

**AUTONOMIC NERVOUS SYSTEM IN PATIENTS WITH CIRRHOSIS OF THE LIVER**

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**Abstract**

A comprehensive clinical and instrumental, laboratory, psychovegetative examination of 139 patients with cirrhosis of the liver of various etiologies (viral, alcoholic, combined) and severity according to Child-Pugh was carried out. The comparison group was represented by 104 patients with chronic hepatitis of viral, alcoholic and combined etiology. The control group consisted of 30 healthy people, comparable in gender and age. In patients with cirrhosis of the liver, as well as in patients with chronic hepatitis, emotionally labile, neurotic traits and high personal anxiety prevailed. The tendency to sympathicotonia depended on the severity of liver damage. The predominance of tone and reactivity of the sympathetic part of the autonomic nervous system is a compensatory enhancement of adaptive mechanisms.

**Keywords:** autonomic nervous system, autonomic reactivity, autonomic tone, personal anxiety, cirrhosis of the liver.

**Introduction**

Currently, there is an increase in the number of chronic liver diseases of various etiologies in all industrialized countries, especially among the able-bodied population. Cirrhosis of the liver (CL) is one of the six main causes of death at the age of 35-60 years and ranges from 14 to 30 cases per 100 thousand population. Etiological factors of the CL They are diverse, but alcohol and hepatotropic viruses play a leading role. The CL frequency of combined (alcohol + virus) genesis is high. In recent years, significant progress has been made in the study of the etiology, clinic and treatment of the pathology in question. However, many aspects of this problem still remain poorly understood, in particular, it relates to the functional state of the autonomic nervous system (ANS), which coordinates the work of the central nervous system and internal organs, regulates all vital processes in the body. Pathological conditions lead to a violation of the interaction of psychovegetative processes, which leads to altered reactions of the body to internal and external stimuli. Studying the state of the ANS will make it possible to predict the course of the disease and



optimize treatment tactics. ANS dysfunction is a determinant factor the development and severity of many diseases, especially the cardiovascular system and gastrointestinal tract. There are practically no such pathological forms in the occurrence and course of which the ANS would not play a role. In some cases, it is an essential factor of pathogenesis, in others it occurs a second time in response to damage any systems and tissues of the body. As a rule, vegetative disorders are secondary, occurring against the background of many mental, neurological and somatic diseases, which determines their pronounced syndromality. The existing methods of ANS research (measurement of blood pressure, heart rate, orthoclinostatic, oculocardial and other tests) are simple to perform and do not require additional costs when conducting them. Dynamic studies of the ANS activity using other methods (cardiorhythmography) are also used in normal and pathological conditions. Chronic liver pathology is accompanied by neuropsychiatric abnormalities that aggravate the course of the underlying disease. In the genesis of developing symptoms, a certain role along with liver cell insufficiency is played by the personality's reaction to a chronically progressive disease. Often, mental disorders are the first manifestation of chronic hepatitis and cirrhosis of the liver, persist throughout the disease and cause certain difficulties in the treatment of such patients. Out of the field of view of clinicians, there are often various options for the attitude of patients to their illness, treatment and rehabilitation. All this underlines the importance and relevance of timely and adequate diagnosis of mental disorders in patients in general somatic hospitals.

The aim of the study was to study psychovegetative disorders in patients with cirrhosis of the liver, depending on the severity of the disease.

#### **MATERIALS AND METHODS**

139 patients with CL (68 men and 71 women, average age  $(49.8 \pm 11.2)$  years) of various etiologies (viral — 36 (26%), alcoholic - 68 (49%), combined - 35 (25%) patients) and severity according to Chiles-Pugh: class A — 50 were examined (36.0%), class B — 44 (31.6%), class C — 45 (32.4%) patients. The comparison group consisted of 104 patients with chronic hepatitis (CH) of viral (27 (26%) patients), alcoholic (51 (49%)) and combined (26 (25%) patients) etiology. The control group was formed from 30 healthy people, comparable in gender and age. The diagnosis of "CL" and "CH" was made on the basis of anamnestic data, the results of an objective study, general clinical and biochemical indicators characterizing the functional state of the liver, as well as ultrasound examination of abdominal organs, esophagogastroduodenoscopy, determination of serological markers of viral hepatitis by ELISA, the replicative phase of virus development by reverse transcription — polymerase chain reaction. In a number of cases, a pathomorphological study of liver biopsies was carried out with the determination of the index of histological activity of hepatitis and the stage of liver fibrosis.

To identify the psychological characteristics of patients, an adapted standardized multifactorial questionnaire for personality research (SMPR), a self-assessment test of the level of personal and reactive anxiety of Spielberg were used— Hanina.



The study of the ANS was carried out by determining the initial vegetative tone by calculating the vegetative index of Kerdo (VIC), the index of minute volume (IMV) of blood, minute volume of blood (MVB), vegetative reactivity using the ocular-cardiac reflex (Dagnini—Ashner) and vegetative support of orthostatic test activity.

The initial vegetative tone was calculated according to the formulas:

$VIC = (1 - DB/HR) \times 100$ , where DAP is diastolic blood pressure;

Heart rate — heart rate in 1 min. By at an index equal to zero, vegetative equilibrium takes place, if the indicator is positive, then sympathetic tone prevails, and at negative values, parasympathetic prevails;

$IMV = (PD_f \times HRS_f) / (PD_n \times HRS_n)$ , where PD is pulse blood pressure, the numerator indicates the results of PD and heart rate, and the denominator indicates the indicators corresponding to age and gender norms for PD and heart rate (Kassirsky I.A., 1971). Normally, IMV is approximately equal to 1.

With an increase in sympathetic tone, the IMV value increases to 1.5—1.8, and with an increase in parasympathetic tone, the IMV value decreases to 0.7;

$MVB = (91 + PD/2 - 0.6 \times DAD - 0.6 \times V) \times HR$ , where 91 and 0.6 are correction coefficients; B is the age in years. Normally, the MVB is 4.4 liters, with an increase in sympathetic tone, this indicator increases, and if parasympathetic tone prevails, the MVB decreases. Considering everything indicators (VIC, IMV, MVB), it is possible to conclude about the predominance of sympathetic (sympathicotonia) or parasympathetic (vagotonia) influences or relative vegetative equilibrium (eitonia). When examining the ocular-cardiac reflex, the heart rate slows down. Normal vegetative reactivity is observed when the heart rate slows down for 6-12 strokes. A more pronounced slowing of heart rate corresponds to increased vegetative reactivity (parasympathetic reactions predominate). If there is a slowing of the heart rate by less than 6 beats, then reduced vegetative reactivity is determined. The absence of slowing down or increasing heart rate indicates perverted vegetative reactivity (sympathetic reactions predominate). In the study of vegetative reactivity, it is necessary to evaluate the initial vegetative tone, on which the body's response to the stressor depends. If the initial level is sharply changed, then the vegetative reactivity, Vegetative support of activity is understood as the ability to maintain optimal the level of functioning of the organs and systems of the body is adequate to the form, intensity and duration of activity. During the orthostatic test, the excitability of the centers of sympathetic innervation was determined by the degree of pulse increase (DPI) or by the increase in pulse (IP) in the first minute after the change of body position. DPI is expressed as a percentage relative to the original pulse. The excitability of the centers of sympathetic innervation is normal: weak (up to 9.1), average (9.2—18.4), lively (18.5—27.7). The excitability of the centers of sympathetic innervation is increased: weak (27.8—36.9), noticeable (37.0—46.2), significant (46.3—55.4), sharp (55.5—64.6), very sharp (64.7 or more).

The assessment of the state of the ANS allows to establish the possibilities of adaptive reactions of the body, to control the state of the regulatory processes of the cardiovascular system in a number of pathological conditions and the action of drugs, to carry out mathematical data processing.



Statistical data processing was carried out using the Statistica 6.0 program (StatSoft, USA). The groups were checked for the normality of the distribution of features using the Lilliefors criterion. The distribution of features in the compared groups did not obey the laws of normal distribution ( $p < 0.05$  for the Lilliefors criterion), therefore, the nonparametric Mann—Whitney criterion was used to compare the indicators between the groups. Since the distribution of features in the compared groups did not obey the laws of normal distribution, the description of quantitative data was carried out using the representation of the median  $Me$ , as well as the 25<sup>th</sup> The percentile is the lower quartile  $Q1$  and the 75th percentile is the upper quartile  $Q3$ . The results for all the methods used were considered statistically significant at  $p < 0.05$ .

## RESULTS

The examined patients complained, on the basis of which pain, dyspeptic and asthenovegetative syndromes were identified. There were no statistically significant differences in the frequency of occurrence of the described clinical syndromes between groups of patients with CL, depending on the severity. Thus, the pain syndrome in class A CL was expressed mainly by the severity in the right hypochondrium (90% of cases), with class B and C CL — pain in the right and left hypochondrium (55%), in the epigastric region (40% of cases). Quite often in patients CL had dyspeptic syndrome in the form of gastric and intestinal dyspepsia. The highest incidence rates were complaints of intolerance to fatty foods, bitterness in the mouth and nausea (up to 80%), as well as decreased appetite, heartburn and flatulence (up to 60% of cases). The frequency of these complaints increased with the severity of the disease. Such manifestations of asthenic syndrome as general weakness, decreased performance, and sleep disorders were noted in almost all patients with cirrhosis, regardless of the severity of the disease. Irritability, anxiety, and depression were found in 60-80% of cases in patients with CL class B and C. Dysregulation on the part of the autonomic nervous system was expressed by complaints of headache, hyperhidrosis of the palms, palpitations and lack of air, which were also more often observed in patients with CL class B and C (50-60%) in contrast to patients Class A CPU. Jaundice syndrome was detected in 93 patients with CL, the incidence of which increased depending on the severity of the disease: with class A CL — at 19 (38%), with a class B CL — at 32 (73%) and a CL Class C — in 42 (93%) patients. This syndrome is an indicator of the activity of the process and at the stage of cirrhosis may be a reflection of liver failure. Hepatomegaly with class C CL was observed in 30 (67%) patients, with class B CL — in 27 (61%), with class A CL— in 25 (50%) patients. A characteristic manifestation of cirrhosis is hemorrhagic syndrome, which was observed in 40 (89%) patients with class C CL, 20 (45%) patients with class B CL and 16 (32%) patients with CL class A. This syndrome has a complex genesis: it can be a manifestation of parenchymal hepatic insufficiency and vascular decompensation with the development of hypersplenism syndrome. Splenomegaly and the presence of varicose veins of the esophagus, which were more common in class C CL, are characteristic signs of decompensation of the CL by vascular type (41 patients — 91%). Edematous ascitic syndrome as a characteristic sign of decompensation of the CL, and encephalopathy



syndrome, which is one of the manifestations of liver failure, also corresponded to the severity class of cirrhosis of the liver. Cytolysis syndrome was detected in the majority of patients (in 80% of cases), regardless of the severity of CL according to Chiles-Pugh. Hepatodepressive (registered with a decrease in albumin and PTI levels) was statistically significant ( $p = 0.005$ ) more common in class C CL. Cholestasis syndrome and immunoinflammatory were statistically significant ( $p = 0.005$ ) more often observed in patients with class A CL in contrast to patients with CL Class B and C. When analyzing the average (by T-points) personal profile of SMPR in patients of the main group (CL class A, B and C according to Chiles-Pugh) and the comparison group (chronic hepatitis) statistically significant differences ( $p < 0.0001$ ) in emotional reactions and disorders of psychological status were revealed in comparison with the examined control groups. An increase in the average indicators of the SMPR psychological test (more than 50T points) observed in patients with cirrhosis and hepatitis is defined by some authors as an actual mental state characterizing the patient's reaction to diseases. This applied equally to the scales of the neurotic triad (hypochondria, depression, hysteria), which determine the psychological portrait of a chronic patient and the type of response to the disease, and the other scales of the SMPR profile, which carry information about deeper psychological changes in personality. In the studied groups, an increase in the parameters of the SMPR test, reflecting the severity of certain trends in the actual mental condition was observed on separate scales: hypochondria, depression, hysteria and paranoia. It should be noted that depressive reactions prevailed in patients in the cirrhosis group, whereas in the group of chronic hepatitis — reactions of anxiety and emotional lability. The relationship between the severity of cirrhosis of the liver by Chiles-Pugh classes and the psychological status of patients was revealed. High personal and reactive anxiety in patients with CL, unlike representatives of the control group and the comparison group, was confirmed using a self-assessment test of the level of personal and Spielberg—Khanin reactive anxiety. It should be noted that patients with CL, regardless of the severity of the course of the disease (CL class), had an increased level of both reactive and personal anxiety. The data obtained indicate the presence of neurotic disorders, emotional and psychosomatic disorders in patients with cirrhosis of the liver. Thus, the psychological portrait of a patient with CL turned out to be the following: emotionally labile, tends to demonstrate the disease and seeks sympathy, prone to hypochondria, fixation on pessimistic thoughts about his illness or beliefs in the erroneous diagnosis, the presence of another disease, selfish, anxious, dissatisfied with himself and his capabilities. To any endogenous or exogenous stimulus in a living organism, a reaction occurs, which is essentially protective and adaptive. These changes are reflected in the evaluation indicators of the autonomic nervous system, being a signal of a violation of the adaptive properties of the body. In the study of patients with CL, the tone of the ANS (according to the Kerdo vegetative index), the relationship of vegetative indicators of the cardiovascular system with the severity of cirrhosis has been established. VIC in patients with class A CL has a negative value, which indicates the predominance of parasympathetic tone. With the aggravation of the disease (CL class according to Chiles-Pugh) the VIC indicator acquires a positive value, which indicates the predominance of



sympathetic tone. These differences are statistically significant ( $p < 0.05$ ). By indicators IMO and IOC have the same pattern: with Class A and B CPUs, IMO is less than 1.0 and the IOC is less 4.4 l, which indicates the predominance of parasympathetic tone, with a CPU of class C IMO greater than 1.0 and The IOC is more than 4.4 liters, which indicates the predominance of sympathetic tone. In the control group, the initial vegetative tone was closer to eitonia, and in the comparison group — to moderate vagotonia. Vegetative reactivity, which characterizes the direction and degree of change in indicators reflecting the state of the ANS at the time of transition from one state to another, allows us to determine the dominant type of vegetative reaction to stress. Sympathetic type reactivity prevails in the group of patients CL of class C ( $p < 0.05$ ), according to the parasympathetic type in the group of patients with CL of class A and B ( $p < 0.05$ —0.01). The normal type of reactivity was registered in the examined control group. In the patients of the comparison group, normal vegetative reactivity was observed in half of the cases, the remaining responses were almost equally common: 24% — parasympathetic, 26% — sympathetic. When assessing the vegetative support of activity in the group of patients with CL, increased excitability was observed ( 22.85 - 12.25), without significant differences between classes of cirrhosis (CL with class A 28.19 - 13.18, with class B 27.84 - 11.48, with class C 27.48 - 12.5), but these indicators were statistically significantly different from the control and comparison groups ( $p < 0.05$ ).

The results obtained show that there are a number of differences in the vegetative maintenance of activity in patients with cirrhosis with varying degrees of severity of the disease, in patients with hepatitis and in healthy individuals. The study indicates a tendency to sympathicotonia in patients with a more severe course of the disease. Predominant predominance of tone, reactivity and maintenance the activity of the sympathetic department of the ANS is a compensatory enhancement of adaptive mechanisms and indicates the desire of the body to preserve homeostasis. Thus, the study of the psychovegetative state of patients is one of the necessary conditions in predicting the severity of liver damage.

## CONCLUSION

1. The psychological characteristics of patients with various classes of cirrhosis of the liver are characterized by emotionally labile, neurotic features and high personal anxiety.
2. With an increase in the class of cirrhosis of the liver, depressive and paranoid personality traits become more pronounced.
3. Indicators of vegetative tone in patients with cirrhosis of the liver with an increase in the Chiles-Pugh class are shifted towards an increase in sympathetic influences.
4. Vegetative reactivity according to the sympathetic type is characteristic of cirrhosis of the liver of class C, according to the parasympathetic type — for classes A and B.
5. The study of vegetative activity revealed increased excitability regardless of the class of cirrhosis of the liver.

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