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PROTECTIVE ROLE OF THE ACTIVATOR OF ATP-SENSITIVE K^+ CHANNELS OF FLOCALINE ON MODELS OF EXPERIMENTAL NEPHROPATHIES

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Potassium (K^+) channels in kidneys have various functions starting from ion balance support and volume regulation to the regulation of renin synthesis and finally angiotensin II generation. The results of renal ATP-sensitive K+ channels (KATP channels) activators studies are ambiguous that gives evidence of the complexity of this research. The reason may be that modern representatives of potassium flow activators are not selective regarding renal KATP channels and have adverse effects. Unlike the reference drugs (the other potassium flow activators) the new KATP channels activators including Flocalin contain the fluorine atom in their molecule that determines higher selectivity and significantly lower toxicity.

The aim of our study was to study the effect of Flocalin KATP channels activator on the dynamics of proteinuria in rats with different models of experimental nephropathy.

The experiments were made on 84 laboratory non-linear white rats 0,15-0,17 kg. The model of sublimate nephropathy was made by a single subcutaneous injection of mercuric dichloride. Hypoxic histohemic nephropathy (HHHN) was modeled with the patented method of sequential administration of sodium nitrite and 2,4-dinitrophenol. The rats with experimental nephropathies were divided into two series for the analysis of acute and chronic kidney damage induced by sublimate and of hypoxic origin. In each series the rats from Group I were left without correction and the rats from Group II received intraventricular probe administration of Flocalin in the dose 5 mg/kg during 7 days. To the rats with acute nephropathy we administered Flocalin from the first day of pathology modeling, whereas the rats with chronic nephropathy received Flocalin from the 30^{th} day after nephrotoxins administration. After the last dose of Flocalin all the rats went through water load in the amount of 5 % of body weight and were placed into exchange cages for two hours for urine collection. Euthanasia of rats was done under light ether anesthesia. For glomerular filtration rate (GFR) assessment we measured creatinine level in the urine by the method of Folin. Plasma creatinine was assessed by the method of Popper in Merson modification. Protein concentration in the urine was determined by sulfosalicylic method. For the possible interrelation between the dynamics of proteinuria and biochemical state of the nephrocytes at all stages of experiment after the course administration of Flocalin we studied particular indexes of energy metabolism – alkaline phosphatase (AP) in renal cortex and succinate dehydrogenase (SDH) in renal cortex and medulla. Statistical processing was performed with «Statgrafics». The significance of differences of the results was assessed with parametric Student's t-test.

Flocalin use causes a decrease in standardized by glomerular filtration rate proteinuria: by 4,5 times and 1,2 times in rats with both acute and chronic sublimate nephropathy; and by 1,6 and 2,1 times, simultaneously, under the conditions of hypoxic injury of nephrocytes. Antiproteinuric effect of Flocalin during both acute and chronic periods of nephropathy was accompanied by an increase in enzymatic activity of alkaline phosphatase (by 18,1 % and 49,9 % – in rats with sublimate nephropathy; by 18,1 % and 4,0 % – in rats with HHHN) and succinate dehydrogenase (by 36,3 % and 56,7% in rats with sublimate nephropathy; reaches control level in rats with acute HHHN and increases by 71,2 % in rats with chronic HHHN) in kidney cortex.

Thus, Flocalin induced KATP channels activation has led to the decrease of proteinuria in the rats with acute and chronic kidney damage caused by the nephrotoxic effect of sublimate and combined histohemic hypoxia. The elevation of protein excretion standardized by GFR has pointed at the predominant tubular origin of proteinuria due to primary damage of the proximal part of nephron regardless of the etiology of nephropathy. The use of Flocalin was followed by the increase of AP and SDH activity in renal cortex of rats in acute period of sublimate nephropathy and HHHN, as well as in chronization of these pathological processes. Combination of the antiproteinuric effect and the improvement of energy supply of the functional state of the nephrocytes in renal cortex

points at the nephroprotective effect of KATP channels activation with Flocalin predominantly in the proximal part of the nephron.

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CHRONORHYTHMOLOGIC FEATURES OF LIPIN ON ANTIOXIDANT PROTECTION INDICATORS IN RATS WITH MODEL PATHOLOGIES

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Any biological system of the organism is subjected to the natural functioning organization. Renal function has a conspicuous circadian periodicity. Thus, circadian rhythms of biochemical parameters in organs and tissues are indicators of the body state, including kidneys. Many pathological processes are accompanied by a violation of the temporal organization of physiological functions, which is also characteristic of the pathogenesis of the acute renal failure development.

The aim of the given study was to establish chronorhythmic indicator changes of antioxidant protection of renal tissues under the conditions of model pathology with a single injection of lipin.

The experiments were conducted on 21 adult outbred white rats, weighing 120-160 g. Acute renal failure was caused by intramuscular administration of 50% glycerol solution at a dose of 10 mg/kg. Lipin was administered at a dose of 500 mg/kg once intraperitoneally in 40 min after administration of glycerol. To perform biochemical studies, kidney tissue was collected after decapitation of rats for the 12th hour of the experiment with a 6-hour interval: 4 times a day - at 8 am, 2 pm, 8 pm and 2 am.

Antioxidant effects were evaluated by the content of lipid peroxidation products (malondialdehyde (MDA)) and proteins (protein oxidation products (POP)).

The obtained data on MDA content in the animal kidney tissues with model pathology reached a minimum value at 8 pm and a maximum one at 2 am, which was 1.6 times higher than control group and remained high at 8 am. Lipin reduced the MDA content on the background of acute renal failure by 1.3 times during the period of its maximum value by 2 hours, and at 8 am the effect of the drug reduced the MDA content by 1.2 times. The POP content reached its peak in the affected animals at 8 pm (1.3 times) compared with the control group. Lipin with a single injection had the greatest effect (in 1.4 times) on the intensity of the POP formation at 8 pm.

Thus, in animals with model pathology there were changes in the structure and nature of circadian rhythms that characterized antioxidant protection. The correction of model pathology by lipin should be noted to enhance since 8 pm till the end of the experiment.

Therefore, the treatment of acute renal failure should be prescribed taking into account the rhythm of antioxidant protection processes and the use of antioxidant drugs is recommended mainly in the afternoon.

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HISTOLOGICAL CHANGES IN THE KIDNEY STRUCTURE IN THE DYNAMICS OF FEVER DEVELOPMENT

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Fever is a typical pathological process characterized by a shift of the thermoregulatory reference point to a higher level of body temperature regulation due to the influence of pyrogenic substances. Fever development includes three stages: rising of temperature, maintenance of high temperature and decrease in body temperature.

The aim of our experiment was to study the histological changes the kidney structure in the dynamics of fever development and detect the mechanisms of damage to nephrocytes of the kidney cortex, medulla and papilla in conditions of the fever development.

Research was conducted on 60 non-linear white male rate weighting 130-180 g, maintained under the standard vivarium conditions with a constant temperature and humidity. Aseptic fever was induced according to recommendations by a single subcutaneous injection of pyrogenal at a