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Dynamic Changes of Cytokines in the Occurrence of Chronic Liver Damage in an Experimental Condition

A. N. Aripov[1*], L. L. Akhunzhanova[2], O. A. Aripov[3], A. U. Nabiev[4]

[1,2,3,4]Republican Specialized Scientific and Practical Medical Center of Pediatrics of the Ministry of Health of the Republic of Uzbekistan*

Corresponding Email: [1]tolmas4th@mail.ru*

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Abstract: ***This article presents the characteristics of liver fibrosis in rats with chronic heliotrin intoxication, indicators characteristic of the formation of animal serum fibrosis, an increase in the level of inflammatory-stimulating cytokines IL-1ß, IL-2, IL-6 and IL-17 was observed in dynamics. Induction of cytokines IL-1ß, Il-2, IL-6 and IL-17 was detected in the dynamics of the development of experimental heliotrine hepatitis, the maximum increase in their number was established on the 35th day of the development of heliotrine hepatitis compared with intact animals. Thus, in studies, profound changes in the immunoregulatory function of cytokines were observed as the lesion process intensified in experimental chronic hepatitis. These changes were especially evident in Anna as the disease progressed. From the conducted studies, it can be concluded that an important topical issue is the identification and correction of liver damage processes at the earliest possible stages.***

Keywords: Chronic Liver Diseases, Liver Fibrosis, Hepatotoxins, Cytokines, Pro-Inflammatory, Anti-Inflammatory.

1. INTRODUCTION

Currently, chronic liver diseases against the background of a pandemic of viral hepatitis In the world are one of the urgent socio-economic and clinical-epidemiological problems of modern medicine. As a result of this pathology, there is a steady increase in morbidity, disability and mortality [1, 2, 3]. About 2 billion people are infected with hepatotropic viruses in different countries of the world. people, 350-400 million of them. It is considered a chronic carrier of this infection, and about 400,000 people die from chronic viral liver diseases, in particular chronic viral hepatitis C as a result of the development of cirrhosis of the liver and hepatocellular carcinoma [4, 5]. Due to the significant strength of the spread, duration, adverse effects of chronic hepatitis and low effectiveness of treatment, interest in the study of

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hidden mechanisms is increasing pathological processes occurring in them at the level of cells, organelles, membranes. Changes in metabolism in the liver can occur under the influence of various etiological factors-infectious agents, ingestion of hepatotoxins. In recent years, the understanding of the mechanisms of fibrogenesis has been expanded, which has led to an understanding of the narrowing of fibrosis and very accurate assumptions that effective treatment provides a favorable prognosis even at severe stages of fibrosis [6, 7]. Despite these achievements, a comprehensive study of the mechanisms of liver fibrosis development remains an urgent task of modern medicine [8]. In this regard, a number of scientific works are being carried out under experimental conditions to identify chronic severe liver lesions in laboratory white rats and confirm them with the help of modern research methods.

The purpose of the study: Dynamic monitoring of changes in the levels of proinflammatory cytokines in the blood of experimental animals with chronic heliotrine hepatitis.

2. MATERIAL AND METHODS OF RESEARCH

100 mongrel white male rats weighing 100±10 g were used as the object of the study.. All the research animals were kept in the same conditions for care and feeding [9]. The chronic toxic form of hepatitis In experiments was caused by the administration of heliotrin to the studied animals in decreasing doses, starting with the lethal dose: 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 body weight. In order to assess chronic toxic liver damage, experimental animals were divided into groups and objective and instrumental examinations were performed at weekly intervals. Chronic toxic liver damage or chronic intoxication was confirmed hematologically, biochemically and morphologically on the 35th day of the experiment [10, 11]. In diseases accompanied by inflammation, in particular, among the mechanisms leading to the pathogenesis of hepatitis, tissue damage is noted due to energy imbalance, excessive peroxidation and the development of secondary immunodeficiency. The relationship between these systems is carried out by various pro-inflammatory and anti-inflammatory cytokines. With the development of inflammation, the formation of cytokines that stimulate inflammation is noted: interleukin - 1β (Il - 1β), interleukin-2 (Il-2), interleukin-6 (IL-6) and interleukin-17 (IL-17). These indicators were determined in the blood serum by IEA using special chips. Based on the conducted studies, the obtained results were compared with the control group of mukhakamasi, and statistical processing of the results was carried out using the methods of R.B. Strelkov presented in [12].

3. 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 gh was 238.6% and 281%, respectively, compared with the levels of these indicators in the control group. It was found that the total amount of protein decreased to 46% compared

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to the control group, while the total amount of bilirubin increased to 138.1%. There was also an increase in the amount of alkaline phosphatase and HHD to 10.3 and 145%, respectively, compared with the control group.

Table 1. Changes in the functional state of liver enzymes in chronic heliotrine hepatitis.

Experimental groups	Intackt group	Control group
Doses in mg/kg	Dist. water	Heliotrin
ALT u /l	95,8±2,4	268,9±9,6
AST u /l	156,6±4,8	373,6±11,21
Total protein (g/l)	85,6±4,8	58,7±2,9
Albumin g/l	48,5±2,9	33,3±3,6
Total Bilirubin mkmol/l	2,15±0,96	5,12±0,96
Koeffitsient of de Rits (AST/ALT)	1,63±0,22	1,35±0,11
ALPh, u /l	394±4,48	434,4±6,52
LDH, u /l	625,5±11,6	1532,5±22,4
HHD u /l	1,15±0,11	1,46±0,11
Amilase (u /l)	495,7±11,22	442,6±6,48

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

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.

Dynamic monitoring of cytokine changes in the blood of rats with chronic heliotrin intoxication. Increased cytokine secretion and their manifestation will depend on the type of pathogenetic factor, but they have not been widely studied. Despite their limited life cycle, proinflammatory cytokines are very aggressive towards host cells. The completion of their production occurs mainly due to the action of anti-inflammatory cytokines, which either suppress synthesis or inactivate anti-inflammatory factors. The balance between pro-inflammatory and anti-inflammatory cytokines is an important component of pathogenesis, determines the severity of pathological reactions and is prognostically important for determining the inflammatory outcome [13, 14].

Table 2. Dynamic changes of cytokine degree in the blood of rats with chronic heliotrin intoxication.

Experimental groups	Intackt group	Control group		
Doses in mg/kg	Dist. water	Heliotrin		
		1st week	2nd week	3rd week
IL-17 pg/ml	1,8±0,048	2,51±0,12	2,29±0,089	3,47±0,089

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IL-6 pg/ml	0,31±0,012	1,27±0,048	1,87±0,072	1,91±0,072
IL-2 pg/ml	0,39±0,012	1,31±0,011	1,96±0,012	1,98±0,012
IL-1beta pg/ml	0,12±0,006	0,23±0,011	0,31±,0,0,8	0,33±,0,0,8

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

The results of studies on the activity of cytokines stimulating inflammation in chronic course showed that the hyperproduction of intenleukins during 3 weeks of the study, in particular, increased the level of IL-6 in the blood to 1.91±0.072 pg/ml, the level of IL-2 in the blood to 1.98±0.012 pg/ml, Il-1beta and IL-17 to 0.33±0.0.8 pg/ml, an increase was observed, as well as to 3.47±0.089 pg / ml. The presented results indicate the observation of regulation of the production of inflammatory-stimulating forms of cytokines in experimental animals with chronic heliotrine hepatitis. An imbalance in the ratio of pro-inflammatory and anti-inflammatory factors caused the destructive nature of inflammation and its exacerbation. Also during the study, the results of studies on the activity of cytokines that stimulate inflammation in chronic course showed that the hyperproduction of intenleukins, in particular, during 5 weeks of experiments, can lead to an increase in the level of IL-6 in the blood to 3.17± 5.0 pg/ml, the level of IL-2 in the blood to 3.23 pg/mlml, Il-1beta and IL-17, respectively. 333 and increased to 253%.

Table 3. Dynamic changes of cytokine degree in the blood of rats with chronic heliotrin intoxication.

Experimental groups	Intackt group	Control group		
Doses mg/kg	Dist. water	Heliotrin		
		1st week	4th week	5th week
IL-17 pg/ml	1,8±0,048	2,51±0,12	4,09±0,12	4,55±0,024
IL-6 pg/ml	0,31±0,012	1,27±0,048	2,37±0,048	3,17±0,012
IL-2 pg/ml	0,39±0,012	1,31±0,011	2,51±0,011	3,23±0,072
IL-1beta pg/ml	0,12±0,006	0,23±0,011	0,41±0,011	0,52±0,012

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

The presented results indicate the observation of the regulation of the production of inflammatory-stimulating forms of cytokines in experimental animals with chronic heliotrine hepatitis. An imbalance in the ratio of pro-inflammatory and anti-inflammatory factors caused the destructive nature of inflammation and its exacerbation.

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4. CONCLUSIONS

Thus, in studies, profound changes in the immunoregulatory function of cytokines were observed as the lesion process intensified in experimental chronic hepatitis. These changes were especially evident in Anna as the disease progressed. From the conducted studies, it can be concluded that an important topical issue is the identification and correction of liver damage processes at the earliest possible stages.

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