COMENIUS UNIVERSITY IN BRATISLAVA

JESSENIUS FACULTY OF MEDICINE IN MARTIN

40th STUDENT SCIENTIFIC CONFERENCE

PROGRAM and ABSTRACTS

April 30, 2019

Martin, SLOVAK REPUBLIC

Univerzita Komenského

1969 2019 JLF UK

40th Student Scientific Conference
Jessenius Faculty of Medicine in Martin
Comenius University in Bratislava

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PROGRAM AT GLANCE

Date: April 30, 2019

Place: Aula A Novomeského 9, Martin
Aula B Novomeského 9, Martin

Registration: April 30, 2019, 7.30 or before the beginning of sections

Opening ceremony (Aula A – Novomeského 9) **08.00 – 08.30**

Invited lecture: Prof. Kamil JavoUka, MD., DrSc.
A brief history and importance of Student Scientific Activities in Martin

Aula A

A1: Section of Clinical Disciplines 08.30 – 10.30

- coffee break

A2: Section of Non-Medical Study Programs 10.45 – 11.45

- coffee break

Aula B

B1: Section of Theoretical Disciplines 08.30 – 10.00

- coffee break

B2: Section of Pre-Clinical Disciplines 10.15 – 11.45

- coffee break

Closing ceremony (Aula A – Novomeského 9) **12.30**

Duration of lectures: **8 minutes, discussion – 4 minutes**

Language: Slovak, Czech or English

PROGRAM IN DETAILS

„AULA - A“

SECTION OF CLINICAL DISCIPLINES

(8.30 – 10.30)

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[3] Department of Hematoonkology, FNO

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[1] 1st Department of Internal Medicine, JFM in Martin, CU in Bratislava
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[2] University of Ostrava, Faculty of Medicine, Czech Republic

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Clinic of Neurosurgery JFM in Martin, CU in Bratislava

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coffee break

„AULA - A“

SECTION OF NON-MEDICAL STUDY PROGRAMS

(10.45 – 11.45)

„AULA - B“

SECTION OF THEORETICAL DISCIPLINES

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Department of Medical Biology and Division of Oncology/Biomedical Center Martin, JFM in Martin, CU in Bratislava

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[2] Department of Molecular Medicine, Biomedical Center Martin, JFM in Martin, CU in Bratislava

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Tutor: Mgr. Petra Priščáková, PhD.

Institute of Medical Biology, Genetics and Clinical Genetics, Faculty of Medicine, CU in Bratislava

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Department of Medical Biophysics, JFM in Martin, CU in Bratislava

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AWARDING AND CLOSING CEREMONY

(12:30)

NOVOMESKÉHO 9, AULA A

ABSTRACTS

All abstracts are available in English at http://www.jfmed.uniba.sk/veda/svoc/

PLASMA LEVELS OF VASCULAR ENDOTHELIAL GROWTH FACTOR AND SELECTED HEMOSTATIC PARAMETERS IN ASSOCIATION WITH TREATMENT RESPONSE IN MULTIPLE MYELOMA

Aneta Knazurova

Tutors: Juraj Sokol, MD., PhD.; Matej Hrncar, MD.; Jan Stasko, MD., PhD.

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Introduction: Multiple myeloma (MM) belongs to a group of neoplastic plasma cell disorders. It is characterised by a clonal proliferation of plasma cells in the bone marrow as well as the presence of monoclonal protein in urine or blood. Several abnormalities in patient's haemostasis have been described in association with MM, which may result in bleeding or thrombosis.

Material and Methods: We focused on measuring concentrations of serum levels of D-dimer, vascular endothelial factor, and von Willebrand factor in patients with MM, either newly diagnosed, or relapsed. We measured these concentrations before treatment, during therapy and after treatment. We aimed to prove that all these factors correlate with the total body mass of tumour. We expected these parameters to decrease throughout the therapy.

Results: As expected, we observed abnormal levels of all three parameters in the blood samples taken before treatment, which may contribute to a higher risk of venous thromboembolism in patients with MM. We also observed higher levels of these parameters in newly diagnosed MM patients compared to relapsed MM patients due to more significant alteration in angiogenic and coagulation activity. These levels gradually decreased as the therapy proceeded. This results from the fact that the total body mass of tumour was reduced throughout the therapy.

Conclusion: We proved the correlation between plasma levels of D-dimer, vascular endothelial factor, and von Willebrand factor with the treatment response in multiple myeloma through the decrease in their levels as the total body mass of tumour was reduced.

NEW METHOD AN ABDOMINAL ADVANCEMENT FLAP OF COMBINED BREAST RECONSTRUCTION

Júlia Bartková

Tutor : Assoc. Prof. Martin Boháč, PhD., MHA, FEBOPRAS

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Introduction: An Abdominal advancement flap is often used as one of methods of the breast reconstruction with prosthetic materials and dermal matrix after radical mastectomy. We modified the old method of abdominal advancement flap and compared the patients treated with classic and new method.

Material and Methods: An abdominal advancement flap is a flap that is pulled up using the skin and the subcutaneous tissue that was under the original inframammary fold and creates the shape of the lower part of the breast by making a neo-inframammary fold. In this new modified method the fixation of the mobilized skin is realized by using a long-term absorbable material installed into the subcutaneous region within the range of the footprint of the new breast which is fixed transpectorally by specialized skeletonized needles. We monitored and compared two groups of patients. In the first reference group of 11 patients during the breast reconstruction was used expander/implant and acellular dermal matrix. In the second group of 11 patients was used besides standard completions also new method of abdominal advancement flap.

Results: Using this modified method of abdominal advancement flap, we discovered its relation with initial expansion volume which was 44 percent bigger than at classical method. In the first group of patients we registered three post-operative complications and in the second group, we noticed two complications.

Conclusion: This method has more aesthetic and functional effect with the minimal morbidity of the donor site compared to the „conventional method“. This method leads to aesthetically better formed lower part of new breast.

RETROSPECTIVE ANALYSIS OF PATIENTS AFTER ACUTE ISCHAEMIC HEMISPHERIC STROKE

Marek Bašista

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Introduction: Ischaemic stroke accounts for the most common type of stroke (85% of all stroke cases). Our goal was to evaluate neurological status of patients at the onset of a stroke (entrance examination) and after a longer period of time.

Material and Methods: To achieve this goal, in the first step we analysed 126 of 262 healthcare records of patients hospitalized at Clinic of Neurology during year 2016. All of them were diagnosed with the same diagnose code. In total 66 patients (average age 68 years, 41 males and 25 females) had acute ischaemic hemispheric stroke. According to records, we evaluated their National Institute of Health Stroke Scale (NIHSS) on admission, CT/MR proof of ischaemia, presence of arterial hypertension (grade if given), diabetes, dyslipidaemia, atrial fibrillation (or any other cardiac arrhythmias) and total duration of hospitalization at Clinic of Neurology. At the time of patients' discharge, we calculated modified Rankin Scale (mRS) and NIHSS. Furthermore, we allocated patients according to TOAST classification into 5 groups based on stroke etiology.

In the second step we will contact our patients (in April 2019, which is at least two years since 2016) via phone call in order to obtain similar information as in the first step: mRS, whether after disposal from hospital patient developed decubiti, another stroke, myocardial infarction or any other significant change in health condition. We will also ask about patients' current medication – mainly antiaggregants and anticoagulants. Additionally, we will determine whether or not the patients have been living in the retirement home and for how long.

Results: We observed reduction of NIHSS at the time of discharge as well as correlation between cardioembolic stroke and atrial fibrillation occurrence.

Conclusion: Research is still in progress, final results will be available at 40th Student Scientific Conference 2019.

IS THE T-LYMPHOCYTES DETECTION IN NON-SMALL CELL LUNG CARCINOMA IMPORTANT FOR THE INDICATION OF AN ANTI-PD-1/ANTI-PD-L1 IMMUNOTHERAPY ?

Pavol Čuj

Tutor: Prof. Lukáš Plank, MD., CSc.

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Introduction: The immunotherapy represents a new treating modality for patients with non-small cell lung cancer (NSCLC) which are escaping immune destruction by expressing PD-L1 (programmed death-ligand 1). Anti-PD-1/anti-PD-L1 treatment enables anticancer immune reaction recovery. This therapy requires identification of a positive immunohistochemistry (IHC) PD-L1 expression at various cut-off levels, but also other new biomarkers for better patients' selection are being analysed. In our pilot study we focused on possibility of evaluation of $CD3^+$ T-cell load in the tumour tissue reflecting a local anticancer immune reaction.

Material and Methods: Our series consist of 39 NSCLC resection biopsy samples, which were analysed for CD3 and PD-L1 (clone 22C3) IHC expression. Both IHC parameters were evaluated semiquantitatively; PD-L1 expression (in tumour cells only) on scale negative (<1%) versus positive (1 – 49%, respectively >50%) and $CD3^+$ lymphocytes presence on scale without infiltration (marked as 0), low (1) versus high (2) $CD3^+$ infiltration, both in tumor stroma and at its margins. Detected parameters were correlated to NSCLC grade, for squamous cell (SQ), adenocarcinoma (ADC) and other carcinoma types respectively.

Results: Due to a limited number of cases, we can only summarise following trends: a/ in well differentiated SQ both stroma and edge of tumour - non-tumour tissue is less frequent and less intensive infiltrated, than in those structures of less differentiated SQ; b/ also in ADC group we recognized a trend of more frequent and more extensive $CD3^+$ T-cell infiltration in lower differentiated (G3) compared to higher differentiated (G1/G2) types c/ same statement applies to sarcomatoid carcinomas, d/ these trends apply to all types of NSCLC irrespectively to negative or positive PD-L1 expression, or to the level of its positivity.

Conclusion: In our study we proved a possibility of analysis of local NSCLC anticancer immunity by detection of CD3+ T-cell infiltration. The implementation of these analysis to routine practice complemented with eventually $CD8^+$ T-cells detection and/or other parameters seems to help in searching for biomarkers of anti-PD-L1 immunotherapy.

THE ROLE OF VWF, FVIII, ADAMTS13 AND INFLAMMATORY RESPONSE IN THE OUTCOME OF ACUTE ISCHEMIC STROKE

Petr KOVÁŘ

Tutors: Václav PROCHÁZKA, MD., PhD. MSc.[1]; Prof. Jirka MAČÁK, MD., CSc.[2]; Jaromír GUMULEC, MD.[3]

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Introduction: In the University Hospital of Ostrava, about 135 acute stroke interventions are annually carried out. The risk of acute stroke relapse is increased if prothrombotic changes of haemostasis or cardiac arrhythmia are present. In such cases, the patients are more likely to suffer from increased thrombus adhesion to cerebral arteries endothelium.

Material and Methods: The group of patients in our study, who have undergone the extraction of thrombus, regularly experience cardioembolic strokes. By means of light microscopy, the extracted thrombi are used to detect vWF, thrombocytes, erythrocytes, plasma proportion including components and granulocytes.

The aim of the study is to analyze the functions of blood platelets in peripheral blood, and the presence of selected signs of activation of coagulation and prothrombotic changes of haemostasis, and related immunohistochemical findings in the proper thrombus removed from cerebral blood vessels.

Conclusion: The study reveals worse prognosis for patients with high activity of vWF/FWIII, and, simultaneously, low ADAMS13 activity. The research also proves inflammatory nature of emboli with increased level of vWF.

TYPICAL AND ATYPICAL RISK FACTORS IN PATIENTS PRESENTED WITH STEMI IN UNIVERSITY HOSPITAL IN MARTIN - RETROSPECTIVE ANALYSIS

Martin Jozef Pec

Tutors: Michal Mokan, MD., PhD.[1]; Frantisek Nehaj, MD.[1]; Juraj Sokol, MD., PhD.[2];

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Introduction: Ischaemic heart disease (IHD) is the single most common cause of death and its frequency is increasing. ST-segment elevation myocardial infarction (STEMI) is defined as a myocardial injury with necrosis, a significant elevation of cardiac troponin values in a clinical setting consistent with myocardial ischaemia. Key risk factors for coronary heart disease (CHD) that cannot be changed are age, gender, family history and factors that can be changed are dyslipidemia, high blood pressure, diabetes, smoking, overweight/obesity, excessive alcohol/stress, being active. This study concerns not only well known risk factors mentioned above, but also the impact of demographic factors, weather and other interesting features in patients presented with STEMI.

Material and methods: 221 patients with STEMI were analysed who underwent primary percutaneous coronary intervention (pPCI) referred to University Hospital Martin in 2015. Modifiable and non-modifiable clinical risk factors, impact of weather, demographic parameters and selected biomarkers were retrospectively analysed.

Results: The majority of 221 patients with STEMI were male (n=145, 65%) and the rest were female (n=76, 35%); the mean age of patients was 62.3 years (+/- 11.76). Patients with positive family history of cardiovascular disease (CVD) were n=52, 23.5%; with diabetes (n=49, 22.2%), hypertension (n=135, 61.6%), most of them were smokers (n=64, 29%), with no previous history of myocardial infarction (MI), neither anticoagulation (n=205, 92.3%) or antiplatelet therapy (n=175, 78.8%). The lowest probability of occurrence of MI was on Sunday (n=22, 10%).

Conclusion: According to data-driven analysis not only typical clinical risk factors and lifestyle, but also specific weather conditions could trigger the manifestation of IHD. A further investigation could reveal the impact of atypical risk factors on IHD.

COMPUTATIONAL FLUID DYNAMICS OF NASAL AIRFLOW - FIRST EXPERIENCE

Plášek, M. [1,2], Kobližková, P. [1,2]

Tutors: Prof. Pavel Komínek, MD., PhD., MBA; Petr Matoušek, MD., PhD., MBA

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Introduction: The pattern of the nasal airflow is crucial for normal nasal breathing as well as it can be a pathophysiological underlay of nasal symptoms. Pathological conditions such as septal deviation/perforation can change nasal airflow and cause nasal obstruction. Nowadays, nasal airflow is simulated especially by computational fluid dynamics (CFD). At first, airflow in physiological nasal cavity was simulated to get preliminary data.

Material and methods: 3D model of nasal cavity was made according to CT scans of patient who did not have problems with nasal breathing and nasal airflow was simulated in „healthy nose".

Airflow was simulated during „inspiration" with constant physical attributes - isotermic, incompressible air without gravitation. The walls of model were firm, without considering moving or deformation, it means without considering mucosal changes. The pattern of airflow was turbulent with pressure grade 120Pa between entrance (nasal entry) and output (nasal choana). We defined seven localities (from nasal entrance to nasopharynx) where the velocity, resistance and main nasal airflow was detected.

Results: Our results showed different airflow between right and left nasal cavity. Main nasal airflow was detected in the inferior meatus as well as in the middle part of common nasal meatus.

The highest resistance was measured out in the area of internal nasal valve. The highest velocity was detected in the area of nasal entrance with consecutively deceleration towards to nasopharynx.

Conclusion: It seems that there is not only one physiological pattern of nasal airflow. Next simulation will be during pathological conditions (data will be compared). There is a great potential to apply knowledge of nasal (patho)physiology to clinical rhinology and rhinosurgery to improve treatment of patients.

Supported by the Institutional Support of the Ministry of Health RVO FNOs/2018

EARLY COMPLICATIONS IN PATIENTS AFTER DECOMPRESSIVE CRANIECTOMY - INCIDENCE AND POSSIBLE RISK FACTORS

Jakub Soršák

Tutors: Martin Hanko, MD.; Assoc. Prof. Branislav Kolarovszki, MD., PhD.

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Introduction: Decompressive craniectomy is a neurosurgical procedure designed to rapidly control an otherwise refractory intracranial hypertension. As it is often performed as an emergent life-saving operation, the patients' outcome and further care is frequently affected by various complications.

Methods: In a retrospective study of 117 patients who underwent decompressive craniectomy in our clinic during a five-year period (2013-2017) we assessed a rate of procedure-related and procedure-nonrelated early complications (occurring during the first 3 weeks post-op). We also analysed an impact of possible risk factors which might have affected the incidence of complications and also the rate of early postoperative death (up to 72 hrs post-op).

Results: At least one early procedure-related complication was recorded in 73.50% of patients with subdural hygroma being the most frequent one (occurring in 36.62% of the patients), however reoperation was necessary in 13.68% cases only. At least one procedure-nonrelated complication was present in 46.15% of patients. Early death occurred in 9.40% of the patients. Male sex, alcohol abuse, liver disease, traumatic brain injury and presence of an acute subdural haematoma, postoperative thrombocytopenia and hyperglycaemia were identified as risk factors for at least one type of postoperative complication. Intake of clopidogrel and acetylsalicylic acid, liver disease, preoperative thrombocytopenia, postoperative hyperglycaemia and increased thrombin time were related to increased risk of early postoperative death.

Conclusions: There is a substantial risk for development of early postoperative complications in patients who undergo decompressive craniectomy. If supported by data from studies describing patients' outcome with an adequate follow-up, our report may improve the decision-making process concerning the indication of decompressive craniectomy and therefore targeting this surgery to the salvageable patients.

EFFECTS OF BISOPROLOL ON THE LEVEL OF DABIGATRAN

Linda Soršáková

Tutors: Juraj Sokol, MD., PhD.[1]; František Nehaj, MD.[2]; Jela Ivanková, MA.[1]

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Introduction: Dabigatran is a direct thrombin inhibitor used for stroke prevention in patients with nonvalvular atrial fibrilation (NVAF). Besides anticoagulation, management of NVAF involves almost universal need for control of heart rate. Therefore many patients receiving dabigatran treatment might also require bisoprolol therapy. However, there is a possibility that bisoprolol as significant P-glycoprotein inhibitor might interact with dabigatran.

Methods: Dabigatran was administrated twice daily and Bisoprolol fumarate 5 mg tablet was taken in the morning after dabigatran. Blood samples were taken 12 hours after previous dabigatran dose administration, followed by next blood sample after 2 hours. Hemoclot thrombin inhibitor assay (Hyphen BioMed, Paris, France) was used according to the manufacturer's instructions for the quantitative determination of dabigatran plasma levels.

Results: A total of 29 patients with NVAF were enrolled and they were divided into two groups: with (group 1) or without (group 2) concomitant bisoprolol therapy. Group 1 (n=18): the mean age was 72.39 years (range 56–85 years), 12 patients were women, and the mean CHA2DS2VASc score was 3.22. Dabigatran doses were 110 mg (56%) or 150 mg (44%) twice a day. Group 2 (n=11): the mean age was 68.64 years (range 51–86 years), 4 patients were women, and the mean CHA2DS2VASc score was 2.73. Dabigatran doses were 110 mg (55%) or 150 mg (45%) twice a day. The dabigatran plasma level was significantly higher at baseline and at hour 2 in patients treated with bisoprolol compared with patients without bisoprolol therapy (baseline: 161.35 vs. 87.94 ng/mL; after 2 hours: 236.87 vs. 151.00 ng/mL).

Conclusion: We demonstrated the interaction between dabigatran and bisoprolol, which is modulated with dabigatran dosage and concomitant treatment with proton-pump inhibitor and digoxin.

NURSES PROFESSIONAL VALUES SCALE: ADEQUATE TRANSLATION PROCESS

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Introduction: Addressing professional values is one of the important areas of nursing. Nurses are required to have knowledge and awareness concerning professional values as standards to provide safe and high-quality nursing care. The aim of study was to develop a Slovak version of the *Nurses Professional Values Scale – Three* for further validation and research.

Material and methods: The method of adequate translation of the English questionnaire into the Slovak language was used. We have used two separate translations made by English teachers which were subsequently united by the author and the tutor. The pilot version of the translation was assessed by two bilingual experts from nursing practice and one from academic area (bilingual translation method).The items were evaluated through a recorded interview. The interview was aimed to assess the adequacy of the translation and content understanding of items in our socio-cultural context.

Results: Item *1.Engage in on-going self-evaluation* has been shown to be problematic in terms of understanding. In our conditions it is not common for nurses to self-evaluate as part of their practice on a regular basis. *5. Participate in peer review*. In the context of our practice it is not so common to involve nurses from practice to reviewing process of articles. *22. Confront practitioners with questionable or inappropriate practice*. In this item was problem with understanding of term fidelity („vernosť"). *24. Participate in professional efforts and collegial interactions to ensure quality care and professional satisfaction. 25. Promote mutual peer support and collegial interactions to ensure quality care and professional satisfaction*. Both items were meaningfully identical to the nurses after the first reading, only after multiply reading they see the difference in the meanings.

Conclusion: The problematic items will be modified to clarify their meaning, the problematic terms will be replaced with regard to the adequacy. It is necessary to deal with semantic equivalence of research tool in the Slovak socio-cultural context especially when a foreign-language professional value tool is adopting.

RISK FACTORS FOR FALLS IN PATIENTS WITH SELECTED NEUROLOGICAL DISEASE

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Introduction: Patients with neurological diseases are at risk for falls during hospitalization and the fall is a complication of their underlying health condition. In Slovak clinical practice, the fall is defined as an undesirable (adverse) event and is subject to mandatory reporting from 2014. The aim of the study was to identify the presence of selected risk factors of falling and circumstances related to this adverse event.

Material and methods: Study design: retrospective analysis medical record of patients. The sample consisted of 30 patients who fell during their hospitalization at Neurological Clinic of University Hospital in Martin from 2014 to 2018. For data collection we created a list of selected fall risk factors, a screening tool for fall risk in adult hospitalized patients - Morse Fall Scale (MFS score 0-125), a screening tool for assessment of self-care abilities - Barthel Index of Activities Daily Living (Barthel ADL Index level 0-100) and circumstances relating to fall (place, time, injury after the falling).

Results: The sample was consisted of 19 men and 16 women (N = 30), the most patients (N = 22) had a medical diagnosis of Cerebral Vascular Disease. The mean age of the sample was 72.1 ± 15.0 (min. 29, max. 93) years. There were most common fall risk factors: gait and balance disturbance (N = 30), chronic disease ≥ 4 diagnoses (N = 30), pharmacotherapy ≥ 5 drug groups (N = 28). Patients used an average of 12.9 ± 6.2 (min. 2, max. 31) pcs. of drugs per 24 hours. Falls history in the past year had 8 patients. Four patients had a recurrent fall during hospitalization. The mean score of fall risk by MFS was high 80.0 ± 26.7 (min. 30, max. 125) during admission at unit. Patients had moderate dependence in Barthel ADL Index (58.0 ± 22.4). The patients most often fell in the room (N = 26), during the night shift (N = 19) and the injury as a result of the fall had 18 patients.

Conclusion: The identification of risk factors, including the level of risk for falling, in a particular patient is a preventive intervention to minimize the fall risk of falling during hospitalization.

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FERTILITY CARE

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Introduction: Fertility awareness and preventing the infertility risk factors have significant consequences for public health. The purpose of the study was to determine the female fertility awareness and fertility care.

Material and methods: In this research the cross-sectional quantitative study design was elected. 107 women participated in our research in the age of 18 – 30 (average age : 22.64 ± 3.60). We used questionaire of our own construction focussed on detection of opinions, attitudes of women in the issues of fertility, also foreknowledge, knowledge and practice in relation with their own fertility care. We used descriptive statistics for analysis of obtained information.

Results: The opinions and attitudes of participated women in the case of fertility were mostly positive. Less than one half of women (48.6%) felt foreknowledged. Lack of information was shown in the case of knowledge , which were not sufficient and correct in all the women´s answers. One of the reasons was the internet as the main source of information (27.6%). Also the presented age for pregnancy was not in accordance with the suggested age. Fertility care in most of the women was satisfying. However in 1/3 of women there were some deficiencies in the case of fertility monitoring and observance of the right lifestyle.

Conclusion: It is important to improve women´s fertility awareness including fertility care with regard to demonstrated insufficiencies. Midwives, except of participatng in foreknowledge, should also identify risks related with fertility, and in the case of fertility problems they should advise and suggest all the available solutions and preventive precautions with the aim to improve reproductive health of women.

MATERNITY THROUGH THE EYES OF ADOLESCENTS

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Introduction: Maternity is an important part of a woman's life. Several studies have focused on the impact of attitudes towards motherhood on the implementation of reproductive plans. One particular group that has received considerable attention is adolescents, as they have just entered reproductive age and are facing competing interests, between their educational and career goals, marriage and childbearing. The main goal of the study was to find out details about the reproduction plan of female students; the reasons that influence their decision to have a child, and to discover the influence of several factors on forming opinion on maternity.

Methods: The study was conducted on 200 female students from third and fourth year of the high school (age 18,35±0,48). For the data collection, a questionnaire of own construction was used, containing items focused on socio-demographic data, reproduction plans and factors influencing the opinion on maternity. Descriptive statistics was applied when processing the data.

Results: The results showed, that 78% of the female students are planning to have a family in the future, considering 2 kids as the ideal number. Main reasons were mutual love, attraction of the partner and fulfilled relationship. Among the important reasons influencing their opinion, family and their partner were cited. The participants claimed that the most important conditions for starting a family were marriage, family support and a good job. According to 42,5% of students, the best age to have a first baby is between the age of 20 and 25. However, the majority is of an opinion that the fertility of a woman decreases only after the age of 36.

Conclusion: Despite the fact that the reproductive plans created during adolescence may not correspond to their actual realization, we may consider these results positive. From the point of view of midwifery, we consider the support of a positive image of maternity among adolescents very important, mainly due to rising average age of primiparas potentially leading to complications and decreasing fertility.

SELECTED SOCIAL – DEMOGRAPHIC DETERMINANTS OF ALCOHOL CONSUMPTION IN MEDICAL STUDENTS

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Introduction: The work analyses selected indicators of alcohol consumption in medical students of the Jessenius Faculty of Medicine, Comenius University by gender, years of study (1st vs. 4th), and geographical background (Slovak vs. English study program).
Material and methods: Questionnaire study carried out in academic year 2018/2019 during study period. Reports on drinking of alcohol more than once a months as well as having more than five drinks of spirits, beer and wine during recent month were analysed. The samples included 220 first-year (130 Slovak and 90 English study program) and 171 fourth-year (83 Slovak and 88 English study program) students.
Results: Alcohol consumption more than once a month varied from 53.1% (1st year Slovak women) to 73.7% (4th year Slovak men) showing no significant differences between analysed subgroups. While preference of spirits dominated in the most of Slovak students (1st and 4th year men and women) and 1st year English study program men, others preferred beer (4th year English study men and women) and wine (4th year women). Among Slovak students drinking preferences did not differ between 1st and 4th year. However, consumption of beer, wine and spirits prevailed in 4th year females over 1st year ones (43.1% vs.14.3%, 45.1% vs. 14.3% and 33.3% vs 12.2%, respectively) among English study program students.
Conclusions: Alcohol consumption is widespread both in Slovak and English study program students. However in Slovak students drinking patterns are less favourable (preference of spirits). While Slovak students did not change their drinking patterns during their study, women studying in English increased their drinking intensity indicating predominant role of social environment during the study.

THYMUS VULGARIS L. IN THE CHEMOPREVENTION OF EXPERIMENTAL BREAST CARCINOMA: ANALYSIS OF MECHANISM OF ACTION

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Introduction: There has been a considerable interest in the identification of natural plant molecules for developing effective anticancer agents. Moreover, it is well documented that regular consumption of phytochemicals from whole foods (functional foods) is linked with a risk reduction of the diseases of civilization, including cancer. Based on our previous research, it seems that the mixtures of low-dose phytochemicals present in whole foods may be more effective against mammary carcinogenesis when compared to isolated phytochemicals.

Methods: The anticancer effects of*Thymus vulgaris* L. haulm were evaluated using the chemopreventive model of N-methyl-N-nitrosourea−induced rat mammary carcinogenesis. Thyme haulm was dietary administered at two concentrations of 0.1 % and 1 % during 15 weeks after carcinogen administration. At autopsy, mammary carcinomas were removed and prepared for immunohistochemical and molecular analyses.

Results: Dietary administered thyme (1 %) caused significant decrease in rat tumour frequency by 53 % when compared to untreated control. Analyses of treated rat carcinoma cells showed CD44 and ALDH1A1 expression decrease and Bax expression increase. MDA levels and VEGFR-2 expression were significantly decreased in rat carcinomas in both *T. vulgaris* treated groups. Regarding the evaluations of epigenetic changes in rat tumors, we found a significant decrease in lysine methylation status of H3K4me3 in both treated groups (H3K9m3, H4K20m3, and H4K16ac were not changed), up-regulations of miR22, miR34a, and miR210 expressions (only at higher dose), and significant reductions in methylation status of four gene promoters – ATM, RASSF1, PTEN, and TIMP3 (PITX2 promoter was not changed).

Conclusion: Our results showed tumour-preventive effect of thyme haulm in the breast carcinoma model. This effect of thyme was associated with apparent positive epigenetic modulations in breast carcinoma cells *in vivo*. This work was supported by the grant VEGA 1/0136/19.

INDUCED PLURIPOTENT STEM CELLS AND IN VITRO MODELING OF AMYOTROPHIC LATERAL SCLEROSIS

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Introduction: Amyotrophic lateral sclerosis (ALS) also known as motor neuron disease is serious progressive disorder, caused by deterioration of motor neurons. Currently, no cure or effective treatment exists for ALS. This is partially caused by the lack of suitable *in vitro* models available for research. In this project we reprogrammed ALS patient-derived skin fibroblasts into induced pluripotent stem cells (iPSc) and subsequently into neural precursors. Neural precursors represent unlimited source of cells that can be differentiated into motor neurons and used in disease modeling and therapy development.

Material and Methods: To isolate fibroblasts from skin biopsy of ALS patients we used optimized explant culture protocol. Primary skin fibroblasts were then reprogrammed with synthetic RNA polycistronic vectors into iPSc. Pluripotent cells were adapted to xeno-free culture conditions and expanded for cryopreservation and pre-differentiation into neural precursor cells.

Results: Five clones of ALS-iPSc cells were isolated in initial experiment and one candidate clone was selected for further analyses based on morphology, growth dynamic, factor expression and low affinity toward spontaneous differentiation. Expression of transcription factors (Oct4, Sox2, Nanog) and SSEA4 was confirmed with fluorescently labelled antibodies with immunocytochemistry and flow cytometry. Embryoid body-based and 2D differentiation protocol was used for isolation of rosettes and neural precursors.

Conclusion: With the use of advanced cell engineering protocols and in collaboration with University Hospital Martin we have successfully developed novel *in vitro* model for ALS disease. Further characterization of this cell line will be performed *in vivo*, using athymic mice and large animal model (Gottingen-Minesota minipig, at IAPG AV CR, Libechov, Czech Republic). We also aim to continue in development of new cell lines from other ALS patients.

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MUTATIONS OF *PTEN* GENE IN UTERINE PAPILLARY SEROUS ADENOCARCINOMA

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Introduction: Uterine papillary serous adenocarcinoma (UPSC) is classified as Type II endometrial carcinoma. It is characterised with poor differentiation, deep myometrial invasion, high metastatic potential and worse prognosis. Mutations of *PTEN* tumorsupressor gene are considered as atypical in this type of malignancy. Our study aimed to determine if the sequence analysis of *PTEN* gene would be a useful procedure in the clinical management of UPSCs in the Slovak population.

Material and methods: We analyzed the *PTEN* gene in DNA isolated from paraffin embedded bioptic UPSC samples of the Slovak patients by Sanger sequencing.

Results: We found more mutations than expected according to international standards, and we even described rare mutations in our study group. We found mutations of *PTEN* gene in three from our eight patients, in two cases there were two mutations in heterozygous states (c.389G> A + c.419T> G and c.19G> T + c.1021T> G) and in one case one mutation in homozygous state (c.730C> T). In the COSMIC (*Catalog of Somatic Mutations in Cancer*) database, all the mutations we found are available and labeled as pathogenic mutations so they can be considered relevant for the neoplastic process.

Conclusion: Comparing our results with the TCGA (*The Cancer Genome Atlas*) and COSMIC, which provides approximately 2% and 7 % frequency of *PTEN* mutations in UPSCs respectively, we can assume that *PTEN* gene mutations in UPSC are more common in the Slovak population than the American or as international average. It indicates that *PTEN* gene analysis would be useful in the clinical management of UPSCs from this population. Mutations in the *PTEN* gene can be exploited in the therapy because they increase the sensitivity of the tumor to the inhibitors of the PI3K-Akt-mTOR signaling pathway – PTEN is the main negative regulator of this pathway. Thus, sequencing of the *PTEN* gene may be important for the more effective, targeted therapy of this type of endometrial carcinoma.

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INTERACTION OF EXPIRATION REFLEX WITH MECHANICALLY INDUCED COUGH IN CATS

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Introduction: Expiration reflex differs from coughing by being independent expiratory effort not preceded by an inspiration. The expiration reflex excitability is the highest during expiratory phase of breathing mainly due to close position of medial margin of the vocal folds (more receptors are available to mechanical stimulation). Mutual interactions of both reflexes has not been deeply studied, yet.

Material and methods: Modulation of the cough response by the expiration reflex induced from vocal folds was studied on 8 spontaneously breathing male cats (3.42 ± 0.26 kg) under the pentobarbitone anesthesia. Both reflexes were induced mechanically by a soft nylon fiber. Cough was elicited in the tracheobronchial area. In our protocols the expiration reflexes were induced during the inspiratory phase of cough; during transition of inspiratory to expiratory cough phase including cough expulsion period and within cough quiet expiratory sub-phase. Blood pressure, esophageal pressure (EP) and EMGs of the diaphragm (DIA) and the abdominal muscles (ABD) were recorded and analyzed.

Results: Expiration reflex induced during all selected cough phases has no significant effect on cough number ($p>0.05$). However, expiration reflexes that occurred within the *inspiratory cough phase,* the *transition of inspiratory to expiratory cough phase, or during cough quiet expiratory sub-phase* increased the amplitudes of DIA ($p<0.05$) and ABD ($p<0.05$) EMG as well as inspiratory ($p<0.05$) and expiratory EP ($p<0.05$) during cough.

Conclusion: Our finding indicates strong modulatory effect of co-activated expiration reflexes on cough reflex intensity with no alterations in cough number representing cough responsiveness.

EFFECT OF INDUCED HYPERHOMOCYSTEINEMIA TO PROGRESSION OF NEUROPATHOLOGICAL CHANGES WITH FEATURES OF ALZHEIMER'S DISEASE

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Introduction: Hyperhomocysteinemia has been considered to be one of the risk factors for neuropsychiatric disorders, including Alzheimer's disease (AD), which is a neurodegenerative disorder that results in massive hippocampal and neocortical neuronal loss leading to dementia and eventual death. The exact pathomechanism of AD is not fully explored but it could be partially prevented by properly addressing its modifiable risk factors, as its treatment, prognosis and rehabilitation is limited. The newer strong modifiable independent risk factor, hyperhomocysteinemia (hHcy) has created such new opportunity. However, the molecular background underlying these mechanisms linked with hHcy and ischemic stroke is poorly understood.

Material and methods: Rat model of global forebrain ischemia-reperfusion injury (IRI) was induced by 4-vessels occlusion lasting 15 min of ischemia followed by reperfusion period of 24 hours. hHcy was induced by subcutaneous injection of Hcy (1.2 μmol/g) once a day in duration of 21 days. Animals were sacrificed, brain were fixed in 4 % paraformaldehyde and proceed for cryosectioning followed by histological analyses.

Results: The results showed remarkable neural cell death induced by hHcy already after 24-hour repefusion in brain cortex and neurodegeneration is further aggravated by global IRI. We demonstrated degeneration of cortical neurons, alterations in number and morphology of tissue astrocytes, neurons and their processes. The fluorescent immunohistochemical analyses detected presence of proteins associated with AD development as well. **Conclusion:** These findings suggest that the combination of risk factor of hHcy with IRI aggravates neurodegeneration processes and leads to development of AD-like pathology in cerebral cortex.

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MEASUREMENT OF LOW FREQUENCY ELECTROMAGNETIC FIELDS DURING DIFFERENT MODES OF THE MOBILE PHONES

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Mobile phones (MPs) and mobile communication have become a part of our everyday routine in a few decades. It is well known that the MPs emit radiofrequency (RF) electromagnetic fields (EMFs). However, a sparse research has been devoted to study combined RF and low frequency (LF) EMFs interactions that are also produced by the MPs.

Therefore, the aim of our research was to measure the values of LF magnetic field emitted by MP in several modes. Our research was focused on the MPs, which were not older than 5 years as they are mostly used by people nowadays. The measurements were conducted as follows: 1st - the mobile phone was switched into stand-by mode with the charger plugged in, 2nd - without charger while the screen was turned off and further turned on. 3rd - was to measure the values of EMFs in typical everyday scenarios such as calling modes in 2G and 3G networks. For measurements the broadband RF field meter NARDA 550 and LF NARDA 50D (Germany) were employed. Each measurement was performed 5 times in two frequency ranges: 5-200Hz (LF1) and 120Hz – 10kHz (LF2). Thus, total number of measurements was 140 for each MP.

Our results showed that there are notable differences in the values of EMF for different modes. The highest values were measured during a speaking mode on the front (LCD) side within LF1 range (23,2168 ± 8,34μT). The lowest values were measured within LF2 on the front side with the LCD off when the charger was unplugged (0,03316 ± 0,00346μT). It was interesting, that high performance MPs at low price had higher values in each measurement comparing to the others.

We found out that LF EMF emitted by the MPs should not be neglected and must be incorporated in the research, which looks for the possible detrimental effects of EMFs to the living systems including humans.

N-ACETYLCYSTEINE REDUCES INFLAMMATION AND OXIDATIVE STRESS IN DOUBLE-HIT MODEL OF LUNG INJURY IN RATS

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Introduction: Hyperoxia and subsequent accumulation of reactive oxygen species (ROS) during intensive care unit supportive ventilation induce inflammatory response and together lead to lung tissue damage. These processes make the lung tissue more sensitive to secondary bacterial infection. Lung intrinsic antioxidant mechanisms can significantly reduce the effect of ROS and may be enhanced by therapeutical antioxidants such as N-acetylcysteine (NAC). We hypothesized that NAC therapy reduces inflammation and oxidative stress in experimental hyperoxia and lipopolysaccharide (double-hit) induced lung injury.

Material and methods: Adult male rats (Wistar, n=15, b.w. 290±35g) were anaesthetized, tracheotomised and the endotracheal tube was inserted. Animals were ventilated with following settings: frequency (f) of 50/min, fraction of inspired oxygen (FiO_2) 1.0, inspiration time (Ti) 50 %, tidal volume (V_T) of 6 ml/kg. Bacterial infection was mimicked by intratracheally instillation of LPS (500 µg/kg b.w.; 2.2 ml/kg b.w; E.coli, 055:B5). Animals with hyperoxia and LPS were treated with N-acetylcysteine intravenously. Controls received sterile saline and were ventilated with FiO_2 0.4. After 5 hrs of ventilation the animals were overdosed by anaesthetics. Cytokine induced neutrophil chemoattractant-1 (CINC-1), caspase 3 (Casp-3), hydroxyproline, thiobarbituric acid reactive substances (TBARS), 3-Nitrotyrosine (3NT) and total antioxidant capacity (TAC) were determined in lung tissue. Total count of leukocytes in blood was evaluated.

Results: In comparison with control, hyperoxia and LPS increase 3NT ($p=0.015$), Casp-3 ($p=0.001$) and decrease TAC ($p=0.025$) in lung and total count of leukocytes in blood from 3rd hour of experiment. In animals with hyperoxia and LPS, NAC administration significantly reduces Casp-3 ($p=0.001$) and increases TAC ($p=0.024$) and total count of leukocytes (4th hour $p=0.050$, 5th hour $p=0.005$), and tended to reduce CINC-1 and hydroxyproline (both $p=0.055$).

Conclusion: N-acetylcysteine therapy improves antioxidant lung capacity and thus reduces inflammation and oxidative stress in experimental double-hit model of acute lung injury.

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MIDD/MELAS: ONE MUTATION, TWO SYNDROMES; IS REALLY THE LEVEL OF HETEROPLASMY A CAUSAL DISCRIMINANT BETWEEN THE TWO SYNDROMES?

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MIDD / MELAS (mitochondrial diabetes and deafness syndrome / mitochondrial encephalomyopathy with lactic acidosis and stroke-like episodes) are distinctive hereditary mitochondriopathies (mitochondrial syndromes) with a maternal patern of inheritance and wide range of phenotypic manifestations. MIDD is clinically relatively well manageable progressive disease with, from the point of view of quality of life, mostly softer symptomatics than MELAS. MELAS is a progresive neuromuscular disorder with very limited therapeutic options, often complicated by a wide range of other metabolic and psychological complications that have a significant impact on a life of the patient.

Approximately 85% of MIDD / MELAS cases are due to the p.A3243G mutation in the mitochondrial gene *MT-TL-1* encoding for the mitochondrial tRNA for Leu. Based on current research, it is assumed that the major discriminator deciding whether an individual develops MIDD or MELAS might be the degree of heteroplasmy, that is to say, the percentage of mutated copies of the mitochondrial chromosome from the total copy number of the mitochondrial chromosome per cell.

However, in the family studied by our team we found that the degree of heteroplasmy is not a discriminant of the phenotypic manifestation of the MIDD / MELAS mutation. Moreover, we have identified family members who, despite the high degree of heteroplasmy and in one case advanced age, show no symptoms of either of the two disorders. The results of metabolomics analyse (MS platform-based targeted metabolomics technology / Waters Xevo TQ MS) which has been conducted in our laboratory indicates that the composition of probiome of the patient might discriminate age of onset and progression of either MIDD or MELAS.

THE EFFECT OF BETANIN PRECONDITIONING AFTER JEJUNAL ISCHEMIA-REPERFUSION INJURY: IMMUNOHISTOPATHOLOGICAL ANALYSIS OF THE LUNG

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Ischemic-reperfusion injury (IRI) can progress to SIRS and finally MODS. The aim of the study is to test the effect of betanin in the lung. Ischemia was induced through arterial clipping. Animals were separated into groups treated with betanin (B) and the control group (A). The B group was injected with betanin 30 minutes prior to 1 hour of ischemia, after which, a reperfusion period of 1, 4 and 24 hours followed. The same followed in the A group using 0,9% saline solution. Biopsies were taken for histological analysis. The histopathological injury index (HII) in the A group showed a continuous significant increase of the tissue damage from the 1st hour to 24th. In the B group a significant decrease was measured from the 4th hour to the 24th. A constant decrease of MPO levels in group A was noticed from the 1st hour to the 24th. PCNA in group A shows a continuous increase. Significant difference in the two groups is observed after 24 hours. The population of mastocytes in group A is decreasing and the number of antitryptase positive mastocytes falls. COX–2 in group A was increasing from the 1st hour until the 24th. In group B the levels of the enzyme immunoreactivity were consistently lover. The results of HII and the constantly falling levels of PCNA lead to the conclusion that betanin prevented the lung tissue from the effects of IRI. The constantly lower quantity of MPO in the B group shows that betanin prevented the chemotaxis of the inflammatory cells, which is supported by lower levels of COX-2. A lesser effect of betanin could be the difference in the inhibition of iNOS production. In absence of betanin, the activity of mastocytes was amplified whereas in its presence a gradual degranulation and regranulation was observed suggesting that betanin antagonizes or inhibits the degranulation, reduces the chemokinetic load and tones down the immune reactions provoked by mastocytes.

COUGH RESPONSE TO TRPA1-RELEVANT STIMULI DOES NOT DIFFER BETWEEN GENDERS IN GUINEA PIGS

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Introduction: Chronic cough represents a troublesome problem in clinical practice – mostly in postmenopausal women. On the other hand, basic cough research in guinea pig model is performed almost exclusively on males, therefore the gender bias is present in this area of biomedical research and the assumption that results obtained in basic research are translatable into clinical practice is dubious.

Material and methods: Dunkin-Hartley guinea pigs (10 males, 10 females) were repeatedly exposed to an aerosol of 10mM cinnamaldehyde or allyl-isothiocyanate in double chamber whole-body plethysmograph HSE 855. Airflow trace and sound from the head chamber were recorded for subsequent off-line analysis. Measurements of cough response were performed at least a week apart in order to prevent tachyphylaxis. Statistical analysis of obtained data was performed in GraphPad Prism 7.0 for Windows – ANOVA or non-parametric tests were used as appropriate. Statistical significance $P < 0.05$ was considered significant.

Results: Number of coughs remained stable both for cinnamaldehyde (8.5±3.25 vs 5±1.875; 5.5±1.375 vs 3.5±1.375; 4±0.875 vs 3.5±1.375) and allyl-isothiocyanate (1.5±0.875 vs 2±1.875; 2±1.25 vs 2.5±1.375; 1±0.875 vs 2±0.5) challenge. Data are presented as male vs female group, median ± interquartile range. Cough latency showed a similar pattern. Statistical analysis did not reveal differences in challenges between genders nor within repeated measurements of cough response obtained in one gender.

Conclusion: This set of experiments, in addition to experiments with capsaicin and citric acid challenge (already presented), show that cough response in female guinea pigs is comparable to that obtained from males and it remains stable over time.

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CYTOKINES AS BIOLOGICAL MARKERS OF LOW GRADE RENAL CELL CARCINOMA AND IT'S RECURRENCE

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Introduction: The evidence of various cytokines involved in renal cell carcinoma (RCC) pathogenesis, a tumour that has a late manifestation, poor prognosis and increasing rate, has emerged. The aim of this study was to identify the cytokines relevant for routine use to achieve earlier detection of RCC.

Material and methods: We analysed 62 samples: 48 from patients with histologically verified RCC (22 were females, in age 70.3 ± 10.7 years; 26 males, in age 61.5 ± 12.2 years), and 14 controls (3 males of 39 ± 7.4 years; 11 females of 41.1 ± 11.4 years). RCC tissue samples and macroscopically healthy renal parenchyma were obtained from patients underwent nephrectomy. Urine samples were collected pre-surgically from each patient and from controls. The Bio-Plex assay and commercial Bio-PlexTM Human Cytokine Standard 27-Plex were used to detect cytokine levels. The tissue concentrations were then normalised to total protein concentration. The haemoglobin amount was quantified in urine to eliminate false positive results. The acquired data were subjected to multiple statistical analysis.

Results: In tissue samples, the significantly elevated cytokine levels that strongly correlated to tumor grade, were observed in VEGF (p means the difference in cytokine concentration of RCC tissue vs healthy parenchyma; in order grade 1 (NG1), NG2, NG3 and NG4: 0.05, 0.05, 0.01 and 0.001), IP-10 (0.05, 0.05, 0.051 and 0.01) and MIP-1β (0.05, 0.05 and 0.01). Eotaxin and IL-15 reached the highest concentration in NG3 and NG4. In patient's urine samples PDGF, IL-15, eotaxin, MCP-1 and MIP-1β reached significantly higher levels compared to controls. The level-grade correlation was observed in eotaxin (0.01, 0.05, 0.01 and 0.01) and MCP-1 (0.01, 0.01, 0.01 and 0.01). Other cytokines (IL-15, MIP-1ß a PDGF) were increased only in higher grades of the disease.

Conclusion: Our study confirms that the cytokines with the highest prognostic value in RCC are VEGF, IP-10 a MIP-1ß. The most relevant for routine screening, improving diagnostics and/or therapy of RCC, eotaxin and MCP-1 appear to be.

THE CHRONIC EFFECTS OF ERDOSTEINE IN THE SETTINGS OF ALLERGIC INFLAMMATION

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Introduction: Derivate of cysteine erdosteine, has not only mucolytics properties, but it also has other pharmacodynamics characteristics, that make this molecule an object of observation in conditions of experimentally induced allergic airway inflammation.

Material and methods: For experiment were used guinea pigs, which were divided into 4 groups. The control group OVA^- represents healthy guinea pigs treated 21 days with saline, negative control group OVA^+ represents 21 days allergen sensitized guinea pigs without treatment, positive control group OVA^+ was treated with reference antiasthmatics salmeterol and antitussive drug codeine; the therapeutic group OVA^+ was treated with erdosteine in a dosage 10 mg/kg administrated daily as a peroral water solution within the last ten days of sensitization. Tracheal smooth muscle reactivity and cough reflex were assessed under *in vivo* conditions using double - chamber body plethysmograph. Bronchodilatatory effect of erdosteine was measured after exposure of histamine and cough reflex was provoked by citric acid aerosol. Ciliary beat frequency (CBF) and concentration of the inflammatory cytokines were estimated via *in vitro* methods. CBF was analyzed by inverted phase contrast microscope and recorded by high-speed video camera. The inflammatory cytokines were determined in BALF by using Bio-Plex Pro Rat Cytokine Th1/Th2 Immunoassay Panel.

Results: The findings showed, that erdosteine has comparable bronchodilatation effect with $beta_2$ agonist salmeterol without significant effect on cough reflex. 10-days administration of the erdosteine stimulated CBF, but not more than salmeterol. The observation of inflammatory regulating cytokines resulted in a slight decrease of pro-inflammatory IL-5 and IL-13 and the positive increase of regulatory IL-10.

Conclusion: The study claim, that erdosteine in the settings of allergic inflammation has a bronchodilatory, anti-inflammatory effect and may directly contribute to mucus clearance by CBF stimulation.

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