MITOCHONDRIAL DYSFUNCTION IN LIVER OF RATS WITH HYPOXIA INDUCED BY COMBINED THERMAL INJURY

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Damages associated with disorder of work of mitochondria form the basis of specific clinical manifestations of diseases. Burns are one of the most important problems of modern medicine. Pathological changes developing in the liver in burn disease lead to the hypoxia and the disruption of many organism functions. A comprehensive study of the processes occurring in the conditions of oxygen lack is vital in the burn disease [1]. Disorders of free radical homeostasis are the most important pathological changes induced in organs and tissues in hypoxia, which lead to oxidative stress [2]. Energy and oxidative metabolism of hepatocytes in normal and thermal injury are determined by the state of the respiratory chain of mitochondria, which depends on the functioning of the liver [3]. The aim of this work was to study the biochemical parameters of liver mitochondria in combined thermal damage.

Materials and Methods. The experiment was carried out on male rats of Wistar line weighing among 200 – 250 g. All animals were kept in standard vivarium conditions in cages with free access to food and water. After the quarantine (14 days) two groups of animals were formed: control group 1 (n=10) of intact healthy animals; experimental group 2 (n=10) of animals with combined thermal injury (CTI; 20% contact burns and thermal inhalation impact of hot air and combustion products). Animals were taken out of the experiment on days 1, 7, and 14 post-injury by decapitation under anesthesia (Zoletil 100 + Xyla VET). Mitochondria were obtained by differential centrifugation. For the mitochondria identification, an electron microscopic study was conducted. In the liver mitochondria, the intensity of free radical oxidation (FRO), the activity of catalase, superoxide dismutase (SOD), succinate dehydrogenase (SDH) and cytochrome c oxidase were evaluated. The research results were processed using Statistica 6.0 (StatSoft Inc., USA).

Results. In the first phase of the study, the polymorphism of mitochondrial fractions: small and large mitochondria with intact membranes were present in the examined samples. A part of the mitochondria had a dense matrix and clear-cut cristae. In addition to mitochondria with preserved structure, swollen mitochondria with violation of intra-mitochondrial architectonics were found. In some mitochondria a change of the electron density of the mitochondrial matrix, its focal lysis, clarification as well as shortening, fragmentation, and reduction of cristae were observed.

Mitochondria are the indicators of the functional state of cells involved in metabolism via the Krebs cycle and transport of electrons in the respiratory chain [3]. An increase of intensity of FRO in the liver mitochondria on days 7 and 14 post-injury was registered. Meanwhile, total

antioxidant activity of blood plasma and catalase activity in erythrocytes in case of thermal injury were decreasing on all test days after the burn, as compared to the control group.

Towards days 7 and 14, SOD activity significantly decreased in comparison with the healthy animals. The study of SDH and cytochrome c oxidase showed a decrease in specific activity of enzymes in the liver mitochondria on days 1, 7, and 14 after CTI. The most pronounced decrease in the activity of SDH and cytochrome c oxidase was observed on day 14 after the burn. The decrease in the activity of SDH in the conditions of O_2 deficiency, developing in the cells in CTI, is due to the activation of fumarate reductase reaction. Fumarate reductase reaction is the reverse of the reaction catalyzed by SDH in the composition of the complex II system of tissue respiration. In this process, free oxygen radicals that can directly inactivate SDH are quickly formed [4].

Thus, the obtained results confirm information about the presence of oxidative stress manifested in the enhancement of FRO and the decrease of general and enzymatic activity of antioxidant defense system in CTI. This leads to the development of systemic disorders during the burn. Reasons for the imbalance in the system of prooxidants – antioxidants may be the impairment of lipid and protein profile of mitochondria in CTI. On the other hand, the activation of the FRO in the mitochondria during the burn can be one of the causes of damage of the liver tissue. The decrease in activity of SDH and cytochrome c oxidase at CTI indicates a reduction of aerobic metabolism, enhancement of anaerobic oxidation in the cell and decrease of energy supply of the cells. These changes appear from the disruption of electron transport in the mitochondrial membrane and deficiency of ATP production.

Conclusion. A presence of oxidative stress during CTI was revealed, as well as a comprehensive mechanism of its formation, implicating both activation of FRO and decrease in antioxidative capacity imbalance. Inhibition of energy supply of cells, reduction in the cell aerobic and increased anaerobic oxidation were revealed.

References

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