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IMPROVEMENT OF DIAGNOSTIC MEASURES FOR CHRONIC LIVER DAMAGE IN RATS

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Abstract: This article describes the work on the formation of a model of chronic liver diseases in the conditions of pathology research, which is considered relevant today. In this regard, in order to timely and effective treatment of chronic liver diseases, a number of research works are being carried out aimed at improving their diagnosis at early stages. In the conducted studies, death was observed in 30% of animals in the experimental group exposed to heliotrin, a substance with liver-damaging properties. At the same time, although the biochemical parameters of the blood also underwent significant changes, it was noticed that the platelet growth factor also increased in proportion to these signs.

***Keywords*:** Heliotrin, liver damage, liver fibrosis, chronic liver diseases, toxic hepatitis.

Introduction. It is known that chronic hepatitis is a diffuse inflammatory process in the liver, which continues without improvement for more than 6 months and can turn into a more severe disease fibrosis or cirrhosis of the liver. HCV is not only a major medical problem, but also has significant social and economic significance, since it affects the able-bodied population, and the available medicines are expensive and not always effective enough. The risk of chronic acute viral hepatitis B is up to 10% in adults (with only 2% with jaundice) and 90% in children born to infected mothers [1, 2, 3, 4].Despite the successes achieved in the study of the pathogenesis of viral liver lesions, to date, the issues of assessing the course and prognosis of the outcomes of chronic viral hepatitis remain open. This problem is actively studied by domestic and foreign researchers. New areas of research, such as metabolomics, proteomics, in which the connection of individual molecules with pathological processes is established, may open up new markers for detecting liver pathology and monitoring therapy. The most common diagnosis of chronic viral hepatitis B and chronic viral hepatitis C is based on the detection of hyperfermenemia, as well as uar markers. The progression of chronic liver diseases is the main pathway leading to damage and activation of the fibrogenesis process. Meanwhile, the basis of liver failure is precisely the irreversible dysfunction of liver fibrosis, the subsequent development of cirrhotic changes. Predicting the course of the disease and timely implementation of therapeutic measures are crucial for determining the severity of fibrosis, and the ability to identify patients with mild or moderate fibrosis allows treatment until the process of liver damage reaches irreversible changes [5, 6]. Due to the lack of effective methods of treating liver fibrosis, the search for new methods aimed at functional restoration of the liver remains relevant. The problem of improving the quality of medical care, in particular, the quality of laboratory research, remains relevant not only for our republic, but also one of the most important in the whole world. [7]. In the pathomorphological picture of toxic hepatitis with ascites in humans, attention is drawn to the severe lesion of the liver parenchyma and the phenomena of fibrosis and necrosis of the central zones of liver fragments. Similar changes were found in the liver of experimental animals with heliotrin poisoning [8, 9]. It is important to note that such toxic hepatitis can occur as a result of poisoning with industrial poisons

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such as carbon tetrachloride and acrylonitrile. Despite the successes achieved in the study of the pathogenesis of viral liver lesions, to date, the issues of assessing the course and prognosis of the outcomes of chronic viral hepatitis remain open [10].

In this regard, in order to timely and effective treatment of chronic liver diseases, a number of research works are being carried out aimed at improving their diagnosis at early stages.

The purpose of the work. Determination of viability of experimental animals and platelet growth factor in rats with chronic liver pathology under study conditions.

Material and methods of research. The experiment was performed on white female laboratory rats weighing 100 ± 10 g, obtained from a vivarium of used animals kept under standard conditions on a normal food and water diet. Manipulations with animals were carried out according to the manual [11].

Toxic liver damage was modeled by intragastric administration of heliotrin in low doses according to the scheme: 10 mg/100 g per kg of body weight, 7 mg/ 100 g per kg of body weight, 5 mg/ 100 g per kg of body weight, 3 mg/100 g per kg of body weight. All animals were divided into 6 groups of 10 individuals each. From the experiment, rats were removed by decapitation after 1, 3 and 5 weeks. The activity of ALT, AST, alkaline phosphatase, LDH, the level of total protein, direct bilirubin and glucose were determined in the blood serum. Chronic toxic liver damage or chronic intoxication was confirmed hematologically, biochemically and morphologically on the 35th day of the experiment [12, 6].

PDGF is known to be a powerful mitogenic and chemotactic factor for mesenchymal cells such as fibroblasts, blood vessels, smooth muscle cells, glomerular mesangial cells and some types of brain cells. PDGF increases the healing rate - a growth factor that affects the healing of various injuries, cuts and wounds that occur on the skin. In inflammation, the expression of PDGF receptors increases in the affected area. Diseases such as glomerulonephritis, liver cirrhosis, lung fibrosis, atherosclerosis and vasculopathy will be associated with excessive PDGF receptor signaling. In this regard, quantitative indicators of platelet growth factor BB (PDGF-BB) were determined by enzyme immunoassay in the blood serum of experimental animals, various sample media and biological fluids. In this case, a complex with a measurement range from 4.6 to 2000 pg/ml and a sensitivity of 4.6 pg/ml was used [13-17].

Results and their discussion. *Hematological and biochemical analysis of rat blood during the development of chronic heliotrine hepatitis.* Toxic damage to the liver in rats as a result of the introduction of heliotrin led to a violation of the functional state of liver cells. As a result of these functional disorders, the activity of transaminases (AST and ALT) in the blood serum of rats with chronic HH was 2,4 and 2,8 times respectively, compared with the levels of these indicators in the control group. It was found that the total amount of protein decreased to 1,5 times compared to the control group, while the total amount of bilirubin increased to 1,4 times. There was also an increase in the amount of alkaline phosphatase and HHD to 1,1 and 1,5 times, respectively, compared with the control group. Thus, as the degree of liver damage worsened, as can be seen from the table, significant changes in biochemical parameters were also observed. in subsequent studies, the amount of cytokines was mainly tracked dynamically, and it was analyzed whether these changes were proportional to biochemical changes in the blood.

As a result of the introduction of heliotrin, a substance with hepatotoxic properties, according to the scheme, lethality was observed in animals in the study group during the study. In total, from 1 to 5 weeks of the study, death was recorded in 30% of laboratory rats in the group (Table 1).

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Table 1. Viability of animals under the influence of hepatotoxic substances.

№	Experimental groups	Viability of experimental animals		
		Number of animals	Number of deaths	Viability in %
1.	Intackt group	10	0	100
2.	Control group (ChHH)	50	15	70

It is worth noting that in this experiment, mortality in experimental animals was observed mainly in higher amounts in the acute phase of the process. Death occurrence in general, changes in the liver caused by a toxic substance were detected during in-depth laboratory tests.

Investigation of the effect of a toxic substance on platelet growth factor (PDGF) in conditions of chronic heliotrine hepatitis.

Prolonged use of the hepatotoxic substance heliotrin in rats in descending order of high doses led to chronic liver damage and, as a consequence, to a number of changes in the body. Along with the aforementioned changes caused by the hepatotoxic substance, platelet growth factor (PDGF) levels also increased up to 1.8 times or up to 85% compared to the intact group, which was not injected with heliotrin. This can lead to an increase in PDGF levels and an increase in the process of fibrosis in the liver. That is, the processes of reparative regeneration in the liver slow down, which ultimately increases the likelihood of severe liver cirrhosis.

Table 2. Changes in platelet growth factor (PDGF) in chronic toxic hepatitis.

№	Experimental groups	Doses in mg/kg	Platelet growth factor (PDGF) in pg/ml
1.	Intackt group	Dist. water	10,4 ± 0,8
2.	Control group (ChHH)	Heliotrin	18,5±1,1

Note: * - differences compared to the data of the control group-P<0.005

Thus, in chronic heliotrine hepatitis, along with markers in the blood that characterize the disease, significant changes in platelet growth factor were observed. These changes began to manifest themselves from the first weeks of the disease and manifested themselves in the form of more pronounced irreversible signs at week 5.

Conclusions. In the conducted studies, death was observed in 30% of animals in the experimental group exposed to heliotrin, a substance with liver-damaging properties. At the same time, although the biochemical parameters of the blood also underwent significant changes, it was noticed that the platelet growth factor also increased in proportion to these signs.

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