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THE IMPORTANCE OF LABORATORY TESTS IN DIAGNOSIS AND MONITORING OF CHRONIC VIRAL HEPATITIS "B"

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Abstract: Despite the ever-expanding Ob it knowledge about the causes of chronic wi - tier infections, many questions concerning the mechanisms of the onset and progression of this disease, remain open.

The aim of the study was to study the pathogenesis of chronic HBV infection by identifying the relationship between clinical and laboratory parameters and apoptosis indices characterizing the processes of damage in patients with chronic hepatitis. It was revealed that the level of ALT and AST in the blood of children with CHB exceeds the control value by 4.3 times and 2.9 times, respectively. Cholestasis rates are also significantly increased. The bilirubin content - by 87.4%, the GGT activity - by 75.2%, the alkaline phosphatase activity - by 3.7 times. The lipid profile of blood serum changed significantly: the content of TC increased by 90%, LDL - by 74.1%, VLDL - by 62.5%. HDL content decreased - by 62.5%. The content of MDA increased 4 times, DC - 1.9 times. CT activity decreased by 65.9%. The content of pro-apoptotic signaling molecules TNF-, and NO - products in the blood of children with CHB increases markedly 4.5 and 1.9 times, respectively. With D 16 $^{+}$, CD 95 $^{+}$ increased 2.5 and 6.4 times, respectively. The increase in NO - products in the blood of children with a chronic course of the disease, once again confirms the assumption that the transition of OHS to the chronic form is due, to a certain extent, to the failure of the immune system and impaired immunoregulatory processes due to the acceleration of apoptotic processes.

Keywords: chronic hepatitis B markers apopto for

Chronic hepatitis B (CHB) is one of the urgent problems of hepatology . The significance of chronic HBV infection is determined not only by its widespread occurrence, but by the possibility of an unfavorable development of the process with an outcome in liver cirrhosis in 20% of adult patients infected with HBV in childhood . There is no doubt that chronic viral liver damage is an immune-mediated infection [1 , 8]. Achieving stable remission in patients with CHB is also not possible without a significant improvement in the parameters of the body's immune system [2,9]. The range of possible mechanisms by which viruses can affect the immune system are widely discussed in the modern literature . Biochemical and immunological research methods are among the studies that contribute to the disclosure of the mechanisms of prolongation of pathological processes [4].

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However, unambiguous data that comprehensively characterize these processes have not been obtained , many questions remain unresolved, both with the pathogenic properties of hepatotropic viruses and with the nature and patterns of development of immunopathological processes leading to the progression of liver damage and fibrosis with an outcome in the formation of hepatocellular carcinoma in during the natural course of this infectious disease .

Thus , despite the advances achieved in recent years in the study of the pathogenetic basis of chronic hepatitis, there is an obvious incomplete research in this area. Given the widespread prevalence of chronic HBV infection among children , the high incidence of adverse outcomes with disability and significant mortality at the final stages of the natural course, they represent one of the most pressing problems of modern medicine [4,5,7].

The purpose of the study : The study of the pathogenesis of chronic HBV infection by identifying the relationship of clinical laboratory and immunological parameters characterizing the processes of damage in the liver of patients with chronic hepatitis B .

Material and research methods . 4 0 children with chronic hepatitis B were examined . In each case, the diagnosis was verified on the basis of clinical and instrumental symptoms, clinical and laboratory syndromes, serological results, PCR diagnostics data. As a control, a group of practically healthy children in the amount of 12 people was examined .

Research methods : The diagnosis of CVHB was established on the basis of traditional laboratory research methods. Etiological diagnosis verification performed detection in blood serum DNA HBV (method of polymerase chain reaction - PCR), HBV serologic markers (HBeAg , HBsAg) by ELISA. We determined the levels of ALT, AST, total bilirubin (OB), direct bilirubin (PB), total protein and its fractions, alkaline phosphatase, GGT. All sera were obtained prior to treatment. A general blood test included the mandatory determination of the number of leukocytes, erythrocytes, platelets, ESR . Lipid complex - MDA in biological material - by reaction with TBA (L.I. Andreeva et al , 1989). Determining the level of DC in -by m- dy Z **.** Platcer **.** The metabolic block of studies included the determination of the content of cholesterol, LDL triglycerides, HDL in the samples under study using reagents from Vital D iagnostic a (Russia). In the blood serum, the ELISA method determined the indices of the content of immunoglobulins of classes A (IgA), M (IgM), G (IgG); levels of the main pro-inflammatory (interleukin 12-IL-12, tumor necrosis factor alpha-TNFα), C D 16 $^{+}$, CD 95 $^{+}$, IL-4, IL-6, IL-8, IL-10

Research results .

First of all, we studied some biochemical blood parameters reflecting the functional state of the liver in children with CHB. The results of these studies are presented in Table 1.

Regarding the mechanisms of lipid metabolism disorders in chronic liver pathology, it should be noted the importance of lipid peroxidation processes . The LPO process is assigned the role of a mechanism that ensures the availability of lipid and protein components for the action of phospholipases and proteases. Activation LPO affect important physical-chemistry cal membrane

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properties - permeability, viscosity, phase state and equally affects all intracellular membranous structures and subcellular formation, exerting yuschee destabilizing effect on membrane cells .

Condition of free radical oxidation of the lipid membranes of lymphocytes was evaluated by the level of the primary product - diene conjugates (DC) and the final product - malonic dialdehyde (MDA). In a comparative assessment of LPO and AOS in CHB patients , we obtained the following results (Table 1).

The lipid profile of blood serum of children with CHB changed significantly: the content of OC increased by 90%, LDL - by 74.1%, VLDL - by 62.5%. HDL content decreased - by 62.5%. The content of MDA increased 4 times, DC - 1.9 times. Catalase activity decreased by 65.9%. SOD activity decreased from 42.3 ± 3.2 U / L to 26.35 ± 1.54 U / L.

N Indicators of cytolysis indicate that AST and ALT levels in the blood of children with chronic hepatitis B exceeds the control 4 , 3-fold and 2 , 9 -fold, respectively. Cholestasis rates are also significantly increased. The total blood bilirubin was increased by 87.4%, the GGT activity was increased by 75.2%, and the alkaline phosphatase activity was increased by 3.7 times. And the enzyme activity increased in proportion to the progression of the pathological process (p <0.05).

Table Itza 1 Indicators of cytolysis and cholestasis in the blood of children with chronic hepatitis B

Index	The control	Ill s CHB
Total cholesterol, mmol / l	2.55 ± 0.21	4.87 ± 0.31 *
Low density lipoproteins, mmol / l	3.33 ± 0.18	5.80 ± 0.21 *
High density lipoproteins, mmol / l	1.45 ± 0.08	1.04 ± 0.02 *
Very low density lipoproteins, mmol / l	0.56 ± 0.04	0.91 ± 0.04 *
Triglycerides, mmol / l	0.84 ± 0.06	2.33 ± 0, 1 8 *
MDA (nmol / ml)	1.84 ± 0.12	7.31 ± 0, 44 *
DC (nmol / ml)	6.72 ± 0.42	12.87 ± 1 , 0 9 *
SOD in erythrocytes (U / L)	42.3 ± 3.2	26.35 ± 1, 54 *

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Catalase in erythrocytes (H_2O_2 / min / mg protein)	15.22 ± 1.34	10.03 ± 0, 97 *
ALT (E / l .)	16,33 ± 2.22	72.18 ± 4.12 *
AST (E / l .)	14.67 ± 1.0 1	40.84 ± 3.32 *
Total bilirubin (μ mol / l)	14.14 ± 2.10	34.5 0 ± 3.2 *
ALF (U / l)	155.2 ± 11.2	597.2 ± 9932.5 *
GGT (U / l)	35.6 ± 2.5	62.40 ± 4.8 *

* - reliability in relation to control (P <0.05)

Additional indicators blood count was significantly reduced hemoglobin, leucocytes and increased level of SOE (Table Itza .2)

Table 2 Indicators of a general blood test in patients with CHB

Index	The control	CHB
Hemoglobin (g / l)	112 ± 7 , 7	100 ± 5 , 3 *
Platelets (× 109 / L)	226 ± 1 6 , 2	203.5 ± 1 2 , 5
Leukocytes (× 109 / l)	6.3 ± 0.5	3.7 ± 0.2 *
ESR (mm / hour)	3.6 ± 0.4	12.6 ± 0.8 *

Note: * - P < 0.05 reliability calculated in relation to control

The greatest deviation in children with chronic hepatitis B patients is observed in the T - link of the immune response. The T-cell link of immunity plays a central role in the elimination of the virus. The study found that with chronic hepatitis B in children, the total number of leukocytes in the blood decreases. With the reduction of general of the number of leukocytes observed reduced

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levels of lymphocytes. The dynamics of a decrease in the number of lymphocytes, depending on the severity of the pathology, is especially noteworthy. The decrease may be associated with both a violation of the proliferative activity of lymphocytes.

Among the mechanisms of cellular defense in antiviral immunity, the leading place is occupied by CD8 + -cytotoxic lymphocytes, the main function of which is aimed at eradication of the pathogen, which is due, on the one hand, to their ability to directly cause the death of infected cells, and on the other hand, to the ability to produce antiviral factors. In the course of our study, the relative content of CD8 + lymphocytes in patients with CVH did not statistically significantly differ from the corresponding control indicators.At the same time, the study of the concentration of natural killer cells (CD 16) revealed an increase in their absolute content in children of both groups . Thus, with moderate activity, the content of CD 16+ lymphocytes (10^9/ l) was 211.4 ± 16.2, i.e. exceeded the control value by 25.8% ($p < 0.05$), with pronounced activity - up to 242.0 ± 19.610 ^{9}/ l. The indicators of the relative content of CD 16+ lymphocytes (%) decreased and amounted to 9.56 ± 0.9 and 8.11 ± 0.61, respectively, with the control value of 11.6 ± 1.02%. CD 16 activation is a response to excessive formation of the relative number of CD 25 cells, which averaged 26.63 ± 1.35% with moderate activity and 27.7 ± 2.8% with pronounced activity ($p < 0.05$)

Table 3 . Some parameters of apoptosis in children with X HB

Indicators	Value control	CHB
TNF-α (pkg / ml)	38.44 ± 3.48	162 ± 13.5 *
With D16 $^+$ (%)	16.1 ± 1, 3 4	40 , 5 ± 3 , 41 *
CD95 $^+$ (%)	3,48 ± 0, 25	2 2 , 2 5 ± 1, 8 6 *
With D8 $^+$ (%)	20.43 ± 1.10	29.15 ± 1.63 *
Ig A (mmol / l)	7 , 25 ± 0, 52	8.44 ± 0, 51
Ig G (mmol / l)	5 6 , 44 ± 4 , 0 2	6 4 , 12 ± 5 , 12
Ig M (mmol / l)	1 , 12 ± 0.0 7	1 , 96 ± 0.1 6 *
NO (μmol / l)	13 , 23 ± 0, 88	25,67 ± 1 , 54 *

* - reliability in relation to control ($P < 0.05$)

As can be seen from the presented data (table 3), the content of proapoptotic signaling molecules TNF-, and NO - products in the blood of children with CHB increases markedly. The level of TNF- in the blood of children compared with the control increases 4.5 times. The level of NO - 1.9 times, C D 16 $^+$, CD 95 $^+$ increased 2.5 and 6.4 times, respectively.

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The increase in NO - products in the blood of children with a chronic course of the disease, once again confirms the assumption that the transition of OHS to the chronic form is due, to a certain extent, to the failure of the immune system and impaired immunoregulatory processes due to the acceleration of apoptotic processes. [10]. The results obtained indicate an increase in the concentration of profibrogenic factors in the serum of patients with CHB.

The results of our studies mostly coincide with the conclusions of researchers who consider high viral load (with HBV infection) [7], an increase in the cytotoxic activity of lymphocytes [10], damage to hepatocytes [3] with an increase in cytolytic syndrome as the determining factors in the development of pathological liver fibrosis , as well as a violation of cytokine regulation [6].

T mayor manner presented data indicate that the laboratory studies indicators indispensable not only at the stage of diagnosis, they are less necessary to assess the severity and prognosis of the disease.

Conclusions:

1. Children with CHB have a marked decrease in the number of T- and imbalance in B-lymphocytes
2. A high level of CD 8+ lymphocytes in the liver parenchyma is observed in chronic hepatitis, which is due to HBV replication (when HBsAg is detected in patients (r = 0.5).
3. Regenerative proliferation of hepatocytes in patients with chronic hepatitis with HBV infection increases with the growth of clinical (according to the activity of serum ALT , r = 0.52) damage criteria, ensuring the preservation of liver function.

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