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INFLUENCE OF THE SELECTIVE ESROGEN RECEPTOR MODULATORS ON THE EXPRESSION AND SYNTHESIS OF HSP 70 PROTEINS IN CARDIOMYOCYTES OF RATS WITH EXPERIMENTAL ACUTE MYOCARD INFARCTION

S.V.Pavlov, K.V.Levchenko, Y.V. Nikitchenko, O.M.Kamyshniy, D.Robota
State medical University, Zaporozhye, Ukraine.

A considerable number of experimental and clinical studies devoted to the study of the metabolic therapy in the acute period of myocardial infarction have been conducted in recent years. However, the molecular and biochemical processes of ischemic metabolic adaptation still remain underexplored. Currently, cytoprotectors are being searched actively among compounds and factors that can induce the HSP70 synthesis. However, most of these compounds/factors have a rather weak pharmacological activity; some significantly increase the content of these proteins, causing the development of adverse reactions. In this aspect, what deserves special attention is estrogen which potentiates theHSP70 proteins entry into the cell based on the mechanism of their biological effect[1-3].

Materials and Methods. The experimental part of the work was performed on 120 sexually mature male rats 190-230 gr of weight. Small-focal acute myocardial infarction was modeled by the 3 days introduction of coronary spasm agent -pituitrin (1 unit/kg subcutaneously) and $\beta_{1,2,3}$adrenomimeticisoprenaline (200 mg/kg intramuscularly). Tamoxifen citrate (0.1 mg/kg) (#EF3300) and toremifene (0.1 mg/kg) (#1705834) were selected as SERMs. Capicor metabolite tropic agent (6 mg / kg) (No. 11114) was selected as a reference drug. To analyze the expression of HSP 70 genes, a reverse transcriptase polymerase chain reaction method

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was used in real time mode. The intensity of the biosynthesis of HSP 70 proteins in cardiomyocytes was investigated by the use of the immunoassay method. The cardioprotective effects of the investigational drugs were evaluated by their ability to influence the energy metabolism and the oxidative stress.

Results.In assessing the state of the cardiomyocytes antioxidant system in rats with acute myocardial infarction, we have found a significant increase in the content of nitrotyrosin, more than 89% in relation to the intact group of animals. The identified pathobiochemical changes took place against the background of the cardiomyocytes energy deficit, as evidenced by a statistically significant drop in EH; EP; TKD respectively 45%; 62% and 80%. It is important to note that when investigating the nature of the expression/synthesis of HSP70 proteins in cardiomyocytes, we have fixed a multi-directional pattern of expression and synthesis of this protein. Thus, on the 4th day of myocardial infarction, a significant increasein the expression of mRNA HSP70, by more than 90%, was recorded in the control group of rats. However, when analyzing the concentration of HSP 70 protein in cardiomyocytes, we have recorded a decrease in its content by more than 74%.

Along with this, administering of tamoxifen (0.1 mg/kg); Toremiphene (0.1 mg/kg) andCapicor (6 mg/kg) to animals with acute myocardial infarction led to a modulating effect on the nature of the expression and synthesis of HSP 70 protein. The data analysisof themRNA HSP70 expressive activity has demonstrated that the SERM andthe Capicor reference druga reable to modulate the expression of HSP 70 under hypoxia. In addition, a course administering of SERM led to limitation of the oxidative stress amplification and improving energy exchange in cardiomyocytes. The established spec-

trum of pharmacological effects of SERM determines the viability and relevance of further researches in this direction.

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