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HEAT SHOCK PROTEIN HSP60 IN CARDIOMYOCYTES OF THE LEFT VENTRICLE OF THE HEART OF RATS WITH ARTERIAL HYPERTENSION

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Abstract: In cardiomyocytes, ATP-dependent high-molecular HSP70 and HSP90 play an important role in protecting the myocardium from damaged proteins, which appear, in particular, as a result of increased oxidative stress. The molecular chaperone HSP60 is of particular importance for cardiomyocytes, since it is responsible for the assembly of mitochondrial matrix proteins. The features of HSP60 expression in left ventricular cardiomyocytes were studied in arterial hypertension, insulin-dependent diabetes mellitus, and their combination. The experiment was performed on 38-week-old male Wistar-Kyoto rats and 38- and 57-week-old SHR rats.

Keywords: heat shock proteins, HSP60, myocardium, arterial hypertension, diabetes mellitus.

INTRODUCTION

Heat shock proteins are actively studied due to their ability to exhibit cytoprotective properties against the background of various types of cellular stress. They participate in many intracellular processes, such as protein folding, assembly of multimolecular complexes, and maintenance of the correct form of enzymes. Their production increases in response to the influence of a wide range of stress factors, including oxidative and thermal stress, ischemia, and functional overload [1].

MATERIALS AND METHODS

Protective properties of heat shock proteins in muscle cells, including cardiomyocytes, play a special role in maintaining their functional state. Contractile activity of the myocardium requires constant monitoring of the quality of the sarcomere protein composition, including their synthesis, maintenance of the correct structure, refolding, utilization in proteosomes or processing to molecular peptides. The pathogenesis of myocardial damage of various origins at the cellular and subcellular levels is mediated by disturbances in the composition and functional properties of cardiomyocyte proteins. In particular, there is an increase in oxidative stress, post-translational modifications, a decrease in protein stability, contributing to their improper coagulation. These damaged proteins exhibit toxic properties in relation to cardiomyocytes, which, in particular, occurs during the development of heart failure.

RESULTS AND DISCUSSION

A number of studies have shown that heat shock proteins act as intracellular chaperones, protecting the genetic material of the cell, preventing the initiation of apoptosis via the mitochondrial pathway, as well as necrotic cell death [2]. A special term, the “stress surveillance system” (SOS), was introduced for the mechanism of perception of the extracellular pool of heat shock proteins, which is presumably a form of cellular

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communication under stressful conditions [3]. However, the mechanisms of release of heat shock proteins with different molecular weights under pathological conditions, activating alternative communication pathways, have been poorly studied. Induction of heat shock protein synthesis caused by metabolic disorders activates antioxidant intracellular processes, reducing cellular acidosis, and also inhibits the generation of inflammatory mediators [4]. At the same time, it was found that the body's response to heat stress is weakened in patients with type 2 diabetes mellitus. In particular, HSP70 expression is reduced in patients with diabetes mellitus [2]. In all experimental groups, the HSP60 content in the cytoplasm of LV cardiomyocytes significantly decreased compared to the control. With a longer course of hypertension (SHR rats aged 57 weeks) and with a combination of hypertension and diabetes mellitus, the decrease in HSP60 expression was less pronounced than with hypertension at a shorter term (SHR rats aged 38 weeks) and with isolated diabetes mellitus. The following picture was observed in a qualitative analysis of LV myocardial sections after an immunohistochemical reaction for HSP60. In the control group, positive staining of the cytoplasm of a significant number of cardiomyocytes was noted. High staining density was determined mainly in the thickness of the myocardium, and in the direction of the epicardium and endocardium, as well as in the areas of the myocardium surrounding the blood vessels, a slight decrease in the number of cells with a positive reaction to HSP60 with a tendency to a decrease in the staining intensity was noted. In cardiomyocytes visualized in longitudinal section, positive staining of the cytoplasm was observed over a significant area.

In the group of rats with AG at the age of 38 weeks, the numerical density of positively stained cardiomyocytes significantly decreased compared to the control group. A mosaic type of distribution of staining of individual cells was characteristic. A relatively higher staining density was observed in the middle layer of the myocardium. Towards the epicardium and endocardium, the number of cardiomyocytes with positive staining significantly decreased. Only local areas with positively stained cytoplasm of cardiomyocytes of low intensity were detected around the vessels. In the group of rats with AG at the age of 57 weeks, the numerical density of cardiomyocytes with a positive reaction to HSP60 also decreased compared to the control group. Staining was mainly observed in the cytoplasm of individual cardiomyocytes, however, in contrast to 38-week-old rats with AG, cardiomyocytes with a positive immunohistochemical reaction were more common in the myocardium. Positively stained cardiomyocytes were mainly detected in the middle layer of the myocardium, as well as in the layer adjacent to the endocardium.

CONCLUSION

Heat shock protein HSP60 is of particular importance for cells with contractile activity: it is responsible for the assembly of mitochondrial matrix proteins. A decrease in HSP60 production can lead to a deterioration in the functional state of mitochondria. In particular, it has been established that HSP60 deficiency in cells is accompanied by increased ROS production and, as a consequence, the development of mitochondrial dysfunction [1]. According to data, maintaining HSP60 at a physiological level in skeletal muscle cells prevents increased oxidative stress caused by SOD inhibition in insulin-dependent diabetes. Thus, a decrease in HSP60 production can be considered as one of the mechanisms of pathogenesis of LV myocardial alteration caused by arterial hypertension and/or diabetes mellitus.

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