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EFFECT OF THE AUTONOMIC NERVOUS SYSTEM ON THE CARDIOVASCULAR SYSTEM IN VIRAL HEPATIC CIRRHOSIS

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Abstract: Today it is known that cirrhosis of the liver can be accompanied by a violation of the functions of the heart, latent at rest, and manifested under the influence of stress factors. Physiological, physical, pharmacological and other causes can serve as stressors. In 2005, a working group consisting of reputable hepatologists and cardiologists adopted the definition of cirrhotic cardiomyopathy. Cirrhotic cardiomyopathy, according to experts, is one of the forms of chronic cardiac dysfunction and is characterized by a decrease in contractility in response to stress and/or a change in diastolic function with electrophysiological features in the absence of other known heart diseases. [4]. In liver diseases, including cirrhosis of the liver, vegetative liver disorders develop. Where there is a decrease in the influence of the parasympathetic nervous system and an increase in the influence of the sympathetic nervous system.

In liver diseases, including viral ones, vegetative disorders develop, leading to

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various complications from the internal organs. Violation of the autonomic nervous system leads to a decrease in the functions of the parasympathetic nervous system and an increase in the sympathetic nervous system. [1;2;5]. In violation of the autonomic nervous system, changes are observed from the gastrointestinal tract, symptoms such as rapid overflow of the stomach, nausea, vomiting, pain in the epigastric areas. In recent years, studies have begun to appear aimed at studying cardiac arrhythmias in liver diseases [3.].

The study of changes in cardiac activity depending on disorders of the autonomic nervous system leading to cirrhotic cardiomyopathy is the main goal of our study.

For the study, 146 patients aged 18 to 60 years were recruited, who were diagnosed with cirrhosis of the liver against the background of viral hepatitis, who were treated at the clinic of the Andijan State Medical Institute. Of these, 70 people had HCV, 76 had HBV, 5 of them had serological markers B and D. The control group consisted of 42 healthy people. Initially, the complaints of all patients, anamnesis and objective clinical condition were evaluated. Also, general clinical, biochemical, blood coagulation and enzyme immunoassays and instrumental studies (ECG, ECG Holter monitoring, ExoCG, Dopplerography of the liver and portal vein - UTT) were performed.

In B and C viral cirrhosis of the liver, an increase in the short-chain peptide cholecystokinin-8 was observed due to impaired utilization in pseudonormokinetic and decompensated portal circulation types than in hyperkinetic portal circulation types (respectively 2.86±0.26 ng/ml, 2.87±0.25 ng/ml, 0.72±0.08 ng/ml $P<0.01$), in as a result of an increase in short-chain peptide in the blood, there is a long-term effect on the activity of the sympathetic nervous system, which leads to a violation of the control of beta-adrenoreceptors, that is, a deterioration in systolic and diastolic activity, a violation of the electrical activity of the myocardium, prolongation of the QT interval, which ultimately leads to the development of cirrhotic cardiomyopathy.

Keywords: contraction of cardiomyocytes; autonomic nervous system, echocardiography, parasympathetic (vagal), liver, QT interval, cholecystokinin

Vegetative disorders are common in liver diseases, including cirrhosis developed on the basis of chronic viral hepatitis. In them, the activity of the parasympathetic nervous system decreases, on the contrary, the activity of the sympathetic nervous system increases. [2; 3; 4;; 5]. The observed changes in the autonomic nervous system are first manifested by a disturbance in the digestion of food in the stomach, and it is accompanied by clinical symptoms such as a

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feeling of rapid satiety, nausea, vomiting, pain in the epigastric area [1.].

In addition to the above, rhythm disorders observed in viral liver cirrhosis and their various manifestations have been actively studied in recent years. Taking into account the above, we performed ECG and overnight Holter monitoring in patients under our observation to study the effects of changes in the autonomic nervous system on the cardiovascular system. In addition, we performed echocardiography examination in patients.

Table 1 below shows the ECG changes observed in different groups of patients with liver cirrhosis developed on the basis of healthy and viral hepatitis.

1table

ECG changes observed in different groups of patients with liver cirrhosis developed on the basis of healthy and viral hepatitis

Indicators	Control group (n=42)	2 group n=29	3group n=65	4group n=52
Slowing of atrioventricular conduction, %	0	1 (3,4%)	3 (4,61%)	8 (15,6%)
Violation of the repolarization process, %	0	3 (10,3%)	21(32, 3%)*	21 (40,4%)*
Left ventricular hypertrophy %	0	4 (13,7%)	18 (27,7%)*	19 (36,5%)*
QT interval index, ms	381± 2,85	416±3,01	424 ±0,55 *	448±1,56 * ** ***

Note: *- P<0.05 – statistical difference compared to the control group; **- statistical difference compared to the 2nd group; ***- statistical difference compared to the 3rd group

As a result of the examination, sinus rhythm was detected in the ECG of all patients under observation. At the same time, in the second group 1 (1.8%), in the third group 3 (4.61%) and in the fourth group 8 (15.6%) subjects, it was noted that conduction through the atrioventricular node decreased, but when they were compared, the differences were not reliable (p>0.05).

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Violation of the repolarization process in the myocardium was not observed in the control group. In the second group3 (10.3%), in the third and fourth groups, 21 people were observed, their percentages were 32.3% and 40.4%, respectively. Disturbance of the repolarization process was more observed in patients of the third and fourth groups and reliably higher ($r<0.03$ and $r<0.007$, respectively) than in the patients of the second group. In the ECG, left ventricular hypertrophy was not noted in the control group. Left ventricular hypertrophy was detected in 4 (13.7%) patients in the second group, 18 (27.7%) in the third group, and 19 (36.5%) in the fourth group. Left ventricular hypertrophy was more observed in the fourth group of patients, and when the indicators were compared between the groups, the differences were reliably higher than those in the second and third groups ($r<0.03$ and $r<0.001$, respectively). In the second group of patients under our observation, the duration of the QT interval increased by 9%, and in the third and fourth by 11% and 15.5%, respectively, compared to the control group ($r<0.004$, $r<0.0003$, $r<0.0009$, respectively). At this point, it was observed that the fourth group increased the duration of this indicator by 7% and 5%, respectively, compared to the second and third group of patients ($r<0.02$ and $r<0.01$).

As we mentioned above, in our observation patients, together with the ECG, his overnight Holter monitoring examinations were performed. Information about them is given in 2 tables.

2 table

Changes observed during overnight Holter monitoring in different groups of patients with advanced liver cirrhosis based on healthy and viral hepatitis

Indicators	Control group (n=42)	2 group n=29	3group n=65	4group n=52
Sinus bradycardia	0	2 (6.8%)	9 (13.8%)	11 (21%)
Sinus tachycardia	0	3 (10.3%)	9 (13.8%)	22 (42.3%)**
Supraventricular extrasystole	0	0	6 (9,2%)	8 (15,4%)
Ventricular Extrasystole	0	1(0,68%)	0	4 (7,7%)
Atrioventriculasr blockage (1 step)	0	1 (3,4%)	14 (21,5%)*	12 (23,1%)*

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Paroxysmal supraventricular Tachycardia	0	0	3 (4,6%)	4 (7,7%)
Splittingofatriums	0	0	0	6 (11,5%)

Note: *-P<0.05 -reliability of statistical difference compared to 2 groups; **-P<0.05 - reliability of statistical difference compared to 3 groups

Sinus bradycardia was observed in 6.8% of the second group of patients, 13.8% and 21% in the third and fourth groups, respectively, during a day-night ECG examination. There was no reliable difference between the groups. Tachycardia was noted in 10.3%, 13.8% and 42.3% of patients in the above three groups of patients, respectively. Tachycardia in the fourth group was found to be more reliable than the other two groups (r<0.004 and r<0.02, respectively). Ventricular extrasystole was detected in 10.3% and 12.3% of patients in the third and fourth groups, respectively, and no reliable (R>0.05) difference between the groups was observed when the indicators were compared. No reliable changes were observed in the indicators of ventricular extrasystole.

Atrioventricular block (AV block) at 1 degree was detected in 1 (3.4%) of the second group, 7 (10.8%) of the third group and 8 (15.4%) of the fourth group. AV block in the third and fourth group of patients Grade 1 was more observed than the second group, and the difference was reliable (r<0.02 and r<0.01, respectively). Paroxysmal supraventricular tachycardias were observed in 1 (1.5%) patient in the third group and in 4 (7.7%) patients in the fourth group. Paroxysmal form of ventricular fibrillation was detected only in 6 patients (11.5%) in the fourth group.

As mentioned above, in patients with viral liver cirrhosis, the QT interval is prolonged in the ECG examination due to the activation of the sympathetic nervous system. In hyperkinetic and pseudonormokinetic types of blood circulation, in contrast to the control group, it was observed that the resistance to mental stress of the autonomic nervous system decreased. Due to the high level of cholecystokinin-8 indicators in the blood of patients with viral liver cirrhosis in the pseudonormokinetic type of the portal circulation system, it has been proven that the autonomic nervous system is more sensitive to mental stress. Prolongation of the QT interval and occurrence of arrhythmias were also observed more often in this group of patients. The obtained results show that the amount of short-chain peptide cholecystokinin-8 in

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the blood of patients with viral liver cirrhosis of the third and fourth groups is higher than the norm, which has a direct effect on the autonomic nervous system. As a result, changes in the myocardium are observed, which in turn are manifested by electrocardiography and various arrhythmias (prolongation of the QT interval, supraventricular and ventricular extrasystoles, paroxysmal supraventricular tachycardias and palpitations) and conduction disturbances that occur during overnight monitoring.

It is worth noting that various rhythm disorders are more often observed in hyperkinetic and pseudonormokinetic types of portal blood flow in liver cirrhosis. Therefore, it is reasonable to use the ECG Holter monitoring method in these classes of the disease.

At this point, taking into account that various changes in the myocardium are observed together with an increase in the short-chain peptide cholecystokinin-8 in the blood of patients, the determination of its amount in the blood can be considered as one of the screening methods with sufficient information in studying the functional state of the heart.

Conclusion. Due to the violation of the breakdown of the short-chain peptide cholecystokinin-8 in the liver due to the increase in its amount in the blood in viral liver cirrhosis and liver cirrhosis developed on the basis of viral hepatitis V and C, the indicators in the pseudonormokinetic type of portal circulation were higher than in the other groups (respectively 0.72±0, 08ng/ml, 2.87±0.25 ng/ml, 2.86±0.26 ng/ml, P< 0.01). As a result, long-term high activity of the sympathetic nervous system leads to a violation of control of β-adrenoreceptors. This condition leads to the development of cirrhotic cardiomyopathy, causing various changes in the heart

As a result of changes in the heart with advanced liver cirrhosis, NT-pro BNP values in the blood were significantly (P<0.001) higher than the control group in all studied groups. The highest rate was found in patients with pseudonormokinetic type of portal circulation

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