



attending children's institutions with age-related immune system in children, as well as genetic disorders of unspecified adaptation.

Frequently sick children include 10-25% of the total number of preschool children, and 68-75% of all cases of ARI in children account for this particular contingent. At present, the pathomorphology of acute respiratory disease tends to have a more severe, complicated course and the increase in frequently sick children contingent. It is in frequently sick children that ARVI most often acquires a prolonged course with associated bacterial complications. The basis of the hypersensitivity of the child's organism to respiratory viral agents, which leads to the formation of frequent morbidity, is formed by the mechanisms of nonspecific adaptation. One of the key proteolytic systems of the body providing the processes of adaptation and protection is kallikrein-kinin system (KKS). One of the most studied KKS genes providing the most important metabolic processes of the body is the tissue kallikrein gene *KLK1* (Tissuekallikrein, *KLK1*, 19q13.33, OMIM 147910). The world literature presents the results of studies of associations of this gene and its functionally significant allelic variants with a number of pathologies. The correlation of some alleles with nonspecific adaptation disorders, the distribution of frequencies of alleles and genotypes of *KLK1* gene in the Ukrainian population has not been adequately studied.

The objective of this study is to analyze the frequency distribution of alleles and genotypes of *KLK1* gene in healthy children and in children often suffering from long-term acute respiratory diseases.

Materials and methods. 51 children aged 1 to 5 years were examined (boys 22 43.1%, girls 29 56.9%) attending pre-school children's institutions. The group of frequently sick children included 28 children who had respiratory infections 6-8 times a year. The group of healthy ones included 23 children who were afflicted with acute respiratory infections no more than 1-2 times a year and who did not have chronic pathology. Anamnestic, general clinical, virological, microbiological, immunological, clinical genealogical, molecular genetic, statistical methods of research were used.

Results and discussion. There were 49 homozygotes for the R53 allele and one homozygote for the 53H allele found. The rate of allele 53H for frequently sick children was 0.036 ($p_H = 0.036$), for healthy children – 0 ($p_H = 0$). The frequencies of alleles of *KLK1* gene were calculated in the total sample of children – $p_R = 0.98$, $p_H = 0.02$. The results obtained are comparable with the literature data for other European populations ($p > 0.05$). Based on the frequencies of alleles analyzed, a theoretical number of genotypes for a panmixis population was determined. The structure of the sample studied corresponds to Hardy-Weinberg ratio, the real distribution of genotypes is statistically significantly different from the theoretically expected in equilibrium ($df = 2$, $st = 5.99$, $\varphi = 2.70$, $p > 0.05$).

Conclusions. The main results of the work are directly related to the practical activities of pediatricians, aimed at increasing the effectiveness of treatment and prevention of complications of acute respiratory viral infection in early childhood. Since, the implementation of genes in a particular phenotype occurs in a diploid set when two alleles interact, the absence of differences in the frequency of alleles in the groups under study can not serve as a characteristic of the neutrality of polymorphism and requires further study. The information obtained about the frequencies of alleles and genotypes from the gene under study can be used to analyze the structure of the population.

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RENAL EFFECTS OF DALARGINE UNDER CONDITIONS OF BLOCKED SYNTHESIS OF PROSTAGLANDINES

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The intrarenal systems that influence the regulation of the activity of the nephron include, among others, prostanoids - prostaglandins F₂, prostacyclins and thromboxane, which are synthesized, act and metabolized directly in the kidney. Analysis of the literature shows that prostaglandins of the intrarenal system are in close connection with endogenous opioids. Thus, according to some researchers, the peculiarities of the mechanism of action of prostanoids can be attributed to their participation in the formation of cellular response to opioids, and enkephalins exhibit the ability to stimulate the biosynthesis of prostanoids.

The aim of the research was to clarify the involvement of prostaglandins in the implementation of renal effects of the synthetic analogue of the opioid peptide leucine-enkephalin Dalargine. Experiments were conducted against the backdrop of blockade of their synthesis, which was achieved by the use of Indomethacin. The analysis of the results of the conducted studies showed that after applying of Indomethacin, that is, under conditions of suppression of the synthesis of prostaglandins, there was a probable decrease in diuresis in 1,7 times and natriuresis - in 1,5 times as compared to the control group of animals. The results of our research correspond to the data of the literature, which testify to sodium retaining and antidiuretic effect of Indomethacin used in the chosen dose.

Separate-repeated use of the synthetic analogue of leu-enkephalin Dalargine in this series of experiments caused a significant increase in urinary excretion - diuresis was higher than in the control group by 1,2 times. There is also an increase in the excretion of sodium ions - 1.5 times as compared to the control group of animals, and probable increase in potassium - 2,7 times.

After combined use of Dalargine and Indomethacin, we observed that diuretic action of the synthetic opioid was maintained despite the antidiuretic effect of the antiprostaglandin preparation. Thus, diuresis under the influence of this combination of preparations was significantly higher in 2.4 times as compared to the similar indicator in the group of animals administered to Indomethacin. Urinary excretion with the combined application of Dalargine and



Indomethacin was close to diuresis values under the influence of a synthetic opioid and exceeded diuresis in the control group of animals (1.4 times). Consequently, the diuretic effect of Dalargin was maintained against the suppression of the synthesis of prostaglandins in the body.

Similar situation was also observed in the study of the removal of sodium ions by the kidneys. In case of application of Dalargin we observed a probable enhancement of sodium thrush, in case using Indomethacin opposite changes occurred, then with co-application of these preparations the effect inherent in a synthetic opioid prevailed.

Excretion of sodium ions in animals receiving Dalargin and Indomethacin exceeded this index as compared to Indomethacin 5.5 times. Natriuresis was also higher than with a separate application of Dalargin in 2.4 times and exceeded the control group's rates by 3.1 times. Thus, with the combined application of these preparations, the natriuretic effect inherent in Dalargin is retained.

Regarding the effect of Dalargin on the excretion of potassium ions, we observed that against the ground of the prostaglandin synthesis blockade, there was a gain in the calcium in each animal group as compared to that of the control. When comparing each other, these indicators did not differ significantly. Thus, with the use of Dalargin against the ground of the blockade of the synthesis of prostaglandins in the body of rats, inherent Dalargin diuretic and natriuretic activity is maintained. The blockade of the synthesis of prostaglandins does not prevent the implementation of the renal effects of a synthetic opioid.

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CEREBRAL LIPID PEROXIDATION PROCESSES AND ANTIOXIDANT DEFENCE IN DYNAMIC ASPECT IN RATS WITH STREPTOZOTOCIN-INDUCED DIABETES COMPLICATED BY ISCHEMIC-REPERFUSION LESION OF THE BRAIN

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According to present views concerning initiation of diabetes mellitus (DM) and its complications oxidative stress possesses a trigger role, which is characterized by exhaustion of the cellular system of the antioxidant defence and increased production of free radicals. Meanwhile numerous attempts to apply antioxidant therapy in case of DM still remain less effective (so called “antioxidant paradox”), which is indicative of the necessity to carry out further studies concerning the nature of oxidative stress against this disease with the purpose to improve pathogenetically substantiated means of struggle against formation of complication with underlying diabetes.

Imbalance of pro-oxidative – antioxidant interrelations plays a valuable role in the development of “ischemic” pathobiochemical cascade in case of acute disorders of the cerebral circulation. DM is known to increase the occurrence of ischemic lesions of the brain and aggravate their course, although pathogenesis of this combined pathology requires a comprehensive study.

The objective of the study was to investigate condition of lipid peroxide oxidation and activity of antioxidant enzymes in the neocortex and fields of the hippocampus of male rats with induced diabetes mellitus in the dynamics of incomplete global ischemia-reperfusion of the brain.

The study was conducted on males of albino nonlinear rats divided into six groups: 1. Control; 2. Rats isolated from the experiment after 20-minute bilateral carotid ischemia with one-hour reperfusion; 3. Rats isolated from the experiment on the 12th day after 20-minute bilateral carotid ischemia; 4. Rats with experimental DM; 5. Rats with DM isolated from the experiment after 20-minute bilateral carotid ischemia with one-hour reperfusion; 6. Rats with DM isolated from the experiment on the 12th day after 20-minute bilateral carotid ischemia.

DM was simulated by a single intraperitoneal introduction of streptozotocin (Sigma, «Aldrich», 60 mg/kg) to male rats aged 2 months. The period of diabetes with duration of 4 months was considered from the moment of streptozotocin introduction. To imitate incomplete global ischemia-reperfusion of the brain under intraperitoneal narcosis (calypsol, 75 mg/kg) both general carotid arteries were isolated by means of the anterior middle cervical access – they were clipped during 20 minutes and then clips were removed for reperfusion. The animals were taken out from the experiment by means of decapitation under calypsol narcosis. After fixation of the brain in liquid nitrogen using the atlas of stereotactic coordinates the cortex of the frontal and occipital lobes and the hippocampus fields CA1, CA2 and CA3 was taken for the examination. In the homogenates of these structures the content of diene conjugates (DC), Malonaldehyde (MDA), activity of superoxide dismutase (SOD), catalase, glutathione peroxidase (GPO) was determined. Statistical significance of differences was estimated by Student t-criterion for independent sampling. The findings are presented in the form of arithmetic means and standard deviation.

In early ischemic-reperfusion period in all the examined structures of the brain without DM the signs of oxidative stress are found which is manifested by accumulation of lipid peroxidation products against the ground of a considerable decrease of superoxide dismutase (SOD) activity. In rats with DM during this period of observation in all the brain structures except CA3 field there are signs of depression of lipid peroxidation processes and activity of antioxidant enzymes.

On the 12th day of ischemic-reperfusion period in rats without DM the content of lipid peroxidation secondary products in the examined brain structures increases against the ground of reduced activity of antioxidant enzymes which is indicative of increasing signs of oxidative stress in this period. In rats with DM in this term of observation the signs of hyporeactivity of the lipoperoxidation/ antioxidant defence system remain unchanged.