SUBSTANTIATION OF MULTI-COURSE ENTEROSORPTION AIMED AT MINIMIZING THE NEGATIVE EFFECT OF CHRONIC INTOXICATION IN THE EXPERIMENT

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ABSTRACT

The markers for assessing the dynamics of chronic hepatotoxicity, which has a 3-stage character, as well as the effectiveness of a single course and multi-course enterosorption (ES) have been substantiated using the chronic toxic liver damage (CTLD) model induced by carbon tetrachloride (CCL_4). The terms when the CTLD model was made were 26 days (stage 1), 10-20 weeks (stage 2), and 36 weeks (stage 3) since the CCL_4 intoxication. Serum aminotransferase activity (ALT, AST), bromsulfalein test values, hexenal-induced sleep duration, medium-weight molecules (MWM) content, serum toxicity level, malondialdehyde (MDA) content in the liver tissue, mitochondria and lysosomes of hepatocytes quantification by electron microscopy were studied. A single and multi-courses of ES (vaulen intragastrically) have been used as a correction method: a single course was carried out within 7 days at terms of 26 days, 10 weeks, 20 weeks, and 36 weeks from the initiation of the experiment. Multi-courses were carried out every month for 7 days. Ultrastructural changes in mitochondria and lysosomes of hepatocytes were studied on 25-30 electron micrographs (EM) taken from 3 animals of each series. Total number, number of primary and secondary lysosomes, mean number of mitochondria on one EM, mean total mitochondrial surface area on EM, mean relative surface area of one mitochondrion, ratio of inner mitochondrial membrane surface area to the outer one multiplied by the mean number of mitochondria on an EM (Sim/SomMit) were counted. Statistical analysis of the results was performed by the Student's t-test, Fisher's exact test and Mann-Whitney-Wilcoxon test.

At the CTLD stage 1, damage processes prevailed. Toxemia, ALT and ALT/AST activity, and lipid peroxidation increased, the absorption-excretion liver function impaired. Marked degenerative mitochondrial changes were seen. Mean surface area of one mitochondrion, mean number of mitochondria on one EM, their mean total area, and the coefficient Sim/SomMit decreased. The total number of lysosomes decreased due to the primary forms. At the CTLD stage 2, compensation reactions predominated. Toxemia, blood toxicity, degree of cytolysis in the liver, lipid peroxidation activity decreased, the absorption-excretion liver function improved. The mitochondrial structure deteriorated. The mean area of one mitochondrion as well as the mean number of mitochondria on one EM increased, the number of young forms decreased, the coefficient Sim/SomMit did not change. The total number of lysosomes increased due to the secondary forms. At the CTLD stage 3, the pathological reactions prevailed over compensation-adaptation. The toxemia increased again, the functional liver state and the ability to bioconversion of xenobiotics deteriorated.

There was noted an altered structure of hepatocytes due to the growth of collagen fibers and the formation of cirrhosis. Mean number of mitochondria on one EM, mean total mitochondrial area on one EM, mean area of one mitochondrion, Sim/SomMit significantly decreased as compared to controls. The number of primary lysosomes sharply decreased, secondary and heterophagolysosomes predominated. A course of ES at the CTLD stage 1 and 2 was accompanied by a significant improvement (especially at stage 1) in all the studied parameters as compared to animals that did not receive the sorbent. At the CTLD stage 3, a single course ES showed a weak positive effect. Multi-course ES in the CTLD improved the functional liver state more significantly and reduced the toxemia and cytolysis. At the subcellular and intraorganoid level, the mitochondrial bioenergetic ability grew, the processes of synthesis intensified, the number of primary lysosomes increased. Decreased endotoxemia and toxic load on the liver can be considered as a mechanism of the ES hepatoprotective effect.

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