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SIGNIFICANT FIBROSIS IN CHRONIC LIVER DISEASES: POSSIBILITIES OF NONINVASIVE SCREENING

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ВЫРАЖЕННЫЙ ФИБРОЗ ПРИ ХРОНИЧЕСКИХ ЗАБОЛЕВАНИЯХ ПЕЧЕНИ: ВОЗМОЖНОСТИ НЕИНВАЗИВНОГО СКРИНИНГА

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The investigation aimed to study the prognostic significance of clinical and laboratory parameters, including markers of the matrix metalloproteinases (MMP) system, for the detection of significant fibrosis (F2–4) in chronic liver diseases (CLD). Seventy-six patients with CLD of viral or alcoholic etiology aged 18 to 64 years were examined. Fibrosis F0–1 was found in 36.8 % of cases, and fibrosis F2–4 – in 63.2 %. Enzyme-linked immunosorbent assay was used to determine the blood levels of MMP-1, MMP-9, and tissue inhibitors of matrix metalloproteinases-1 (TIMP-1). The ratio TIMP-1/MMP-1, TIMP-1/MMP-9 was calculated. Increased risk of fibrosis F2–4 was associated with parameters of liver stiffness ≥7.3 kPa, gamma-glutamyltranspeptidase ≥37 u/l, aspartate aminotransferase ≥53 u/l, ESR ≥8 mm/h, platelets ≤187x10^9/l, age ≥45 years, alanine aminotransferase ≥68 u/l, TIMP-1/MMP-1 ≥36.4, albumin ≤43 g/l, total bilirubin ≥16 μmol/l, TIMP-1 ≥501 ng/ml, international normalized ratio ≥1.08, alkaline phosphatase ≥112 u/l, with the presence of moderate/severe cytolysis. According to multivariate logistic regression, liver fibrosis F2–4 was associated with blood levels of TIMP-1 and platelets, values of ESR. The combination of these parameters had a sensitivity of 70.8 % and a specificity of 100 % in the prediction of fibrosis F2–4. Thus, the levels of TIMP-1 and platelets in the blood and ESR are independent risk factors for significant fibrosis in CLD due to their participation in hepatic fibrogenesis.

Keywords: chronic liver diseases, significant liver fibrosis, matrix metalloproteinases, tissue inhibitors of matrix metalloproteinases, platelets, erythrocyte sedimentation rate, screening

В работе определялась прогностическая значимость ряда клинико-лабораторных показателей, в том числе маркеров системы матриксных металлопротеиназ (ММП), для выявления выраженного фиброза (F2–4) при хронических заболеваниях печени (ХЗП). Обследовано 76 больных ХЗП вирусной или алкогольной этиологии в возрасте от 18 до 64 лет. Фиброз F0–1 встречался в 36,8 % случаев, фиброз F2–4 – в 63,2 %. Методом иммуноферментного анализа определяли содержание в крови ММП-1, ММП-9, тканевого ингибитора матриксных металлопротеиназ-1 (ТИМП-1), рассчитывали соотношение ТИМП-1/ММП-1, ТИМП-1/ММП-9. Увеличенный риск фиброза F2–4 был связан с показателями жесткости печени ≥7,3 кПа, γ-глютамилтранспептидазы ≥37 ед/л, аспарагиновой аминотрансферазы ≥53 ед/л, СОЭ ≥8 мм/час, тромбоцитов ≤187x10^9/л, возраста ≥45 лет, аланиновой аминотрансферазы ≥68 ед/л, ТИМП-1/ММП-1 ≥36,4, альбумина ≤43 г/л, общего билирубина ≥16 мкмоль/л, ТИМП-1 ≥501 нг/мл, международного нормализованного отношения ≥1,08, щелочной фосфатазы ≥112 ед/л, с наличием умеренного/высокого цитолиза.

По данным многофакторной логистической регрессии, фиброз печени F2–4 был ассоциирован с содержанием в крови ТИМП-1 и тромбоцитов, значениями СОЭ. Комбинация этих параметров имела чувствительность 70,8 % и специфичность 100 % в предикции фиброза F2–4. Таким образом, содержание ТИМП-1 и тромбоцитов в крови, а также показатели СОЭ являются независимыми факторами риска выраженного фиброза при ХЗП, что обусловлено их участием в процессах печеночного фиброгенеза.

Ключевые слова: хронические заболевания печени, выраженный фиброз печени, матриксные металлопротеиназы, тканевые ингибиторы матриксных металлопротеиназ, тромбоциты, скорость оседания эритроцитов, скрининг

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Ac – accuracy
ALT – alanine aminotransferase
AST – aspartate aminotransferase
AUC – area under curve
cAMP – cyclic adenosine monophosphate
CI – confidence interval
CLD – chronic liver diseases
GGT – gamma-glutamyl transpeptidase
HBV – hepatitis B virus
HCV – hepatitis C virus
HDV – hepatitis D virus
INR – international normalized ratio
MMP – matrix metalloproteinase
NAFLD – non-alcoholic fatty liver disease
NPV – negative predictive value
OR – odds ratio
PPV – positive predictive value
ROC – receiver operating characteristic
Se – sensitivity
Sp – specificity
TIMP – tissue inhibitor of matrix metalloproteinases

Fibrosis is integral to structural and functional changes in chronic liver diseases (CLD). The development and progression of fibrosis is a turning point in chronic liver pathology, independent of etiology but determining an unfavourable prognosis (formation of liver cirrhosis, hepatocellular carcinoma, and other complications) [1].

The absence of clinical symptoms of fibrosis in CLD requires a biopsy – the «gold» standard in diagnosing histological changes in the liver, the widespread use of which in routine practice is limited for several reasons. In addition, a liver biopsy provides a snapshot of changes in the organ without characterizing the dynamic direction of fibrogenesis (progression or regression) [2].

These limitations have led to the development of non-invasive methods for assessing fibrosis, based either on a «biological» approach – quantifying biomarkers in the blood or on a «physical» approach, measuring liver tissue stiffness. At the same time, existing scales and indices of fibrosis, such as FibroTest, FibroMeter, FibroSpectII, HepaScore, FIB-4, APRI, include serum parameters that are not strictly specific for the liver and in most cases do not relate to markers of fibrogenesis [1].

Matrix metalloproteinases (MMPs) and their tissue inhibitors (TIMPs) control the accumulation and degradation of collagen and other components of the extracellular matrix in the liver [2]. An imbalance in the system of MMPs in the form of their increased expression can lead to intensification of inflammatory changes in the liver [3], and overexpression of inhibitors of matrixins is accompanied by an increase in the severity of fibrosis [2].

However, the relationship between plasma levels of MMPs and TIMPs and necroinflammatory changes in chronic liver diseases [4–10] has not always been observed [7, 11, 12]. Despite this, attempts are being made to use the FibroSpect II, Enhanced Liver Fibrosis score, HALT-C model, which includes the TIMP-1, MMP-3 parameters, in the non-invasive diagnosis of liver fibrosis [5], although the predictive role of MMPs and their inhibitors in assessing the severity of fibrosis in patients with CLD has not been determined. Therefore, searching for simple, non-invasive, inexpensive biomarkers of advanced fibrosis is of clinical importance – for choosing the right therapeutic strategies and predicting outcomes.

The research aims to study the prognostic significance of several clinical and laboratory parameters, including components of the MMP system for diagnosing severe fibrosis (F2–4) in CLD.

Material and Methods. The study included 76 patients with CLD (27 females, 49 males) aged from 18 to 64 years (41 (31; 48) years). Inclusion criteria: histologically confirmed CLD of viral or alcoholic etiology; age over 18 years; signed informed consent to participate in the study. Exclusion criteria: liver pathology of other etiology; clinically significant acute and chronic somatic diseases in the period of exacerbation; drug addiction; mental illness; pregnancy and lactation; malignant neoplasms.

In 59 cases, chronic hepatitis of viral etiology was detected (HBV – 16, HCV – 30, HDV – 13). Child – Pugh class A of liver cirrhosis was detected in 17 patients: viral etiology in 13 (HBV – 2, HCV – 8, HDV – 3), alcoholic in 4.

Liver fibrosis was categorized as absent (F0), minimal (F1), moderate (F2), severe (F3), and cirrhosis (F4). Fibrosis F0–1 was found in 36.8 % of patients, and fibrosis F2–4 – in 63.2 %.

The university ethics committee approved the study.

The blood concentration of MMP-1 (RayBiotech, USA), MMP-9 (Bender MedSystems GmbH, Austria), and TIMP-1 (Aviscera Bioscience, USA), was determined using the ELISA method, followed by the calculation of TIMP-1/MMP-1 and TIMP-1/MMP-9 ratio.

The results were statistically processed by StatTech v. 3.1.7 (Stattech LLC, Russian Federation). Quantitative values had a distribution different from usual and are presented as median (Me) and interquartile range (Q1; Q3). Differences were identified using the Mann – Whitney test. Categorical data are presented as percentages (%), and the χ^2 test was used to evaluate differences between groups with Yates' correction for continuity. The odds ratio (OR) and its 95 % confidence interval (CI) were calculated. The logistic regression analysis method was used to build a mathematical model; ROC analysis was performed; the information content of the models was assessed using the area under

the ROC curve. Sensitivity, specificity, positive and negative predictive value, and accuracy were calculated. Differences were considered statistically significant at $p<0.05$.

Results and Discussion. It was noticed that the patients with F2–4 fibrosis are older, with higher levels of aspartate (AST) and alanine (ALT) aminotransferases, γ-glutamyl transpeptidase (GGT), alkaline phosphatase, total bilirubin, ESR, international normalized ratio (INR), liver stiffness, lower concentration of albumin and platelets in the blood. Moderate/high biochemical activity of the process was more common. In this cohort, the maximum values of TIMP-1 and TIMP-1/MMP-1 were determined, which differed from the corresponding values in F0–1 fibrosis (Table 1).

Table 1

The relationship of clinical and laboratory markers and matrix metalloproteinases with fibrosis in CLD

Parameters	Patients with CLD, n=76	
	F0–1, n=28	F2–4, n=48
Gender (women/men, %)	42.9/57.1	31.2/68.8
Age (years)	37.5 (26,5; 44,0)	43.5 (35.0; 51.0) *
AST (u/l)	33.5 (21.0; 44.0)	58.5 (28.0; 97.5) *
ALT (u/l)	38.3 (23.0; 60.5)	68.0 (31.5; 145.0) *
GGT (u/l)	27.5 (17.0; 38.0)	68,9 (42.5; 143.8) *
Alkaline phosphatase (u/l)	82.0 (64.5; 163.0)	123 (72.0; 226.0) *
Total bilirubin (μmol/l)	14.0 (11.9; 16.9)	19,0 (13.5; 31.5) *
Direct bilirubin (μmol/l)	3.8 (3.0; 5.75)	3.7 (2.95; 8.4)
ESR (mm/h)	5.0 (4.0; 8.0)	9.0 (8.0; 17.0) *
C-reactive protein (mg/l)	0.4 (0.23; 3.4)	0.9 (0.1; 4.4)
Fibrinogen (g/l)	2.6 (2.22; 3.5)	2.64 (2.24; 3.55)
Albumin (g/l)	47.0 (44.5; 48.5)	43.0 (39.65; 46.0) *
Prothrombin time (sec)	16.3 (13.05; 17.25)	15.75 (12.6; 17.45)
Prothrombin index (%)	91.0 (89.0; 99.0)	91.0 (86.0; 97.0)
INR	1.1 (1.0; 1.15)	1.15 (1.09; 1.25) *
Total cholesterol (mmol/l)	4.24 (3.84; 4.67)	4.32 (3.75; 4.59)
Platelets ($x10^9$/l)	234.5 (189.5; 271)	162 (133.5; 213.5) *
Liver stiffness (kPa)	5.7 (5.05; 6.95)	11.55 (8.15; 15.5) *
Moderate/severe biochemical activity (%)	7.1	35.4 *
Mesenchymal inflammatory syndrome (%)	17.9	29.2
Cholestatic syndrome (%)	0	14.6 [1]
TIMP-1 (ng/ml)	494.0 (407.0; 613.0)	640.0 (519.0; 764.5) *
MMP-1 (ng/ml)	23.53 (16.63; 35.7)	21.45 (9.58; 31.8)
MMP-9 (ng/ml)	191.5 (95.5; 365.0)	188.0 (91.4; 528.0)
TIMP-1/MMP-1	19.0 (14.89; 29.31)	29.55 (16.64; 59.6) *
TIMP-1/MMP-9	2.9 (1.45; 5.1)	3.05 (1.15; 7.52)

Note: quantitative data are presented as Me (Q1; Q3), categorical data as %; * – significant differences between groups of patients ($p<0.05$); [1] – $p=0.087$ (criterion Yates's chi-squared test, Mann – Whitney criterion).

An increased risk of F2–4 fibrosis was associated with liver stiffness ≥7.3 kPa, GGT ≥37 u/l, AST ≥53 u/l, ESR ≥8 mm/h, platelet levels ≤$187x10^9$/l, with age ≥45 years old, moderate/severe cytolysis, ALT levels ≥68 u/l, albumin ≤43 g/l, total bilirubin ≥16 μmol/l, INR ≥1.08, alkaline phosphatase ≥112 u/l. The values of TIMP-1 above 501 ng/ml and TIMP-1/MMP-1 more than 36.4 were also associated with an increased risk of developing significant fibrosis. The optimal area under the curve was detected in the following cases: liver stiffness (0.89±0.03), GGT (0.88±0.03), ESR (0.79±0.05), platelets (0.77±0. 05), TIMP-1 (0.72±0.05). The sensitivity and specificity values respectively were: for liver stiffness (89.6 %, 82.1 %), GGT (87.5 %, 75.0 %), ESR (79.2 %, 71.4 %), platelets (66.7 %, 78.6 %), TIMP-1 (79.2 %, 57.1 %). Overall, the diagnostic significance of the studied parameters is presented in Table 2.

Table 2

Diagnostic significance of markers of liver damage and parameters of MMP system in the detection of liver fibrosis F2–4

Parameters	OR (95 % CI)	AUC (M±SE)	Se (%)	Sp (%)	PPV (%)	NPV (%)	Ac (%)
Age ≥45 years old	7.1 (1.9–26.5)	0.66±0.06 *	45.8	89.3	88.0	49.0	61.8
AST ≥53.0 u/l	10.7 (2.8–40.4)	0.69±0.06 *	56.3	89.3	90.0	54.3	68.4
ALT ≥68.0 u/l	6.5 (1.9–21.7)	0.69±0.06 *	52.1	85.7	86.2	51.1	64.5
GGT ≥37.0 u/l	21.0 (6.3–70.4)	0.88±0.03 *	87.5	75.0	85.7	77.8	82.9
Alkaline phosphatase ≥112 u/l	3.2 (1.2–8.6)	0.66±0.06 *	60.4	67.9	76.3	50.0	63.2
Total bilirubin ≥16.0 μmol/l	5.5 (1.9–15.5)	0.66±0.06 *	64.6	75.0	81.2	55.3	68.4
ESR ≥8 mm/h	9.5 (3.2–27.9)	0.79±0.05 *	79.2	71.4	82.6	66.7	76.3
Albumin ≤43 g/l	5.9 (1.9–18.2)	0.70±0.05 *	56.3	82.1	84.4	52.3	65.8
INR ≥1.08	3.3 (1.2–9.1)	0.66±0.06 *	79.2	46.4	71.7	56.5	67.1
Platelets ≤$187x10^9$/l	7.3 (2.5–21.7)	0.77±0.05 *	66.7	78.6	84.2	57.9	71.1
Liver stiffness ≥7.3 kPa	39.6 (10.4–150.9)	0.89±0.03 *	89.6	82.1	89.6	82.1	86.8
Moderate/ severe biochemical activity	7.1 (1.5–33.8)	0.63±0.06	35.4	92.9	89.5	45.6	56.6
TIMP-1 ≥501 ng/ml	5.07 (1.82–14.09)	0.72±0.05 *	79.2	57.1	76.0	61.5	71.1
TIMP-1/ MMP-1 ≥36.4	5.95 (1.58–22.46)	0.65±0.06 *	41.7	89.3	86.9	47.2	59.2

* Statistical significance of the model ($p<0.05$).

Using multivariate regression analysis, the probability of developing fibrosis F2–4 was assessed. The predictive model included 14 factors (age, values of AST, ALT, GGT, alkaline phosphatase, total bilirubin, ESR, INR, albumin, platelets, liver stiffness, as well as the presence of moderate/high biochemical activity, blood levels of TIMP-1 and TIMP-1/MMP-1 ratio), which showed sta-

tistically significant differences between the groups of patients with fibrosis F0-1 and F2–4.

According to the data of logistic regression, the presence of F2–4 fibrosis was independently associated with blood levels of TIMP-1 (OR 1.006; 95 % CI 1.001–1.011; p=0.018) and platelets (OR 0.981; 95 % CI 0.970–0.992; p=0.001), with ESR values (OR 1.298; 95 % CI 1.073–1.573; p=0.008). The chance of detecting F2–4 fibrosis increased by 1.006 times with an increase in TIMP-1 values by one ng/ml, by 1.298 times with an increase in ESR values by 1 mm/h, and by 1.019 times with a decrease in platelets by $1x10^9$/l.

The following equation describes the observed dependence:
$z = -0.994 - 0.019 \times X_{platelets} + 0.006 \times X_{TIMP-1} + 0.261 \times X_{ESR}$, where z – is the objective function; X_{TIMP-1} – TIMP-1 value (ng/ml); $X_{platelets}$ – platelet value ($x10^9$/l); X_{ESR} – ESR value (mm/h); –0.994 – regression constant; 0.019; 0.006; 0.261 – corresponding regression coefficients.

The formula calculates the probability of fibrosis F2–4 : $p = 1 : (1 + e^{-z})$, where e – is the base of the natural logarithm, equal to 2.72, p – is the probability of fibrosis F2–4.

The threshold p-value at the cut-off point was 0.768. F2–4 fibrosis was predicted with a p-value greater than or equal to this value. The diagnostic significance of $p \geq 0.768$ was: sensitivity – 70.8 %, specificity – 100 %, positive predictive value – 100 %, negative predictive value – 66.7 %, accuracy – 73.7 %. The resulting model was statistically significant ($p<0.001$), and the area under the ROC curve was 0.893±0.036 (95 % CI: 0.822–0.964), which indicated a good quality of the model.

Thus, the development of severe morphological signs of liver pathology is closely related to an imbalance in the MMP system. According to our data, significant fibrosis (F2–4) was associated not only with the age of patients, parameters of cytolysis, inflammation and cholestasis, levels of albumin and platelets in the blood but also with the values of TIMP-1 and TIMP-1/MMP-1.

It was previously noticed that the patients with chronic viral hepatitis with significant fibrosis had older age, higher values of AST, ALT, GGT, alkaline phosphatase, INR, average platelet volume, GGT/platelet and neutrophil/lymphocyte ratios, and lower levels of platelets and cholesterol in the blood [13, 14]. Golgi protein 73, antibodies to hepatitis B core antigen, and erythrocyte distribution width were associated with the severity of inflammatory changes in CLD [15]. Increased values of body mass index, AST/ALT ratio, blood glucose, GGT, sizes of liver, spleen, and portal vein, decreased albumin and platelet values, along with age, are considered predictors of the progression of fibrosis in non-alcoholic fatty liver disease (NAFLD) [16, 17]. The risk of development of fibrosis, associated with chronic HBV infection, increased 9-fold in cases of increased GGT/platelet ratio with a cut-off point of 0.229 (OR 9.1; 95 % CI 1.66–50.0; p=0.011) [13], and blood platelet counts less than $196.5x10^9$/l were markers of F2–4 fibrosis with a sensitivity of 71 % and specificity of 67 % [14].

It has been suggested that the relationship between aging and the progression of liver fibrosis is due to age-related decline in hepatic blood flow and liver function [16]. Increased ALT activity was more often associated with minimal fibrosis. In advanced stages of fibrosis, on the contrary, an increase in AST predominated. The interrelation of GGT with severe fibrosis is likely due to changes in pro-oxidant activity (the enzyme controls the metabolism of glutathione – the primary antioxidant molecule in cells) and a modulating effect on endothelial dysfunction [16], which plays an essential role in hepatic fibrogenesis [18, 19].

Several studies have revealed an increase in MMPs and TIMPs proportional to the severity of fibrotic changes in the liver in cases of chronic viral hepatitis [4, 9, 10, 12], NAFLD [5, 8, 20], primary sclerosing cholangitis [11] and biliary atresia [21]. There is also evidence that some MMPs and TIMPs negatively correlate with the severity of fibrosis [4, 6, 7, 9] or are not associated with it [5, 9, 11, 12, 22].

We identified factors associated with F2–4 fibrosis in CLD based on the multivariate regression analysis. These are increased levels of TIMP-1 and ESR and decreased platelet counts.

Previously, the predictive ability of serum parameters of MMP-1 in distinguishing hepatitis and cirrhosis, detecting fibrosis F2–4 or any fibrosis (>F0) [7, 23], as well as MMP-7 in identifying cirrhosis in chronic hepatitis C [9] or severe fibrosis in cases of NAFLD [8] was noticed. Blood levels of TIMP-1 in chronic hepatitis C were associated with the presence of fibrosis [24], and the levels of MMP-2, MMP-9, TIMP-2, and male gender of patients were predictors of fibrosis ≥F2 [22]. The combination of platelet, alpha-fetoprotein, ratios of AST/ALT, and collagen-3-propeptide/MMP-1 was highly significant in the diagnosis of significant fibrosis (F2–4) (area under the ROC curve 0.91) and liver cirrhosis (F4) (area under the ROC curve 0.83) [23]. According to multivariate analysis, risk factors for severe fibrosis in NAFLD included body mass index, platelets, sizes of liver, spleen, and portal vein [17].

The relationship between elevated TIMP-1 values and the severity of fibrosis is due to its ability to inhibit MMPs (especially MMP-1 and -9), preventing apoptosis of stellate cells, and protecting collagen from fibrolysis [2].

Platelets play a dual role in the formation of liver fibrosis. On the one hand, by releasing hepatocyte growth factor, they suppress fibrogenesis and stimulate hepatic mitogenesis by reducing the expression of transforming growth factor-β, type I collagen, and increasing the expression of MMPs [14, 25, 26]. By affecting the redox balance in stellate cells, platelets increase the concentration of intracellular cAMP [27], leading to cell inactivation and decreased collagen production [26].

On the other hand, activated platelets, under certain conditions, reduce the regeneration of hepatocytes, aggravate fibrosis, induce the proliferation and migration of stellate cells, and the synthesis of profibrogenic cytokines by releasing several growth factors, platelet factor 4, Von Willebrand factor and serotonin [25, 28]. They also initiate microthrombosis in the liver, especially near fibrotic areas, and enhance P-selectin-mediated local inflammation due to the recruitment of leukocytes [18, 19, 29].

There is no information on the significance of ESR as a predictor of the severity of fibrotic changes in the liver. It can be assumed that the relationship between ESR and hepatic fibrogenesis reflects the influence of the inflammatory process on the rate of progression of fibrosis, as evidenced by the association of C-reactive protein with steatohepatitis (OR 1.155; 95 % CI 1.029–1.297; p=0.014) and fibrosis (OR 1.130; 95 % CI 1.17–1.257; p=0.024) identified in NAFLD [30]. The proportion of patients with NAFLD with severe steatosis or fibrosis increased with the increasing levels of C-reactive protein in the blood, and the risk of detecting severe liver fibrosis in cases of C-reactive protein levels exceeding 6.68 mg/l increased by three times (OR 3.086; 95 % CI 1.154–8.249; p=0.025) [31].

Conclusion. The levels of TIMP-1, platelets in the blood, and ESR parameters are independent risk factors for significant fibrosis in chronic liver diseases. Their

association with the severity of liver fibrosis is due to their participation in the processes of fibrogenesis – their influence on the activity of stellate cells, the expression of MMPs, and the modification of collagen synthesis. The combination of TIMP-1, platelets, and ESR is highly significant in the diagnosis of F2–4 fibrosis, which allows its use in chronic liver pathology as a non-invasive marker of considerable fibrosis.

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FEATURES OF FORMATION OF PSYCHOPHYSIOLOGICAL DISORDERS IN MINE EXPLOSION INJURY

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ОСОБЕННОСТИ ФОРМИРОВАНИЯ ПСИХОФИЗИОЛОГИЧЕСКИХ НАРУШЕНИЙ ПРИ МИННО-ВЗРЫВНОЙ ТРАВМЕ

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The article discusses issues related to cognitive impairment in patients who have suffered mine blast trauma (MBT). The main group comprised 61 patients (58 men and three women). The average age was 45.5±4.7 years. The patients were divided into two groups: the first group – 31 (50.8 %) patients with a history of isolated traumatic brain injury (TBI) of mild to moderate severity; the second group – 30 (49.2 %) patients with a combination of mild and moderate TBI with somatic complications (amputation of the lower limb at different levels). The control group consisted of 30 healthy individuals. In the main group, sharply reduced levels of cognitive wave amplitude were noted. This was based on the difficulty in perceiving and processing incoming signals. As a result of the study, it can be argued that after MBT, patients perceive complex external perceptual events, objects, and phenomena worse. At the same time, there was a decrease in the communicative activity of patients with the onset of depression, which, in terms of level and severity, dominated in patients of the second group due to limited movement and difficulties in self-care.

Keywords: mine blast injury, traumatic brain injury, cognitive impairment, evoked potentials

Рассмотрены вопросы, связанные с когнитивными нарушениями у пациентов, перенесших минно-взрывную травму (МВТ). Основную группу составил 61 пациент (58 мужчин и 3 женщины). Средний возраст 45,5±4,7 лет. Пациенты были разделены на 2 группы: первая группа – 31 (50,8 %) пациент с изолированной черепно-мозговой травмой (ЧМТ) легкой и средней степени тяжести в анамнезе; вторая группа – 30 (49,2 %) больных с сочетанием нейротравмы легкой и средней степени тяжести с соматическими осложнениями (ампутация нижней конечности на разных уровнях). Контрольную группу составили 30 здоровых лиц. В основной группе отмечены резко сниженные показатели амплитуды когнитивной волны, что, вероятно, определяло сложности в восприятии и переработке поступающих сигналов. По результатам исследования можно утверждать, что после МВТ сложные внешние перцептивные события, объекты и явления хуже воспринимаются пациентами. При этом происходило снижение коммуни-