PRAXIS implementation is being done in the clinical units of hospitals in Granada. The performance of the PRAXIS application has been tested in some subjects during the year 2013-14. The results have been very positive. A high degree of satisfaction of students and clinical tutors have been achieved. The students' competences lists are available for incorporation into their academic curriculum itinerary. Necessary modifications to improve PRAXIS performance for the academic year 2014-15 have been allowed by this first contact of students and clinical tutors with PRAXIS. Modifications will be in order to get a better adaptation to the needs of students an clinical tutors.

CONCLUSION

Adaptation of Medicine Degree Requirements to EHEA requirements and the improve of coordination between clinical units (SAS) and teachers responsible (UGR) will be permitted by this software. In addition, the mapping of individual skills of each student, the assessment of the technical ability of students and evaluation of clinical tutors teaching will be possible with PRAXIS.

LEGALIZATION OF ABORTION: HOSPITALIZATIONS RELATED TO LEGALLY INDUCED ABORTION

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AIM

We aim to determine the frequency and profile hospitalizations among cases of legalized induced abortions on public hospitals in Portugal.

INTRODUCTION

Portugal is one of those countries that have recently liberalized abortion. Before this measure, illegal abortions caused several fatalities, remaining unknown their exact number. Statistic data prove that since 2007 induced abortion has largely increased in Portugal and maternal death due to clandestine abortion has fallen. (1,2) After a February 2007 referendum, abortion was legalized in Portugal on April 10th 2007, allowing the procedure to be done until the tenth completed week for any indication and being all costs supported by the National Health Service. Though it is known that prior to 2007 most abortions took place either outside the country or illegally, and even though relevant research has been conducted, we don't have complete and reliable data about the real number and the complications of the procedure. Since 2007, induced abortions must be registered online and sent to DGS, research on legal abortions has been done and several scientific meetings were held.(3) However, all this does not and cannot cover all the relevant information, which makes us aware of the much we still have to learn about the new Portuguese reality and that's why we truly believe in the importance of this study.

METHODS

All cases coded with ICD-9-CM 635.xx were selected from a database provided by the ACSS – Administração Central dos Serviços de Saúde related to all the hospitalizations reported on the public hospitals of Portugal. The code 635.xx assembles all the cases of legally induced abortion executed until the 10th completed week. The data obtained referred to all the admissions (hospitalizations) in the public hospitals of Portugal occurred from 2000 to 2010. Demographic variables used were patients' age group, patients' residence by NUT II regions (mainland Portugal is currently divided in five NUT II regions: North, Central Region - from here onwards referred as "Center -, Lisbon, Alentejo and Algarve)13, hospital localization, length of stay (days).

RESULTS

A total of 16128 women, with a correspondent diagnosis (DDX1 to DDX20) matching the code 635(legally induced abortion - ICD-9-CM) were included in our study. The cases reported were registered between 2000 and 2010 where a substantial increase was seen after 2007 (mean increase of 673,3 cases per year). However, the increase was less substantial between the year 2009 to 2010(where the value was 79 cases per year) Hospitalizations vs Total number of abortions However when we compare the number of hospitalizations coded with 635(legally induced abortion) and the total number of abortions performed on public hospitals, provided by INE(National institute of statistics) we may see that the proportion of hospitalizations has diminished substantially since 2005(1,21 hospitalization/case of abortion), stabilizing in 2009 (0,2 hospitalization/case of abortion). Legally induced abortion and birth rate The relation between the number of births and the number of legally induced abortions coded in our data is shown below. As it can be seen, from 2000 until 2006 a small increase (mean of 63,74 cases coded with 635/100 000 newborns/year) was registered, but when compared with the mean annual variation of the ratio from 2006 until 2010(673,24 cases coded with 635/100 000 newborns/year) we may see that since the legalization of the procedure the number of cases coded had a 10 time augment. Age The mean age of women who were submitted to legally induced abortion and needed hospitalization before the liberalization of the procedure was 30,76 years old, as since 2007 a shift has been verified where the mean age has

LEGALIZATION OF ABORTION: HOSPITALIZATIONS RELATED TO LEGALLY INDUCED ABORTION

Pinho Gonçalves M.
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diminished and stabilized in 29,38 years old. Regions A differentiated analysis was executed to determine the frequency of cases on each NUT'sII region. The regions evaluated were: North, Lisbon, Center, Alentejo and Algarve (when referring the hospital), where Lisbon had the highest percentage of LIA performed (54,7%), followed by North (with 26,5%), then Center (11,2%), Algarve (4,6%) and Alentejo (2,9%).

CONCLUSION

Our study approaches a period that shows the evolution of legally induced abortion in two different periods in Portugal, one before the liberalization of abortion (that occurred in 2007) and the other after the liberalization. From 2000 to 2006 a constant but slow augment on the number of hospitalizations related to legally induced abortion was verified (from 637 to 963 cases coded w/ 635 ICD-9-CM), however in 2007 with the approval of the law we may see that the number of cases grew from 2007 until 2009 (1449 to 3577 cases) a much more significant increase that is related with the liberalization and a much more availability on the assessment to induced abortion by public hospitals. In 2010 stabilization on the total number of hospitalizations is noticed once the numbers from 2009 and 2010 are similar (3577 compared to 3656) which follows what happened on many developed countries some years after the legalization, where the total number of abortions stabilized.(4) Comparing the number of abortions registered on INE with the total amount of hospitalizations related with legally induced abortion, we have seen that since the approval of the law, the ratio between the two variables has diminished from 1,39 in 2003 to 0,20 in 2009 which may be due to the majority of cases reported before the approval of the law being of more severity and requiring hospitalizations more often than the rest of cases since the liberalization. Accessing the values of the number of births in Portugal and comparing them with our data allows us to understand the impact at a demographic level of the approval of the law in 2007. As we can observe the ratio of cases coded with 635 / 100 000 newborns has increased from a value of approximately 913 in 2006 to 3595 in 2009,this may be due to the diminished birth rate registered in Portugal throughout the accessed years but also because of the increased number of abortions. The mean age of women who were hospitalized due to the procedure that follows legally induced abortion varied before and after the approval of the law. Before 2007 the mean age was 30,87 years old and after it was equal to 29,38. The reason of those values may be found on the increased number of younger women that started to replace the illegal induced abortion before 2007 by the legal one which as fewer risks and is totally supported by national health system.

CORRELATIONS OF OSTEOPROTEGERIN WITH CARDIOVASCULAR RISK FACTORS IN A RISK POPULATION

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AIM

The aim of our study was to determine the relationship between OPG and cardiovascular risk factor in a risk population represented by postmenopausal women.

INTRODUCTION

Osteoprotegerin (OPG) is a molecule involved in both bone metabolism and arterial calcification. Even though in experimental studies OPG had protective vascular effects against wall calcification, in clinical studies is was associated with prevalence and severity of cardiovascular disease. The role of OPG in vascular pathology is still a subject of debate.

METHODS

Circulating OPG was measured in 100 postmenopausal women without overt cardiovascular diseases but with multiple cardiovascular risk factors. Linear correlations and multiple regression were used assess the relationship between OPG and various cardiovascular risk factors.

RESULTS

OPG correlated with age (r=0.22,p=0.01), years since menopause (r=0.23,p=0.01), abdominal circumference (r=0.24,p=0.01), BMI (p=0.25,p=0.002), C-reactive protein (r=0.24, p=0.01). OPG was also increased in patients with hypertension compared with those without hypertension (p=0.04) and in patients with diabetes compared with those without diabetes (p=0.03). In multiple regression analysis the independent predictors of increased OPG were age (ÃŸ=0.19, p=0.01) and C-reactive protein (ÃŸ=0.20,p=0.01). 20% of the patients were diabetics, 36% were obese and 55% had hypertension.

CONCLUSION

Circulating OPR positively correlated with classical cardiovascular risk factors and with C-reactive protein, a mediator of systemic inflammation. We may speculate that OPG may be a marker of increased cardiovascular risk in postmenopausal women.

EFFECTS OF ESTROGEN RECEPTOR AGONISTS IN THE EXPRESSION OF ESTROGEN RECEPTOR ALPHA IN THE FEMALE MEDIAL PREOPTIC NUCLEUS

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AIM

The aim of this work was to study the effect of the administration of the agonists of estrogen receptor (ER)α and ERβ on the total number of ERα-immunoreactive neurons in the medial preoptic nucleus of female rats.

INTRODUCTION

The medial preoptic nucleus (MPN) is a sexually dimorphic group of neurons located in the preoptic area that is important for the integration of olfactory and hormonal stimuli necessary for the coordination of sexually differentiated functions and behaviors. The MPN expresses abundantly both subtypes of estrogen receptors (ERs), ERα and ERβ [1] whose activation is able to modulate MPN physiological and behavioral responses [2]. Very few studies have investigated the effects of gonadal steroids in the expression of ERα in the MPN of female rats being most of the knowledge about this subject obtained by measuring mRNA ERα levels.

METHODS

3 months-old female ovariectomized Wistar rats were injected with oil, estradiol-benzoate (EB), the ERα agonist, PPT, the ERβ agonist, DPN, and the combination of both agonists PPT+DPN. Rats were sacrificed by intracardiac perfusion of a fixative solution and their brains were sectioned and processed for immunohistochemistry using a rabbit anti-ERα antibody. The total number of ERα-immunoreactive MPN neurons of female rats was estimated by using a stereological method – the optical dissector. The results were statistically analyzed using one-way analysis of variance (ANOVA) followed by post-hoc Tukey's HSD test.

RESULTS

EB treatment resulted in a significant reduction in the total number of ERα-immunoreactive neurons in the MPN that was also seen after the administration of PPT and PPT+DPN. The administration of DPN induced a higher decrease in the total number of ERα-immunoreactive MPN neurons comparatively to all other treatment groups.

CONCLUSION

The results demonstrate that the activation of the ERα induces the down-regulation of the receptor, which results in a decrease in the total number of neurons that express the receptor. The sole activation of the ERβ further decreases the total number of neurons that express the ERα, corroborating the repressive action of ERβ over ERα [3]. The fact that there is no difference in the total number of ERα-immunoreactive neurons in the MPN of animals injected with PPT and PPT+DPN, suggests that the repressive action of ERβ is inhibited when both ERs are simultaneously activated. In conclusion, this study contributes to the understanding of the influence of estradiol, and each ER agonist on the total number of neurons expressing ERα in the MPN, an area involved in important behavioral answers.

THE ROLE OF AKT SIGNALLING PATHWAY IN THE TOXIC EFFECT OF EXTRACELLULAR ASYN, IN VITRO

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AIM

The aim was to investigate the role of insulin-dependent Akt signalling pathway activation in neuronal dammage caused by extracellular secreted ASYN.

INTRODUCTION

ASYN is regarded as an essential mediator of Parkinson's disease pathogenesis. Although ASYN is considered as exclusively intracellular protein, recent data suggest it can be detected extracellularly. Deregulation of the PI3K/Akt signalling pathway is observed in neurodegenerative diseases including Parkinson's disease. Insulin-dependent Akt signaling pathway activation plays an important role in CNS.

METHODS

Experiments were conducted in all-trans retinoic acid differentiated human neuroblastoma SH-SY5Y cells stably expressing wt ASYN (intracellular ASYN), as well as in SH-SY5Y cells exposed to secreted ASYN, present in conditioned medium (CM), collected from ASYN-overexpressing cells (extracellular ASYN). The production of ASYN, its presence in conditioned medium and activation of Akt (pAkt) were monitored using immunoblotting. The cell viability was assessed using crystal violet assay.

RESULTS

The crystal violet assay demonstrated decrease in cell number after 6 days of differentiation with all-trans retinoic acid and applying conditioned medium (31,1% ± 3,4 compared to control untreated cells (100%), $p<0,01$). Western blot analysis showed decrease in phosphorylated, active Akt form (pAkt) after applying conditioned medium. Cell viability analysis revealed significant increase in cell viability treated with CM after incubation with insulin (from 47,6% up to 62,3%, $p<0,01$).

CONCLUSION

Extracellularly secreted ASYN induce cell death of differentiated SH-SY5Y cells, possibly via the PI3K/Akt signalling pathway inhibition. Incubation with insulin leads to an increase in cell viability, suggesting that insulin could be an intriguing strategy in modulation of Parkinson's disease.

EFFECT OF SELECTIVE REMOVAL OF CHOLINERGIC AFFERENTS IN THE RETROSPLENIAL CORTEX ON THE PERFORMANCE OF RATS IN AVERSIVELY MOTIVATED ACTIVE AVOIDANCE TEST

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AIM

The goal of this study was to evaluate the role of the cholinergic innervation of the retrosplenial cortex in the active avoidance behavior of rats

INTRODUCTION

Despite the cytoarchitectonic organization of the retrosplenial cortex (RC) and its anatomical connections with other brain regions are well characterized, very little is known about its functional role. Even less is known about the specific contribution of cholinergic afferents to the behavioral functions of this cortical area. Yet, cholinergic neurotransmission is believed to play a critical role in neuronal plasticity and various behavioral processes. Prior studies showed that bilateral excitotoxic lesion of the RC produces severe impairments in the acquisition of the active avoidance response in rats, regarding both response latency and correctness. In this study, we decided to evaluate the effect of a selective removal of cholinergic afferents from the RC on the performance of rats on the very same task.

METHODS

Adult male Wistar rats were used in this study. Selective removal of retrosplenial cholinergic afferents was achieved by bilateral stereotaxic infusions of the conjugated immunotoxin 192 IgG-saporin into RC. One month later, the rats were trained on a two-way shuttle-box active avoidance task. Retention test was performed 24h later. Consequently, animals were perfused and their brains were processed using standard histological procedures. The brain sections were immunostained for vesicular acetylcholine transporter protein (VAChT) and the degree of the cholinergic lesion in each animal was assessed by counting VAChT-positive fiber varicosities using image analysis software Fiji. The location of the RC and the boundaries between its layers were determined in Nissl-stained sections using the rat brain atlas of Paxinos and Watson.

RESULTS

Although rats that received 192 IgG-saporin were able to learn the active avoidance task, their performance was significantly inferior to that of sham-operated controls (60% of correct responses vs. 90% of correct responses in control rats; $P<0.05$). Furthermore, 24h later, control rats still showed 90-95% of correct responses, while rats treated with immunotoxin returned to the baseline level of performance ($P<0.001$). Postmortem histological analysis has revealed that bilateral intracortical infusions of 192 IgG-saporin produced dramatic loss of VAChT-positive fiber varicosities in the infusion areas, reaching 75-80% in the retrosplenial layers I and V. The densities of cholinergic varicosities in RC positively correlated with the performances of rats on the retention test.

CONCLUSION

The present findings support the notion that RC is strongly implicated in instrumental behaviors, such as discriminative avoidance. Cholinergic activity in the RC, originating in the medial septum/diagonal band of Broca nuclei, appears to be important, but not determining factor for the encoding of consistent stimulus-response associations. However, consolidation of these associations is critically dependent on the structural and functional integrity of the septo-retrosplenial cholinergic pathway.

AGE-RELATED ALTERATIONS IN ACUTE CENTRAL CORTICOTROPIN EFFECTS REGARDING THE PARAMETERS OF ENERGY BALANCE

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AIM

We hypothesized that anorexigenic and hypermetabolic responsiveness to acute corticotropin-releasing factor (CRF) administration change with different dynamics in male and female Wistar rats during aging.

INTRODUCTION

In the background of middle-aged obesity and aging anorexia complex age-associated alteriations in the catabolic (anorexigenic, food intake (FI) reducing; metabolic rate (MR) enhancing) and anabolic (FI- increasing, MR-reducing) peptide systems are assumed, since they also appear in other mammals. CRF is an important central metabolic mediator. Our previous studies revealed age-related shifts in the responsiveness to intracerebroventricular (ICV) CRF infusion in male Wistar rats: anorexigenic effects were especially pronounced in the oldest, hypermetabolic response was detected in the youngest and oldest rats. Middle-aged rats did not show catabolic responsiveness to CRF. Responsiveness to acute central melanocortin agonist and acute periferal cholecystokinin (CCK) administration on energy homeostasis show similar age-related patterns. Responsiveness to other catabolic mediator administrations (e.g. to those of ICV CCK injections) continously decrease with aging.

METHODS

The effects of ICV CRF injections on energy balance [FI, body weight (BW), oxygen consumption (VO2), core temperature (Tc)] were analysed in male and female Wistar rats of different age-groups: young adult, younger/older middle-aged, aging and old (3-, 6/12-, 18- and 24-months, respectively). Anorexigenic responsiveness (0.3 ug) was tested during 120-min re-feeding following 24-h fasting. Thermoregulatory analysis (1 ug) was performed using calorimetry for VO2 complemented by thermocouples recording Tc and tail skin temperature indicating heat loss.

RESULTS

ICV CRF injection suppressed FI, increased VO2 and Tc in young rats. In males, all effects declined with aging. Females showed significant responsiveness in all age-groups.

CONCLUSION

Age-associated alterations in the responsiveness of male rats to acute central CRF injections were similar to those of ICV CCK injection. Gender differences may be explained by endocrine factors (anorexigenic estrogens) or differences in body weight and body composition.

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CATABOLIC EFFECTS OF CENTRAL LEPTIN INFUSION DURING AGING

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AIM

Leptin is a catabolic adiposity signal. Aging has been associated with leptin resistance. It has not been clarified, how age-related leptin resistance affect the anorexigenic and hypermetabolic components of leptin effects. In the present study we aimed t

INTRODUCTION

In the course of aging we observe well-defined changes in the regulation of energy homeostasis: middle-aged people tend to gain weight and develop obesity, while old people show anorexia with sarcopenia. As these trends are also observed in other mammals, alterations in the activity of catabolic and anabolic peptides may also be assumed in the background. Leptin is a peptide hormone produced in white adipose tissue acting mainly in the hypothalamus by altering the expression of neuropeptides. It has complex catabolic activity: suppresses food intake (anorexigenic) and enhances energy expenditure leading to weight loss.

METHODS

Male Wistar rats of different age-groups (4-months young adult, 6-months younger middle-aged, 12-months older middle-aged, 18-months aging and 24-months aged) were used. Their right lateral cerebral ventricle was cannulated for intracerebroventricular (ICV) infusions and a biotelemetric transmitter was implanted into their abdominal cavities. Core temperature and heart rate (indicating metabolic rate) were registered during a 7-day ICV infusion (1 µg/µl/h leptin or 1 µg/µl/h pyrogen-free saline, Alzet osmotic minipump) in a biotelemetric (MiniMitter, VitalView) system. Body weight and food intake were measured daily manually. For statistical analysis of the data repeated-measures ANOVA was used.

RESULTS

Leptin-induced anorexia remained significant in all age-groups. This suppression was weak in the aging (18-months old) group but returned to a higher value in the 24-months old rats. Leptin resistance of older animals affected hypermetabolic actions. Heart rate values did not change during the leptin infusion in the two oldest group and hyperthermia was missing in the 24-months old rats. Weight reducing effect of leptin was strong in young, diminished in middle-aged and aging animals, and became significant again in the oldest group.

CONCLUSION

According to our observations, leptin-induced anorexia and hypermetabolism change in disparate ways with aging. Overall catabolic effects become pronounced again in old rats.

IS THE PROCESS OF ENTOSIS A WAY TO ESCAPE FROM CHEMOTHERAPY?

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AIM

We aim to verify the hypothesis that one cell invades into another cell to escape from a harmful effect of exogenous compounds.

INTRODUCTION

Cell-in-cell structures occur in different human tumors and correlate with enhanced malignant phenotype. Entosis is a process that results in creating cell-in-cell structure. It starts when two epithelial cells detach from the basement membrane. Then one of them activates Rho kinase pathway, which leads to the polymerization of actin filements, and invades into another cell creating cell-in-cell structure. Only invading cell is active by engaging its cytoskeletal elements. The invaded cell is passive and does not activate Rho kinase pathway. In the first step of entosis the inner cell is not altered and maintains a proper mitochondrial membrane potential. As a result of this process the inner cell may undergo lysosomal degradation, divide or leave the outer cell and then function normally. The biological role of entosis remains unknown.

METHODS

The experiments were performed on BxPC3 pancreatic cancer cell line. CFDA-SE (green fluorescent dye), CMPTX (red fluorescent dye) and doxorubicin (chemotherapeutic agent that shows red fluorescence) were used to evaluate the distribution of exogenous compounds to inner and outer cells. For this purpose the cells were incubated with different concentrations of above-mentioned fluorochromes for different time intervals and were observed under a confocal microscope. In the next experiment cells were incubated with increasing concentrations of Rho kinase inhibitor and cisplatin to assess their influence on the number of cell-in-cell structures. After 24 hours the cells were stained with CFDA-SE and Hoechst. Then, twenty randomly chosen images were taken from each field under a confocal microscope to evaluate the number of cell-in-cell structures in each case.

RESULTS

We observed that the concentration of CFDA-SE and CMPTX fluorescent dyes in the inner cell is lower than in the outer cell. Such relation occurs regardless the time of incubation and concentration of fluorochromes, but it does not concern all cell-in-cell structures. Doxorubicin was distributed equally to inner and outer cell in all cases. Rho kinase inhibitor decreases the number of cell-in-cell structures in a dose-dependent manner, while cisplatin increases the number of cell-in-cell structures in a dose-dependent manner.

CONCLUSION

Lower concentration of fluorescent dyes in the inner cells means that inner cells are less exposed to some exogenous compounds than outer cells. Cisplatin promotes creating cell-in-cell structures. If this chemotherapeutic agent presented similar property to CFDA-SE and CMPTX, it would mean that cells escape from its harmful effect by invading into another cells. When the chemotherapy was over, the inner cells would leave the outer cells and function normally. If this hypothesis was true, preventing cells from invading into another cells for example by using Rho kinase inhibitor may increase the effectiveness of treatment.

IS BUTYRATE AND IRINOTECAN COMBINATION A NEW THERAPEUTIC APPROACH FOR COLON CANCER?

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AIM

The aim of this study is to evaluate the effect of the combination of butyrate and irinotecan on three CC cell lines.

INTRODUCTION

High levels of dietary fiber is related with a lower risk for developing colon cancer (CC). Microbial fermentation of fiber by the gut produces short chain fatty acid, such as butyrate. Butyrate is an important energy source for colonocytes and it plays an important role in maintenance of the colon homeostasis. It was reported that butyrate may be a chemopreventive agent. Irinotecan is used as second-line treatment, but, there remains the doubt about the benefits and risks, namely, the large interindividual variability in pharmacogenetic behavior. The use of natural compounds to turn the resistant cells more sensitive to the chemotherapy seems to be a possible solution.

METHODS

C2BBe1, WiDr and LS1034 cells were separately incubated with increasing sodium butyrate (1-50 mM) and irinotecan (0.1-100 μM) concentrations. In order to obtain the IC50 (half maximal inhibitory concentration) after 48, 72 and 96 h, cell proliferation was evaluated through MTT assay. Flow cytometry was performed to study the butyrate effect on cell viability and types of death, apoptosis (evaluating the BAX/BCL2 ratio), the expression of reduced glutathione (GSH), as well as, the effects of the combination on cell cycle and cell viability. To see if butyrate influences the chemoresistant mechanism in LS1034, 99mTc-MIBI uptake studies were performed. LS1034 cells were incubated with butyrate for 1, 2 and 4h before adding 99mTc-MIBI. At different times, samples of cell suspension were collected, centrifuged, separating the pellet from the supernatant, in order to calculate the 99mTc-MIBI uptake. In vivo studies with xenotransplanted were conducted, in order to ascertain the effect of butyrate in combination irinotecan on tumor growth. WiDr cells were inoculated on the back of Balb/c nu/nu mice and during several day the body weight and tumor size were monitorized.

RESULTS

It was observed that as butyrate incubation time increases, cell proliferation decreases, being obtained lower IC50 values. The combination of butyrate and irinotecan significantly decreased cell proliferation compared to monotherapy, in all cell lines, being the LS1034 the most sensitive to the combination at longer incubation times. Regarding cell viability, when butyrate concentration increases, cell viability decreases in all cell lines. When C2BBe1 and LS1034 cells are incubated with higher butyrate concentrations, there is an increase in BAX/BCL2 ratio, and also a slight increase in GSH expression, comparing to control. In all cell lines, combination of butyrate and irinotecan, decreased cell viability, and induced alterations on cell cycle. Results showed a prominence for cells to stay in G0/G1 phase, except for WiDr cells. It was also found, that when LS1034 cells are exposed to butyrate, a higher uptake of 99mTc-MIBI is observed, comparing to control. The results obtained in vivo suggest that butyrate and irinotecan combination inhibit synergistically tumor growth.

CONCLUSION

Butyrate and irinotecan act synergistically against three CC cell lines, despite of the different genetic background and organ localization. Butyrate may influence the chemorresistance mechanism of LS1034 cell line. Butyrate in combination with chemotherapeutic agents can be a solution for CC treatment. Such understanding can guide decisions about which CC patients might benefit from butyrate pharmacologic therapy.

METHYLATION PATTERN IN MYELODYSPLASTIC SYNDROME – COMPARATIVE STUDY BETWEEN BONE MARROW AND PERIPHERAL BLOOD

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AIM

Our aim was to compare DNA methylation status in bone marrow (BM) aspirate and peripheral blood (PB) of Myelodysplastic Syndrome (MDS) patients at diagnosis.

INTRODUCTION

DNA methylation status was one of the earliest discovered epigenetic regulators of gene expression and aberrant methylation of gene promoter region is responsible for inappropriate gene silencing, mainly tumor suppressor genes, and it has been associated with cancer initiation and progression. Blood-based specimens may be a potential source of non-invasive DNA methylation cancer biomarkers. Peripheral blood leukocytes from patients with solid tumors exhibit complex and distinct cancer-associated DNA methylation patterns, which might be seen as epigenetic biomarkers with significant clinical potential. However, peripheral blood cell methylation profiles are largely unknown in hematopoietic cancers.

METHODS

We compare DNA methylation status of the tumor suppressor genes, p15, p16, p53, DAPK and MGMT, and of TRAIL (TNF-Related Apoptotic Inducing Ligand) receptor genes, TRAIL-DcR1, -DcR2, -DR4 and -DR5, in 68 Myelodysplastic Syndrome (MDS) patients at diagnosis, in genomic DNA obtained from BM aspirate and PB samples, after informed consent. Genomic DNA was isolated by standard protocols and modified by sodium bissulphite. The MS-PCR for each gene was performed using two sets of primers, one for methylated DNA and other for unmethylated DNA. $\chi 2$ Test was used to analyses association between groups and Kappa statistics to evaluate concordance, results were considered statistically significant when $p<0.05$.

RESULTS

We observed a good concordant results between BM and PB samples in 69,1% of patients for p16, 70,6% for p15 (p=0,005), 57,4% for DAPK, 76,5% for TRAIL-DcR1 (p=0,041), 69,1% for TRAIL-DcR2, 72,1% for TRAIL-DR4 and a discordant results for TRAIL-DR5 gene, since only 48,5% of the tested samples were concordant. In some cases discrepancies were also bidirectional, with cases presenting demethylated PB and methylated BM aspirate and vice versa. No patient presented p53 and MGMT genes methylated.

CONCLUSION

Our results show a correlation between gene methylation patterns in PB and BM aspirate in MDS patients. Although DNA methylation patterns measured in PB may have great potential as informative biomarkers of cancer risk and prognosis, large systematic and prospective studies will be needed.

BUPARLISIB, ANOTHER STEP IN THE QUEST TO CURE HAEMATOLOGICAL MALIGNANCIES.

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AIM

The aim of this study is to evaluate the effect of Buparlisib (BKM), a Class I Phosphatidylinositol 3-kinase (PI3K) inhibitor, in four models of haematological malignancies.

INTRODUCTION

PI3K, is an intermediate signalling molecule that act by producing phosphorylated lipids that transduce signals from the cell surface to the cytoplasm. These signals are received by G-coupled proteins and receptor tyrosine kinases and are responsible for the activation of multiple effector pathways such as BTK, AKT, NF-KB and JNK/SAPK. Therefore, PI3K play a very important role in key cellular processes like apoptosis, DNA repair, senescence, angiogenesis, motility and cell metabolism. This molecule are tightly regulated in normal cells, however, several studies show that the dysregulation of PI3K pathway in several neoplasias. Additionally, mutations in PI3K sub-units are not only associated with the tumorigenesis but also with the resistance to anti-neoplasic therapies. Buparlisib (BKM) acts by inhibiting the PI3K Class IA (p110α, p110β, p110δ) and IB (p110γ) catalytic sub-units in a dose dependant manner. Therefore, we look at the PI3K as a potential target in the treatment of haematological malignancies.

METHODS

For this purpose, we used four in vitro models of haematological malignancies, Myelodysplastic Syndrome (F-36P cells), Multiple Myeloma (H929 cells), Erythroleukemia (HEL cells) and Acute Promyelocytic Leukemia (NB-4 cells). Cell lines were cultured in absence and presence of different concentrations of BKM ranged from 0,5μM to 10μM. We used both daily (0,5μM) and single dose (0,5μM; 1μM; 2,5μM; 5,0μM; 7,5μM; 10μM) administration schemes. In order to evaluate the BKM effect in these cell lines, we determined the cell viability at 24, 48 and 72 hours using a Resazurin Assay. Cell death was analysed using optical microscopy (May-Grunwald Giemsa staining), and by flow cytometry (FC) using the Annexin V and Propidium Iodide double staining. To analyse some mechanisms involved in cell death we used the ApoStat, a probe that identify and quantify caspase activity.

RESULTS

Our preliminary results show that BKM reduces cell viability in time, dose and cell line dependent manner. The half maximal inhibitory concentration (IC50) at 72 hours of exposure was between 2,5 μM and 5 μM in the HEL cell line; 7,5μM in the NB-4 cell line; 10 μM in the F-36P cell line; and over 10 μM in the H929 cell line, meaning that these cells among those used in the study are the more resistant to BKM. The daily administration scheme of a small dose of BKM reveal a positive effect in the HEL, F-36P and mainly in NB-4 cell line, where we observed the highest pronounced effect. In the multiple myeloma cell model (H929 cells) the daily administration scheme doesn´t produce effect. This compound induces cell death by apoptosis, confirmed by morphological analysis and by the increase in activated caspases expression levels.

CONCLUSION

PI3K reveals a promising target for novel anti-cancer therapeutics, since BKM have the ability to induce apoptotic cell death. In conclusion, our results suggest that BKM could be a new potential therapeutic approach in haematological malignancies.

REPRODUCTIVE AGEING AND ANTIOXIDANTS: EFFECT IN UTERINE FUNCTION

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AIM

Test whether specific antioxidant therapy would ameliorate age-related impaired reproductive capacity.

INTRODUCTION

The decision of postponing the choice of childbearing until the late 30s poses important medical problems because at this age there is not only a significant increase in female infertility but also an increase in the risk for the occurrence of pregnancy–related disorders and serious complications. A biological process that appears to be involved in the loss of reproductive capacity is the cell redox status, namely an age-related imbalance in redox homeostasis consequent to enhanced local production or scavenging of reactive oxygen species. Thus, it is plausible to hypothesise that the reduced reproductive capacity and adverse pregnancy outcome in aged females is funded on a redox imbalance.

METHODS

Uterine samples of mice aged 11–15 weeks or 43-45 weeks were obtained. Protein carbonylation was determined in uterine epithelium by fluorescent immunohistochemistry techniques. Reproductive outcome was evaluated by counting the number of viable foetus and re-absorption sites. Hematoxylin and eosin staining of uteroplacental compartment was used for histological examination. SOD activity and expression were determined in placental bed by spectrophotometry and western blotting, respectively. Females aged 43-45 weeks were treated, prior to and during pregnancy, with a SOD mimetic (TEMPOL, 1 mM) or a NOX inhibitor (apocynin, 5 mM) and reproductive outcome and uteroplacental histology were re-evaluated. Results are presented as mean ± standard error mean.

RESULTS

The non-pregnant uterus of the aged female mice was hypertrophied and contained cysts, when compared to young mice. Moreover, protein carbonylation was increased. Pregnant aged females showed an age-related decreased in the number of viable foetuses [young females 6.0 ± 1.2 (n=9) and aged females 2.0 ± 0.4 (n=6), P=0.03 (Student's t test)]. Moreover, this decrease was accompanied by a significant reduction of the uterine decidua height. Total SOD activity was significantly increased in placental bed of reproductively aged female mice [1.6 ± 0.2 fold increase P=0.04 (Student's t test)]. This increase in SOD activity was accompanied by an increase in the expression of SODII. Anti-oxidant treatment increased the number of foetuses from aged female mice [control 2.0 ± 0.4 (n=9), TEMPOL 3.5 ± 0.9 (n=4) and apocynin 4.2 ± 0.6 (n=5), P=0.05 (ANOVA)]. Moreover, treatment with a SOD mimetic increased significantly foetuses weight [control 1.30 ± 0.06 (n=9) and TEMPOL 1.52 ± 0.01 (n=4), P=0.02 (Student's t test)] and improved decidua thickness.

CONCLUSION

These findings demonstrate a correlation between uterine oxidative imbalance and a decrease in female reproductive outcome and support the view that the uterine environment is fundamental for reproductive success.

EFFECTS OF AGING AND CARDIOVASCULAR RISK FACTORS ON EXPRESSION OF SIRT1 AND SIRT6 IN THE HUMAN CORPUS CAVERNOSUM

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AIM

The aims of this work are to prove the presence of Sirtuin 6 in human corpus cavernosum and to access differences of Sirtuin 1 and Sirtuin 6 expression between groups of samples obtained from young, healthy aged and aged with cardiovascular disease risk f

INTRODUCTION

Sirtuins 1 and 6 belong to the family of mammalian sirtuins (SIRT 1-7) that are isoenzymes that exert NAD+-dependent deacetylase and ADP-ribosylation activities. It has been described that SIRT6 and SIRT1 are mainly active in the cell nucleus, where they regulate histone acetylation status, chromatin structure and DNA repair, presenting an important role in the modulation of the biological process of aging in human tissues [1]. In fact, it was previously demonstrated that SIRT6-depleted cells present Werner syndrome phenotype, a premature aging disorder, and that upregulation of SIRT6 could counteract age-related features [2]. The expression of each member of sirtuin family present tissue-specificity, and recently SIRT1was detected in Human corpus cavernosum (CC) [3]. Based on this evidence, we hypothesized that SIRT6 could also be expressed in this high-vascularized tissue that present an important age-dependent loss of function. Indeed, aging is considered the most important independent risk factor for erectile dysfunction (ED), further to other cardiovascular disease risk factors, such as diabetes, hypertension or obesity. ED is considered by some researchers equivalent to endothelial dysfunction and a marker of cardiovascular disease [4,5]. The aims of this study were to determine whether SIRT6 is present in human CC, and to access differences of expression between groups of samples obtained from young, healthy aged and aged with cardiovascular disease risk factors (CVDRF) individuals.

METHODS

Samples of human CC were collected from patients submitted to penile corporoplasty after informed consent or from healthy organ donors without erectile dysfunction (ED) or known CVDRF at the Hospital of S. João Porto and divided in three groups (Young - 16 to 35 years, Aged – 59 to 74 years with or without CVDRF). The samples were excised and immediately fixed in formalin solution or frozen at -80ºC for molecular analysis. Dual immunolabelling of SIRT6 with specific marker of smooth muscle cell (α-actin) was performed employing appropriate antibodies. Images were acquired in an Apotome microscope (Carl Zeiss System) connected to an Axiocam MRm camera. For quantification of SIRT1, 6 and actin as housekeeping gene expression levels in the CC, RNA was extracted and converted to cDNA. Real-time PCR reactions for amplification of SIRT1 and SIRT6 were carried out employing appropriate primers. SIRT6 protein levels were also assessed in samples from all groups by Western blotting (WB).

RESULTS

SIRT6 was detected in the nuclei of α-actin- labelled fusiform smooth muscle cells in the human CC. In what concerns molecular analysis, a band with apparent molecular weight of 40 KDa, corresponding to SIRT6 was detected by WB. In line, amplification products corresponding to SIRT1 and SIRT6 mRNAs were detected in all individuals. Real-time PCR results showed a significant increase in SIRT6, but not SIRT1, expression in cavernous tissue of aged men with CVDRF comparatively with those obtained from the healthy counterparts. No statistical differences were observed between young and aged tissues for any of the evaluated mRNAs.

CONCLUSION

Our results demonstrate for the first time the expression of SIRT6 in the human CC tissue employing different technical approaches. We also proved for the first time that SIRT6 is upregulated in aged men with CVDRF when compared to aged individuals without CVDRF. SIRT6 is a highly specific histone deacetylase that promotes proper chromatin function in several physiologic contexts, including telomere and genome stabilization, gene expression and DNA repair. It has been proposed that Sirt6 regulates mitochondrial acetylation and reactive oxygen species generation, and therefore prevents genomic instability, and maintains metabolic homeostasis thus impacting on several pathways relevant for inflammation, metabolism and aging. In consistent with this hypothesis, the increased expression level of Sirt6 in aged men with CVRF could be a defence mechanism to counter the inflammation associated to endothelial dysfunction.

ROLE OF PKG-RELATED PATHWAYS IN THE DIASTOLIC RESPONSE TO ACUTE MYOCARDIAL STRETCH UNDER ISCHEMIC CONDITIONS

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AIM

Characterization of molecular signaling mechanisms underlying myocardial diastolic adaptation to acute stretch and identification of potential therapeutic targets to restore it under ischemic conditions.

INTRODUCTION

Acute myocardial stretch induces both systolic and diastolic adaptive responses. The mechanisms responsible for diastolic adaptation remain largely unknown. However, in the presence of ischemia, this response is not observed. Therefore, we aimed to evaluate the role of cGMP-dependent protein kinase (PKG) and associated signaling pathways in the diastolic adaptive response to acute myocardial stretch under ischemic conditions.

METHODS

Rabbit papillary muscles (0.2Hz, 30ºC) were acutely stretched from 92% to 100% of Lmax in a modified Krebs-Ringer solution (A) under basal conditions. Group B was stretched during ischemia and other protocols were performed in the ischemic setting in the presence of (C) 8-Bromo-cGMP (an agonist of PKG, 10-5 M, n=7), (D) B-type Natriuretic Peptide (BNP, 10-6 M, n=7), (E) S-Nitroso-N-acetylpenicillamine (SNAP, a nitric oxide donor, 10-5 M, n=9), (F) Sildenafil (phosphodiesterase 5 inhibitor, 10-6 M, n=7) and Sildenafil combined with either (G) BNP (n=8) or (H) SNAP (n=6) Immediate and delayed responses to muscle stretch were evaluated. Results are presented as mean±standard error of mean ($P<0.05$).

RESULTS

Under basal conditions (group A), after immediate increase in myocardial passive tension (PT) induced by acute myocardial stretch, there was a significant and time-dependent decrease in PT of 46.2±1.8% in the 15 minutes following stretch. Under ischemic contitons (group B), diastolic response to acute stretch was completely abolished throughout the 15 minutes of ischemia (increase in PT of 3,5±8,1%). The presence of an agonist of PKG (group C) promoted a significant decrease in PT of 20,6±3,2% after stretch during ischemia, as did the addition of sildenafil (group F, decrease in PT of 14,9±5,3%). The presence of either BNP (group D) or SNAP (group E) did not significantly improve the diastolic adaptation to acute stretch (decrease in PT of 5,6±6,7% and 9,2±6,2%, respectively). The simultaneous addition of sildenafil with BNP (group G) or SNAP (group H) elicited a synergistic effect, with the fall in PT being significantly greater than those observed when either drug is added alone (decrease of 30,3±6,4% and 34,1±4,7%, respectively).

CONCLUSION

The impaired diastolic response to stretch under ischemic conditions can be reversed by PDE5 inhibition and the improvement of the diastolic response by BNP or NO was only observed in the presence of sildenafil. These results suggest that PDE5 inhibition may be a promising therapeutic target to boost cardiac adaptation to hemodynamic overload during acute myocardial ischemia, presumably acting through rescuing of PKG phosphorylative function.

STUDYING THE EFFECT OF OXYGEN INHALATION ON CUTANEOUS MICROCIRCULATION BY THE WAVELET TRANSFORM

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AIM

Our aim was to assess the responses in the lower limb skin microcirculation evoked by the application of a 100% normobaric oxygen inhalation protocol.

INTRODUCTION

Cutaneous microcirculation is an accessible vascular bed [1] and potentially representative [2] for the evaluation of peripheral vascular function and dysfunction mechanisms [3]. Laser Doppler Flowmetry (LDF) is a noninvasive technique widely employed for this purpose [4]. It provides a complex signal comprising several components at characteristic frequency ranges. These are related to the heart (0.6-2Hz), respiration (0.15-0.6Hz), myogenic activity in the vessel wall (0.052-0.15Hz), sympathetic activity (0.021-0.052Hz) and endothelial (nitric oxide-mediated) activity (0.0095-0.021Hz) [5]. Wavelet analysis is a mathematical tool capable of partitioning non-stationary systems, as is the case of LDF [6].

METHODS

This protocol consisted of three phases: resting for 10 minutes (phase I), provocation for 10 minutes (phase II) and recovery for 10 minutes (phase III). A group of 30 healthy subjects (22,3 ± 3,7 years old) comprised of 15 males and 15 females, with previously informed consent was studied. All procedures complied the ethical standards for human research by the Declaration of Helsinki and subsequent amendments. Local blood flow, expressed in arbitrary units (AU) was assessed by LDF (Periflux PF 5010 system, Perimed, Sweden) on the inferior side of the second toe of a randomly chosen lower limb. The LDF signal, sampled at 32Hz, was partitioned using a Morlet wavelet transform (MATLAB). The amplitudes of the above mentioned components of the LDF signal were compared for each phase of the protocol by the Wilcoxon matched-pairs signed-rank test. The amplitudes of the components were compared in relation to gender using the independent-samples Mann-Whitney U test. A 95% confidence level was adopted.

RESULTS

Spectral analysis revealed highest amplitude values for the sympathetic and endothelial components, indicating that LDF signal was predominantly from sympathetic and endothelial origin. Results show that all components' amplitudes are reduced during oxygen inhalation, although only significantly for the cardiac, sympathetic and endothelial components. During recovery, only the respiratory component failed to return to baseline. Males showed consistently higher components' amplitudes than females for the resting phase, although only significantly for the respiratory component. Significantly higher values in males were also found for the respiratory and myogenic components during provocation, suggesting different levels of involvement of these mechanisms in different genders. There were no gender differences found during recovery.

CONCLUSION

These results seem to confirm the usefulness of the wavelet transform in assessing the contribution of each LDF signal component to a physiologic response evoked for the study of lower limb microcirculation.

GHRELIN'S EFFECTS IN DIABETIC RETINOPATHY: INHIBITION OF CHOROID RETINAL CELLS MIGRATION AND PROLIFERATION UNDER A HYPERGLYCEMIC ENVIRONMENT

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AIM

The purpose of this work is to investigate the effect of ghrelin in a primate choroid retinal cell line cultured under hyperglycemic conditions and its effect on the early changes of diabetic retinopathy in an animal model of streptozotocin-induced type 1

INTRODUCTION

Ghrelin is a 28-aminoacid acylated peptide, isolated from the X/A-like cells of the gastric fundus and acts on several organ systems, such as the eye. It has been demonstrated that ghrelin is implicated in the pathophysiology of proliferative retinopathy. However, these actions differ depending on the stage of the disease.

METHODS

A RF/6a cell line was used in the in vitro assay. Cell migration was assessed using the wound-healing assay under increasing (0-300 mM) glucose concentrations. To test its effect, ghrelin was added (10-5-10-10 nM) to the cell cultures for 24h. Positive controls had VEGF added to the medium. Colorimetric immunoassay was used for the quantification of cell proliferation, based on the measurement of BrdU incorporation during DNA synthesis. Glucose and ghrelin concentrations were the same as the ones used on the migration assay. We defined 10 mM of glucose as the basal condition and 250 mM as the hyperglycemic environment. For the in vivo studies, diabetic Wistar rats received intravitreal injections of either ghrelin (81 nM) or saline every 4 weeks for 3 months. Vascular permeability was assessed using the evans blue assay.

RESULTS

Increasing concentrations of glucose show a reduction in the migration distance. On the other hand, concentrations of glucose from 0 to 100 mM seem to potentiate cell proliferation, but in higher concentrations (150-300 mM), it has no effect. At a concentration of 10-8 nM ghrelin potentiates the inhibition of migration induced by the hyperglycaemic medium, and inhibits the migration induced by VEGF. At 10 and 100 mM of glucose, ghrelin (10-7 and 10-6 nM) seems to inhibit the proliferation enhanced by glucose. Regarding the in vivo model, diabetic animals treated with intravitreal ghrelin injections showed no alteration in vascular permeability, when compared with diabetic controls.

CONCLUSION

Ghrelin inhibits cell migration in choroid-retinal cells under hyperglycemic media and reduce cell proliferation at normoglycemic and high glucose environments. In a DM1 animal model, ghrelin appears to have no effect on the vascular permeability.

NEUREGULIN-1 PRESERVES RIGHT VENTRICULAR DIASTOLIC FUNCTION IN ANIMAL MODEL OF PULMONARY ARTERIAL HYPERTENSION

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AIM

Analyse the presence and possible underlying mechanisms of right ventricular diastolic dysfunction in an animal model of pulmonary arterial hypertension and the role of NRG-1 in this context.

INTRODUCTION

Neuregulin (NRG)-1 is involved in the preservation of left ventricular performance. Nevertheless, the role of NRG-1 in pulmonary arterial hypertension(PAH) and right ventricular(RV) diastolic stiffness is unknown (1,2). This study analysed the presence and possible underlying mechanisms of RV diastolic dysfunction in an animal model of PAH and the role of NRG-1 in this context.

METHODS

Wistar rats randomly received monocrotaline (MCT,60mg/Kg,sc) or vehicle. After 14 days, rats received NRG-1 (40ug/Kg/day,ip) or vehicle. The study resulted in 4 groups: control(CTRL,n=16);CTRL+NRG(n=15);MCT(n=13); MCT+NRG(n=18). RV invasive hemodynamic studies and sample collection were performed 25-28 days after MCT administration. Isolated cardiomyocytes were stretched to measure resting tension and phosphorylation of titin isoforms was analyzed (ProQ Diamond and SYPRO Ruby protein gel stains). Only significant results ($p<0.05$) are given.

RESULTS

RV diastolic stiffness (β) was increased in MCT rats (MCT vs CTRL:0.016±0.002 vs 0.008±0.001). However, NRG-1 treatment attenuated this change (MCT+NRG:0.007±0.001). Histological analyses revealed increased cardiomyocyte cross-sectional areas (MCT vs CTRL:536.67±59.46 vs 375.39±47.43μm2), indicating RV hypertrophy. In addition, the amount of RV fibrosis was enhanced in PAH tissue (MCT vs CTRL:2.04±0.17 vs 0.98±0.07%). NRG-1 also attenuated both changes (MCT+NRG:409.01±19.72μm2 and 1.00±0.17%, respectively). MCT-group isolated cardiomyocytes developed higher passive force when compared to CTRL-group cells at the sarcomere lengths of 2.0 (MCT vs CTRL:1.90±0.43 vs 1.43±0.29N/m2), 2.2 (MCT vs CTRL:3.66±0.69 vs 2.68±0.24N/m2), and 2.3μm (MCT vs CTRL: 5.76±1.15 vs 3.86±0.87N/m2). NRG-1 restored passive force development to levels similar to the CTRL-group, at 2.0, 2.2, and 2.3μm (MCT+NRG:1.28±0.25, 3.04±0.55, and 3.63±0.89N/m2, respectively). CTRL+NRG-group cells developed less passive force compared to CTRL-group (CTRL+NRG:1.16±0.31, 2.27±0.38, and 3.05±0.54N/m2, at 2.0, 2.2, and 2.3μm respectively). Titin phosphorylation was reduced in RV tissue of MCT rats (MCT vs CTRL:1.06±0.38 vs 1.62±0.85,arbitrary units) and increased in MCT+NRG group (2.28±0.61).

CONCLUSION

RV diastolic stiffness is increased in MCT rats, with important contributions from increased fibrosis and intrinsic stiffening of the RV cardiomyocyte sarcomeres. NRG-1 treatment decreases the passive force and thus myocardial stiffness, either in rats with RV hypertrophy or in healthy animals. These findings show that NRG-1 pathway regulates systolic and diastolic function at the cellular level, suggesting a potential therapeutic role of this pathway in PAH.

COMPERSION OF ASTIGMATISM AND VISUAL FUNCTION BEFORE AND AFTER REFRACTIVE SURGERY BY TWO METHODS (WAVEFRONT-GUIDED ABLATION PRK AND ASPHERIC ABLATION)

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AIM

To compare visual performance and astigmatism before and after refractive surgery by two methods (wavefront-guided ablation PRK and aspheric ablation)

INTRODUCTION

Nowadays, with the growing acceptance of refractive surgery is to try to discover safer and more effective methods. One effective and safe method is refractive surgery of photorefractive keratectomy procedure that can be done several different ways. However, many patients are seeking surgeries have a high astigmatism and further studies to determine the best method of surgery is performed on people who are nearsighted or who their astigmatic value was low and fewer studies could be found that their method is to determine the best method in target group with high astigmatism. We examined safety and effectiveness of two wavefront-guided photorefractive keratectomy and photorefractive keratectomy surgeries in aspheric method in astigmatism correction.

METHODS

In this study, 144 eyes of 71 patients who had refractive astigmatism of myopic astigmatism and were sought surgery randomly operated in two methods of wavefront-guided photorefractive keratectomy and aspheric method and 6-month after testing operative visual function, including visual acuity, corrected or uncorrected, and the refraction and also aberrometry and topography and contrast sensitivity tests were done and the data were analyzed to SPSS statistical software version 15

RESULTS

Both methods are resulted in significant reduce of refractive errors. Also in each 4 groups of surgery including astigmatic less than 3 with wavefront method and Astigmatic more than 3 with wavefront method , Astigmatic less than 3 with spherical method and Astigmatic more than 3 with spherical visual acuity method in uncorrected and corrected visual acuity improved. Higher-order aberrations in the pupil of 6 mm in all 4 groups increased however, in less than 3 cylinders wavefront method also an increase in 5-mm pupil was observed. About studying Contrast sensitivity of contrast sensitivity in wavefront method we observed more contrast sensitivity in cylinder groups less than 3 diopter compared with more cylinders of 3 but no Significant differences was observed in spherical method between the two groups of cylinders of less than 3 diopter and no more than 3 diopter.

CONCLUSION

Both surgeries with wavefront-guided photorefractive keratectomy and aspheric methods were successful to improve visual acuity and refractive defections and significant differences were observed between the two methods and two cylinder groups less than 3 diopter and cylinder more than 3 diopter however in cylinder group less than 3, more high order aberrations in wavefront method was observed in comparison with than 3- with spherical wavefront. In contrast sensitivity and aberrometry tests better results were observed in aspheric method compared to the wave fronts method.

ROLE OF PRE- AND POSTCONDITIONING TO AVOID NOXIOUS OXIDATIVE STRESS INDUCED BY PNEUMOPERITONEUM

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AIM

The aim of our investigation was to evaluate the potential protective effects of postconditioning compared to preconditioning during laparoscopic surgery in rat models. Based on our previous experiments preconditioning has a beneficial effect.

INTRODUCTION

Pneumoperitoneum, widely used in laparoscopic surgery, increases the intraabdominal pressure over the 7-10 mmHg physiological pressure of the portal blood flow. This leads to hypoperfusion of the abdominal organs, and promotes the buildup of reactive oxygen species (OFR) and inflammatory cytokines, which in turn impair the body postoperatively and slow down the recovery.

METHODS

The experiments were conducted on 70 female Wistar rats. Pneumoperitoneum was created with Veres needle, inserted tranumbilically into the abdominal cavity. Rats were divided into 7 groups (n=10/group, each): Group I.: Sham; Group II.: Pneumoperitoneum with 5 mmHg for 60 min; Group III.: Preconditioning with 5 mmHg (insufflation and desufflation for 5 min followed by pneumoperitoneum with 5 mmHg for 60 min); Group IV.: Postconditioning with 5 mmHg (pneumoperitoneum with 5 mmHg for 60 min followed by 5 min desufflation and 5 min insufflations) V.: Pneumoperitoneum with 10 mmHg for 60 min; Group VI.: Preconditioning with 10 mmHg (insufflation and desufflation for 5 min followed by pneumoperitoneum with 10 mmHg for 60 min); VII.: Postconditioning with 10 mmHg (pneumoperitoneum with 10 mmHg for 60 min followed by 5 min desufflation and 5 min insufflations). Blood samples were taken 2 hours after the procedure. Oxidative stress parameters: lipid peroxidation indicated by malondialdehyde (MDA) concentration, reduced glutathione (GSH), sulfhydril (-SH) levels and the endogenous antioxidant superoxide-dismutase (SOD) activity were measured. Inflammatory cytokines: TNF-α and IL-6 levels were also detected. Tissue samples were reserved for histology and for Western blot.

RESULTS

MDA concentrations were significantly higher in each group compared to the control group. In the case of MDA postconditioning with 10mmHg had significantly better effect than preconditioning. GSH concentrations were significantly decreased in all groups compared to the sham group. In sulfhydril levels there were no differences between groups. SOD enzyme: a pressure of 10 mmHg elicited significantly greater damage than 5 mmHg. SOD activity was significantly increased in 10 mmHg pre- and postconditioned groups compared to the 10 mmHg pneumoperitoneum group. TNF-α and IL-6: the concentrations were significantly higher in each group compared to the control group. In the 10 mmHg pre- and postconditioned groups the concentrations were significantly decreased compared to the 10 mmHg pneumoperitoneum group.

CONCLUSION

Based on our results the elevated intraabdominal pressure due to pneumoperitoneum induces oxidative stress, which is dependent on the applied pressure. Therefore it is advisable to use the minimal required pressure which still does not influence the surgical technique. Pre- and postcondiotioning even at low pressure are able to reduce surgical stress following laparoscopic procedures, but to explore the mechanism requires further investigations.

DOES IMPLANTATION OF ADIPOSE STEM CELLS ON THE GRANULATION TISSUE INCREASE CHANCE FOR HEALING LARGE TISSUE DAMAGE? A CASE REPORT OF PATIENT WITH RECURRENCE PERIANAL FISTULA TREATED BY THE CELL BASE THERAPY.

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AIM

We present a case of a a 32-year old male with recurring, large perianal fistula treated by ASC injected into granulation tissue 3 weeks after fistulectomy.

INTRODUCTION

Recurrent form of perianal fistula destroy the sphincter apparatus and lead to an incontinence. Regenerative medicine provides a novel approach to healing fistulas using autologous stem cells. Recently, several studies have been designed for a single stage fistulectomy combined with application of Adipose-derived Stem Cells (ASC) and fibrin glue.

METHODS

Adipose tissue was obtained surgically from subcutaneous tissue. ASCs were isolated and cultured to reach 10^7 cells. Suspension of cells in 2 ml of Ringer were injected sub-superficially into granulation tissue, around internal opening of the fistula tract 3 weeks after fistulectomy. No tissue glue was applied.

RESULTS

After a 6-month follow-up, the fistula tract at the site of implantation was totally obstructed by healthy fibrous tissue, forming a scar, which closed the tract and internal opening. No complications and adverse events were noted.

CONCLUSION

Successful application of ASC into the granulation tissue opens up a new strategy for treating perianal fistulas. This encouraging result requires further trials to evaluate the clinical efficacy.

POSTER PRESENTATIONS

CRITICAL CARE AFTER ALLOGENEIC HEMATOPOIETIC STEM CELLS TRANSPLANTATION IN PEDIATRIC PATIENTS: CASE CONTROL STUDY.

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AIM

The aim of this study is to characterize the outcome of treatment in pediatric allogeneic hematopoietic stem cells transplant recipients who required intensive care unit (ICU) admission and to compare it with patients who did not need treatment in ICU.

INTRODUCTION

Hematopoietic stem cells transplantation (HSCT) is a lifesaving procedure performed in both malignant and non-malignant disorders. It consists of myeloablative or non-myeloablative chemotherapy followed by reconstitution with autologous or allogeneic hematopoietic stem cells. After the main part of the therapy, inevitable side effects are: pancytopenia, immunosuppression, tissues toxicity and, in allogeneic transplants, graft-versus-host disease. Although most of the treatments with HSCT finish successfully, the outcome is not always satisfying and complications might be observed. Severe post-transplantation condition might be an indication of treatment in the intensive care unit (ICU).

METHODS

The data came from The Department of Transplantation of University Children's Hospital in Cracow, Poland, and were collected in years 2005-2014. Medical histories with laboratory tests results and one year follow-up of 100 pediatric patients (mean age = 8.5±5.6 years; 30% females) after allogeneic HSCT were analised. In this cohort, 15 patients (mean age 9.6±6.2 years; 53% females) required treatment in ICU during the follow-up period.

RESULTS

In 93% of the patients requiring ICU admission, myeloablative conditioning was used before transplantation. There is a significant relationship between usage of myeloablative protocol and later requirement of treatment in ICU (p=0.038). Most of the patients treated in ICU had oncohematological diseases (87%) and the most common underlying pathology was acute lymphoblastic leukemia (47%). There is a significant relationship between a type of a disease (oncohematological vs. non-oncohematological) and a need for ICU admission (p=0.007).

CONCLUSION

Myeloablative conditioning before transplantation and oncohematological diseases as the underlying pathology, correlate with high rate of admissions to ICU. HSCT remains a dangerous procedure with many possible complications and it should be reserved for patients with life-threatening diseases. Post-HSCT admission to ICU has generally poor prognosis with high mortality resulting mainly from multiple organ failure.

EFFECTS OF ACUTE HIGH-INTENSITY EXERCISE ON PLASMA IL-17 CONCENTRATION IN ELITE ATHLETES

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AIM
The aim of this study was to clarify the dynamics of IL-17 in association with acute high-intensity exercise in elite athletes.

INTRODUCTION
The T-cell subset Th17 is activated by IL-23, and produces a proinflammatory cytokine IL-17. During acute exercise, IL-6 increases dramatically following muscle damage, this response may also stimulate the induction of IL-17 and IL-23 after exercise.

METHODS
Sixteen water polo players (age: 22.1±2.6 yrs; height: 195.0±4.1 cm; body mass: 100.5±13.8 kg; %body fat: 17.0±2.9) and sixteen physically inactive controls (age: 21.8±2.2 yrs; height: 184.5±5.9 cm; body mass: 90.2±7.8 kg; %body fat: 17.3±1.4) participated in this study. Venous blood samples were collected before, immediately after and 30 minutes after the acute high-intensity exercise on treadmill. Plasma IL-17 and interferon gamma concentrations were analyzed using enzyme-linked immunosorbent assays (ELISA).

RESULTS
Any statistical differences in body composition variables (body mass, body mass index, body fat percentage) were not found between athletes and controls ($p > 0.05$). Basel plasma IL-17 level was higher ($p<0.05$) in athletes compared with controls, while no significant changes were observed regarding plasma interferon gamma level. In athletes, plasma concentrations of interferon gamma and IL-17 increased significantly immediately after the exercise and decreased in 30 minutes recovery ($p<0.05$). In controls, plasma concentrations of interferon gamma increased significantly immediately after the exercise and decreased in 30 minutes recovery ($p<0.05$). There was no change in the concentration of IL-17 in control group ($p > 0.05$).

CONCLUSION
These findings suggest that acute high- intensity exercise promote IL-17 concentration in elite athletes.

ANALYSIS OF THE ASSOCIATION BETWEEN RS3024505 POLYMORPHISM AND IBD IN SERBIAN POPULATION

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AIM

The aim of this study was to analyze the association between rs3024505 polymorphism and IBD in Serbian population.

INTRODUCTION

Inflammatory bowel disease (IBD) is a chronic disease of the intestinal tract with complex etiology. Crohn's disease (CD) and ulcerative colitis (UC) represent the most common clinical forms of IBD. It is assumed that a regulatory cytokine, interleukin (IL)-10, has important role in the pathogenesis of IBD. Single nucleotide polymorphism (SNP) rs3024505 that is located downstream of IL-10 gene and is believed to affect its expression, has been previously associated with UC and CD.

METHODS

Study included 94 IBD patients and 93 healthy controls. Genomic DNA was isolated using standard method with columns. Genotyping was done using quantitative Real Time PCR with commercially available TaqMan probes.

RESULTS

In IBD group, CC genotype was found in 56 (59,57%), CT in 35 (37,23%) and TT in 3 (3,19%) patients, while among healthy controls, CC genotype was found in 51 (54,84%), CT in 30 (32,26%) and TT in 12 (12,9%) subjects. There was a statistically significant difference between healthy controls and all IBD patients and between controls and group of IBD patients without those with undifferentiated disease ($p=0.0495$ and $p=0.0381$, respectively). In contrast, genotype distribution in controls and CD or UC patients, and allele frequencies in all groups were similar.

CONCLUSION

The association between rs3024505 SNP and IBD patients in Serbia suggests potential role of IL-10 in the pathogenesis of IBD.

POSITIVE AND NEGATIVE REGULATION OF TOLL-LIKE RECEPTORS SIGNALLING PATHWAYS IN INNATE IMMUNE RESPONSES

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AIM

In this review, we describe some of the molecules involved in the fine-tuning of TLR signalling in innate immunity and how they modulate the host's defences.

INTRODUCTION

Recognition of pathogen-associated molecular patterns (PAMPs) by pattern recognition receptors (PRRs) is the host's first line of defence against microbial invasion. Toll-like receptors (TLRs) were the first type of PRRs to be discovered and are the best characterised. They trigger innate immune responses through the activation of MyD88 or TRIF-dependent signalling pathways. Positive and negative regulation of these pathways can be achieved by a wide range of mechanisms, at different compartments of the cell.

METHODS

RESULTS

CONCLUSION

The molecules described may become therapeutic targets for the treatment of acute and chronic inflammation and auto-immune diseases.

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Physiology & Immunology
Poster Presentation

RAT CORNEAL ENDOTHELIUM PRIMARY CELL CULTURES

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AIM

The purpose of this work is the optimization of cell culture conditions to establish primary cultures of corneal endothelium.

INTRODUCTION

Corneal endothelial dysfunction is the main indication for corneal transplantation worldwide. Corneal endothelium is the most important layer of all corneal layers, once it is responsible for corneal hydration and nutrient diffusion maintaining corneal transparency. Corneal endothelial cells are characterized by their unique hexagonal shape that allows corneal endothelium to fulfill its functions. It is described that these cells have no proliferative ability in vivo, responding to wounding and cell loss with cell enlargement and migration. Corneal transplants are often difficult due to possible failure by rejection, critical corneal endothelial cell counts from donor corneas and even for low donor corneas. Therefore ex vivo expansion may be crucial allowing treatment improvements and further corneal endothelial cells studies.

METHODS

After gathering the tissue through peeling of Descemet's membrane from cornea-scleral buttons from Wistar rats under surgical microscope, cell culture was established. For this purpose we tried several different conditions. The variables considered were enzymatic digestion, culture medium, serum, supplementation and plate coating. Digestion of the collected tissue was performed through 0.02% collagenase medium for 12 hours which was then upgraded to 0.04% collagenase medium for 24 hours. Other digestion approach used was the enzyme dispase at 1u/ml for 40 minutes. After digestion optimization, culture conditions were also improved. For that matter six different protocols were tested: medium with 15 % FBS in poly-l-lysine coated plates, medium with 15% FBS in collagen coated plates, medium with 15% BSA in poly-l-lysine coated plates, medium with 15% BSA in collagen coated plates, medium with 15% FBS in plates without coating and culture medium with methylcellulose where suspension sphere colonies would be formed and then seeded in one of the conditions above. All six protocols included FGF and EGF supplementation.

RESULTS

The digestion protocol regarding 0.04% collagenase medium for 24H turned effective while the lower time and concentration collagenase and dispase lead to low cell separation. Sphere formation protocol allowed obtenning of colonies however the posterior adherent cultures were not achieved. The best results obtained were with 15 % FBS medium in poly-l-lysine coated plates or in uncoated plates. It was possible to maintain the adherent culture for several days.

CONCLUSION

After applying all the protocols we could clarify which ones were effective. FBS was essential to corneal endothelial cell growth. Regarding plate coating its absence allowed cell culture establishment nevertheless poly-l-lysine coating had faster cell growth. Notwithstanding it is necessary to perform immunocytochemistry studies in order to prove this cell culture origin.

UROCORTIN-2 IMPROVES RIGHT VENTRICULAR FUNCTION IN PULMONARY ARTERIAL HYPERTENSION

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AIM

This study analyzed the effects of UCN-2 treatment in an animal model of RV HF, secondary to pulmonary arterial hypertension (PAH).

INTRODUCTION

Urocortin (UCN)-2 is a peptide highly expressed in the cardiovascular system and it has shown promising therapeutic effects in several studies in both humans and animal models of heart failure (HF). However, the role of UCN-2 in right ventricular (RV) failure is still unknown.

METHODS

Male Wistar rats (180-200g) randomly received monocrotaline (MCT, 60mg/Kg, s.c.) or vehicle. After 14 days, animals from these groups were randomly assigned to receive treatment with either UCN-2 (2.5µg/Kg/day, i.p.) or vehicle. The study resulted in 4 groups: control (CTRL) (n=12); CTRL+UCN-2 (n=10); MCT (n=9); MCT+UCN-2 (n=8). RV Pressure-Volume measurements were performed 24-25 days after MCT administration. Only significant results (mean±SEM, $p<0.05$) are given.

RESULTS

MCT group developed PAH, as shown by: increased RV end-systolic pressure (MCT vs CTRL: 59±3 vs 26±1 mmHg) and end-diastolic pressure (MCT vs CTRL: 6.7±0.9 vs 3.5±0.7 mmHg), RV dilatation (MCT vs CTRL: 270±17 vs 215±12 µL), and decreased cardiac output (MCT vs CTRL: 29±3 vs 63±3 mL/min) and ejection fraction (MCT vs CTRL: 37±6 vs 72±2%). UCN-2 treatment resulted in attenuation of RV pressure increase (RVESP: 42±2 mmHg; RVEDP: 4.7±0.6 mmHg), dilatation (RVEDV: 212±4 µL), and in improved cardiac function (CO: 48±2 mL/min; EF: 58±2%).

CONCLUSION

UCN-2 chronic treatment significantly reduced the worsening of RV function in PAH. These findings suggest that the UCN-2 pathway has a relevant role on the pathophysiology of PAH and RV failure, representing a potential therapeutic target.

RIGHT VENTRICLE PRESSURE OVERLOAD-INDUCED HYPERTROPHY IS ATTENUATED BY NEUREGULIN-1

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AIM

The main goal of this study was to investigate the effects of NRG-1 treatment in RV hypertrophy (RVH), in an animal model of pressure overload of the RV through pulmonary artery banding (PAB).

INTRODUCTION

Neuregulin (NRG)-1 is implicated in the preservation of left ventricular (LV) performance in pathophysiological conditions. Nevertheless, the role of NRG-1 in right ventricular (RV) function in pathological conditions is unknown.

METHODS

Seven-week-old male Wistar rats (180-200g) were randomly submitted to a mild PAB, severe PAB or sham operation. Two weeks after surgery, rats were arbitrarily assigned to receive therapy with rhNRG-1 (40µg/Kg/day) or vehicle. The study resulted in 6 experimental groups: SHAM (n=8), SHAM+rhNRG-1 (n=5), mPAB (n=8), mPAB+rhNRG-1 (n=9), sPAB (n=12) and sPAB+rhNRG-1 (n=11). Hemodynamic studies and sample collection for histology studies were performed 3 weeks after PAB surgery.

RESULTS

Mild PAB animals (end systolic pressure: 61 ± 2 mmHg) developed RV hypertrophy (cardiomyocyte cross sectional area: 472 ± 48 vs 269 ± 35 mm2, mPAB vs SHAM), without loss of function (cardiac output: 71 ± 3 vs 65 ± 5 mL.min-1; ejection fraction: 71 ± 6 vs 69 ± 3 %, mPAB vs SHAM). The sPAB group (end systolic pressure: 97 ± 6 mmHg) developed RV hypertrophy (628 ± 32 mm2), with impaired function (cardiac output: 50 ± 4 mL.min-1; ejection fraction: 57 ± 6 %).

CONCLUSION

In conclusion, we show that NRG-1 treatment has cardiac specific effects on the RV and is able to decrease hypertrophy in response to pressure overload in an animal model of PAB. These results suggest that the NRG-1 pathway has a relevant role in the pathophysiology of right ventricular dysfunction, representing a potential therapeutic target in these conditions.

MOLECULAR MECHANISMS UNDERLYING THE BENEFICIAL EFFECTS OF NEUREGULIN-1 IN PULMONARY ARTERIAL HYPERTENSION

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AIM

This study investigated the underlying molecular mechanisms to the beneficial effects of rhNRG-1 in myocardial function, MCT-induced PAH.

INTRODUCTION

Pulmonary arterial hypertension (PAH) is a syndrome based on diverse etiologies and pathogenesis, potentially leading to right ventricular heart failure and death. Neuregulin (NRG)-1 has been implicated in several physiological processes regulating cardiac development, as well as cardiac and vascular homeostasis. It was previously shown, in an experimental model of MCT-induced PAH, that NRG-1 treatment is able to restore PAH-induced severe abnormalities in cardiac function and structure. This study investigated the underlying molecular mechanisms to the beneficial effects of NRG-1 in myocardial function, in the same animal model of induced PAH.

METHODS

Male Wistar rats randomly received monocrotaline (MCT, 60mg/Kg,sc) or vehicle. After 14 days, animals received NRG-1 (40µg/Kg/day,ip) or vehicle, resulting in 4 groups: CTRL; CTRL+NRG-1; MCT; MCT+NRG-1. RV sample collection for were performed 21-24 days after MCT administration. Only significant results (mean±SEM, $p<0.05$) are given.

RESULTS

NRG-1/ErbB system components expressions in MCT animals are changed. We observed increased levels of NRG-1 in RV (11.1±2.8 vs 1.0±0.3 AU, MCT vs CTRL), which were reversed by NRG-1 treatment (MCT+NRG-1: 0.7±0.5 AU), and decreased levels of ErbB4 in all MCT animals (MCT: 0.6±0.2 and MCT+NRG-1: 0.7±0.15 AU). We also found increased levels of ErbB2 (2.0±0.3 AU), ADAM-17 (2.1±0.3 AU) and ADAM-19 (2.7±0.3 AU), and increased eNOS expression (2.0±0.3 AU) in the RV of MCT animals that not reversed with NRG-1 treatment. MCT treatment led to altered GLUT1 expression (4.1±0.5 AU) and NRG-1 treatment attenuated this increase (1.7±0.3 AU). GLUT4 was increased in all animals treated with NRG-1 (CTRL+NRG-1: 1.4±0.1; MCT+NRG-1: 1.5±0.2 AU). Increased RV caspase 3 (MCT: 4.4±0.4 AU) and plasmatic expression of IL-6 and TNF-α (IL6: 2.7±0.7 AU; TNF-α: 1.7±0.3 AU) were attenuated by NRG-1 treatment (caspase 3: 1.7±0.3 AU; IL6: 2.0±0.4 AU; TNF-α: 1.5±0.4 AU). Moreover, we found that the increased expression of BNP (17.5±2.2 AU), ET-1 (5.0±1.2 AU) and HIF-1α (4.3±1.1 AU) observed in MCT animals was attenuated or reversed with NRG-1 therapy (MCT+NRG-1: 5.6±1.9; 1.7±0.7; 1.4±0.1 AU, respectively).

CONCLUSION

In conclusion, we show that NRG-1 treatment is able to restore the changes in expression of markers of cardiac overload, hypertrophy and hypoxia induced by PAH. These beneficial effects of NRG-1 are associated with the modulation of different signaling pathways, namely apoptotic, metabolic, survival/ proliferation, and inflammation pathways.

RECOMBINANT HUMAN GROWTH HORMONE (RHGH) IN PRADER-WILLI SYNDROME THERAPY- BENEFITS AND ADVERSE EVENTS.

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AIM

The aim of the study is to evaluate effects of rhGH treatment of patients with Prader- Willi Syndrome. In particular to investigate the evolution of obesity on basis of BMI-SD, growth velocity, weight, disturbances in lipid and glucose metabolism and to a

INTRODUCTION

Prader- Willi Syndrome (PWS) is a genetic disorder characterized by hypothalamic- pituary dysfunction, which can cause short stature, loss of lean body mass, increased fat mass, hypogonadism and morbid obesity. Therapy with recombinant human growth hormone (rhGH) is the primary treatment for PWS. One of main goals of rhGH treatment is to improve linear growth velocity, however in case of WPS the most important aim is to normalize a body composition. Long-term tolerance in PWS children treated with rhGH is not well known and the data are still required.

METHODS

A retrospective study based on medical records of twelve patients (pts) was conducted. 8 boys and 5 girls, median age 13.4 ±5.64 years (5-17 yrs), treated with rhGH in 2013, were included to the study. Patients had PWS confirmed by genetic testing. Treatment duration was 5.9±2.62 yrs (2-11yrs).

RESULTS

During the treatment weight standard deviation score (SDS) increased from 0.16 to 0.93 and height SDS from -1.38 to 0.55. Weight SDS recorded raised after median 3 yrs of treatment (to 1.15) and after 4 yrs of treatment noted downturn (0.93); height SDS had been increased progressively. BMI-SD at the beginning of the treatment was 1.31, now totals 1.29.

CONCLUSION

Growth hormone affects variety of metabolic paths. Treatment with rhGH much increased the rate of growth in PWS pts. In PWS pts treated with rhGH, BMI-SD should be strictly monitored, not to allow the development of obesity and severe metabolic disorders as a result. Failure to achieve this goal is a case of discontinuation of rhGH therapy. However it should be kept in mind, that BMI is not sensitive surrogate measure for changes in body composition, particularly if lean tissue mass increased in parallel with decreased fat mass. IGF is a sensitive parameter suitable for determining an appropriate dose of rhGH.

THE SIGNIFICANCE OF GLUCOKINASE INACTIVATING MUTATIONS IN THE REGULATION OF CARBOHYDRATE METABOLISM - CLINICAL CHARACTERISTIC OF PATIENTS WITH MODY 2

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AIM

To analyze the clinical features of children and adolescents with MODY2, characterized by a genetically confirmed mutation of glucokinase (GCK).

INTRODUCTION

Mutations in the glucokinase (GCK) has an important role in the regulation of glucose levels in the blood.Heterozygous inactivating mutations in the GCK gene can result in glucose dysregulation. Type 2 of maturity onset diabetes of the young (MODY 2) is characterized by an autosomal dominant inheritance with high penetrance.

METHODS

Thirty eight patients with MODY 2: 21 girls and 17 boys, with a mean age 12.3 (±5.3) yrs, treated in the Department of Pediatric and Adolescent Endocrinology in Cracow in 2002-2013 were included into the study. Retrospective analysis of clinical data was performed.

RESULTS

Three percent of all diabetic patients in our center have a diagnoses of MODY 2. The mean age at diagnosis was 10.2 (± 6) years. 14 patients (37.8%) presented with an impaired fasting glucose (IFG) in a routine screening, 3 patients (7.8%) were admitted with symptoms of hyperglycemia, one patient (2.6%) was obese and 16 patients (43.2%) had monogenic diabetes melitus (DM) diagnosed previously in their family. Before a confirmation of GCK mutation, 9 patients (23.7%) were diagnosed as diabetes mellitus type 1 and 6 (15.7%) were on insulin treatment. Nine mutations of the GCK gene were identified. The most common mutations were GGG/AGG (10 patients, 34.4%) and GTG/CTG (7 patients, 24.2%). Autoantibodies typical for Type 1 DM were detected in 2 patients (5.2%). Autoimmune diseases were not observed in this group of patients. One pt was obese and one underweight. The fasting glucose level ranged between 5.2 and 9.2 mmol/l with the mean 6.57 (±0.93) mmol/l. 120' oral glucose tolerance test (OGTT) was normal in 3 patients, 2 had a result characteristic of DM 1, and 33 had impaired glucose tolerance. The mean HbA1c level was 6.13% (±0.39) and mean c-peptide level was 2.13 (±0.65) ng/ml. Seven patients had an elevated LDL and 4 patients had elevated total cholesterol. Three patients in the same family had Gilbert disease .

CONCLUSION

Our study revealed that symptoms presenting by some pts may differ from those characteristic for other types of diabetes to asymptomatic with normal fasting glucose level. There is no strong correlation between the certain type of mutation and the clinical characteristic in presented group and the phenotypic heterogeneity can be observed within the same family. The prevalence of dislipidemia revealed in some pts is not characteristic for that type of diabetes and described rather in adult cases. Two-times higher incidence of Gilbert disease in our pts than in general population seems to be due to family relationships among some of them.

BRAIN OXYMETRY AND CARDIAC OUTPUT DURING SLEEP IN LOW FIO2 USING AN ALTITUDE SIMULATOR.

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AIM

To evaluate if brain oxygen saturation decreases to pathologic values during sleep at a simulated altitude of 3500 metres and to compare the haemodynamic response between top-level athletes and non-athletes.

INTRODUCTION

High performance athletes have used real and simulated altitude for some time with two main goals: to increase hematocrit through prolonged exposure to hypoxia and to increase sport performance through training in these conditions [1]. One very common method is known as €˜live high, train low', where the individual sleeps at high altitude but exercises at sea level. Instead of travelling on a daily basis, this is accomplished with the use of altitude simulation systems - composed of a specially designed tent connected to a generator that lowers the amount of oxygen available inside the tent by nitrogen dilution - normobaric hypoxia [2]. Although the efficacy of this training method remains controversial, professional and amateur athletes worldwide use it everyday. Our aim is to evaluate the physiologic impact of this practice, focusing on brain oxygen saturation and other haemodynamic parameters - cardiac output (CO), stroke volume (SV), total peripheral resistance (TPR), blood pressure, (BP), heart rate (HR) and breathing rate (BR). As of May 2014, we found no research assessing brain oxygen or cardiac output variation during exposure to simulated altitude. This study was approved by the Ethics Committee of Centro Hospitalar do Porto.

METHODS

Our sample was composed of 6 male, ultra-long-distance running (>42km), top-level athletes, aged 30-40. We used a control group of 6 healthy male non-athletes, with similar age. No female subjects were selected as to control the most variables by avoiding possible influence by menstrual cycle or oral contraceptives use. These were all volunteers, and informed consent documents were signed by all before any testing.

RESULTS

Mean age among athletes was 32.7±5.2 years and 34.0±6.3 in the control group, with a p-value of 0.697. There is no significant difference between both groups. Body-mass index was 21.7±1.2 and 25.1±2.7 kg/m2 in athletes and controls, respectively. This has a p-value of 0.019, showing a significant difference between both groups, explained by different weights (66±6kg vs. 80±14kg; p= 0.044) but similar heights (174±5cm vs. 177±9cm; p=0.358).

CONCLUSION

The first conclusion we can take from this study is that the protocol can be followed without major problems or limitations. Every volunteer fell asleep easily and quickly after lying down inside the tent, all monitors running and lights out. In the sleep quality questionnaire, all mentioned a good sleep, not different from that at home, and without any symptoms showing poor blood perfusion (such as headaches or disorientation). The one single factor that was pointed out by all as being the most uncomfortable were the cuffs necessary to continuously measure pulse waves (arm and fingers - LiDCO monitor).

THE POTENTIAL IMPORTANCE OF EARLY THERAPEUTHICAL INTERVENTIONS IN FEMALE PATIENTS WITH BIPOLAR DISORDER

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AIM

The aim was to determine the gender differences in relationship between DUB (calculated as time from the onset of symptoms to the application of first mood stabilizer) and the ability to maintain an adequate remission over 24 months period following hospi

INTRODUCTION

Affective disorders are more frequent in females. The studies also underlie the gender differences in severity of affective symptoms. In addition, delay of treatment (longer duration of untreated illness) has been associated with more severe course of illness in various psychiatric disorders. However, the data on the association between duration of untreated illness in bipolar disorder (DUB) and the course of illness and its outcome, viewed through the gender differences, are still inconsistent.

METHODS

The study used retrospective design and included patients with BAD (n = 118). The inclusion criteria were: diagnosis according to ICD-10 criteria with BAD, age 18-65, inpatient treatment in the period 2005 – 2010, regular check-ups in posthospital period ≥ 24 months. The exclusion criteria were: history of any other psychiatric illness apart BAD, substance or alcohol abuse, organic mental disorder, acute or chronic physical diseases.

RESULTS

The average DUB was 126.71 ± 93.75 months. Female patients had longer DUB ($z = -2.735$, $p=0.006$) and more frequently failed to maintain remission for more than 24 months ($\chi 2 = 6.735$, $p = 0.009$).

CONCLUSION

Interventions for monitoring of DUB, its diminishing duration, early detection and recognition, and timely treatment, resulting in better course and outcome of BAP, are needed. Particular attention should be paid to the female patients, bearing in mind not only the more frequent presence of affective symptoms in the population but also the weaker ability to maintain the remission.

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Neurosciences Poster Presentation

THE EFFECTS OF ANTIPSYCHOTIC TREATMENT ON BONE MASS AND BODY COMPOSITION IN ANIMAL MODEL OF SCHIZOPHRENIA

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AIM

The aim was to investigate long-term effects of haloperidol and clozapine treatment on bone mass and body composition in phencyclidine (PCP) animal model of schizophrenia.

INTRODUCTION

Schizophrenic patients, on long-term antypsychotic therapy, have decreased bone mineral density (BMD) and increased fracture risk. Perinatal phencyclidine administration to rodents represents an animal model of schizophrenia.

METHODS

Six groups of animals were subcutaneously treated on 2nd, 6th, 9th and 12th postnatal day (PN), with either PCP (10 mg/kg) or vehicle (0.9% saline). On PN35, one NaCl and one PCP group begun receiveing haloperidol (1mg/kg/day; NaCl-H, PCP-H groups) and one NaCl and one PCP group begun receiving clozapine (20mg/kg/day; NaCl-C, PCP-C groups) dissolved in drinking water. The rest NaCl (controls) and PCP groups received drinking water. BMD, bone mineral content (BMC) and fat mass were measured in vivo by dual X ray absorptiometry (DXA) on PN60 and PN98.

RESULTS

A long lasting reduction of total BMD was observed on PN60 and PN98 in PCP group compared to control animals and highly significant decrease in PCP-C group on PN98. Total BMC was decreased on PN60 in PCP, PCP-H and PCP-C groups. On PN98, BMC was decreased in NaCl-H and NaCl-C groups and highly significantly decreased in PCP, PCP-H and PCP-C groups. There was a decrease in total fat in PCP and PCP-H groups on PN60 and NaCl-H, PCP-H and PCP-C groups on PN98.

CONCLUSION

The results demonstrate that PCP administrated perinatally reduces bone mass. The changes in BMC caused by PCP were not normalized upon anti-psychotic treatment, but drugs have influenced fat content.

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Neurosciences Poster Presentation

EFFECTS OF AGING ON THE VENTRAL TEGMENTAL AREA AND THEIR PROJECTIONS TO THE MEDIAL PREFRONTAL CORTEX OF THE RAT

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AIM

The dopaminergic system is important for cognitive function, but little is known about its changes related to the decline of this function in normal aging. Therefore there has been a considerable effort to address the mechanisms involving this system in a

INTRODUCTION

The dopaminergic system, which plays a role in several functions such as locomotion, addiction, behavior and emotion, comprises many scattered cell groups throughout the CNS. The VTA is a central part of the midbrain dopaminergic cell populations, comprising the A10 cell group. One of the brain areas targeted by VTA dopaminergic projections is the mPFC, which consists of four main divisions: the medial agranular, the anterior cingulate, the prelimbic and the infralimbic areas. As a whole, it has been implicated in diverse functions including attention, decision-making, goal-directed behavior, emotion and working memory.

METHODS

Male adult (6 months-old) and aged (24 months-old) Wistar rats were used. Cognitive abilities of the animals were assessed using the Morris water maze test. At the end of the experimental period, rats were anesthetized and then killed by transcardiac perfusion. Then the brains were serially sectioned in the coronal plane and the sections containing the mPFC and the VTA were sampled at regular intervals of 160 µm and immunostained for tyrosine hydroxylase (TH). The total number of VTA TH-immunoreactive (TH-ir) neurons and the numerical density of the mPFC TH-ir varicosities were estimated using the optical fractionator.

RESULTS

Statistical analysis (Student´s t-test) revealed no significant aging related changes in the number of VTA TH-ir neurons (p=0.40). A two-way ANOVA test (treatment Ã— subregion) showed no significant effect of treatment ($F(1,24) = 1.14$, $p = 0.30$), subregion ($F(2,24) = 0.26$, $p = 0.77$) or interaction between the two variables ($F(2,24) = 0.05$, $p = 0.95$), on the density of mPFC TH-ir varicosities.

CONCLUSION

We found no significant differences in the number of TH-ir neurons in the VTA of aged rats and in connections to the mPFC. Therefore, the cognitive changes observed with aging can not be explained by changes in the number of VTA TH-ir neurons or in the density of mPFC TH-ir varicosities. The observed cognitive changes could be explained, for instance, by changes in the dopamine receptors and/or in other neurotransmitors and their signaling balance with dopamine.

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Neurosciences Poster Presentation

PROSPECTIVE STUDY OF HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH MYOTONIC DYSTROPHY TYPE 1

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AIM

The aim of the study was to assess changes in HRQoL in patients with DM1 during 5-year period.

INTRODUCTION

Myotonic dystrophy type 1 is the most common form of muscular dystrophy in adults. In the clinical presentation of DM1, besides dominant myotonic signs and progressive muscular weakness, there are also signs of multisystemic affection. All these factors could seriously damage health-related quality of life (HRQoL) in patients with DM1. Since there is not a causal therapy for DM1 yet, measuring QoL in these patients are very important and can lead to better prevention, as well better rehabilitation and symptomatic therapy. However, there are not any prospective studies of HRQoL in these patients so far.

METHODS

This study included 44 patients with DM1, 29 were tested again after 5 years. The SF-36 questionnaire, Serbian version, was a measure of HRQoL.

RESULTS

HRQoL was reduced in patients with DM1 with no difference in physical and mental domains. The best results were obtained for bodily pain (BP), role emotional (RE) and mental health (MH). The worst results were for role physical (RP) and general health (GH). For this period, the amelioration ($p<0.05$) was found in role emotional (RE) (36.8±45.7/60±44.9), mental composite score (MCS) (48.8±21.6/58.5±22.9) and total SF-36 score (47.8±21/57.5±24.5).

CONCLUSION

All patients have decreased HRQoL in mental and physical domains. After 5-year period, the amelioration was observed in emotional functioning in everyday tasks. This is significant because it is in contrast with assumption that DM1 progressively leads to deterioration in all domains, including emotional and cognitive. These results enable better insight into the progression of DM1 and patient's adaptation to it. In order to obtain more accurate interpretation of results, it is necessary to continue research including more patients.

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Neurosciences Poster Presentation

EFFECTS OF ALARIN ON THE REGULATION OF ENERGY BALANCE IN RATS

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AIM

Our aim was to analyze the thermoregulatory and food intake-related effects of alarin in rats.

INTRODUCTION

In the background of obesity, regulatory alterations in energy balance affecting peptide systems may also be assumed. Regulation of energy balance does not only involve maintenance of body weight but also that of metabolic rate and core temperature. The contribution of alarin, a new member of the potentially orexigenic galanin peptide family to the regulation of energy metabolism has been recently suggested (Boughton, 2010). Elimination of the first five amino acids of alarin (Ala6-25Cys) abolished its orexigenic effect, moreover the fragment also showed specific antagonist activity (Fraley, 2013).

METHODS

Adult male Wistar rats received full-length alarin in various intracerebroventricular (ICV) doses (1, 3 or 15 ug) at cool or slightly subthermoneutral ambient temperatures. In other tests Ala6-25Cys (2.5 ug) was administered with or without full-length alarin to investigate its potential antagonistic thermoregulatory effects. We also tested the effects of a scrambled alarin peptide (3 ug) containing the same amino acids as alarin, in random order. In semi-restrained animals oxygen consumption (VO2, indicating heat production), heat loss (assessed by tail skin temperature) and core temperature (Tc) were recorded in an indirect calorimeter system. In freely moving animals the spontaneous and fasting-induced food intake were automatically recorded in a FeedScale system.

RESULTS

Upon ICV alarin injection, even at cooler ambient temperatures an increase in VO2 and continuous tail skin vasoconstriction induced a rise in Tc. This effect was not dose-dependent, however, the administration of Ala6-25Cys prevented this action and scrambled alarin did not induce any effect. Fasting-induced food intake was significantly reduced by alarin.

CONCLUSION

Alarin appears to elicit a hypermetabolic, hyperthermic thermoregulatory response and an anorexigenic effect in rats. Such responses characterize catabolic rather than anabolic mediators. Ala6-25Cys seems to act as an antagonist also to the thermoregulatory effects. Further investigations are needed to clarify the complex role of alarin in energy homeostasis. (FFG, 822782/THERAPEP, SROP 4.2.4.A/2-11-1-2012-0001, SROP-4.2.3-12/1/KONV-2012-0028, 34039/KA-OTKA/13-02)

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Neurosciences Poster Presentation

EXPOSURE TO KETAMINE INDUCES CHANGES IN IMPULSE BEHAVIOUR AND IN DENDRITIC MORPHOLOGY

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AIM

The aim of the research is to evaluate and characterize the effect of ketamine exposure in impulsive behaviour and dendritic morphology of Nucleus Accumbens and Striatum.

INTRODUCTION

General anesthetics (GA) are drugs used to allow patient interventions without physiological and psychological stress. GA exposure has been related to cognitive changes and social impairment such as increase in risk of leaving prematurely labor market and dependency on social transfer payments. Exposure to GA is known to induce changes in dopamine through dopaminergic pathway structures. Our goal is to characterize GA effect in dopaminergic function using the Variable Delay-to-Signal (VDS) test is a validated procedure that allows the evaluation decision impulsivity in rodents, which is a dopaminergic dependent function.

METHODS

Twelve animals (Wistar Rat) were used for the procedure. The VDS protocol was realized in a square operant box where a stimulus (light) is presented with variables intervals of standby and signals the permission of an action (put the nose in an opening) associated with a reward (sugar pellet). It consists in two periods: the learning tasks (10 sessions) and the test itself; where the beginning of each repetition is signaled by a flash of light from the square operant box; after 3s illuminates a light in the place where the animal should put its nose. If the animal does the action before the signal (early response [ER]) stops the test and initiates a period of punishment of 5s (no light). Every right actions release a sugar pellet. After the learning period; the rats were divided into 2 groups of 6 animals: i) non-anesthetized [NA] or ii) subjected to intraperitoneal anesthesia with ketamine [KT] (100 mg/kg for induction and 50 mg/kg for maintenance) for a period of 3 hours for 3 consecutive days and VDS test performed 6 hours after the last exposure to GA. It was evaluated the absolute number of ER, the ER per minute and the latency to ER and to collect the sugar pellet.

RESULTS

The data results are presented as (average± standard deviation) and the analysis performed using 1-way ANOVA followed by post-hoc test.

CONCLUSION

According to the results, the multiple exposures to ketamine improve the parameters related to impulsivity when compared to the NA animals.

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Neuroscience Poster Presentation

PAIN IN METASTATIC CANCER: PATHOBIOLOGY AND CLINICAL MANAGEMENT.

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AIM

Review metastatic cancer pain: i) animal models, ii) mechanisms, iii) current treatments, iv) potential future treatments.

INTRODUCTION

Cancer is a major health problem that affects and kills 12.7 million and 7.6 million people worldwide, respectively. With the ageing and growth trends of world population, it is predicted that in 2030 cancer prevalence and mortality will almost duplicate. Cancer pain occurs most often in breast, prostate, kidney and lung cancers. Bone cancer pain is experienced by patients in a complex manner, either with ongoing pain, breakthrough pain or both. Furthermore, multiple mechanisms have been described in the genesis of cancer pain. Consequently cancer pain treatment is presently difficult and cannot give full relief to patients.

METHODS

A systematic review of the most relevant articles published in the field of cancer pain in the last 5 years until May 2014 was performed.

RESULTS

Cancer pain (CP) arises mostly from bone metastasis. Though bone is innervated by Aβ, Aδ and C fibres, these fibres are nearly undetectable within metastatic tumour masses and in adjacent bone. So, animal models are necessary to study the multiple mechanisms involved in cancer pain. Current models favour local over systemic injection of cancer cells with advantages both in inter-animal comparison studies and in correlation with pain behaviour in humans, resulting in more suitable models for the study of cancer pain. Multiple CP mechanisms affecting both cellular and neurochemical organizations which result in peripheral and central sensitization have been described. Up-regulation of the neurotrophins NGF and BDNF results in genesis and maintenance of pain. Another mechanism that might be involved in CP is the activation of acid-sensing ionic channels (ASICs) in the presence of a lower pH in bone microenvironment that leads to a state of hyperalgesia. The elevation of pro-inflammatory cytokines and chemokines in the bone microenvironment also correlates with both peripheral and central components of pain. CP is also related to oxidative molecules that are responsible for the higher sensitivity of NDMA receptors and calcium conduction in nerve fibers which contribute to higher levels of pain in these patients. Activation of both microglia and astrocyte had also been demonstrated in spinal cord associated with increased levels of c-fos, dynorphin, TNF-α and IL-1. Current treatments for cancer pain follow the "WHO analgesic ladder", starting with NSAIDs for mild pain and escalating pain relief potency to weak opioids for moderate pain and strong opioids for severe pain. These analgesic drugs may be associated with adjuvant therapies to alleviate side effects and to provide better pain control. Other drugs such as bisphosphonates and steroids, and therapies as radiotherapy, radiosurgery and column surgery may be used too. Potential future treatments are being studied and they essentially involve modulating specific cancer pain mechanisms instead of general pain relief through opioid receptors.

CONCLUSION

Metastatic cancer pain remains a prevalent condition with no effective treatment. However, with the discovery of many new mechanisms, new therapeutic strategies may emerge and provide a better quality of life to these patients.

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Neurosciences Poster Presentation

CLINOID PROCESS PNEUMATISATION: FREQUENCY AND PREDICTORS

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AIM

The aim of this study is to estimate the frequency of the ACP pneumatisation and its potential predictors.

INTRODUCTION

Anterior clinoid process (ACP) may be pneumatised by the sphenoid, ethmoid, or both sinuses. If bony destruction in the middle cranial fossa is considered preoperatively, radiographic evaluation of ACP pneumatisation should be done in order to prevent cerebrospinal rhinorrhoea. Many studies report on the ACP pneumatisation, but its occurance is not fully investigated yet.

METHODS

The study was conducted among 279 adult patients who underwent sinus CT. There were 170 females (60.93%) and 109 males (39.07%). Two dimensional images in transversal and coronal planes were studied to evaluate pneumatisation of left and right ACP. Only patients without skull base pathology were included in the study. Statistical analysis was performed using STATISTICA v. 10 for Windows (Statsoft, Poland).

RESULTS

Air cells were present in 140 of the 558 examined processes, resulting in overall pneumatisation of 25.09%. Bilateral pneumatisation was found in 13.62% of patients. There was a prevalence of pneumatisation in females than in males (27.06% vs. 22.02%; $p>0.05$), especially in the letf ACP (31.18% vs. 19.27%, $p=0.028$). Presence of air cells in ACP was most common on the left than on the right side (26.52% vs. 23.66%; $p>0.05$). Anterior clinoid processes were more often connected to the sphenoid sinuses than to the ethmoidal cells (52.15% vs. 48.75%; $p>0.05$). There were no statistically significant association between age, occurance and side of ACP pneumatisation.

CONCLUSION

The ACP pneumatisation is present in over 25% of patients. It is more common in females than in males. Left side turned out to be affected more frequent than the right side.

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Neuroscience Poster Presentation

ANATOMIC VARIATIONS OF THE INTRACRANIAL VERTEBROBASILAR SYSTEM ON MSCT AND MR ANGIOGRAPHY

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AIM

The aim of this study was to determine anatomic, tophographic and morphofunctional variations and morphometric analyses of the intracranial vertebrobasilar system and their branches.

INTRODUCTION

Vertebrobasilar system (VBS) is an important vascular network that supplies blood to the important brain structures. VBS shows a high incidence of abnormalities in the form of hypoplasia, fenestrations and asymmetrical configuration of the blood vessels.

METHODS

This research represents retrospective study of CT and MR scans of 200 patients. CT angiography included 100 patients (44 males (44,0%) and 56 females (56,0%)), average 61,38±13,15 years of age and MR angiography included 100 patients (54 males (54,0%) and 46 females (46,0%)) with average 61,38±13,15 years of age. The following arteries were measured: basilar artery – BA, distal vertebral arteries – VAs, posterior inferior cerebellar arteries – PICAs, anterior inferior cerebellar arteries – AICAs, superior cerebellar arteries – SCAs and posterior cerebral artery – PCAs. Our study was conducted to analyze the diameter, asymmetry and existence of variations in the form of hypoplasia, fenestrations, asymmetry and dolichoectasia of the vertebrobasilar system.

RESULTS

The mean values and standard deviations of diameters on CTA are: BA 3.52±0.72 mm, VAs 2.88±0.82 mm, PICAs 1.27±0.55 mm, AICAs 0.95±0.41 mm, SCAs 1.31±0.30 mm and PCAs 2.21±0.40 mm. The mean values and standard deviations of diameters on MRA are: BA 3.70±0.78 mm, VAs 2.69±0.88 mm, PICAs 1.13±0.42 mm, AICAs 0.94±0.46 mm, SCAs 1.29±0.34 mm, PCAs 2.28±0.52 mm. The common variations encountered were fenestration and dolichoectasia of the basilar artery and hypoplasia, agenesia, asymmetry and duplication of other vertebrobasilar arteries.

CONCLUSION

The anatomic features of the branches of the vertebrobasilar circulation may be different from well-known normal anatomy. Our study identified frequent VBS variations. The values obtained in our study correspond to the literature data. CT and MR angiography provide accurate and detailed assessment of vertebrobasilar circulation.

PS219

Neurosciences Poster Presentation

DEVELOPMENT OF NEW PROTEIN KINASES INHIBITORS: A CONTRIBUTION FOR THE TREATMENT OF AMYOTHOPHIC LATERAL SCLEROSIS

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AIM

A drug discovery project with the aim of finding new lead compounds for the treatment of Amyothophic Lateral Sclerosis has been developed. In this context the synthesis and characterization of new small molecules based on PHA767491 structure (2-((9H-purin

INTRODUCTION

ALS is a progressive neurodegenerative disease that affects neuronal cells in the brain and in the spinal cord. When the motor neurons die, the ability of the brain to initiate and control muscle movement is lost. Studys show that ALS is caused by mutations in one of at least 32 known genetic loci including SOD1 and TAR DNA-binding protein 43 (TDP-43). TDP-43 is a cellular protein that plays a significant role in RNA metabolism. Hyperphosphorylated cytoplasmic and intranuclear inclusions of TDP-43 have been found in brains of patients with ALS. Recent studies showed that the protein kinases CK1, GSK3, and also the CDC7, are related with ALS. CDC7 is a serine/threonine kinase and its activity is controlled by binding to its activator DBF4. PHA767491 is a potent ATP mimetic inhibitor of CDC7 that reduces TDP-43 phosphorylation and prevents TDP-43-dependent neurodegeneration. This compound is characterized by a low-molecular-weight, good solubility in water, and good metabolic stability, but low cellular permeability in the PAMPA assay.

METHODS

AM076 analogous were obtained by means of 6-mercaptopurine and a series of monobromide acetophenones. After then the compounds were the N-acetylated. The synthetized compounds were characterized by NMR 1D (1H, 13C) and 2D (COSY, HSQC e HMBC), as well as by elemental analysis and HPLC-MS. The biologic assays were made in vitro using the prepared compounds to study their inhibitory capacities.

RESULTS

Seven AM076 analogous with high purity were synthetized. Several compounds were active towards CDC7 kinase. No activity was found toward CK1 and GSK3 kinases.

CONCLUSION

Regarding the AM076 analogous, the seven compounds synthetized were obtained with moderated yields and high purity. Moreover, the N-acylation process using acetic anhydride and triethylamine gave the pretended derivatives in moderated yields and high purity. From the preliminary results of the biological screening one can conclude that the inhibition of CDC7 kinase activity is affected by the bulky groups located in the para position of the side chain of the referred derivatives. On the other hand, it was observed a loss of activity when the substituents were placed in the meta position of the side chain. No inhibitory activity was detected toward CK1 and GSK3 kinases. The synthesis of a more consistent library is on progress that will allow in a next future the establishment of structure-activity relationships and consequently the improvement of efficacy of this type of scaffold toward the kinases targets.

TOTAL FAT CONTENT AND FATTY ACID COMPOSITION IN SNACK FOODS FROM SERBIAN MARKETS

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AIM

The aim of work was to determine fatty acid compisition and trans fatty acids in snack food and inflenece on health

INTRODUCTION

"Fast food" that also includes snack products is part of the daily diet especially in children and adolescents. According to the national legislative,- snack products are classified as: chips, chips' related products, flips/crisps, products based on pellets, expanded products, fried and dry-roasted natural products –like seeds, nuts. Most of the snack products could be reach sources of saturated fats which are scientifically proven to have an adverse effect on health, leading to increased levels of LDL cholesterol, triglycerides. The aim of this study was to analyze the fatty acid content of snack products available in the market of Serbia that are commonly consumed in our student population.

METHODS

A total of 15 commercial snack products commonly used in adolescent population were obtained from the market in order to determine fatty acid composition. These samples were classified as: corn flips products (5), potato chips (4), popcorn (2), roasted corn (2), roasted peanuts (2). All samples were purchased at random in local supermarkets and health food stores in Belgrade. They were manufactured by different manufacturers. Extraction of fats was carried out according to the nature of products. We applied the method of direct extraction with an organic solvent (method by Soxlet). Apparatus consists of a condenser, extractor, extraction/boiling flask and heater for achieving optimum temperature. About 10 g of each sample was weight (± 1 mg) and transferred into the cellulose capsule and the capsule transferred to the extractor, closed with wad and connected with the rests of the Soxlet's apparatus. The flask where the extracted fats were collected was previously brought to constant weight. The extraction medium was organic solvent (chloroform). The flask was heated on the heater. After several hours of the extraction, the solvent was evaporated in the vacuum evaporator bellow 40ËšC and the residue in the flask was dried until constant weight was measured. From the difference in weight of the flask before and after extraction total fat content was determined. After acid hydrolysis of fats to fatty acids, fatty acids were derivatized into the corresponding methyl esters. Qualitative and quantitative composition of fatty acid methyl esters was determined on Agilent Technologies 7890A Gas Chromatography System with FID detector. A 100 m fused silica capillary column of 0,25 mm internal diameter coated with cyano-propil-polysiloxane as stationary phase (HP 88) was used. Identification of chromatographic peaks was carried out by comparasion of their retention times using appropriate standards of fatty acid methyl esters (Sigma).

RESULTS

The total fat content varied significantly between the groups and within the same snack group. The lowest content of total fat was recorded in roasted corn (9.45%), while the highest content had roasted peanuts (73.64%). The greatest variation within the same group showed roasted corn where the fat content was in a range from 9.45% to 25.53% and the roasted peanuts with the range of 36.86% to 73.64%. Based on the results obtained with gas chromatography, we concluded that all snack products had the highest content of monounsaturated oleic acid, while the content of polyunsaturated fatty acids were low. The most common monounsaturated fatty acid-oleic fatty acid was in the range of 2.76% in popcorn, to 46.04% in the one sample of roasted peanuts, while linoleic fatty acid was the most common polyunsaturated fatty acid in analyzed snack food with the highest content in flips products (10.29%). The content of saturated fatty acids was in the range of 4.76% in sample of flips to 16.10% in one sample of chips. Analyzed chips products had the highest content of saturated fatty acids. The most common saturated fatty acid was palmitic, with highest percentage in chips (14.37%, while the content of stearic saturated fatty acid was low. Some of analyzed snack products were sources of trans-fatty acids, like flips products and popcorn.

CONCLUSION

Since snack foods are very popular among young population they can be important sources of selected nutrients in their everyday diet. This study indicated that certain snack food had large amounts of fat, but the content of undesirable saturated fats was relatively low. The determined fatty acid profiles in snack foods were significantly influenced with the quality of lipids used in their production.

INVESTIGATION OF THE ANTI-TUMOR ACTIVITY OF NEWLY SYNTHESIZED ZINC (II) COMPLEX ON HL-60 AND L929 TUMOR CELL LINES IN VITRO

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AIM

The aim of this study was to investigate cytotoxic potential of newly synthesized Zn(II) complex towards human promyelocytic leukemia (HL-60) and mouse fibrosarcoma (L929) cell line, and to investigate the mode of cell death induced by this complex.

INTRODUCTION

Malignant diseases are one of major health problems nowadays in the developed countries.

METHODS

Cell viability was determined using acid phosphatase assay. Flow cytometric analysis was used to determine the cell cycle distribution and intracellular production of reactive oxygen species, following the staining with propidium-iodide and dihydrorhodamine 123 (DHR), respectively.

RESULTS

Cell viability showed that novel Zinc complex displays moderate cytotoxic activity following 48-hour treatment. The IC50 values, i.e. concentration of Zinc complex that decreased cell number to 50% compared to untreated cells, for HL-60 and L929 cell line were 63,54 ± 0,32μM and 41,74 ±1,17 μM, respectively. DNA fragmentation analysis revealed that treatment with Zn(II) complex (100μM, 48h) resulted in statistically significant increase in percentage of cells in subG0 phase to 17,31% and 22,5% in HL-60 and L929 cell line, respectively, compared to untreated cells ($p<0.05$). Besides, Zn complex induced formation of reactive oxygen species (ROS), that reached the peak after 6 h of incubation, as measured by DHR fluorescence. The role of ROS in cytotoxic action of novel Zn complex was confirmed by pretreatment with scavenger N-acetylcysteine (NAC), as NAC-pretreatment reduced the cytotoxic action of Zn(II) complex.

CONCLUSION

The novel Zn(II) complex displays fair anti-tumor activity to HL-60 and L929 cell lines in the micromolar concentration range. The observed anti-tumor effect seems to be, at least in part, mediated by ROS overproduction, which then seems to activate the apoptotic mechanism.

INHIBITION OF GLUCOSE UPTAKE IN HUMAN FIRST TRIMESTER TROPHOBLASTS BY XANTOHUMOL, MEDIATED BY TYROSINE KINASES, MAMMALIAN TARGET OF RAPAMYCIN AND C-JUN N-TERMINAL KINASES INTRACELLULAR PATHWAYS, HAS CONSEQUENCES UPON THE PROCESS OF PLACENTATION

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AIM

The aim of this work was to investigate whether modulation of glucose transport by some polyphenols in first trimester extravillous trophoblasts (EVTs), cells that regulate the process of placentation, affects cell viability, proliferation, growth and mig

INTRODUCTION

METHODS

To do this, glucose uptake by HTR-8/SVneo human first-trimester EVT cell line and its modulation by selected polyphenols was studied by measurement of cellular incorporation of 3H-2-deoxy-D-glucose (3H-DG). Additionally, the effect of XH upon glucose cellular metabolism (extracellular lactate quantification) and upon the viability (lactate dehydrogenase leakage assay), proliferation (3H-thymidine cellular incorporation), culture growth (sulforhodamine B (SRB) assay) and migration capacity (wound-healing assay) of HTR-8/SVneo cells were studied. Finally, MCT-mediated transport was measured by quantification of 14C-butyrate (14C-BT) uptake by HTR-8/SVneo cells.

RESULTS

Acutely (30 min), the polyphenols quercetin, epigallocatechin-3-gallate, xanthohumol (XH) and resveratrol concentration-dependently inhibited 3H-DG uptake by inhibiting both GLUT and non-GLUT-mediated uptake. XH was found to be the most potent inhibitor of 3H-DG uptake by HTR-8/SVneo cells and, at 100 μM, it significantly reduced the Vmax while not affecting the Km of 3H-DG uptake.

CONCLUSION

Altogether, these results show that XH potently and non-competitively inhibits glucose uptake by EVTs, an effect that seems to be mediated by mTOR, TK and JNK intracellular pathways. Our results also show that the cytotoxic and antiproliferative effects of XH over EVTs are mainly due to glucose deprivation.

NEW INTRACELLULAR SIGNALING INHIBITORS AS TARGETED THERAPEUTIC APPROACHES IN MULTIPLE MYELOMA

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AIM

The aim of this study is to evaluate the potential therapeutic of new intracellular signaling inhibitors in Multiple Myeloma (MM), namely inhibitors of mTOR (Everolimus), survivin (Silibinin), proteasome (Gambogic Acid) and of IkB (Parthenolide).

INTRODUCTION

MM is a plasma cell dyscrasia characterized by clonal proliferation of malignant plasma cells in the bone marrow microenvironment. Currently, Bortezomib (a proteasome inhibitor, PI) is used as a first line treatment for MM. A complex signalling network is activated in plasma cells, allowing the survival, proliferation and avoiding apoptosis. The knowledge of these changes would enable the use of new drugs in this pathology.

METHODS

For this purpose, we used a Multiple Myeloma cell line, the H929 cells. Cells were cultured in absence and presence of different concentrations of Everolimus, Silibinin, Gambogic Acid and Parthenolide alone, and in association with Bortezomib. To evaluate the effect of these inhibitors on cell viability we used the Resazurin Assay. Cell death was determined by optical microscopy (May-Grunwald Giemsa staining), by flow cytometry (FC) using the Annexin V and Propidium Iodide double staining, and by the expression levels of the activated caspases, using the Apostat probe. The effect of the drugs in cell cycle was determined by flow cytometry using Propidium Iodide incorporation.

RESULTS

Our results show that all of the tested compounds induced cell death in a time- and dose-dependent manner, with IC50 values, after 72h of treatment, of 17,5 μM for Everolimus, approximately 150 μM for Silibinin, less than 150 nM for Gambogic Acid and 12,5 μM for Parthenolide. These compounds induced cell dead mainly by apoptosis, confirmed by the increase of activated caspases expression levels and morphological characteristics. These drugs also induce cell cycle arrest in G0/G1 phase, mainly the mTOR inhibitor. The association of lower doses of these inhibitors with a small dose of Bortezomib shows an additive cytotoxic effect.

CONCLUSION

In conclusion, our results suggest that inhibition of multiple signalling pathways could be used as a new potential approach in the treatment of MM as in monotherapy as in combination with bortezomib.

INVESTIGATION OF ANTI-TUMOR ACTIVITY OF NOVEL SYNTHESIZED PALLADIUM COMPLEX TO HUMAN PROMYELOCYTIC LEUKEMIA CELL LINE IN VITRO

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AIM

The aim of this study was to investigate the cytotoxic potential of novel Pd4 complex on HL60 human promyelocytic leukemia cell line.

INTRODUCTION

Acute promyelocytic leukemia is a form of acute myeloblastic leukemia characterized by hemorrhagic episodes, severe thrombocytopenia and infiltration of the marrow with hypergranular promyelocytes. Ultrastructurally, the promyelocytes show many splinter granules. Incresaing number of patients and inadequate response on the therapy lead to searching for potential hemoterapeutics.

METHODS

Cell viability was determined using acid phosphatase assay. Cell cycle analysis, phosphatidyl serine externalization and pan-caspase activity were determined flow cometrically, using appropriate fluorochromes (propidium-iodide, annexinV-FITC/propidium-iodide and Apostat). Pan-Caspase activity was determinated by commercial test.

RESULTS

Cell viability showed that novel Pd complex displays good cytotoxic activity following 24 and 48-hour treatment (IC50 values 14,46±15%μM and 3,27±15%μM, respectively). DNA fragmentation analysis revealed marked increase in percentage of cells in subG0 phase to 12,39% in applied concentration of 5μM, compared to 0.88% of cells in the control (untreated) samples. We have showed increase in the number of annexin positive cells: 10,44%(2,5 μM) i 38,91%(5 μM) after treatment, compared to 8,2% in the control samples. In treated cells, caspase activation was 1,9 times higher in comparation with control cells.

CONCLUSION

The novel Pd4 complex displays good anti-tumor activity to human promyelocytic leukemia cell line in the micromolar concentration range. The observed anti-tumor effect seems to be, to important part, mediated by the apoptotic mechanism.

INVESTIGATION OF ANTI-TUMOR ACTIVITY OF NOVEL ZINC (ZN(II)) COMPLEX ON HUMAN PROMYELOCYTIC LEUKEMIA CELL LINE IN VITRO

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AIM

Aim of this paper is to investigate cytotoxic effects of novel Zinc complex on cell line HL-60 (human promyelocytic leukaemia).

INTRODUCTION

Leukaemias are malignancies of white blood cells. Since different types of leukaemias react differently to current therapeutic protocols, and those protocols have severe side effects there is apparent need for new, more efficient chemotherapeutic agent for treatment of this neoplasm.

METHODS

Cell viability was determined using MTT test. Analysis of cell cycle distribution, externalisation of phosphatidyl-serine, pancaspase activity and oxidative stress were conducted on flow cytometer using fluorophores propidium iodide, annexin/propidium iodide, ApoStat, dihydrorhodamine and dihydroethidium.

RESULTS

The investigated novel Zinc complex showed cytotoxic effect after 24 hour and 48 hour exposition of cells (IC50 values 50,3 ± 9,6μM and 43,03 ± 5,3 μM, respectively). After 24 hour treatment with this complex 27,45±4,8% of cells have translocated phosphatidyl-serine to the outer layer of their membranes, pancaspase activity was 3,89 times greater than in control cells, and an there was an increase in the number of cells with fragmented DNA from 2,12±0,2% to 13,17±0,9%. Dihydrorhodamine staining showed 1,78 times greater production of free radicals in cells treated for one hour, and dihydroethidium staining showed a 5 time increase in free radicals production when the cells were exposed to the Zinc complex for 2 hours. By adding antioxidant N-acetylcysteine the IC50 concentration raised to 83,78±6,7μM after 24 hour treatment.

CONCLUSION

Novel Zinc(II) complex has cytotoxic effect on HL60 cells. By adding N-acetylcysteine cytotoxic effect is decreased. The results show that primary type of cell death is apoptosis, which is probably induced by oxidative stress.

EFFICACY OF SYSTEMIC TREATMENT OF CLEAR CELL RENAL CELL CARCINOMA WITH SUNITINIB.

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AIM

The primary aim of this study is to evaluate survival of ccRCC patients treated with Sunitinib and determine factors influencing PFS and OS.

INTRODUCTION

Clear cell Renal Cell Carcinoma accounts for 3% of all malignant tumors. 30% of patients have distant metastases at the moment of diagnosis what is associated with poor prognosis. Systemic treatment usually begins with Tyrosine Kinase Inhibitors, in Poland – Sunitinib but also other options, like mTOR inhibitors are available on the market.

METHODS

The medical records of 153 (117M, 36F) patients with metastatic ccRCC treated at the Department of Oncology of Military Institute of Medicine in Warsaw were reviewed. Mean patients' age was 59 (25-80) years. Patients stared therapy between January 2007 and June 2011. Analysis of hypothetical prognostic and predictive factors were performed with statistical test (Student's t-test, Chi-square) comparing patients with OS>3years and below, and PFS>1 year versus below. Evaluated factors included: sex, BMI, presence of cardiovascular diseases, hypertension, diabetes, baseline levels of blood parameters, hypertension and hypothyroidism occurring during treatment.

RESULTS

Median PFS on Sunitinib was 14,9 months (mean 17,1).Median OS since nephrectomy was 48,5 months (mean 66,3). Patients with PFS>1 year had significantly higher baseline level of RBC (4,65 v 4,35, p=0,043), HGB (13,5 v 12,18, p=0,00004) and MCV (90,14 v 83,7, p=0,01) and lower PLT (227,45 v 307,77, p=0,005) and Glu (100 v 117, p=0,006). Other factors were insignificant. During the treatment they presented statistically higher frequency of side effects: hypertension (45% v 19%, p=0,0005) and hypothyroidism (25% v 1.%, p=0,00006). This group presented also lower level of Neutrophyles (1,7 v 2,6), platelets (136 v 182) and higher of Creatynine (1,66 v 1,36), WBC (9,06 v 7,41), Alt (69 v 36) and Ast (75 v 35). In the group of patients with OS>3 years only significant differences were observed with baseline WBC (6,77 v 8,15, p=0,03), RBC (4,86 v 4.35, p=0,001), HGB (13,89 v 12,43, p=0,00001), PLT (213 v 289, p=0,014) and frequency of hypertension (55% v 23%, p=0,0012) and hypothyroidism (30% v 7%, p=0,0001) during treatment. According to Pearson correlation test, OS highly depends on PFS on first line drug, r=0,79.

CONCLUSION

Analyses of group of patient with long survival (PFS>1y, OS>3y) reveals that patient with high red blood cells parameters and low platelets and glucose are highly probably to benefit more from treatment with Sunitinib. In the group of short survival patients, observed low frequency of side effects – hypertension, hypothyroidism, reno- and hepatotoxicity suggest that used dose of Sunitinib (50mg) is inappropriate and should be increased. Safety and efficacy of higher doses of Sunitinib should be reevaluated in new clinical trials. Sunitinib Induced Hypertension and Hypothyroidism are important prognostic factors for patients with ccRCC. Presented data are highly important in selection of individual treatment for patients with ccRCC.

PHOTODYNAMIC THERAPY IN VIVO EFFECT OF TWO PHOTOSENSITIZERS IN A RETINOBLASTOMA HETEROTOPIC ANIMAL MODEL

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AIM

To evaluate the therapeutic outcome of two photosensitizers heterotopic animal model of retinoblastoma.

INTRODUCTION

Retinoblastoma (RB) is a rare but aggressive tumor of retina that affects children. There is a great effort for ensure better quality of life and preserve the eye of the children however therapies currently available can lead to secondary neoplasias. Photodynamic therapy (PDT) is a non mutagenic therapeutic modality for treating cancer. Our previous in vitro studies showed the potential of the photosensitizers we developed in retinoblastoma cell line Y79. Therefore, now we intend to evaluate in vivo outcome in an heterothopic animal model.

METHODS

The retinoblastoma cell line Y79 was propagated according to standard procedures. 18 Balb/c nu/nu nude female mice were injected subcutaneously with a suspension of 107 cells. Animals were divided in tree two groups. The Group I, the control group, with 6 animals, was not submitted to PDT. The Group II, with 6 animals, was treated with a bromated hydroxyphenylporphyrin and the Group III, with 4 animals, was treated with meso bis 5-15-[(2-bromo-5-pentaacetilgliconilcarboniloxi)fenil]porphyrins. Animal were injected intraperitoneally with 2mg/kg when tumor reached 200 mm3 of volume. Animal were protected from light during 48 hours, and tumor area was irradiated with an appropriate Ceramoptec laser system. Animals were monitored daily and registered any signs of disease, during 12 days.

RESULTS

This heterotopic animal model of RB has proved to be reproducible and of simple obtainment and monitoring. In Group I, control group, we observed a solid round tumor. Tumors of animal from Group II showed a decreased tumor volume, with significant differences related to the control ($p= 0.022$). After the irradiation tissues in the tumor area showed, in some animals, necrosis that was replaced by scarring during the follow-up. In animals from Group III, we observed that tumor volume growth more slowly compared with the ones from Group I.

CONCLUSION

Bromated hydroxyphenyl porphyrin photosensitizer used has a significant effect over the growth of RB xenotransplants. These promising results can lead to further studies in order develop new options for managing retinoblastoma.

INCIDENCE AND MORTALITY FROM MALIGNANT TUMORS OF REPRODUCTIVE ORGANS AND BREAST AMONG YOUNG WOMAN IN BELGRADE

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AIM

Aim of this descriptive epidemiological study was to analyze trends of incidence and mortality rates of malignant tumors of reproductive organs and breast in a population of young woman (15-39) in Belgrade in the period of 1999-2010.

INTRODUCTION

Malignant tumors of reproductive organs and breast among young woman become particularly significant due to family planning.

METHODS

The main sources of illness incidence and mortality from malignant tumors in woman population of Belgrade from 1999-2010 were taking from the cancer registry of central Serbia. In mortality and incidence analyses age specific and standardized mortality rates per 100 000 female population as well as linear trend were used. Linear regression coefficient in time trend analysis of rates was accessed by the Fisher's test.

RESULTS

In Belgrade, average standardized incidence rate of breast cancer among woman 15-39 years in Belgrade was 15.5/100 000 while mortality was 2.0/100 000. In cervical carcinoma standardized rate of incidence was 16.0/100 000, while mortality was 1.4/100 000. Considering endometrial cancer the value was 1/3/100 000, and mortality was 0.1/100 000. In ovarial cancer values were 15.3/100 000 and 0.6/100 000 respectively. The significant increasing tendency in observed period was registered only for breast cancer (p=0.005) while other mortality trends were out of statistical significance.

CONCLUSION

According to incidence and mortality rates of explored malignant disease and their changes in the previous 12 years in population of young woman in Belgrade, it could be established that malignant tumors of reproductive organs and breast were important health problems in our population.

INHIBITION OF METLAPROTEINASES INDUCES APOPTOSIS AND CELL CYCLE ARREST IN HEMATOLOGICAL NEOPLASIAS

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AIM

The aim of this study was to evaluate the therapeutic potential of Batimastat (BB-94), a matrix metalloproteinases inhibitor, in in vitro models of hematological neoplasias.

INTRODUCTION

The bone marrow microenvironment is the main support of normal hematopoiesis, although it is also important in processes involving the development of neoplastic clones. The matrix metalloproteinases (MMPs) are an important player in bone marrow microenvironment, since they can degrade all the protein components of the extracellular matrix, being also involved in cancer development and progression. Since the majority of actual therapeutics for hematological neoplasias fails in some patients leading to relapses, the use of MMPs inhibitors may become a new therapeutic approach for these patients.

METHODS

For this purpose, we used four hematological neoplasia cell lines, two Acute Promyelocytic Leukemia cell lines (NB-4 and HL-60 cells, with and without the translocation t(15;17), respectively), one Multiple Myeloma cell line (H929 cells), and one Myelodysplastic Syndrome cell line (F-36P cells). We detected gene basal expression levels of MMP-2, -8 and -9, and Tissue Inhibitor Metalloproteinase (TIMP)-1 and -2 by semi-quantitative PCR, and the protein basal expression of MMP-2, -8 and -9, by Flow Cytometry (FC) using specific antibodies. All cell lines were cultured in absence and presence of different concentrations of BB-94 ranged from 0,1 μM to 10 μM, in a daily or single dose administration. To evaluate the effect of this inhibitor on cell viability and cell density we used the Trypan Blue Assay. Cell death was determined by optical microscopy (May-Grunwald Giemsa staining), and by FC using the Annexin V and Propidium Iodide double staining. It was also evaluated the activation of caspases, using the Apostat probe, and cell cycle by FC. In order to understand the role of BB-94 in cell proliferation, we evaluated the ERK 1/2 and AKT expression by Western Blotting.

RESULTS

Our results showed that BB-94 reduces cell viability and proliferation in a time, dose and cell line dependent manner. We found that the half maximal inhibitory concentration (IC50) at 48 hours of exposure was, approximately, 7,5 μM for NB-4, 10 μM for H929and F36-P, and between 7,5 and 10 μM for HL-60. The daily administration schedule seems to be more effective in the reduction of cell viability and proliferation when compared to the same doses in single administration, except in H929 cell line. BB-94 induced cell death by apoptosis with activation of caspases, in a dose-dependent manner. The cytotoxic effect of BB-94 seems to be more active in NB-4, the APL cell line with the t(15;17) translocation, and this effect seems to be independent of MMPs expression levels. The antiproliferative effect is confirmed through of cell cycle analysis, which revealed an arrest in G0/G1 and S phases, in HL-60 and NB-4 cell lines, respectively. In Western Blot analysis it was observed an increase of ERK expression in the cells treated with BB-94 when compared to the cells without treatment, in every cell line except H929. On the other hand, BB-94 induced an increase in AKT expression in HL-60 cell line, while in H929 a decreased was observed, compared to control.

CONCLUSION

In conclusion, our results suggest that BB-94 is a potential new targeted therapy in hematological neoplasias and also support a role for the ERK and AKT signaling pathway in BB-94-induced apoptosis. However, therapeutic efficacy may depend on the cell type and genetic characteristics of the neoplasia, as well as the therapeutic schedule used.

8-PRENYLNARINGENIN STIMULATES ANGIOGENIC PATHWAYS

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AIM

To evaluate the effect of 8PN on angiogenic pathways and to verify the dependence on the activation of the ER.

INTRODUCTION

8-Prenylnaringenin (8PN) is a polyphenol and a powerful phytoestrogen with a binding affinity to estrogen receptors (ER) alpha three times higher than ERβ [1]. 17β-Estradiol stimulates angiogenesis [2]. Recent work has attributed angiogenic properties to 8PN [3], but its effect on the modulation of angiogenic process is not consistent.

METHODS

Human umbilical vein endothelial cells (HUVEC) were stimulated with vascular endothelial growth factor (VEGF) and treated with 10µM 8PN. ERα and ERβ gene expression was evaluated by RT-PCR. HUVEC were also treated with an ERβ antagonist (PHTPP). VEGFR2, pAkt, pERK 1/2 and Tie2 expression was quantified by western blotting. Ang2 was evaluated by ELISA assay. The modulation of angiogenic pathways by 8PN was confirmed in vitro by quantification of tubular structures formed by HUVEC cultivated in matrigel. Quantifications are expressed as mean ± SEM. Results were evaluated by ANOVA followed by Bonferroni. A difference between experimental groups was considered significant whenever p‰¤ 0.05.

RESULTS

HUVEC only transcribed ERβ. 8PN tend to increased the expression of VEGFR2 (128.8 ± 16.1%) in a process apparently dependent on ERβ and improved the expression of pERK (127.6 ± 16.8%) in a process dependent on ERβ. It stimulated the release of Ang2 (122.3 ± 0.3%) and the expression of Tie2 (140.6 ± 6.1%) independently of ERβ and didn't affect the expression of pAkt (98.8 ± 6.7%). Matrigel assay showed an increase in the formation of tubular structures (143.2 ± 4.4%) after treatment with 8PN.

CONCLUSION

8PN manifested pro-angiogenic properties involving pathways regulated by binding to ERβ and pathways independent of this stimulation. This finding can be interesting, considering pathologies associated to poor angiogenesis, as myocardial ischemia, peripheral arterial disease and neurological diseases.

RADIOSENSITIVE AND RADIORESISTANT COLORECTAL CANCER CELL LINES: RESPONSE TO DIFFERENT TREATMENT MODALITIES

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AIM

In this study we aimed to compare cell viability, DNA damage, oxidative stress and GSH expression of sensitive parental colorectal cancer cells to its radioresistant derivatives, after treatment with 5-fluorouracil (5-FU), radiation alone and combined the

INTRODUCTION

Chemoradiation as neoadjuvant treatment for locally advanced rectal cancer is one of the most common approaches, since it allows downstaging and improves local control. After exposure to radiation, there is a succession of physical, chemical and biological processes, which include interactions between charged particles and the atoms of the cells, formation of free radicals and enzymatic reactions due to cellular damage. To understand how radioresistant cells behave after treatment is extremely important in order to improve treatment modalities.

METHODS

Parental WiDr cell line and the radioresistant derivative WiDr/10r, previously obtained by our group, were used to study radioresistance. Cells were submitted to 20 μM of 5-FU for chemotherapy and irradiated with 0, 2 and 10 Gy for radiation alone, in a Varian Clinac 600 linear accelerator with a 4MV photon beam. Cells treated with combined therapy were exposed to 20 μM of 5-FU three hours prior irradiation and then irradiated with the same doses. Cell viability, oxidative stress and GSH expression were assessed by flow cytometry 96 hours after treatment and DNA damage was measured by comet assay immediately after treatment.

RESULTS

WiDr cells showed a significant decrease of cell viability after exposure to 10 Gy and to 5-FU + 10 Gy, comparing to their derivative radioresistant cells WiDr/10x (respectively 49.1±5.0% compared to 66.0±8.1%, p=0.008; and 50.9±2.4% compared to 63.8±4.2%, p=0.003). Besides, they showed a significant increase of necrosis, regarding 10 Gy (30.9±8.5% compared to 19.3±4.2%, p=0.001), 5-FU (22.5±5.2% compared to 17.8±2.7%, p=0.009) and 5-FU + 10 Gy (27.0±6.6% compared to 16.2±2.3%, p=0.015).

CONCLUSION

These results showed that radioresistant WiDr/10r cell line is less affected by higher doses of radiation, regarding cell viability and oxidative stress. However, radioresistant cell line acquired more DNA damage than radiosensitive cell line, which means that cells can carry DNA damage and still be viable and resistant to treatment.

EXPRESSION OF HORMONAL RECEPTORS IN BREAST CANCER STEM CELLS

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AIM

With this work we intend to evaluate the expression of HR in TN and HR positive (HR+) CSC

INTRODUCTION

In clinical practice, breast cancer (BC) is stratified into 3 groups: tumors that express hormonal receptors (HR), tumors overexpressing Her2, and finally those which do not express HR and do not overexpress Her2, triple negative (TN) BC. Estrogen receptor-α (ER-α) and progesterone receptor (PR) are HR that are used in clinic as markers for diagnostic and treatment purposes. The recent theory of cancer stem cells (CSC) refers to a small tumor cell population that has the main characteristics of stem cells. It is believed that CSC are responsible for tumor progression, recurrence as well as resistance to therapy.

METHODS

The breast cancer cells lines MCF-7, HR+, and HCC1806, TN, were submitted to the mammosphere forming protocol. The first CSC generation (MS1) was cultured in adherent conditions. This procedure was repeated in order to obtain successive generations of CSC (MS1, MS2 and MS3) and the CSC-derived cells in adherent conditions (G1, G2 and G3). After obtaining the various generations of CSC and CSC-derived cells total protein extracts were prepared in order to evaluate the expression of ER- α and PR by Western blot.

RESULTS

In the cell line HCC1806, CSC and adherent-derived populations had null expression for both receptors. The expression of ER- α was lower in MS1 ($p<0.001$), in MS2 ($p<0.001$) and MS3 ($p<0.05$). However the adherent population had a similar expression of this receptor comparing to the parental cell line. The expression of PR was also lower in MS1 ($p<0.001$), in MS2 ($p<0.001$) and MS3 ($p<0.001$), however the adherent population showed no difference comparing to MCF-7.

CONCLUSION

The lower expression of both HR in CSC can represent an undifferentiated phenotype of these cells. However when submitted to adherent culture conditions cells regain the original phenotype. The undifferentiated phenotype of CSC suggest that targeting agents for HR may not be effective, at least in a long term perspective considering recurrence and distant metastization.

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Oncology & Molecular Biology Poster Presentation

LIDOCAINE A NEW THERAPEUTICAL APPROACH IN ORAL SQUAMOUS CELL CARCINOMA: AN IN VITRO STUDY

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AIM

With this work, we intend to evaluate the therapeutic efficacy of local anesthetic, lidocaine, in oral squamous cell carcinoma (OSCC) cell lines.

INTRODUCTION

Oral cancer, most commonly oral squamous cell carcinoma (OSCC), represents about 90% of oral cancer patients, has a worldwide incidence around 300 000 cases / year. A substantial number of these patients may become resistant to chemotherapy or relapse having a particularly poor survival rate. Thus, identification of innovative therapies is greatly needed. Local anesthetics, such as lidocaine, have been reported to produce good pain control in patients with head and neck tumors and to inhibit cancer cell proliferation, invasion and migration. However, mechanisms underlying these effects are not fully understood, namely in OCSS.

METHODS

For this purpose we maintained in culture two OSCC cell lines, the HSC-3 (metastatic) and BICR-10 (in situ) cells, in absence and in presence of different concentrations of lidocaine in monotherapy (daily or single dose administration) or in association with conventional chemotherapeutic drugs (Cisplatin or 5-Flurouracil). Cell viability was assessed by the rezasurin assay and cell death by Optical Microscopy (May-Grunwald staining) and flow cytometry (FC) using the Annexin V/Propidium Iodide double staining. Cell cycle (using propidium iodide incorporation), caspases levels (apostat kit), mitochondrial membrane potential (JC-1 probe), reactive oxygen species levels (hydrogen peroxide, H2O2; superoxide anion, O2•-, evaluated by 2,7-diclorofluorescein and dihidroetidium, respectively) and the antioxidant defense (Reduced Glutathione (GSH) using mercury orange) were evaluated by flow cytometry.

RESULTS

Our results show that lidocaine induces antiproliferative and cytotoxic effects in a dose, time, administration and cell type dependent manner. HSC-3 cells seem to be more sensitive to lidocaine effect than BICR-10 cells, as the IC50 at 48 hours was 4 – 4.5 mM and 5 – 6 mM, respectively. Furthermore, lidocaine induces cell death mainly by apoptosis and late apoptosis/necrosis, which may be related with the increase in caspases and superoxide anion levels and the decrease of mitochondrial membrane potential as well as with the pre-G1 peak in cell cycle. Lidocaine decreases GSH levels in HSC-3 cells compared to BIRC-10 cells, which may contribute for the higher sensitivity of HSC-3 cells to lidocaine. Moreover, in both cell lines when we administrated lidocaine daily at low concentration, as well as in combination schedule with conventional chemotherapy we observed synergist cytotoxic effect.

CONCLUSION

Our results suggest that lidocaine constitute a new therapeutic adjuvant approach in OSCC, namely in metastatic cancer.

HUMAN AMNIOTIC MEMBRANE-DERIVED PROTEINS: A NEW APPROACH FOR HEPATOCELLULAR CARCINOMA TREATMENT?

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AIM

The aim of this study is to evaluate the effect of hAM proteins extracts (hAMPE) in protein synthesis and metabolic activity in three human HCC cell lines. DNA induced-damage will be also evaluated.

INTRODUCTION

Hepatocellular carcinoma (HCC) is a primary liver cancer. HCC is a leading cause of cancer death worldwide, mainly due to its ability to withstand conventional therapies. For the last years, the regenerative properties of human amniotic membrane (hAM) were explored in the treatment of liver diseases. Several studies indicated hAM as a possible option in the treatment of liver diseases, particularly in the treatment of hepatic cirrhosis and fibrosis. Nevertheless, until now, there are still no studies exploiting the application of hAM in the treatment of HCC

METHODS

hAM were obtained from caesarean sections with informed consent according to the guidelines of Ethical Committee of Coimbra Hospital and University Centre (Coimbra, Portugal). hAM were washed with phosphate buffered solution and subjected to mechanical actions in order to extract proteins, which were quantified using Nanodrop®. To study the effect of hAMPE in HCC, studies were performed in three human cancer cell lines: HuH7 (mp53), HepG2 (wp53) and Hep3B2.1-7 (p53 sub-expressed). Cells were incubated with 1µg/µL of hAMPE for 24h or 72h. After, sulforhodamine B (SRB) and MTT assays were performed to assess protein synthesis and metabolic activity, respectively. In order to evaluate DNA damage, comet assay was carried out.

RESULTS

After 24h of treatment with hAMPE, protein synthesis decreased 24% in HuH7, 39% in Hep3B2.1-7 and 46% in HepG2 cell line. Metabolic activity decreased 77% in Hep3B2.1-7, 31% in HepG2 and 29% in HuH7 cells after treatment. Regarding 72h treatment, protein synthesis decreased 85% in Hep3B2.1-7, 89% in HuH7 and 91% in HepG2 cell line. Metabolic activity value decreased 32% in HuH7, 65% in HepG2 and 83% in Hep3B2.1-7 cell line after treatment. Through comet assay it was observed that Hep3B2.1-7 tail moment (product of tail length and total DNA fraction in tail) increased 3 times. The tail moment of HepG2 increased 13 times after 72h treatment. There is no difference between hAMPE treated and untreated HuH7 cells tail moment.

CONCLUSION

The treatment of HCC cell lines with hAMPE decreases the protein synthesis and the metabolic activity as the time treatment increased,, indicating the time-dependence of this treatment strategy. The results also show the increase of DNA damage, confirming that hAMPE may have a promising role in the HCC therapy.

EVALUATION OF THE EXPRESSION OF MICRORNAS 21, 125B AND 155 IN HEMATOLOGICAL NEOPLASIAS

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AIM

The aim of this study was to evaluate the expression of miR-21, miR-125b and miR-155 in different hematological neoplasias both sensitive and resistant to chemotherapy.

INTRODUCTION

MicroRNAs are small, single stranded non-coding RNA molecules that regulate gene expression at post-transcriptional level. MicroRNAs have been shown to be involved in a wide range of biological processes such as cell cycle control, apoptosis, differentiation and proliferation. In addition to their important roles in healthy individuals, microRNAs have also been implicated in a number of diseases including a variety of cancers. In this way, microRNAs are intensely studied as candidates for diagnostic and prognostic biomarkers and predictors of drug response.

METHODS

In this study we used different hematological neoplasia models, HEL cells (erythroleukemia cell line), NB-4 and HL-60 cells (Acute Promyelocytic Leukemia (APL) cell lines, with and without the translocation t(15;17), respectively), F36P cells (Myelodysplastic Syndrome cell line) and K562 cells (Chronic Myeloid Leukemia cell line in blast crisis). In our lab, we developed two Imatinib resistant cell lines, the K562-RC (continuous resistance) and K562-RD (discontinuous resistance). The RNA from the cells was extracted using TRIzol. We converted RNA into cDNA using a specific primer of qRT-PCR, miRNA TaqMan MicroRNA Assays and the reagents from TaqMan MicroRNA Reverse Transcription Kit. After cDNA synthesis, we executed the amplification of miR-21, miR-125b, miR-115 and RNU6B by qRT-PCR. For each microRNA we used “TaqMan MicroRNA Assay” with specific primers and probes.

RESULTS

Our results showed in all cell lines low expression levels of miR-21, however the K562-RC and F36P cells presented the higher expression levels. Besides that, we observed in HL-60, HEL and F36P cell lines an increase of expression of miR-125b, with levels between 1,2 and 2,1, whereas in K562 cells there was a lower expression (0,01). In K562 and NB-4 cells the expression of miR-155 was absent. Moreover, HEL and K562-RC cells had the lower levels of miR-155 expression and HL-60 cells the highest.

CONCLUSION

In conclusion, our previous results show some interesting expression patterns of these microRNAs related with cancer cell response to therapy and mutational status, opening new perspectives to continue this study in patients.

VITAMIN C AND OXALIPLATIN: A POTENTIAL SYNERGISTIC EFFECT AGAINST COLON CARCINOMA

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AIM

The aim of this study was to evaluate the synergistic effect of a combination between oxaliplatin and AA in two different human CC cell lines.

INTRODUCTION

Colon cancer (CC) is a major health problem with more than one million new cases diagnosed worldwide every year. The efficacy of standard tumor therapy has reached a plateau, therefore additional innovative therapies are being developed. Researchers are now looking for therapies with greater efficiency and less toxicity. Ascorbic acid (AA) works as a pro-oxidant at pharmacological concentrations, promoting the formation of reactive oxygen species which can induce cancer cell death. It has been proved that AA doesn't protect cancer cells from chemotherapy but plays a protective role in normal cells. At the same time AA can enhance tumor growth inhibitory effect conferred by usual therapies regardless tumor type.

METHODS

WiDr, and LS1034 (multidrug resistant) cell lines were cultured in appropriate culture medium and incubated in absence and with different concentrations of AA and Oxaliplatin (Oxa) alone or in combination during different periods of time. The half maximal inhibitory concentration (IC50) and the interaction index were calculated after 24, 48, 72 and 96 hours by sulphorhodamine B (SRB) assay.

RESULTS

Results obtained with SRB assay showed that the cytotoxic effect of these two drugs depends on the cell line under study, incubation time and administered concentration. We could observe that combined therapy allowed the decrease of IC50 values of Oxa comparing with monotherapy IC50 values, for all conditions and both cell lines. When a combination with a proportion of 75% of AA IC50 and 25% of Oxa IC50 was performed, a 15-fold decrease on IC50 value of Oxa was obtained for LS1034 cells and a 60-fold decrease for WiDr cells, comparing with monotherapy. A synergistic effect was observed in almost all conditions, namely for longer periods of treatment (48, 72 and 96 hours).

CONCLUSION

Our study showed that combined therapy allowed not only the decrease of oxaliplatin concentration maintaining the same anti-proliferative effect but also obtaining synergistic effect for longer incubation periods. The data obtained could contribute to the development of a promising therapy in CC with reduced doses of conventional chemotherapeutic drugs and consequently, a decrease in secondary effects.

MDR1 (C3435T) AND MRP1 (G1666A) POLYMORPHISMS - ROLE IN MYELOID NEOPLASIAS' DEVELOPMENT

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AIM

To investigate the influence of MDR1 (C3435T) and MRP1 (G1666A) polymorphisms as risk factors for myeloid neoplasias development, namely MDS, AML and CML.

INTRODUCTION

Polymorphisms have been observed in several hematopoietic malignancies and some evidences suggest that they have a role in the cancer development, namely in Acute Myeloid Leukemia (AML), Myelodysplastic Syndromes (MDS) and Chronic Myeloid Leukemia (CML). The ATP-binding cassette (ABC) transporter superfamily contains membrane proteins that translocate a variety of substrates across extra- and intra-cellular membranes. Genetic variation in these genes can cause or contribute to a wide variety of human disorders, including neurological disease, retinal degeneration, and cancer, but can also modify drug response. MDR1 (ABCB1) and MRP1 (ABCC1) are transporters from this superfamily, therefore, they can play a part in the development, progression and therapy response of neoplastic malignancies.

METHODS

This study enrolled 168 samples from patients diagnosed with myeloid neoplasia (MN) (including 76 MDS, 43 AML, 49 CML) and 111 healthy controls (CTL). The genetic polymorphisms of MDR1 (C3435T) and MRP1 (G1666A) were accessed by RFLP-PCR. The strength of association between polymorphisms and disease risk was assessed by odds ratio (OR) with 95% confidence interval (CI95%).

RESULTS

Our results show that allele C from MDR1 is predominant in control and in all patients (CTL=52,3%; MDS=55,9%; AML=51,2%; CML=59,2). Besides that, the CT genotype from this gene is the more prevalent in CTL and MN patients (CTL=46,8%; MDS=48,9%; AML=46,5%), with exception of CML that presents higher frequency of CC genotype (40,8%). For MRP1, we observed that allele A is more frequent in all studied individuals (CTL=72,5%; MN=73,4%; MDS=74,8%; AML=77,9%; CML=68,6%). Moreover, we observed that AG genotype is the most frequent in CTL, MN and CML (CTL=54,9%; MN=51,4%; CML=60,0%), whereas AA genotype prevails in MDS and AML (MDS=50,5%; AML=55,8%). The GG genotype presents a very low frequency and was only observed in MDS and CML patients (MDS=1,0%; CML=1,4%). Besides that, our results also suggest that CC genotype might be a risk factor for the CML development, with an odds ratio of 1,70-fold (CI95% 0,84-3,44; p=0,14). However, when we analyzed the genetic profiles of these two polymorphisms, we observed that the association between genotype CT from MDR1 and AA from MRP1 results in increased risk for AML development of 2,5-fold (CI95% 1,03-6,10; p=0,05).

CONCLUSION

Our results suggest a contribution of these genetic polymorphisms, mainly the genetic profiles, to myeloid neoplasia development. However, their role in progression and therapy response remain unknown. To clarify these issues a larger systematic and prospective studies will be needed.

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Oncology & Molecular Biology Poster Presentation

SHIKONIN INHIBITS THE PROLIFERATION OF DIFFERENT HEMATOLOGICAL NEOPLASIAS

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AIM

The aim of this study was to evaluate the potential therapeutic of Shikonin (SHK), a β1 integrin inhibitor, in in vitro models of different hematological neoplasias.

INTRODUCTION

Several studies have demonstrated that β1 Integrin play an important role in adhesion of hematopoietic cells to the bone marrow microenvironment. The β1 Integrin facilitates cancer cell adhesion, migration, invasion, proliferation, and survival by activating intracellular signaling pathways, such as ERK/MAPK and PI3K/AKT signaling pathways. Shikonin is a β1 Integrin inhibitor that seems to have anti-proliferative qualities by inactivating these signaling pathways and others. Therefore the use of SHK could be a potential therapeutic approach in different hematological neoplasias.

METHODS

For this purpose, we used four hematological neoplasias cell lines: HEL cells, an Erythroleukemia cell line; NB-4 cells, an Acute Promyelocytic Leukemia cell line with the translocation t(15;17); F-36P cells, a Myelodysplastic Syndrome cell line; and H929 cells, a Multiple Myeloma cell line. The cells were cultured in absence and presence of different concentrations of SHK, ranged from 0,5μM to 10μM, in a single dose and in daily dose. For evaluate the effectiveness of SHK on cell viability, cell lines were analyzed by the Rezasurin Assay and it was calculated the half maximal inhibitory concentration (IC50). Cell death was determined by optical microscopy, using the May-Grunwald Giemsa staining, and by flow cytometry (FC), using the Annexin-V and propidium iodide double staining. It was also evaluated by FC the activation of caspases using the Apostat probe.

RESULTS

Our preliminary results showed that SHK reduce cell viability in a time, dose and cell type dependent manner, being the HEL cells the more sensitive and the H929 cells the lowest. In fact, we found that the IC50 at 72 hours of exposure was approximately 0,5 μM, 1,0 μM, 1,0 μM and 2,5 μM for HEL cells, NB-4 cells, F-36P cells and H929 cells, respectively. The administration of SHK in a daily dose seems to reduce more cell viability, especially in NB-4 cells, compared with cells treated with a higher concentration of SHK in single dose. Besides the antiproliferative effect, SHK induces cell death by apoptosis, confirmed by morphological and FC studies which may be related with the observed increase in activated caspases expression levels.

CONCLUSION

In conclusion, our results suggest that SHK might be used as a new therapeutic approach in different hematological neoplasias. The same was also described to other types of cancer, however at least in hematological cancers, the therapeutic efficacy may depend on the schedule of drug administration used.

PS205

Oncology & Molecular Biology Poster Presentation

MAY OUR DIET INTERFERE WITH TUMOR AGGRESSIVENESS IN COLON CANCER CELLS?

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AIM

To study whether butyrate (obtained from diet) interferes with the aggressiveness provoked by Warburg effect in colon cancer cells.

INTRODUCTION

Colorectal cancer is one of the most common and deadly cancers in developed countries. One of the principal risk factors that can lead to a higher incidence of this tumor is a diet rich on read meat and fats. Diet, essentially dietary fibers, become an increasingly critical factor in preventing this type of cancer. The fermentation of dietary fibers by colon's bacteria leads to the production of short chain fatty acids. This work highlights on butyrate, the main energy source of colonocytes and with a preponderance on the maintenance of colon homeostasis. Butyrate is a histone deacetylases inhibitor referenced as an inducer of apoptosis and promoter of differentiation in tumor colon cells.

METHODS

WiDr and C2BBe1 cell lines were cultured with low glucose content (5mM). To perform the uptake studies, cells were incubated with or without butyrate (3mM for WiDr cells and 6mM for LS1034), 1 and 4 hours before the incubation with 18F-FDG (25µCi/ml). At different times, samples of cell suspension were collected, centrifuged, separating the pellet from the supernatant, in order to evaluate 18F-FDG uptake percentage. To evaluate the cytoplasmic and membranar expression of GLUT-1, -3, -5 and -12 after butyrate exposure for 1 and 24 hours, flow cytometry was used. To evaluate the lactate production, the coupling between glycolysis and the Kreb's cycle, and the turnover of Kreb's cycle with or without the presence of butyrate, glucose uniformly labeled with carbon-13 was added to the medium without glucose. NMR technique allowed us to evaluate different parameters, including butyrate uptake by tumor cells.

RESULTS

In WiDr and C2BBe1 cell line we observed that incubation with butyrate decreases 18F-FDG uptake. No differences were observed between different incubation periods with butyrate. Taking into account GLUTs expression, in WiDr cells we observed a higher expression of GLUT-12 at the membrane. With butyrate exposure, a decrease in GLUT-12 membranar expression was observed. In C2BBe1 cell line butyrate, in some cases promoted an increase in GLUTs expression. With NMR technique it was possible to confirm the uptake studies, in that butyrate induced a decrease in lactate production in both cell lines. When WiDr cells are exposed to butyrate, the coupling between glycolysis and Kreb´s cycle increased. In both cell lines it was possible to observe that butyrate interferes with glucose consumption and that oxidative metabolism was more pronounced.

CONCLUSION

The results obtained suggest that butyrate (obtained from diet) interferes and in some cases attenuate the Warburg effect, decreasing tumor aggressiveness. With these studies is indeed marked the importance of a balanced / personalized diet in colon cancer prevention and treatment.

A POSSIBLE INVOLVEMENT OF ADIPOCYTOKINES IN MONOCLONAL GAMMOPATHIES – A PRELIMINARY STUDY

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AIM

This work explores the role of adipocytokines, namely adiponectin, leptin, resistin, MCP-1 and TNF-α in the pathogenesis of Monoclonal Gammopathies (MG) and correlate these adipocytokines levels with patient's clinical characteristics.

INTRODUCTION

Multiple myeloma (MM) is a neoplastic disease characterized by the growth of malignant plasma cells in the bone marrow (BM) with a subsequent overproduction of a monoclonal protein. This malignancy starts with a monoclonal gammopathy of undetermined significance (MGUS) and the BM microenvironment is believed to have a central role in the transition to MM by producing cytokines. Adipocytokines are a group of hormones produced by the adipose tissue that play an important role in energy homeostasis, hematopoiesis, immunity, inflammation and angiogenesis. There are studies that have shown that adipocytokines may have a role in the pathogenesis of some cancers such as colon and breast cancer. Recent evidence showing that increased body mass index has a positive association with both mortality and incidence of MM, suggests that adipocytokines may have a role in the pathogenesis of MM.

METHODS

A total of 34 patients with monoclonal gammopathies [15 MGUS and 19 MM patients, those 3 with smoldering MM (SMM) and 16 with symptomatic MM (symMM)] and 37 healthy individuals were included in this study, after informed consent. MGUS patients had an average age of 70,9 years (41-90 years), 60% female and 40% male. MM patient's had an average age of 73,5years (56-86 years), being 52,6% female and 47,4% male. Adiponectin, leptin, resistin, MCP-1 and TNF-α levels were quantified on the peripheral blood (PB) and BM using ELISA commercial kits.

RESULTS

Our preliminary results shown higher levels of resistin in PB of MG (15,65±13,96ng/mL), namely in MM (18,90±16,78ng/mL) patients compared to controls (9,22±5,33ng/mL). Besides that, resistin levels in PB are higher in symMM patients (20,91±17,61ng/mL) when compared with controls and SMM patients (8,17±1,79ng/mL). The adiponectin levels were lower in symMM patients (6,93±5,70µg/mL) compared with patients presenting SMM (14,84±3,23µg/mL). However, adiponectin was higher in SMM patients (14,84±3,23µg/mL) than those with MGUS (8,60±4,86 µg/mL). Furthermore, symMM patients that exhibit an IgG monoclonal component had higher levels of MCP-1 in both PB (194,05±93,36ng/mL) and BM (484,35±323,48ng/mL). On the other hand, patients with κ light chains show higher levels of MCP-1 in PB (242,25±155,39ng/mL). According to ISS classification, stage 3 patients, also show higher levels of MCP-1 in PB than those on stage 1 (stage 3: 200,97±88,18ng/mL; stage 1: 109,59±3,97ng/mL).

CONCLUSION

Our study suggests that adipocytokines may be envolved in the pathogenesis of MM by creating a pro-inflammatory state in the BM that contributes to the carcinogenesis process. These findings might contribute to a better understanding of this malignancy and may allow the improvement of prognosis classification.

ROLE OF INSULIN IN TOXICITY MEDIATED BY EVEROLIMUS

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AIM

With this work, we intend to study the role of Insulin, as an activator and its interference in Everolimus toxicity, an inhibitor of the PI3K/Akt/mTOR pathway in oral cancer cell lines.

INTRODUCTION

Oral cancer (OC) is a subtype of head and neck cancer (HNC) that arises from the oral cavity. OC holds the eighth position in cancer incidence ranking worldwide, with oral squamous cell carcinoma (OSCC) being responsible for more than 90% of all of them. The current curative treatment modalities are usually surgery and radiation, with chemotherapy added to decrease the possibility of metastasis. On the other hand, some studies have shown a higher prevalence of cancer in diabetic patients, namely oral cancer.

METHODS

For the purpose of the study, two oral cancercell lines (HSC-3 and BICR-10) were used, incubated with Insulin (100nM) and mTOR inhibitor, Everolimus, in different therapeutic protocols. Cytotoxicity was evaluated by the Alamar Blue assay. Flow cytometry (FC) was used to analyze cell cycle, cell death mechanisms, using Annexin V/Propidium Iodide assay. FC was also used to analyze Cyclin D1 and PDGFR expression.

RESULTS

Our results showed that mTOR inhibitor, Everolimus, had cytotoxic effects in monotherapy in a dose, time and cell-dependent manner, inducing cell death preferentially by apoptosis. By cell cycle analysis, everolimus showed an antiproliferative effects with an increase of G2 phase and decrease in S phase.

CONCLUSION

Our work showed that Insulin can have an important role in chemotherapy resistance in oral cancer which can affect therapeutic protocols in diabetic patient with oral cancer.

PS56

Internal Medicine Poster Presentation

ACUTE CORONARY SYNDROME WITH ST SEGMENT ELEVATION (SCACST) IN PATIENTS WITH CRITICAL AORTIC VALVE STENOSIS - A CASE REPORT.

1- Hurtado Olmo, P. Student of third year of medical degree. 2- Cárdenas Cruz, A. Professor of Department of Medicine at the School of Medicine of Granada. 3- Romero Palacios, PJ. Professor of Department of Medicine at the School of Medicine of Granada

School of Medicine of the University of Granada. Department of Medicine.

AIM

Introduce students in the differential diagnosis of acute coronary syndromes through the presentation of a clinical case.

INTRODUCTION

For the study of acute coronary syndromes, it is presented the case of a patient whose complaint is dyspnea and chest pain of sudden onset.

METHODS

A thorough investigation of his personal history is made. The following data are of interest: active smoker from age 20 of 72 packs of cigarettes per year; type II diabetes mellitus treated with insulin, hypertension of difficult control, retinopathy, dyslipidemia.

RESULTS

We make a differential diagnosis with pathologies such as aortic dissection, myopericarditis, pulmonary thromboembolism / thromboembolic disease, hiatal hernia, esophageal spasm, pneumonia, pneumothorax.

CONCLUSION

For the case study a wide range of resources are used.

PS57

Internal Medicine Poster Presentation

AN APPROACH TO MAJOR SYNDROMES THROUGH A CLINICAL CASE: CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD).

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AIM

To introduce students to the process of diagnosing using day-to-day tools as practice guidelines and diagnostic algorithms by putting forward a clinical case in a handy device as it is an app.

INTRODUCTION

Medical students are getting prepared to develop a career in which they will have to face clinical cases every day. That is why it is important to acquire diagnostic skills by solving real clinical cases. Furthermore, COPD is the fourth leading cause of death worldwide and it is often over-diagnosed.

METHODS

For the study of the different COPD phenotypes, it is propounded the case of a middle-aged man who complains of frequent exacerbations, related to acute bronchitis. In addition, the patient presents a MRC dyspnea grade 2.

RESULTS

The analysis of the data obtained from the patient and the tests shows that the patient does fulfill two of the major and two of the minor diagnostic criteria agreed by consensus for the diagnosis of the Overlap Phenotype COPD-Asthma. The patient´s COPD phenotype is defined as “mixed COPD-asthma” by using the diagnostic algorithm proposed by the GesEPOC guidelines. Severity is established by the BODE/BODEx multidimensional scales and by assessing airflow obstruction, dyspnea, level of physical activity and history of exacerbations. Finally, it is decided the appropriate treatment for the patient according to his phenotype and his severity.

CONCLUSION

Students get used to apply their knowledge about a major syndrome, as COPD is, and to follow the practice guidelines to solve clinical cases.

PREVALENCE OF METABOLIC SYNROME IN OBEESE WOMEN WITH POLYCYSTIC OVARY SYNDROME

Milica Bokan

AIM

Comparing the prevalence of metabolic syndrome in a population of obese women with PCOS, with a population of obese control women (CW).

INTRODUCTION

Women with polycystic ovary syndrome (PCOS) have a higher prevalence of the metabolic syndrome (MetS) in relation to a control women.

METHODS

The study included 100 women with PCOS and 50 healthy women. In all patients we determined body mass index (BMI), waist circumference (WC) and blood pressure. The metabolic syndrome as defined by NCEP ATP III criteria (The National Cholesterol Education Program Adult Treatment Panel III, NCEP ATP III) and the whole group is further divided into PCOS group with and without MetS. In the follicular phase of the menstrual cycle were determined basal glucose, insulin, HDL, triglycerides, testosterone, SHBG, HOMA, and FAI. All analyzes were performed with correction for age and BMI.

RESULTS

For the PCOS women, mean age was 30.15 ± 2.04 years, and mean BMI was 30.99 ± 3.37 kg / m² (HC: 31.00 ± 2.77 years, BMI: 30, 40 ± 3.07 kg/m²). Metabolic syndrome was present in 43% of PCOS and in 12% of CW. We showed significant differences in anthropometric (BMI, WC, systolic and diastolic blood pressure) and biochemical parameters (fasting glucose and insulin, HOMA index, HDL, triglycerides, SHBG and FAI) between PCOS with MetS and PCOS without MetS.

CONCLUSION

Our women with PCOS had significant disorder of lipid metabolism, insulin resistance and hyperandrogenic profile that may be the reason for the existence of a significantly higher incidence of MetS.

PS101

Internal Medicine Poster Presentation

DIAGNOSTICAPP: A SOFTWARE TO RESOLVE CLINICAL CASES.

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AIM

Making a smartphone app based on resolution of clinical cases that allow to obtain basic medical competences and progress the training level in clinical medicine.

INTRODUCTION

Compared to other spheres of society, it has been observed that medical teaching has not yet entirely integrated the benefits that acquiring and developing mobile apps. Exploding that field can report an improvement in quality and excellence of Universities and in Medical Specialty programs.

METHODS

In consequence, a software was designed which allows the user to play and interactively solve clinical cases that have been previously designed for this purpose on an online website. The user accesses to a clinical history and after that he or she must suggest a differential diagnosis and request some medical examinations that will be used for establishing the final diagnosis and treatment. After that, the software evaluates heuristically the clinical judgment used for the resolution of the case, and shows the correct clinical aptitudes that have been achieved during the process. In both cases, the system has been optimized for simple and intuitive usage. Also, the user gains admission into useful information like Clinical Practice Guidelines (CPGs), Diagnosis and Management Algorithm, hyperlinks to medical webpages.The Website platform was set out for the educational field. In accordance to this, it is possible to create and manage student groups, and assign specific cases for each group, which will later be evaluated for each individual student.The system works with several databases similar to Spanish Hospitals currently manage, as: International Classification of Diseases (ICD-9); Anatomical, Therapeutic, Chemical classification system (ATC Code); Resource-based relative value scale (RVRVS) from Hospital Universitario Virgen de las Nieves, Granada; Group of medical examinations and surgical procedures from Hospital Universitario Virgen de las Nieves, Granada.

RESULTS

For one hand, the student can practice his knowledge by dealing with real situations and solving it with the most similar resources that a doctor can do. On this way, the student learns to develop his reasoning ability and properly strategies depending on the context.

For the other hand, the professor obtains new work and evaluation methods absolutely different than classical methodology.

CONCLUSION

Consequently, this digital system sets up an useful tool for student and practicing doctors just like their mentors. It stablishes a fresh interaction way between pupils and tutors, in line with the Bologna Process European Higher Education Area context. Due to all of these reasons, this approach is considered an innovation in its field.

PS104

Internal Medicine Poster Presentation

CARDIOVASCULAR RISK FACTORS AND ANTIOXIDATIVE ENZYMES AMONG OBESE POSTMENOPAUSAL WOMEN

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AIM

The aim of this study was to determine antioxidant enzymes glutathione peroxidase (GPx) and superoxide dismutase (SOD) activities among healthy normal weight and overweight postmenopausal women, as well as to identify relationship between these enzymes ac

INTRODUCTION

Oxidative stress in obesity may be an important pathogenic mechanism in the obesity-associated metabolic syndrome, which includes the coexistence of several risk factors for atherosclerosis. In obese patients, antioxidant defense is altered and it's relationship between central adiposity is still an open question.

METHODS

This study was performed in 45 normal weight (56.51 ± 4.64 years) and 115 overweight (56.24 ± 5.05 years) healthy postmenopausal women. The GPx and SOD enzyme activity was measured spectrophotometrically. Waist circumference was measured and body mass index was calculated. Biochemical parameters were determined as follows: C-reactive protein, total cholesterol, high density lipoprotein cholesterol (HDL-c), low density lipoprotein cholesterol (LDL-c), triglycerides, and glucose.

RESULTS

A significantly higher C-reactive protein, triglycerides, and glucose levels ($p<0.001$), as well as significantly lower HDL-c levels were found in overweight compared to the normal weight females ($p<0.001$). Nonsignificant difference in SOD and GPx levels between overweight and normal weight females was found ($p>0.05$). In overweight group, significant negative correlation were observed between GPx plasma activity and glucose levels ($p=0.042$) and significant positive correlation between SOD activity and triglyceride level ($p=0.027$).

CONCLUSION

The results obtained in this study showed no statistical significant difference both of GPx and SOD enzyme activity among healthy normal weight and overweight postmenopausal women.

PS108

Internal Medicine Poster Presentation

URINARY OBSTRUCTION: CLINICAL CASE OF AN IMPORTANT UROLOGICAL SYNDROME

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AIM

Acquirement of basic capacities for the diagnosis of urological syndromes through a clinical case by using an interactive application.

INTRODUCTION

The medical action is governed these days by clinical practice guidelines, which contain lots of algorithms. And, as everyone knows, it is easier to learn them by using them, which means facing up real clinical cases.

Moreover, new technologies are enjoying a boom and are established in all medical fields. So that, this urological case combines both facts, the need to learn how to use the clinical guidelines, and the use of new technologies for learning.

METHODS

Solution of an authentic clinical case of urology with real information and the results of complementary diagnostic exams, in order to follow the direction of clinical practice guidelines.

The patient undergoes a thorough questioning, and physical and radiological exams to get a correct diagnosis (urinary obstruction) and treatment (surgery). Moreover, the evolution of the patient will be shown and evaluated.

RESULTS

By using the clinical guidelines to analyse the information of the syndrome revealed by the exams, the patient was diagnosed as having a stenosis of his urethra. He had an operation and his evolution is being followed in case he needs to have a new operation.

CONCLUSION

Practice guidelines and diagnosis algorithms can be learnt by solving real clinical cases. Furthermore, that training could be made more enjoyable and accessible by using new technologies (such as mobile apps), and that could result in an easy familiarization of students and health staff with the use of clinical practice guidelines, which are in continuous updating.

PS138

Internal Medicine Poster Presentation

TOWARDS EFFECTIVE TREATMENT AND MANAGEMENT OF SICKLE CELL ANEMIA (NIGERIA CASE STUDY)

Ajuwon Olugbenga Tunji

AIM

it is the aim of study to present an effective and wholesome approach in the control, treatment and management of major complications of sickle cell disease especially in a developing country like Nigeria with limited medical and health resources, taking

INTRODUCTION

Sickle cell disorder is by far the commonest inherited disorder in the world and three quarters of cases occur in Africa. Statistics have it that the gene which is responsible for the sickle cell disease is most prevalent in Africa

METHODS

Patients with the Sickle cell disorder where referred by Doctors from the Lagos State General Hospitals to the National Sickle Cell Centre (Specialized Clinic for Sickle cell patients). Within the study period of May 2012 to November 2013, consecutive patients were also incorporated into the study.

RESULTS

Over the study period, from inception in May 2012 to November 2013, the data obtained were recorded and analyzed using the SPSS data analysis tool. Comparison was made between the years of the study period.

CONCLUSION

Throughout the period of study, the results obtained showed that, the morbidity and mortality rates reduced progressively and substantially. More astounding is the fact that these result were obtained without the administering any of the attested prophylactic measures such as daily oral penicillin (Gaston et al., 1986), pneumococcal vaccination (Kaplan, Sarnaik & Schiffman, 1986) and daily oral hydroxyurea (Charache et al., 1995).

PS139

Internal Medicine Poster Presentation

PLAIN ABDOMEN RADIOGRAPHY IN CASUISTRY OF MEDICAL INSTIUTION SPECIALIZED FOR ONCOLOGY

Petar Zlatanovic, Natasa Stankovic, Jovana Stevic
PhD MD Zorica Milosevic

AIM

Evaluation the role of PAR in investigation of complaints in oncologic patients threw the experience of medical oncologic institution and assessment of rational usage of this diagnostic procedure. These types of studies would indicate to big savings in co

INTRODUCTION

Plain abdomen radiography (PAR) is a picture of organs on film during X-ray passage threw pacient's body. It preceds to other radiological studies. The most important indication is in differntiation between acute abdomen and other conditions.

METHODS

The HELIOS data system was used from Institute for radiology and oncology Serbia for acquiring data. In study participated 30 patients who uderwent PAR in the second half year 2013. It was preformed retrospective study on patients with abdominal complaints in order to determine frequence of PAR in corelation with clinical data.

RESULTS

6 patients (20%) had acute abdomen and even 24 patients (80%) had not. The most common complaint for PAR usage was abdominal pain – 56%. The most common malignancies were gynecological – 57%. Average radiation exposure was 56 msV, which is 18,6 more than those dose that man can get from natural sources. Total price of all PAR was 960 pounds.

CONCLUSION

The role of PAR is undoubted in an initial evaluation of patients with symptoms of acute abdomen, especially in oncological patients in whom etiology is multiple. The study also showed an irrational usage of PAR, not sticking to good practice guides and patients exposure to great amount of radiation. Therefore, there is a constant need for clearer and better defining of indications for PAR and introducing good practice guides. Key words: plain abdomen radiography (PAR), acute abdomen, good practice guides, radiation dosage.

PS140

Internal Medicine Poster Presentation

MICROBIOLOGICAL ASPECTS OF HOSPITAL ACQUIRED INFECTIONS AT THE INTENSIVE CARE UNIT OF UNIVERSITY HOSPITAL "ST. GEORGE "- PLOVDIV

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AIM

To determine the distribution and antibiotic resistance of the most common bacterial isolates from patients of ICU at University Hospital "St. George "- Plovdiv in 2011 and 2012 and to propose measures for their control and limitation.

INTRODUCTION

Nosocomial infections caused by multidrug-resistant microorganisms will become uncontrollable if their spread is not limited. This applies to intensive care units mostly because of the specificity of careand sharply increasing number of microbial isolates.

METHODS

We studied isolates from pathological material of patients evidenced by routine and automated microbiological methods. To determine the significance of the results was used the statistical analysis method.

RESULTS

The most frequent isolates in the clinic are non-fermentative Gram negative bacteria - Acinetobacter baumannii (40% from 2011and 56% from 2012) and Pseudomonas aeruginosa (18% and 23.5%), followed by Enterobacteriaceae Klebsiella pneumoniae (9, 9%; 22.4%) and Escherichia coli (5,6%; 13,63%). The resistance of the strains to carbapenem antibiotics protected with beta-lactamase inhibitor increases.

CONCLUSION

At the ICU of University Hospital "St. George "Plovdiv there is an unfavorable trend for the prevalence of gram-negative flora, represented mainly by multidrug-resistant Acinetobacter baumannii. Despite the lack of sufficient data to distinguish colonization from infection in these patients, the results show worrying trends. They are a prerequisite for an increased number of hospital aquired infections with resistant bacteria that requiring the implementation of fast and adequate control measures.

PS141

Internal Medicine Poster Presentation

MASSIVE THROMBUS FORMATION WITH ENLARGEMENT OF LEFT ATRIUM

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University Hospital"St.Geogi" Plovdiv, Bulgaria

AIM

Enlargement of left artium can be arivented with huge thrombus formation. Various factors are implicated in the formation of thrombosis among which the localleft atrial factors seem to play a major role.Complete removal of huge thrombus can be facilitated

INTRODUCTION

Large left atrium is a condition characterized by huge enlargement of the left atrium with a diameter exceeding 55mm. It is most commonly associated with long standing rheumatic mitral valve disease. We present 54 years-old female patient with rheumatic mitral stenosis associated with enlargement left mitral atrium occupied a 10x9x6cm. The patient underwent successful mitral valve replacement and thrombectomy through an inverted T-shaped biatrial incision. Enlargement of let atrium is commonly associated with long standing rheumatic mitral valve regurgitation or mixed mitral disease with predominant regurgitation. The exact etiology is not known. Both increased left atrial pressure and weaking of left atrial wall by rheumatic pancarditis are impricated in its development. The condion can be associated with atrial fibrillation, thrombembolic complications, hemodynamic and respiratory complications. We present a case of enlargement of left atrium with predominant mitral stenosis associated with atrial fibrillation and huge thrombus formation. Patient was successfully managed by mitral valve replacement and removal if left atrium thrombus.

METHODS

Computel tomography (CT), transesophageal echocardiography

RESULTS

Two hundred and ten patients(mean age 60+-7)170 men and 40 women with left atrium thrombus.

CONCLUSION

Surgery with cardiopulmonary bypass is a safe method for treatment.The patient should be medicated with warfarin especially in the presense of atrial fibrillation.

PS142

Internal Medicine Poster Presentation

ROLE OF MSCT IN TREATMENT PLAN OF PATIENTS WITH CHRONIC TOTAL OCCLUSION OF CORONARY BLOOD VESSELS

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AIM

To determine significance of MSCT in treatment plan of PTCI patients with chronic total occlusion of coronary blood vessels.

INTRODUCTION

Nowdays occluded coronary arteries have become major obstacle for cardiologists and interventional radiologists hence solving this problem would lead to reduction in cardiovascular leading cause of death. The development of new preoperative strategies, such as non-invasive MSCT angiography in contrary to invasive selective angiography is getting an important role in preoperative treatment plan of patients with chronic total occlusion (CTO).

METHODS

Percutaneous transluminal coronary intervention was performed on 60 patients in KBC “Bežanijska kosa” from January of 2011 until December 2012. Half of those patients were preoperatively sent on MSCT coronary angiography. Control group of patients (30) underwent PTCI without preoperatively MSCT angiography. After origin of plaque was determined intervention was performed.

RESULTS

Our results have showed highly significant statistical difference ($\chi 2=23.472$, DF=1, $p=0.00012$) between patients that underwent MSCT procedure before PTCI and control group of patients that were not included in MSCT procedure. Among patients that underwent MSCT angiography PTCI was successful in 83% (25/30 patients), while in control group PTCI was successful in 40% (12/30 patients).

CONCLUSION

Multislice computed tomography (MSCT) is increasingly being utilized as a non-invasive diagnostic imaging modality to detect coronary artery disease. Its ability to provide information on the soft tissue (including plaque) surrounding the lumen has been applied to better define the morphological features of CTOs as our results showed twice higher success of PTCI after MSCT angiography.

PS164

Internal Medicine Poster Presentation

THE ASSESSMENT OF EXERCISE CAPACITY AND ITS RELATION TO HEMODYNAMIC PARAMETERS AND NT-PROBNP LEVEL IN PATIENTS WITH IDIOPATHIC PULMONARY ARTERIAL HYPERTENSION AND EISENMENGER'S SYNDROME.

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AIM

To assess six-minute-walk-test (6MWT) distance and maximal oxygen consumption (VO2max) measured during cardiopulmonary exercise testing (CPET) procedure, in patients with different kinds of pulmonary hypertension (PH) and compare them with hemodynamic me

INTRODUCTION

Pulmonary hypertension is a heterogeneous group of diseases defined as an increase in mean pulmonary arterial pressure (mPAP) ≥ 25 mmHg at rest assessed by right heart catheterization. PH leads to progressive deterioration of cardiopulmonary function and significant exercise intolerance. Even though PH patients are frequently evaluated using 6MWT, little is known about other methods such as CPET and their prognostic significance in various kinds of PH. N-terminal fragment of brain natriuretic peptide precursor (NT-proBNP) is a well known biochemical marker, which levels reflects the severity of right ventricular dysfunction in patients with PH.

METHODS

In the study we included 61patients: 38 diagnosed with idiopathic pulmonary arterial hypertension (IPAH)(27 females, 11 males, aged: 52.11±17.03years) and 23 diagnosed with Eisenmenger's syndrome(ES)(11 females, 12 males, aged: 36.13±15.35years). All of the patients underwent 6MWT, CPET, diagnostic right heart catheterization and blood tests in the Department of Cardiac and Vascular Diseases in John Paul II Hospital, Cracow (Poland). Hemodynamic variables including mean pulmonary artery pressure (mPAP), oxygen saturation in aorta (SpO2 A) and pulmonary artery(SpO2 PA), 6MWT distance, VO2max and NT-proBNP level were analyzed in both groups.

RESULTS

Among individuals with ES, mPAP was significantly higher than with IPAH (73.72±22.01 vs. 52.4±21.64mmHg

CONCLUSION

Our research showed that each form of PAH presents with different exercise capacity, peak oxygen consumption and NT-proBNP level. VO2max correlated with mPAP, SpO2 A, SpO2 PA and NT-proBNP only in IPAH group. The 6MWT distance, VO2max consumption were lower in IPAH, while levels of NT-proBNP were higher. Specific course and shorter time of adaptation in IPAH than ES may be the cause of differences in aerobic exercise tolerance, but also in hemodynamic and biochemical parameters.

PS188

Internal Medicine Poster Presentation

CHANGES IN KIDNEY HISTOMORPHOLOGY AND NNOS EXPRESSION IN RATS SUBMITTED TO CHRONIC ETHANOL TREATMENT

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AIM

The aim of this work was to study if there are changes in the numerical, surface and volume densities of glomerular tufts and nNOS-immunoreactivity in renal tubules of ethanol-treated rats.

INTRODUCTION

Alcoholism is associated with kidney disease by directly damaging the kidney or by elevating blood pressure. Under normal physiological conditions, nitric oxide (NO) derived from NO synthase (NOS) influences on renal blood flow, tubular regulation and glomerular filtration. In diabetic rats, an increase in neuronal NOS (nNOS) was found to be related with elevated glomerular filtration rate, giving support to its role in kidney pathogenesis and dysfunction. Despite the knowledge that ethanol consumption induces oxidative stress in the kidney and reduces renal function, there are no data on the effects of chronic ethanol consumption on kidney morphology and on nNOS immunoreactivity.

METHODS

Male Wistar rats at the age of 2 months were divided into 2 groups: Control rats had free access to tap water and Ethanol-treated rats were given a 20% (v/v) ethanol solution as the only available liquid solution for 24 weeks. Rats were anesthetized and killed by transcardially perfusion. The kidneys were collected, sectioned and embedded into paraffin. The numerical, surface and volume densities of the glomeruli were determined by morphometric analysis in periodic acid-Schiff stained sections. nNOS expression in renal tubules was evaluated by immunohistochemistry. Statistical analysis was performed using the Student's t-test.

RESULTS

Ethanol treatment induced a decrease in the numerical density and an increase in the volume density of the glomeruli without changes in their surface density. The percentage of nNOS-immunoreactive renal tubules was higher in ethanol-treated rats.

CONCLUSION

Our findings show that chronic ethanol consumption induces structural changes in kidney and increases nNOS immunoreactivity in renal tubules. The reduction in the glomerular numerical density exhibit by ethanol-treated rats could be due to an increase in its glomerular volume. Similar structural changes had been reported in diabetic rats being related to change of glomerular filtration rate which is an indicator of the early-stage of hypertension nephropathy. Chronic ethanol intake decreases renal tubular reabsorption and our results further showed an increase in nNOS immunoreactivity within renal tubules. This allows us to suggest that an increase in nNOS immunoreactivity induced by ethanol consumption could be seen as one relevant mechanism underlying of chronic ethanol effects on renal dysfunction. This study provides morphological data that contributes to the understanding of the adverse effects of ethanol on renal function. These findings provide further support for the role of nNOS in the pathogenesis of kidney disease due to chronic ethanol consumption.

PS217

Internal Medicine Poster Presentation

E-TRACKING EVALUATION OF CAROTID ARTERY IN CHILDREN WITH KIDNEY DISEASES - PRELIMINARY STUDY

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1-Jagiellonian University, Medical College 2-University Children's Hospital of Cracow

AIM

The aim of our study was to evaluate the usefulness of e-tracking method in the assessment of vascular changes in children with kidney diseases.

INTRODUCTION

Carotid artery ultrasound evaluation with arterial stiffness calculation is an easy and non- invasive method in determination of cardiovascular risk factors

METHODS

The study group consisted of 26 children (14 boys and 12 girls, mean age 15,6 ±2,0 years) treated for kidney diseases at the Department of Pediatric Nephrology. Measurements were performed with ALOKA prosound α 6 ultrasound device using linear transducer 5-10 MHz. Carotid common artery intima-media thickness (cIMT), stiffness parameters as β-index, elastic modulus (Ep), arterial compliance (AC), pulse wave velocity (PWV) and Aix were evaluated using Aloka e-tracking software. Another markers as distensibility coefficient (DC), incremental modulus of elasticity (Einc) and β were calculated as SD scores (SDS) for age and height. Biochemical (cholesterol, estimated glomerular filtration rate- eGFR, proteinuria) and clinical (ambulatory blood pressure monitoring -ABPM, hemodynamic, anthropometric) data were correlated with arterial measurements. The results were analyzed with nonparametric tests in Excel 2007 MS and Statistica 10 Statsoft.

RESULTS

16 of 26 children presented with hypertension (HT) and did not differ from non-HT group regarding height, age and GFR (106,7 vs 125,5 ml / min • 1,72 m2, p=0,077). Children with HT had significantly higher cIMT (0,47 vs 0,395 mm, p=0,005) and cIMTsds (1,62 vs. 0,04, p=0,004) than non-HT. Einc SDS and DC SDS differ in these groups (-0,28 vs 1,72, p=0,012), (-0,3 vs -1,69, p=0,036) respectively. No difference was found in β-index (4,75 vs 4,9) and β SDS (-0,23 vs 1,18) between HT and non-HT.

CONCLUSION

This data cannot conclusively answer the question whether e-tracking is an accurate method of identification of carotid artery changes. However, despite of small sample, this findings confirmed the usefulness of measuring cIMT and other parameters of arterial stiffness as Einc or DC in patients with HT. The study has to be further confirmed in a larger population.

PS223

Internal Medicine Poster Presentation

ACUTE POISONING AS A CAUSE OF ADMISSION AT CENTRO HOSPITALAR DO PORTO

Rocha A; Miguel A; Marinho B; Rodrigues C; Teixeira C; Martins J; Mirada J.; Moreno J.; Rema João; Relvas M.; Vieira P.; Macedo T.
ICBAS-UP; CHP

AIM

Identify areas for improvement, we analyzed all urgent admissions during one year, in a central hospital in Porto, Portugal.

INTRODUCTION

The toxicological emergencies, due to their high frequency and associated morbidity and mortality, are of great importance in hospital emergency departments. Human poisoning has been transformed into one of the most serious public health problems because of the lack of control and prevention which is associated with the population's easy access to a growing and diverse number of substances with varying degrees of toxicity. It thus becomes important to know its prevalence in order to take action in the most appropriate manner.

METHODS

Of all admissions to the emergency room of the Santo António General Hospital (HGSA) in 2013, we selected all patients with a final diagnosis of intoxication/poisoning through the ALERT system registry and the clinical process in SAM, after appropriate institutional permits from the Ethics Committee of this hospital. From the literature review, we identified the most relevant indicators and constituted a survey to collect data for the selected population. After collecting the data, it was processed and analyzed anonymously through the Statistical Package for Social Sciences (SPSS ®) version 22.0.

RESULTS

This study is made up of 809 emergency room episodes of which 509 were pertaining to men and 300 to women. This sample covers cases of patients aged 17 to 92, with an average of approximately 43 years ($\sigma \pm 16.8$) and mode of 21 years.

CONCLUSION

The present study shows that poisonings were more prevalent in males, with alcohol and benzodiazepines being the most frequently used toxics. We highlight barbiturates as one of the least used toxics, which may be a reflection of the limitations imposed to their access.

PS248

Internal Medicine Poster Presentation

IMPLEMENTATION OF A TUTORING PROGRAM IN A MEDICAL SCHOOL: THE ROLE OF STUDENTS

1 - Cardoso, J., 2-Correia, G., 3-Ferreira, MA., 4-Ribeiro, L.

1, 3 and 4 - Department of Education and Medical Simulation, Faculty of Medicine of the University of Porto; 2 and 4 - Department of Biochemistry (U38/FCT), Faculty of Medicine of the University of Porto

AIM

To describe the implementation of a tutoring program and the role of students in this process

INTRODUCTION

The main aim of student-centred learning is to encourage the development of students as independent learners. Research literature suggests that tutoring programs have an important role in facilitating this process, given their inherent social support, guidance and modeling.

METHODS

Different steps were taken to create and implement a formalized tutorial program in the Faculty of Medicine of the University of Porto, including the role of students during this

RESULTS

After one and 6 months, the proportion of established functional-pairs increased from 26% to 72%. The challenges and difficulties identified along the implementation process were mainly related with internal communication procedures. Some of these problems were identified and overcome due to the collaborative work with the freshman student in close contact with his colleagues.

CONCLUSION

The tutoring program was successfully implemented, despite some aspects deserving future attention, as the need for a training program for tutors.

AIMS Meeting

The AIMS Meeting (Annual International Medical Students Meeting), presently in its 5th edition, is a conference meant for all students and young adults involved in Health Sciences. It will be held at the University of Lisbon - Faculty of Medicine (Portugal) on 7-9 March 2014.

This year we will focus on the following subjects: War On Cancer, Vision(ary) Medicine and Innovation in Medicine. The AIMS Meeting also offers you the possibility to engage in enriching workshops as well as pre-courses, and enjoy an entertaining social program.

You can find further information and register for the congress at www.aimsmeeting.org. You can also follow us on Facebook (AIMS Meeting) and Twitter (@AIMSMeeting).

IMSCNS: International Medical Students Congress in Novi Sad

IMSCNS - International Medical Students` Congress in Novi Sad – held as an annual event since 2006, is oriented towards cooperation with Universities and faculties of biomedical sciences all over the world.

This multidisciplinary scientific event will welcome students of medicine, dentistry, pharmacy, nursing and molecular biology. During the 4 days of congress, participants will have the opportunity to present their scientific work, attend lectures and workshops held by renowned experts, exchange ideas and make friendships.

The IMSCNS is an official project of EMSA - Novi Sad, which is supported by EMSA – Europe, Faculty of Medical Sciences, University of Novi Sad and Serbian Academy of Sciences and Arts.

You can register and look for more information at www.imscns.com.

We are delighted to invite YOU to participate in this event, exchange your scientific proficiencies and have an excellent time.

Partners
Conferences

IMSCNS BRAINCOMS:
Brazilian International Congress of Medical Students

Thursday-Saturday, October 9th-11th, 2014, 8:00AM-5:30PM, Universidade Federal de São Paulo (UNIFESP), São Paulo.

An unique experience in which professors, alumni and foreign participants come together to share and discuss groundbreaking scientific works through an students' project like never seen before.

Partners
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KARMIC: International Medical Students Congress in Novi Sad

KARMIC 2014 is an international undergraduate research conference for medical students, presented by Indian Medical Students Association, being hosted by Kempegowda Insitute of Medical Sciences, Bangalore.

With an endeavour to achieve a communal meet of medicos to bring a much needed research temperament closer to the routine medical curriculum, this event hopes to inform and inspire.

After the immense success of the past two, this 3rd edition organized by a vehement lot promises a troika of academia, creativity and layman intrigue.

A unique platform awaits young medical researchers. Learning opportunities will also be abundant what with various pertinent pre-conference workshops and in-house competitive events to be held during the 3-day event.

Partners
Conferences

LIMSC: Leiden International Medical Student Conference

The Leiden International Medical Student Conference (LIMSC) is one of the largest student conferences in Europe, hosted by the Leiden University Medical Center (LUMC) and organized by (bio-) medical students.

At LIMSC students from all over the world will convene in the setting of an international conference. LIMSC provides them with the opportunity to present the results of their (bio) medical-related research projects, either in oral or poster presentation sessions. The sessions will be interspersed with guest lectures by prominent international speakers, interactive workshops, a range of social events and a Career and Internship Fair.

LIMSC is a great opportunity to establish contacts with international colleagues and to build a social and professional international network.

The Ninth edition of LIMSC will take place from 11th till 15th March 2015 in Leiden, the Netherlands.

For more information visit our website (www.limsc.nl) and find us on Facebook! (www.facebook.com/limsc2015)

Partners
Conferences

BIMCO:
Bukovinian International Medical Congress

KARMIC 2014 is an international undergraduate research conference for medical students, presented by Indian Medical Students Association, being hosted by Kempegowda Insitute of Medical Sciences, Bangalore.

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Ain Shams International Medical Students' Congress

AIMSC:
Ain-shams International Medical Students' Congress

On February 1992, an idea lit up in the mind of one of the university's brilliant professors,the late professor Ali Kalifa. The idea was to gather young doctors and medical students from all around the world to empower them to present the results of their scientific research and leaving not as strangers but as friends. Ainshams International Medical Students' Congress (AIMSC) has been growing since then to be one of the oldest most prestigious congresses not only in the Middle East but also in the whole world.

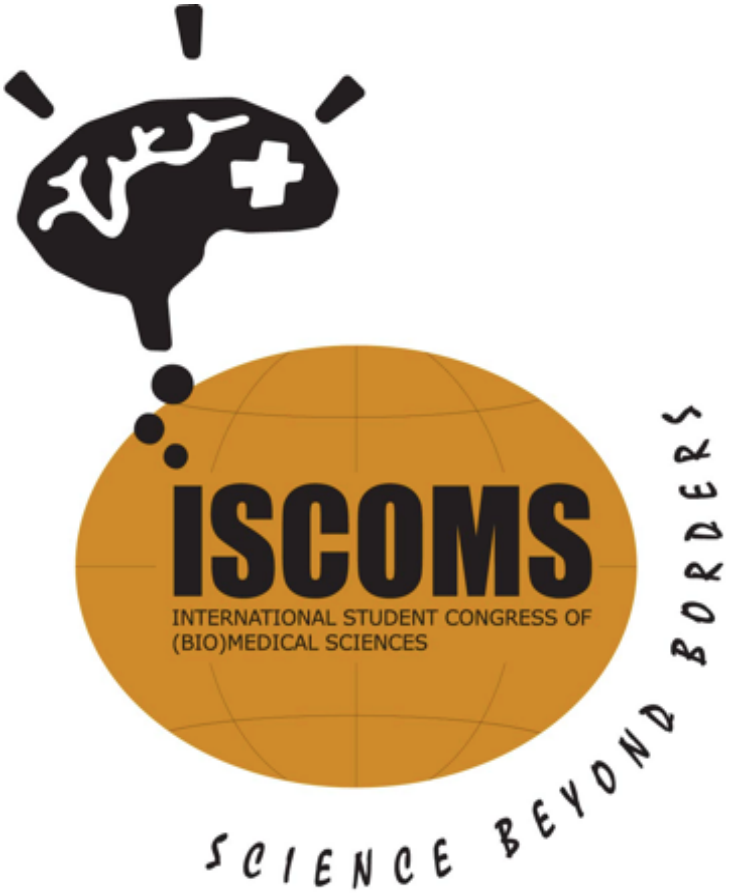
Along the past 20 years, thousands medical students have gathered from different parts of the world to attend AIMSC. Being the 22nd, this year AIMSC will continue its growth upon the gained experience and build on the efforts exerted in the past years to offer you the time of your life not only with our rich intellectual scientific program but also with the fun-packed social program.

Congress Date: 11,12 and 13th October 2014
Pre-congress Tour (Alexandria): 10th October 2014
Post-congress Tour (Hurghada): 14,15 and 16th October 2014
Venue: Egypt, Cairo
Website: www.aimsc-egypt.org

ISMCK'14:
International Student Medical Congress Košice

ISMCK`14 (25.-27.6.2014) in Košice, Slovakia offers medical and PhD students an opportunity to present their research and to exchange ideas on topics through oral or poster presentations in categories: Basic Science, Clinical Medicine, Dentistry, Pharmacology, Public Health and PhD students' works.

Follow us on www.ismck.com and find out more!



ISCOMS:
International Student Congress of (bio) Medical Sciences

The International Student Congress of (bio)Medical Sciences, also known as ISCOMS is one of the world's leading student congresses on (bio)medical sciences.

ISCOMS is not just any regular congress however, it is a non-profit organisation made up of students that aims to promote student research and the international exchange of it. Throughout our three day congress we therefore offer a stimulating venue for student research exchange and give students the opportunity to broaden their social and scientific network.

Our scientific programme includes different researches from students all over the world which are presented in poster, oral or plenary form, all in front of an international and professional audience. Along with these student sessions there will be fascinating keynote lectures and hands-on workshops.

Along with a rich scientific programme we also have an elaborate social programme, filled with dinners and parties giving a chance for all the participants to get to know and have fun with each other and ISCOMS organisation.

Partners Conferences

WIMC: Warsaw International Medical Congress for Young Scientists

This year we'll have the opportunity to gather together for the 10th time at the Warsaw International Medical Congress for Young Scientists. As we are celebrating our ten-year anniversary, special attractions and commemorations are in the works for our participants. Warsaw International Medical Congress marks one of the most significant events of the elite scientific community in Europe. Already in 2005, WIMC hosted students from all around the world. In the course of the decade-long tradition, our congress managed to position itself highest among academic events, uniting the best skilled young adults.

Last year, already over 600 participants, who competed in a wide range of medical sessions, have registered. For this particularly special anniversary congress, we've prepared numerous gems of scientific research, in the form of expert lectures keynoted by doctors renowned in the world of science. We also offer our participants a various selection of fascinating workshops, during which you'll be able to expand your medical knowledge and develop many skills within the health-care profession.

Aside from shared scientific adventures in the course of WIMC 2014, there will be ample opportunity for integration among students from all over the world, getting to know about each others' countries through interpersonal contact, as well as discovering the beauty of Poland and its capital Warsaw with the organizers through many social events.

We are waiting for abstracts until 2nd March 2014!
More information on our website: www.wimc.wum.edu.pl

Questions? Ask us: wimc2014.participants@gmail.com

iMed Conference:

The iMed Conference® is an annual event organised by the Students' Association of Faculdade de Ciências Médicas of NOVA University of Lisbon (AEFCML). It aims to bring the latest scientific innovations to Life Sciences students.

Its 6th edition, taking place in Lisbon on the 10th, 11th and 12th of October 2014, will have Scientific Lectures dedicated to Immuno-Oncology, Man & Machine, Infectious Diseases and Neuropsychiatry. There will also be Keynote Lectures given by the most acknowledged speakers of the Scientific Programme - among which two Nobel Laureates -, as well as the brand-new iMed Sessions, an informal and dynamic kind of lectures focusing on original and unexpected issues.

Similar to the previous editions, the Innovate and the Clinical Mind Competitions will be hosted, giving students the chance to challenge themselves with the presentation of research projects and the resolution of real-time clinical cases, respectively. The best ones will be awarded prizes.

Furthermore, by enrolling in the iMed Workshops, they will also be able to have a more practical approach to the congress themes. There will also be a Social Programme for both speakers and participants, which will include: the iMed Gala, a glamorous dinner and after-party at the Palace of Tapada da Ajuda, a Wine Tasting at São Jorge Castle and a Lisbon Tour around the city.

The iMed Conference is under the High Patronage of the European Parliament, the President of the Portuguese Republic, the Ministries of Health and Education, as well as several bodies dedicated to research and education. It aims to be the Best Congress for Medical Students in Europe.

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