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Abstract

Positive Pharmacological Modulation of Hsp70 In Recovery of Brain Energy Metabolism in Various Models of Cerebral Ischemia

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Abstract: The aim of this research was to analyze the neuroprotective action of drugs with an evidence-based effect on the expression of endogenous neuroprotection factors in various experimental models of cerebral ischemia on Wistar white rats (intracerebral hemorrhage, carotid artery occlusion, prenatal hypoxia) to further substantiate their use in the treatment of CNS damage. The experimental studies were carried out in accordance with the "Regulations on the Use of Animals in Biomedical Research" and with the European Convention on the Protection of Animals Used for Scientific and Other Purposes. The experiment was approved by the Bioethics Committee of Zaporizhzhia State Medical University. In studies it was found that pharmacotherapy of emerging mitochondrial disorders with modulators of HSP70 expression - Cerebrocurin (composition: neuropeptides, S-100 proteins, reelin, factor nerve growth (NGF)), Glutoredoxin, Tamoxifen, (S)-2,6-diaminohexanoic acid, 3-methyl-1,2,4-triazolyl-5-thioacetate significantly ($p<0.05$) stimulates energy production brain. This is expressed in an increase in the content of a number of intermediates of energy metabolism (glucose, pyruvate, succinate, isocitrate, malate) in the brain tissue, as well as an increase in the activity of pentose phosphate shunt dehydrogenase. A significant ($p<0.05$) decrease in the level of lactic acid in the brain indicates a decrease in the proportion of anaerobic glycolysis. The most pronounced energotropic effect was shown by cerebrocurin (150 μl/kg) and (S)-2,6-diaminohexanoic acid 3-methyl-1,2,4-triazolyl-5-thioacetate (50 mg/kg). On the 21st day of treatment of rats with cerebral ischemia, there is a gradual disappearance of severity between animals with simulated pathology and healthy rats, which is associated with actively recovering mitochondrial energy production and cerebral load in general. These changes in energy metabolism correlate with the normalization of oxidant-antioxidant balance and the concentration of HSP70 and HSF-1a in the cytosol and mitochondria of the cerebral ischemia zone and are manifested in a significant ($p<0.05$) decrease in ultrastructural disorders of mitochondria. The energy-tropic and mitoprotective effects of the studied drugs are associated with their ability to protect mitochondrial proteins from oxidative damage by increasing the concentration of HSP70, prolong the lifespan of HSF-1a, and activate alternative energy generation pathways.

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