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«ФУНДАМЕНТАЛЬНІ ТА КЛІНІЧНІ АСПЕКТИ ФАРМАКОЛОГІЇ»

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KLOTHO PROTEIN SYNTESIS INDUCTORS CARDIO PROTECTIVE EFFECT IN EXPERIMENTAL ACUTE MYOCARDIAL INFARCTION

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Recent decades have been marked with a global steady growing trend towards an increase in the incidence of vascular diseases linked to the general population aging, and the increasing incidence rate of diabetes mellitus, arterial hypertension and atherosclerosis. Currently, blood flow medications are widely used in the treatment of hypoxic cardio-vascular disorders, along with medications affecting cell metabolism, specifically, individual units of the adaptive molecular biochemical reactions. Concerning the efficacy of the last mentioned medications, a sufficient amount of experimental and clinical data has been cumulated lately. However, in terms of proof based medicine, the effect of those drugs is controversial and questionable. Therefore, there is an active search for metabolic medications. In this respect, the purpose of our study was to assess the spectrum of Klotho protein inducers expression and synthesis (D-vitamin, Necrostatin-1) cytoprotective action in the experimental model of AMI.

The experimental part was carried out on 40 sexually mature male rats weighing 190-230 g. The AMI was modeled by pituitrin (1 unit/kg subcutaneously) and isoprenaline adrenergic agonist (200 mg/kg intramuscularly) injection within 4 days. The study drugs were injected for 4 days in this way: Vitamin D (5000 IU/day) (GmbH Arzneimittel, Germany) intragastrically and Necrostatin-1 (Nec-25 January mg, Sigma-Aldrich) 1 mg/kg intraperitoneally 20 minutes after the isadrin injection. The incidence of acute myocardial infarction was confirmed by determining it in the blood plasma by the Chemiluminescence Immuno method, Immulate 1000 – troponin (Siemens), by the biochemical method – the total CPK activity (Cormay) and by the enzyme immunoassay – ST2 "The Pressage ST2 Assay" (Critical Diagnostics, cat. No. BC-1065E). The Klotho protein, HSP70 proteins, 8-OHdG, ST2 were detected with the use of the ImmunoChem-2100 enzyme-linked immunosorbent complex (USA).

Results and discussion. Acute myocardial infarction was modeled in experimental animals against the background of an increase in the markers of heart muscle troponin damage, and the activity of total CPK. It is important to note that the experimental markers tended to increase in animals of all experimental groups in comparison with the intact. The ST2 value did not reach the level of 35 ng/ml, given the vitamin D and Necrostatin-1 administration. In addition, vitamin D and Necrostatin-1 experimental therapy resulted in a statistically significant increase of Klotho protein amount in the heart homogenate (by 76.3% and 78.8%, respectively in relation to the test). The administration of Klotho protein synthesis inducers led to the oxidative stress limitation, nucleic acid damage, and was reflected in a significant decrease in the concentration of 8-OHdG in relation to the test, both with the vitamin D administration (by 38.5%) and Necrostatin-1 (by 55.8%) administration. The experimental data we have obtained confirm the viability of further research in this direction. The study of vitamin D and Necrostatin-1 ability to affect the processes of cell death and its type (necrosis / apoptosis) are of special interest in this respect.