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SOD ACTIVITIES IN THE LIVER, KIDNEY, PZH, AND TC HOMOGENATES OF RATS IN THE DYNAMICS OF EXTRAHEPATIC CHOLESTASIS

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Annotation
The work analyzes the activity of soda in the homogenates of the liver, kidneys, pancreas and TC of rats in the dynamics of experimental extrahepatic cholestasis.

Keywords: cholestasis, experiment, obstructive jaundice, antioxidant system, SOD (Superoxide dismutase).

Relevance
Despite the optimization of surgical treatment of obstructive cholestasis, high mortality is mainly due to the development of acute liver failure due to damage to hepatocytes both by endotoxicosis products and by an increased level of free radicals that cause a state of oxidative stress. One of the powerful inducers of lipid peroxidation is endogenous intoxication (EI). Violation of the function and destruction of liver cells leads to the accumulation in the patient's blood of a wide range of toxic metabolites, blockade of oxidative enzymes.
Therefore, an important measure to prevent the development of acute liver failure in obstructive jaundice is
correction of endogenous intoxication through the use of pathogenetic methods for the treatment of acute liver damage.
Aim To determine the activity of antioxidant defense enzymes (AOD) in homogenates of the liver, kidneys, pancreas and small intestine of experimental animals in the dynamics of extrahepatic cholestasis.
Material and methods
The experiments were carried out on 69 outbred male rats of a mixed population with an initial weight of 180-200 g, kept in a laboratory diet in a vivarium. Extrahepatic cholestasis was reproduced in 37 rats by ligation of the common bile duct. Overall mortality in this group was 32.4%. Sham-operated animals (24 rats) served as

controls, which underwent only laparotomy under aseptic conditions. No mortality was observed in these groups. The intact group consisted of 8 rats. The studies were carried out 1, 3, 7 and 15 days after the reproduction of the models. The choice of the timing of the study is associated with the development of significant morphological and functional changes in the liver in experimental cholestasis (27).

The scheme of experience is presented in table 1.

Determination of superoxide dismutase activity. The intensity of lipid peroxidation, which is one of the dominant mechanisms for the development of damage to parenchymal organs by intestinal toxins, is determined not only by the formation of free radicals, but also by the function of the antioxidant system of cells. One of the most significant links in the AOS system is SOD. Superoxide dismutase undergoes enzymatic dismutation of the superoxide radical anion O2- by the formation of hydrogen peroxide, which is subsequently cleaved by another AOC enzyme, catalase, to H2O and inactive triplet oxygen. The determination of SOD activity in our work was carried out according to the method of V.G. Mkhitaryan and G.E. Badalyan. The principle of the method is based on the ability of SOD to inhibit the reduction reaction of nitrotetrazole blue in an alkaline medium. The calculation of the enzyme activity was carried out using the percentage of reduction of nitrotetrazole blue, which was determined from the ratio:

$$T\% = \frac{(E_к - E_0) * 100\%}{E_к},$$

where

Ek is the extinction index of the control sample,

Eo is the extinction index of the prototype;

T% is the percentage of recovery of nitrotetrazole blue.

SOD activity was calculated by the formula:

$$A = \frac{T\% * n * 0,2}{100 - T\% * m}$$

where

A - enzyme activity in conventional unit's / min. mg of protein,

n - dilution of the bioassay;

0.2 - the volume of the sample taken,

m is the amount of protein in the bioassay.

The data obtained were subjected to statistical processing using the Excel-2000 statistical analysis software package with the calculation of the arithmetic mean (M), standard deviation (σ), standard error (m), relative values (frequency, %), Student's t test (t) with the calculation error probability (P). At the same time, the existing

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guidelines for the statistical processing of data from clinical and laboratory studies were followed.

Table 1 Experiment scheme

Series of experiments	Experiment time, days				Total	Lethality, %
	1	3	7	15		
Intact	2	2	2	2	8	-
Control	6/6	6/6	6/6	6/6	24/24	-
Extrahepatic cholestasis	9/6	9/7	9/6	10/6	37/25	32,4

Note: in the numerator, the initial number of animals in groups; the denominator is the number of animals taken for research, taking into account lethality.

Results of Research

According to the literature data, the processes of free-radical and lipid peroxidation are under the control of the AOD system, which consists of an enzymatic and non-enzymatic link. SOD plays an important role in enzymatic AOD. The study of SOD activity in the homogenates of the liver, kidneys, pancreas and TC in animals of the control group showed a tendency to its activation earlier after laparotomy (Table 2).

Table 2 SOD activity (arb. units/min. mg of protein) in the tissue homogenate of experimental animals (M±m)

Groups and terms of the study (days)	Liver	Kidneys	Pancreas	Small intestine
Control	10,906±1,411	4,853±0,499	12,296±0,538	10,831±0,490
Obturation, via:				
1	7,128±0,312 ^{a,b}	5,99±0,381	7,043±0,166^{a,b}	7,350±0,338^{b}
3	11,984±0,646	5,88±0,746	13,740±0,546	11,739±0,616
7	10,943±0,351	7,36±0,416	9,236±0,604^{a}	10,090±0,669
	10,731±0,275	5,34±0,855	10,128±0,594^{a}	11,154±0,973
15	9,181±0,571	3,120±0,161^{a}	12,457±0,918	8,42±0,630^{b}
	10407±1,127	4,910±0,704	12,744±0,853^{a}	10,284±0,417
	7,444±0,488^{a,b}	5,60±0,347	10,338±0,567^{a,b}	10,207±0,553
	10,965±1,021	4,84±0,615	12,082±0,320^{a}	10,407±0,705

Note: 1. The numerator contains the indicators of the experimental group, the denominator - the control group. 2. Significant difference ($P<0.05$); a – from the intact group, b – from the control group.

At the same time, in rats with extrahepatic cholestasis, enzyme activity changed in different directions in the studied organs. Thus, the study of SOD activity in the liver homogenate of experimental animals showed its decrease by 40.5% ($P<0.001$) already 1 day after the reproduction of the model of extrahepatic cholestasis relative to the parameters of control rats. However, later (after 3 days) SOD activity increased statistically significantly by 53.4% compared to the values of the previous period and approached the parameters of the control and intact groups of rats. Apparently, this was a compensatory reaction of the body to the development of cholestasis, since later we observed a gradual decrease in SOD activity in the liver homogenate of experimental animals. The studied indicator by the end of the experiment (after 15 days) was statistically significantly lower than the standard parameters by 32.1%. One of the mechanisms of its decrease can be the development of fibrotic changes in the liver as a result of long-term preservation of cholestasis.

In contrast to the liver, changes in SOD activity in the kidney homogenate were manifested to a greater extent by activation. Thus, 1 day after the reproduction of the model of extrahepatic cholestasis, the extrahepatic activity of SOD in the kidney homogenate increased statistically significantly by 23.5% relative to the indices of intact rats, and did not differ from the values of the control group of animals. This activation was even more pronounced after 3 days, when its values exceeded the parameters of the previous period by 22.9%, control and intact animals by 38 and 51.8%, respectively. However, this activation after 7 days was replaced by inhibition, since the studied indicator significantly decreased by 57.6% compared with the previous period and by 36.4% compared to the values of control rats. It should be noted that the compensatory capabilities of the kidneys, apparently, are significantly higher than in the liver, since the activity of SOD by the end of the experiment significantly increased by 79.5% compared to the values of the previous period and exceeded the control parameters by 15.8%.

The study of SOD activity in the pancreas showed its inhibition only in the early stages of the experiment. Thus, the studied indicator was statistically significantly lower than the normative control parameters by 48.7% of the group of animals 1 day after the reproduction of the model of extrahepatic cholestasis. In the future, its activity increased slightly (by 1.31 times) in relation to the values of the previous period, but still remained below the values of the control group of rats. Gradual activation of SOD persisted in the future, as the studied indicator increased relative to the values of the previous period by 1.35 times and reached the parameters of the control intact group of animals. Only by the end of the experiment (after 15 days) we revealed a tendency

to a decrease in the activity of the enzyme in the pancreatic tissue: a decrease by 14.5% relative to the control values.

The study of SOD activity in the mucosa of the small intestine showed the undulation of its change. Thus, 1 day after the reproduction of the bile duct obstruction model, we revealed a statistically significant decrease in enzyme activity by 37.4% relative to the values of control animals. Subsequently (after 3 days), this inhibition was replaced by an increase in its activity by 37.2% relative to the values of the previous period and approaching the parameters of intact rats. After 7 days, SOD activity again decreased by 16.5% and 18.1%, respectively, to the values of the previous period and control rats. On the 15th day of the experiment, we again observed an increase in SOD activity by 26.1% and its approach to the values of the control group of animals.

Consequently, the dynamics of changes in SOD activity in the studied organs is different and, apparently, to a greater extent is related to their involvement in the pathological process.

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