SESSION 8
TRACE ELEMENTS IN INTENSIVE CARE

ACIZOL IS A NEW EFFECTIVE REMEDY AGAINST ZINC DEFICIENCY

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A series of long-term investigations was carried out within a multiyear study of pharmacological efficiency of original drug preparation Acizol, designed in Russian Federation, at various pathologies. The mechanism of Acizol action is related to its influence on cooperative interaction of haemoglobin subunits, which leads to a decrease in relative affinity between haemoglobin and carbon monoxide, improves oxygen binding (decrease of Hill's constant) and gas transport capacity of blood. These properties of Acizol provide tolerance to hypoxia in tissues most sensitive to oxygen deficiency. Acizol has wide therapeutic effect and is safe at prolonged (90 days) intramuscular, intragastric or oral daily administration to experimental endothermal animals (rodents and dogs). Acizol application cause no pathological shifts in biochemical parameters, has no negative effect on main physiological systems and internal organs. The tested pharmaceutical forms of the preparation possess no irritative action and do not provoke allergic reactions. The preparation normalizes condition of hepatic parenchyma, causes immunomodulatory effect. At tested dosage schemes, Acizol does not show embryotoxic or teratogenic properties, does not affect reproductive function in experimental animals after 90 days of administration. Clinical tests have shown high antitoxic effectiveness of the preparation. There was observed a two-fold decrease in blood carbon monoxide concentration in carbon monoxide poisoned patients an hour after Acizol introduction. The half-life of carbon monoxide in blood was shortened by 5.3 times comparing to ordinary therapy. This resulted in higher consciousness of sufferers during the first hours of treatment, absence of lethal outcomes in the observed group of patients versus 50% lethality in the control group, and two-fold shortening of hospital stay. Therapeutic use of Acizol promoted normalization of lipid exchange (decreased cholesterol, LDL, VLDL level). Clinical presentation of endotoxicosis at daily use of Acizol was considerably less pronounced, that was probably due to not only antitoxic, but also antioxidant, immunomodulatory and adaptogen effects of the remedy. These features have allowed Acizol to be offered as a prophylactic and therapeutic antidote against carbon monoxide and other combustion gases. The results of our investigations clearly demonstrate the wideness of pharmacological action of Acizol. There are strong reasons to suppose, that its properties are based on participation of zinc ions coupled with the optimal ligand (a compound of azole group) in regulation of redox metabolic processes in cells. It is known, that zinc is included in more than 250 enzymatic systems and thus directly influences their activity. This is why zinc deficiency is connected to development of metabolic disorders with various severe pathologies (ischemic heart disease, hepatitis, diseases of lungs, skin, oncological diseases etc.). We also demonstrated treatment of such disorders by zinc preparations by an example of Acizol. Besides optimizing oxygen utilization, Acizol as a zinc preparation balances redox reactions in cells, acting as a universal regulator of energy exchange. It protects membranes, prevents generation of oxygen reactive species induced by heavy metals coming into the organism from exhaust gases or polluted air. Prophylactic application of Acizol in animals, subjected to 14-day intragastric introduction of lead acetate, completely leveled changes in cardiovascular system, thus demonstrating high prophylactic effectiveness of Acizol against poisoning by heavy metal salts. Such pharmacological features of Acizol allow its becoming a remedy of ecological choice. On a big actual material (more than one thousand persons), efficiency of Acizol for prophylaxis and treatment of alcohol intoxication, dermatosis and for recovery of spermatogenesis, was shown. Allowing for the wideness of therapeutic action and pharmacological properties, Acizol can be surely referred to a new class of medications — universal regulator of cell metabolic processes, or redox potential regulator. Thus, we have all the preconditions to assert that Acizol not only optimizes oxygen utilization in the organism, but also is able to solve one of the most widespread and dangerous problems in the world: the problem of zinc deficiency.

COPPER NANOPARTICLES MODIFY ANTIOXIDANT ENZYME ACTIVITIES IN ACUTE MYOCARDIAL INFARCTION

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Copper is an essential trace element necessary for human being. Oxidation regulating enzymes such as superoxide dismutase (SOD), glutathione peroxidase (GP), cytochrome C oxidase, ceruloplasmine etc. comprise Cu in the core of active centres. Copper deficiency or surplus induces pathologies in organs and tissues, cause myocardial injuries. We have studied a single subcutaneous injection of Cu nanoparticles (CuNP) influence on trace elements status in organs and tissues and antioxidant enzymes activities. We have found physico-chemical parameters of nanoparticles as follows: mean size in diameter 124 nm, oxygen percentage 17.35% and phase ratio was 27% crystallized copper against 73% copper (II) oxide. Our study demonstrated that CuNP administration in biotic doses into animal organism induced changes of copper, zinc and Fe contents in organs and tissues along with prominent influence on the antioxidant enzymes activities. SOD and GP activities in the whole blood, heart and liver tissues varied periodically with a significant maximum three days after injection. We have revealed a positive correlation between Cu-Zn SOD activity and blood copper contents: $SOD = 60.7[Cu] + 1.28$ ($r = 0.65$, $p < 0.05$). Copper deficiency in the organism is known to reduce SOD activity. Lack of accessible copper leads to vascular and myocardial injuries in experimental animals. So the data obtained in our work might be significant for prophylaxis of cardiovascular pathologies and in particular myocardial infarction. Really CuNP injection in experimental animals 3 days before experimental coronaroocclusive myocardial infarction procedure, i.e., acute ischemia at elevated level of antioxidant enzymes, led to an increase of SOD and GP activities both in ischemic and non-infarcted myocardial regions. Animal's survival after coronaroocclusive myocardial infarction in experimental (treated) group was nearly twice higher than in control group without CuNP injection. In rehabilitation period after acute myocardial infarction a great attention is paid to immunological status support and enlargement of infections resistance. Copper is known to manifest antibacterial effects and so increase immunity against some infections. We tested CuNP as antimicrobial agent. A dose-depended suppression of bacterial growth was found as for Gram-negative (*E. coli K-12* and *E. coli AB1157*) so for Gram-positive (*St. albus*) after CuNP addition into growth substrate. Therefore CuNP used as preparation for pathology treatment stimulates trace element metabolism and activity of antioxidative enzymes, enzymes activity being increased in non-infarction zone and nanoparticles manifesting antibacterial effect. Such polyfunctional mode of action of CuNP when administrated into the organism with cardiovascular pathology development gives a reason to propose new ways for therapeutic correction of myocardial injury with the help of preparations including CuNP — copper nanoparticles.

IS SELENIUM DEFICIENCY THE CAUSE OF SUDDEN DEATH IN PATIENTS TREATED WITH PSYCHOTROPIC DRUGS?

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INTRODUCTION: Selenium (Se) deficiency is associated with neurological, rheumatismal, inflammatory, infectious, renal, gastro-intestinal, neoplastic and cardiovascular pathological conditions. Moreover, psychotropic drugs are a well-recognized cause of sudden death in treated patients. OBJECTIVE: Aim of this study was to evidence a possible correlation between Se levels in cardiac tissue, treatment with psychotropic drugs, and sudden death. METHOD: Human patients who had recently died from sudden death were investigated prospectively and compared depending on whether post-mortem analyses revealed the lack of psychotropic drugs (group I) or their presence (group II). Patients from group II were further subdivided based on the type and number of detected psychotropic drugs with POP 1: neuroleptics alone or associated with a benzodiazepine derivative; POP 2: meprobamate alone or associated with a benzodiazepine derivative; POP 3: benzodiazepine derivative alone; and POP 4: inhibitors of serotonin reuptake. Se levels were measured by electrothermal atomic absorption spectrometry in post-mortem heart, brain and liver tissues, which were also submitted to histological examination. RESULTS: Dilated cardiomyopathy (45% of cases), left ventricle hypertrophy (36%) and ischemic coronary disease (18%) were found to be associated with histological lesions including reticulated fibrosis, nuclear misshaping, necrosis and myolysis. A significant decrease in myocardial tissue Se levels as compared to control patients (group I) was only found in patients from POP1 and POP2. No changes in Se levels from brain or liver tissues were found. CONCLUSION: These results demonstrate that Se deficiency may be associated with sudden death in patients treated with psychotropic drugs. Se is primarily involved in the functioning of selenoproteins. This is a key element of glutathion-peroxidase (GPx), an enzyme found in the cytosol, mitochondria and extracellular fluids, which exerts protective antioxidative properties against free radicals. The reduction of GPx activity linked to Se deficiency could result in increased oxidative stress within myocardial cells, in augmented pathogenicity of viruses and thus in cardiomyopathy leading to sudden death.

THE MICROELEMENT STATUS AT A STROKE WITH COMORBIDITY DEPRESSIVE DISORDERS

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BACKGROUND: There is an infringement of all kinds of metabolism at stroke, including mineral. At the same time the role of a mineral homeostasis in the development and outcome of stroke is studied insufficiently. The psycho-emotional disorders are burdening current of a stroke, in particular, depression, whose comorbidity reaches 50% (WHO, 1999). OBJECTIVE: To estimate a condition of a mineral homeostasis at patients with an ischemic stroke during the sharp period with depressive disorders and without those in comparison with .patients chronic ischemia of brain. MATERIAL AND METHODS: Research of the element status of the human scalp hair (the maintenance of 17 elements is conducted: cadmium, cobalt, chrome, aluminium, manganese, molybdenum, nickel, lead, scandium, strontium, chrome, tungsten, zinc, silver, barium) at 40 patients. The first group contains10 patients with an ischemic stroke (5 men and 5 women with middle age of 65.6 ± 4.2 years): the second group — 20 persons (12 women and 8 men, middle age of 68.0 ± 3.1 years) with post-stroke depression (PSD).

In control group were 10 patients with a chronic ischemia of brain I—II of degree (8 women, 2 men, middle age 62.8 ± 4.1 years). The diagnostic estimation of a condition of patients and clinical qualification of pathology of nervous and mental spheres was spent according to ICD-10 (1994). The level severity of depression was specified by means of a hospital scale of anxiety and depression (HADS, 1987), Hamilton Rating Scale (HRS, 1967). Was studied the multielement profile in the hair by atomic-emission spectral analysis (AES). Was applied an atomic-emission complex «Grandee». The obtained data compared to normal values of the maintenance of separate chemical elements in hair (WHO, 1996). RESULTS: Depressive disorders at post-stroke patients are revealed in 66.7% of cases. The moderate depressive episode is prevailed. Are revealed: features of element states at a stroke and PSD: the tendency to decrease the maintenance of manganese, strontium and magnesium, at PSD — deficiency of barium. A tendency to low level of aluminium at cerebral vascular pathology and depressions is observed.

SELENIUM ADD-ON THERAPY RESTORES BRONCHIAL AIRFLOW IN RESISTANT BRONCHIAL OBSTRUCTION

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BACKGROUND: The syndrome of resistant bronchial obstruction (RBO) is found in case of bronchial asthma (BA) and chronic obstructive pulmonary disease (COPD). RBO is characterized by permanent daytime symptoms, decreased quality of life (QoL), increased β2-agonists use (6—8 and more inhalations per day), need in corticosteroids (2—3 courses per year). OBJECTIVE: To work out a method of restoring bronchial airflow in case of RBO. MATERIALS AND METHODS: The study was carried out at P.Stradins Clinical University hospital, Riga, Latvia. 18 patients with RBO syndrome received selenium (Se) *per os* 200 μg per day during 6 months additionally to β2-agonists and corticosteroids. RBO was assessed by spirometry with bronchodilatation test: plus % predicted forced expiratory volume in the first second (FEV1) and reversibility (REV) were processed. QoL was estimated using the Juniper Asthma Quality of Life Questionnaire (AQLQ), which comprises 4 domains (obstruction symptoms, limited activity, emotions, and environment). Clinically detectable improvement was defined as an increase in the total AQLQ points score of ≥ 0.5 from baseline. The examination was repeated after 6 months of Se therapy. The data were processed under SPSS 15.0 for Windows. RESULTS AND CONCLUSION: Irreversible obstruction was revealed in all the patients (average FEV1-REV 5.13%), after 6 months of Se use restored bronchial airflow was revealed (average FEV1-REV 16.50). Total QoL score increased for 1.21: from 3.25 to 4.71 ($p < 0.01$). Activity improved for 0.76, emotions — for 0.98, symptoms — for 0.94, environment — for 0.84. Long-term Selenium add-on therapy (200 μg per day *per os* during 6 months) appears to restore bronchial airflow in case of RBO.