THE EFFICACY OF COMBINATIONS OF ANTIDEPRESSANTS AND ANTIDEPRESSANT MONOTHERAPY FROM TREATMENT INITIATION IN PATIENTS WITH RESISTANT DEPRESSION. A RETROSPECTIVE ANALYSIS.

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Objective and the aim of study: Despite the availability of new antidepressants, only 50 – 70% of patients respond to the first antidepressant treatment and less than 40% remit. The aim of this study was to compare the efficacy of antidepressant monotherapies and combinations of antidepressants in the treatment of resistant patients in current clinical practice.

Methods: We reviewed chart documents of resistant depressive inpatients treated at least 4 weeks with a new treatment. Depressive symptoms and clinical status were assessed using Montgomery and Åsberg Depression Rating Scale (MADRS), Beck Depression Inventory–Short Form and Clinical Global Impression at the baseline, week 2 and in the end of treatment.

Results: We identified 81 patients (27 with combinations and 51 with monotherapies) that were suitable for analyses. The combination group achieved higher reduction of MADRS score (14.6 vs. 10.2 pts., $p=0.02$) and response rate ($\geq$ 50% reduction of MADRS, 67% vs. 39%, $p=0.03$). Number needed to treat for response was 4.

Conclusion: Based on our results, we suggest that combinations of antidepressants might be more effective than monotherapy in clinical practice.

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RESPONSE OF DENTAL PULP STEM CELLS AND PERIODONTAL LIGAMENT STEM CELLS TO IONIZING RADIATION

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Mesenchymal stem cells isolated from dental pulp (DPSC) and periodontal ligament (PLSC) are cells with high proliferative potential and ability to self-renewal, comparable with other stem cells. The aim of our study was to evaluate changes in DPSC and PLSC caused by ionizing radiation. Both DPSC and PLSC were irradiated with the doses of 2, 6 and 20 Gy and observed in time period of 13 days. In both cell lines the activation of p53 and its phosphorylations on serines 15 and 392 were detected, the expression of p21 protein increased and the cell cycle was arrested in G2 phase. Ionizing radiation depletes hematopoietic SCs of adult organism by induction of apoptosis.

However, we have shown that irradiation of DPSC and PLSC with the doses up to 20 Gy has no significant effect on cell viability and does not induce apoptosis during the whole interval of experiment. Instead apoptosis we have detected hallmarks of stress induced senescence, such as increase in cell cycle regulator protein p16 and increased activity of senescence-associated β-galactosidase.

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REGIONAL CEREBRAL OXIMETRY AS A NON-INVASIVE METHOD FOR CEREBRAL DAMAGE MONITORING

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Objectives: The common aim in the treatment of patients with brain damage is to maintain adequate cerebral oxygenation. It is necessary to follow high risk regions of brain in view of oxygen content. This study summarises the theoretical and practical aspects of non-invasive continual measurement of regional cerebral oxygenation (rSO_2) using near-infrared spectroscopy with the INVOS (In Vivo Optical Spectroscopy) device in neurosurgical ICU.
Methods: The authors present study results during rSO_2 monitoring of four groups (n_1=10, n_2=16, n_3=18, n_4=30) with brain damage of different etiology and also describe their own practical experiences.
Results: In $group_1$ (patients with spontaneous intracerebral hemorrhage-ICH) we determined significant decline of rSO_2 values (by 20 -30 %) due to usual antihypertension therapy. We treated patients with vasospasm after subarachnoid hemorrhage due to aneurysm rupture ($group_2$) and detected an increase in rSO_2 values by 27 % required for clinical signs burn-out. In $group_3$ we compared results of the encumbrance test with rSO_2 and SPECT in patients prior to extra-intracerebral vascular anastomosis. In $group_4$ we did not prove any possible role of rSO_2 in timing of decompression craniectomy in patients with severe intracranial hypertension.
Conclusion: We determined the potential risk of cerebral hypoxia during usual antihypertensive therapy in patients with ICH. We demonstrated the benefits of rSO_2 monitoring during vasospasm therapy and prior to cerebral revascularization surgery. Clinically proven, rSO_2 is a real-time guide to therapeutic interventions before brain damage occurs.

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PHOSPHORYLATION OF HISTONE H2AX AS AN INDICATOR OF RECEIVED DOSE OF GAMMA RADIATION AFTER LOCAL AND WHOLE-BODY IRRADIATION OF RATS

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Objective: The aim of our study was to decide whether phosphorylation of histone H2AX in peripheral blood mononuclear cell (PBMCs) can be used as an indicator of received dose of gamma radiation after local (chest) and whole-body irradiation of rats. Introduction: DNA double-strand breaks (DSBs) are the most deleterious lesions of genome directly or indirectly induced after exposure to ionizing radiation (IR). IR-induced DSBs trigger activation of ATM (ataxia telangiectasia mutated) kinase, which in turn swiftly phosphorylates serine 139 at the carboxy terminus of histone H2AX; the phosphorylated H2AX is denoted γH2AX.
Methods: To study changes in expression of γH2AX in PBMCs irradiated *in vivo* we used phospoho-epitope specific antibody. The intensity of γH2AX immunofluorescence concurrently with cellular DNA content were quantified by flow cytometry. Reference method was immunocytochemistry. Results: The fluorescence of γH2AX in PBMCs 1 hour after the whole-body irradiation increases linearly in dose-dependent manners. The increase of γH2AX fluorescence 1 hour after local irradiation was remarkable in subsets after higher doses of radiation.
Conclusion: Assessment of phosphorylated histone H2AX in rats PBMCs could by used as a rapid screening indicator for radiation biodosimetry following local and whole-body irradiation.

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PENTRAXIN 3 - A NEW MARKER OF SUBCLINICAL CHORIOAMNIONITIS IN WOMEN WITH PRETERM PREMATURE RUPTURE OF MEMBRANES

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Histological chorioamnionitis (HCA), characterized by high-grade polymorfonuclear infiltration in placental tissue and fetal membranes, habitually indicates the presence of intrauterine infection, and thus, represents a clinically important outcome in pregnancies complicated by preterm labor or preterm premature rupture of membranes (PPROM). Unfortunately, the diagnosis of HCA is not known to the obstetricians and the neonatologists until after delivery, and therefore, cannot be used for clinical management.

The first aim of this study was to evaluate amniotic fluid concentration of PTX3 in patients with PPROM; second aim was to evaluate umbilical cord blood PTX3 concentration in neonates from women with PPROM and to determine whether amniotic fluid and umbilical cord PTX3 concentration are of value in the identification of patients with HCA.

Women with HCA had a significantly higher median amniotic fluid PTX3 concentration than patients without histological signs of inflammation [3.69 ng/mL, interquartile range (IQR) 0.73-15.46 versus 0.8 ng/mL, 0.46–3.09; $p = 0.015$]. No significant differences were observed in the median umbilical cord blood PTX3 concentration between PPROM patients with the presence and absence HCA (3.96 ng/mL, IQR 2.24-6.77 versus 2.95 ng/mL, IQR 1.74-6.93; $p = 0.49$)

In conclusion, our results demonstrate that amniotic fluid, but not the umbilical cord blood, PTX3 concentrations were significantly increased in PPROM subjects with the presence of subclinical histological chorioamnionitis.

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EXPRESSION OF CD95 (APO/FAS) AND CD38 (MULTIFUNCTIONAL ECTOENZYME) ON MONOCYTES OF PATIENTS UNDERGOING CABG SURGERY WITH CARDIOPULMONARY BYPASS

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Conventional cardiopulmonary bypass (CPB) comprises a potent stimulus of immune system activation, which might give rise to postoperative complications. In order to decrease the risks associated with surgery, a mini-invasive technique (mini-CPB) often replaces the conventional CPB. Since monocytes are an important part of regulatory mechanisms of immune system, we followed monocyte activation, represented by enhanced expression of CD95 and CD38, and changes in number of monocytes in patients operated with conventional CPB and patients operated with mini-CPB. The two groups of patients differed in duration of surgery ($p<0.01$) and duration of CPB ($p<0.05$), however, there was no difference in number of monocytes between both groups at post-surgery time. Even though the number of monocytes reached the maximum on the 1st postoperative day, the expression of the markers of monocyte activation, CD95 and CD38, was significantly enhanced on the 3rd postoperative day in both groups. Moreover, on the 3rd day after surgery, the CD95 expression was correlated to the CD38 expression in conventional CPB group ($r=0.77$, $p <0.001$), as well as in mini-CPB group ($r=0.5$, $p=0.03$). Nonetheless, we did not find any relation between the enhanced expression of CD95/CD38 on the 3rd postoperative day and the decreased number of monocytes after the 1st postoperative day; thus we assume CD95/CD38 do not participate in the initiation of apoptosis of monocytes in cardiac surgical patients. Additionally, we did not find any significant difference in the CD95/CD38 expressions between both groups of patients in post-surgery period.

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THE EFFECT OF CARDIAC RESYNCHRONIZATION THERAPY ON SYSTOLIC FUNCTION OF RIGHT VENTRICLE

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Aim: To assess effect of cardiac resynchronization therapy **(**CRT) on systolic function of right ventricle (RV) in responders and non-responders in a prospective study.
Group of patients and methods: In 58 patients with heart failure NYHA class II-IV (average QRS duration 193 ± 33 ms) a biventricular system was implanted between 7/2005 and 5/2008. At baseline, 3 and 15 months after the implantation the following parameters were determined: NYHA, quality of life, 6-min walk test (6MWT), echocardiography including assesment of systolic function of RV by TAPSE (tricuspid annular plane systolic excursion) and ventricular dyssynchrony. A responder was defined as patient who improves in quality of life, NYHA class and/or 6MWT more than 10 %.
Results: 15 months after CRT we found 38 responders (66 %) and 19 non-responders (33 %). In the group of responders we found statistically significant improvement of the systolic function of RV and also significant decrease of RV size after 15 months of CRT (TAPSE resp. before CRT 17,8 ± 4,0 mm, 15 months after CRT 19,4 ± 3,7 mm, $p < 0,05$, RV size before CRT 29,3 ± 5,0 mm, 15 months after CRT 27,8 ± 4,2 mm, $p < 0,05$). In the group of nonresponders these changes were not observed, on the contrary, after 15 months we observed significant progression of tricuspid regurgitation.
Conclusion: 15 months after CRT we found a statistical significant improvement of systolic function of RV and a significant reduction of right ventricular size in CRT responders.

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PRE-HOSPITAL COOLING IN CARDIAC ARREST PATIENTS: LESS FLUID STILL WORKS

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Induction of therapeutic mild hypothermia (TH) may reduce post-cardiac arrest brain injury in patients resuscitated from out-of-hospital cardiac arrest. We decided to assess feasibility and safety of pre-hospital TH induction by rapid infusion of cold crystalloids in the setting of emergency medical system in the Czech republic and, having the target dose of 15-20 ml/kg of 4° C cold normal saline, to assess a pre-hospital cooling effectivity.
Methods: We performed a prospective observational study with a retrospective control group. A total of 40 patients were planned to be cooled by an intravenous administration of 15-20 ml/kg of 4°C cold normal saline during transport to the hospital (TH group). Forty control group patients did not underwent any pre-hospital cooling attempt.
Results: In the TH group, administration of 12.6±6.4 ml/kg of 4°C cold normal saline was followed by a pre-hospital decrease of tympanic temperature of 1.4±0.8°C in 42.8±19.6 min ($p<0.001$). The most effective cooling was associated with a transport time duration of 38-60 min and with an infusion of 17 ml/kg of cold saline. There were no differences in other pre-hospital, in-hospital and safety variables between groups. The coupling of pre-hospital cooling with subsequent in-hospital TH predicted a favourable neurological outcome at hospital discharge (OR 4.1, CI95% 1.1-18.2, $p=0.046$).
Conclusions: Pre-hospital induction of TH by the rapid infusion of cold normal saline has been shown efficient and safe even with the lower dose of coolant as was investigated in the previous studies. When coupled with in-hospital continuation of cooling, it can potentially improve the prognosis of the patients. **Trial registration**: ClinicalTrials.gov NCT00915421.

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RESULTS OF A STUDY EVALUATING THE EFFECTIVENESS OF FORTOSS® VITAL IN THE TREATMENT OF PERIODONTITIS AFTER A PERIOD OF 1 AND 2 YEARS

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The study was designed to evaluate the clinical significance of a synthetic composite material, Fortoss® Vital, in the treatment of periodontal intrabony defects. 26 patients with clinical diagnosis of chronic periodontitis were subjected to data analysis. A total of 47 teeth with various osseous defects received regenerative therapy with Vital, and were followed for a minimum of 2 years. Treatment of the intrabony defects with Vital led to a statistically significant improvement in the mean value of probing depth at 1-year when compared with at the baseline ($p<0.01$). Reduction in probing depth was achieved with minimal recession of the gingival margin, and was maintained over the 2-year observation period with no significant change. Mean values of attachment gain at 1 and 2 years were of clinical significance: 1.68±1.12 mm and 1.93±1.36 mm, respectively. In conclusion, treatment of intrabony osseous defects using Fortoss® Vital yielded clinically favorable responses. Further controlled studies are needed to elucidate the clinical significance of surgical treatment using this composite material.

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EFFECTS OF INTRAVENOUS ANESTHETIC AGENTS ON HEPATOSPLANCHNIC MICROCIRCULATION IN RATS

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Effect of intravenous anesthetic agents on macrohemodynamics including blood pressure, cardiac output, heart rate or vascular resistance and venous return has been in details described frequently. Immediate effects of these agents in hepatosplanchnic region at microcirculatory level are subject of intensive research.

The goal of this study was to evaluate the microcirculatory alterations in hepatosplanchnic region in rat after induction dose and during continuous sedative dose of selected iv anesthetics when using Sidestream Dark-field (SDF).

Male Wistar rats (n = 30) were anesthetized intravenously either with propofol (n=6), ketamine (n=6), midazolam (n=6) or thiopental (n=6) after preceding initial maximal dose of intraperitoneal pentobarbital (60mg/kg) to ensure 90 minutes of surgical anesthesia, also in control group (n=6), where only normal saline of corresponding volume instead of additional anesthetic was given. All animals were tracheotomized and mechanically ventilated. Microcirculatory parameters of the intestinal wall (functional capillary density - FCD of the longitudinal and circular muscle layer), of the liver (functional sinusoidal density - FSD and postsinusoidal venular velocity - PSVV) and of the renal cortex (FCD) were assessed by SDF imaging and LDF at the baseline, just after induction dose and after 30 and 60 minutes of sedation using an appropriate anesthetic agent. Macrohemodynamic data were monitored throughout the study.

When compared to baseline, statistically significant increase of both FSD ($p<0.01$, +25%), PSVV ($p<0.05$, +20%) and intestinal FCD ($p<0.05$, +15%) was observed in propofol group after induction dose, the same increase was confirmed when compared to control group. Statistically significant decrease of intestinal longitudinal ($p<0.05$,-18%) and circular FCD ($p<0.05$,-22%) was observed in ketamine group after induction dose. The midazolam group has shown statistically significant decrease in FSD and ileal FCD after induction dose and during sedation, thiopental group has shown no significant changes in microcirculatory parameters throughout the study.

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