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DISTURBANCES IN THE ENZYMATIC SYSTEMS IN LIVER PATHOLOGY

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Abstract: Changes in the activity of hepatic cell (hepatocyte) enzyme systems are at a stage of development or not fully studied. Among the recent findings is the fact that possible qualitative changes in the catalytic activity of enzymes occur when exposed to hepatotropic toxins.
Key words: membrane, enzyme, mitochondria, monoamine oxidase, organelle, liver, cell, lipid.

At the present stage of studying the pathogenesis of liver diseases, a significant focus is on the research of pathological processes at the level of subcellular structures, their membrane and enzymatic systems. Many works are being conducted in this direction, which provide detailed information on the mechanism of action of pathogenic agents and clarify the localization of the primary site of cellular damage.

In this regard, special interest lies in the study of the metabolism of biogenic amines and other nitrogenous compounds, in terms of the catalytic properties of mitochondrial monoamine oxidases. On one hand, these enzymes are involved in the metabolism of a number of biologically active nitrogenous compounds, and on the other hand, they are enzymes of organelles, the early damage of which has been established in a number of pathological processes in the liver.

In experiments with highly purified monoamine oxidases, it was found that partial oxidation of the thiol groups of these enzymes not only reduces monoamine oxidase activity but also causes a qualitative change ("transformation") in the catalytic properties of monoamine oxidases, with the appearance of the ability to deaminate nitrogenous compounds.

Data obtained in experiments using selective inhibitors of different types of monoamine oxidases led to the conclusion that the transformation process involves type A monoamine oxidases, which are blocked by low concentrations of chlorline, rather than type B monoamine oxidases, for which deprenyl is a selective inhibitor. It turned out that the property of monoamine oxidase type A to undergo qualitative changes in catalytic activity is also realized in the whole organism under conditions of stimulated radical oxidative processes, particularly in the stimulation of lipid peroxidation.

Apart from isolated works indicating the transformation of the catalytic properties of liver monoamine oxidases in such experimental pathological conditions as radiation damage, tumor growth, oxygen poisoning under high pressure, hypervitaminosis D_2, pulmonary tuberculosis, hypercholesterolemia, and liver damage from ethanol, no other information was found in the available literature on this issue.

To investigate changes in the processes of deamination of biogenic amines and other nitrogenous compounds in the mitochondria of hepatocytes, types of liver tissue damage caused by intoxication with hepatotropic poisons (allyl alcohol, hydrazine sulfate, CCl_4, ethyl alcohol) were also chosen, where the precondition for the possible appearance of qualitative changes in the catalytic activity of monoamine oxidase, as a key enzyme in the monoamine metabolism, was the previously observed stimulation of lipid peroxidation processes in the tissue, as well as the

biochemical and electron microscopic identification of mitochondrial structure and function disturbance in hepatocytes.

A significant role in the disruption of enzyme activity is played by the phenomena of destruction of parenchymal liver cells, as the activity of most enzymes is only manifested when the internal structure of cells is preserved. In particular, it was established that a shift in the pH of the environment from the optimal reduces urea synthesis. The degree of manifestation of the liver's urea-forming dysfunction is closely dependent on the number of amino acids to be broken down in it. In some cases, liver dysfunction is more evident under stress conditions.

It was established that in patients with cirrhosis of the liver, with increasing protein load, hyperammonemia, hyperaminoacidemia, and encephalopathy, the protein level correlated with the maximum rate of urea synthesis. In natural conditions, such a specific protein load can be caused by bleeding from varicose veins of the esophagus and stomach in patients with cirrhosis.

The activity of enzymes catalyzing the process of deamination in the liver during acute and chronic diseases has been studied by a large number of researchers. The obtained data indicate various disturbances in the activity of liver aminotransferases during liver diseases. Alanine aminotransferase activity is significantly suppressed in the presence of necrobiotic changes in the liver.

A reliable decrease in the activity of both aminotransferases in liver tissue obtained surgically was observed, with the ratio of Aspartate Aminotransferase (AsAT): Alanine Aminotransferase (AlAT) being, on average, 1.5 times higher in cirrhosis compared to the control group.

In liver diseases, due to disturbances in the processes of glycolysis and glycogenolysis, there is a decrease in the level of energy metabolism. A significant reduction in oxidative ATP resynthesis and oxygen consumption in the liver was noted in patients with cirrhosis.

When studying the activity of esterases and catalases in the liver of patients with infectious and alcoholic hepatitis, fatty degeneration of the parenchyma in varying degrees with slight fibrosis was observed. Some authors believe that determining the activity of enzymes with different intracellular localization allows not only to identify the primary site of damage but also to determine the stage at which cellular dysfunction becomes irreversible.

The first enzymes affected are those in the mitochondria, followed by the damage of lysosomal hydrolases, and, lastly, the activity of endoplasmic reticulum enzymes is disrupted.

It has been shown that an important sign of necrosis is the increased activity of mitochondrial enzymes (aspartate-alanine aminotransferases, etc.) in the blood serum.

Based on clinical, biochemical, and morphological studies, A.F. Bluger concluded that the central role in the pathology of the liver is the syndrome of hepatocyte cytolysis. Electron microscopy revealed that cytolysis of hepatocytes begins with mitochondrial damage, which precedes other fine morphological manifestations of liver damage.

In the mitochondria of hepatocytes, oxidative phosphorylation processes are primarily impaired, leading to disturbances in the permeability of the membranes of subcellular structures, which are not characteristic of the physiological state.

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