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Diagnosis of Asthenic Vegetative Syndrome in Patients with Chronic Viral Hepatitis Based On Correlation Analysis of Heart Rate Variability.

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ABSTRACT

In the given article were studied to increase the probability of detecting of asthenic vegetative disorders in patients with chronic viral hepatitis in the earlier stages of the disease. Based on statistical data analysis ECG and correlation analysis revealed the following correlations the state of severity in patients with autonomic indices circuit detection of autonomic disorders and heart rate variability, the severity of fatigue (one of the symptoms of asthenia) with heart rate variability, asthenia and autonomic dysfunction with the quality of life of patients. Identified correlations indicate that it is possible to increase the probability of detection of autonomic dysfunction in patients with chronic viral hepatitis in the early stages. The variability of heart rate can be used as a marker of fatigue in patients with chronic hepatitis. The suggested approach to the diagnosis of the syndrome in patients asthenic vegetative CVH provides a fairly objective data on the influence of asthenic vegetative syndrome on the quality of life of chronic viral hepatitis patients.

Keywords: asthenia, fatigue, autonomic dysfunction, asthenovegetative syndrome, chronic viral hepatitis, heart rate variability, quality of life.

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INTRODUCTION

Chronic viral hepatitis (CVH) is a serious social and health problem worldwide [1]. In this case, the hepatitis B virus is not only etiological factor of liver disease, but also causes the development of extrahepatic manifestations [2-4]. Clinic extrahepatic manifestations often come to the fore in the form of fatigue and autonomic dysfunction, which leads to a decrease in disability and social isolation of patients [5-7].

There are wide known works which are devoted to the appliance of the method of heart rate variability analyses to evaluate the condition of the autonomic nervous system in patients with chronic viral hepatitis [8-10]. However, this method is not widely used in the clinic due to autonomic dysfunction have low key role [11, 12].

In this context, this paper presents a new approach to asthenic vegetate syndrome diagnosing and uses it to evaluate the patients' quality of life.

The aim of this work was to increase the probability of detecting of asthenic vegetative disorders in patients with chronic viral hepatitis in the earlier stages of the disease.

METHODOLOGY

In the clinical study the electrocardiographic evidence of heart rate variability 157 patients with chronic hepatitis C virus-moderate male (n = 77) and female (n = 80), middle-aged sex $53,7 \pm 0,8$ years were obtained.

The criteria for including in the study group were: confirmation of the diagnosis CVH (presence of antibodies to HCV (anti-HCV), the identification of viral RNA (RNA HCV)), to moderate disease, the lack of anti-virus-therapy and corticosteroids. The pregnant and breastfeeding women, patients with cancer, with severe cardiovascular and renal insufficiency were not taking part in the research work.

In comparison the group of 41 practically healthy (PH) people who do not have any acute and chronic diseases of the male (n = 20) and female (n = 21), middle-aged sex $48,2 \pm 2,3$ years were examined.

Also, to explore options for the current CVH the groups of patients with ABC (48 patients, average age $58,1 \pm 1,0$ years) and jaundice (53 patients, average age $55,4 \pm 1,3$ years), matched by gender composition, were isolated.

All patients received standard therapy according to their indications: lactulose (Duphalac) spironakton; pentoxifylline, ursodeoxycholic acid (Ursosan) and some other preparations.

The study was conducted in RSBH "City Hospital № 2 of Belgorod" and on the clinical basis of the St. Petersburg State Medical Academy named after II Mechnikov.

RESULTS

Functional liver function was evaluated by clinical and biochemical parameters of blood.

To evaluate hepatocellular insufficiency diagnostic table Child-Pugh was used.

Asthenia was identified with the help of the subjective rating scale asthenia (Multidimensional Fatigue Inventory or MFI-20) developed by EM Smets. It contains 20 statements that reflect different aspects of fatigue, and is used to assess the severity of the various forms of fatigue: "general asthenia", "physical asthenia", "reduced asthenia", "lack of motivation" and "mental asthenia". Total score greater than 12 at least in one subscale total score or full scale above 60 are the basis of establishing the existence of fatigue.

To identify autonomic dysfunction syndrome a study scheme for autonomic dysfunction syndrome chart revealing (ADSC) by AM Wayne has been used. The scheme includes a set of questions aimed at identifying signs of autonomic dysfunction and contains 13 items. The total amount of points obtained in the study of

signs according to the scheme in healthy individuals should not be more than 25, in the case of excess can be the sign of autonomic dysfunction syndrome.

To evaluate the state of autonomic regulation it was used the modern methodology (RF patent number 2,233,616) of heart rate variability analysis and the method of diagnosis (RF patent number 31943) using the instrumentation hardware system "Omega". At the same time, along with the classic indicators of heart rate variability (mode, mode amplitude, variation range, the index of autonomic balance, vegetative index rate, adequacy of regulation processes and tension index) autonomic homeostasis index(AHI) was used. AHI calculated from more than 50 major indices: variation, autocorrelation, spectral analysis and quantification of chaosgram and reflects the degree of autonomic imbalance.

Quality of life research was conducted through a questionnaire SF-36, developed by J.E. Ware. All 36 items of the questionnaire are grouped into eight scales: "physical functioning", "role-playing activities," "bodily pain", "general health", "vitality", "social functioning", "emotional state" and "mental health." Grouping scales allows you to get two indicators: "mental and physical components of health."

The evaluation of the differences between the statistical distributions was performed using t-test. The correlation between the studied traits was detected by a linear Pierson correlation coefficient. For qualitative characteristics Spearman rank correlation coefficient was used. To identify the similarity of the phenomena under study two-factor analysis of variance was used. The data obtained in the study were processed on a personal computer using Microsoft Excel and the statistical program SPSS 12.0.

RESULTS AND DISCUSSION

The study of the functional state of the liver of patients with chronic viral hepatitis showed that the majority of patients had ALT elevations ($72,1 \pm 3,3$ U / L), alkaline phosphatase ($250,9 \pm 11,5$ U / L), γ -GTP ($76,4 \pm 3,0$ U / l), total bilirubin ($28,2 \pm 1,5$ mmol / l), markers of HCV.

Subjective rating scale fatigue allowed in patients with CVH to identify the high frequency of the following symptoms: decreased exercise capacity (75%), reduction of labor activity (67%), and an increased sense of fatigue (63%), decreased motivation (56%) and decreased concentration (31%).

Fatigue syndrome using a subjective scale of MFI-20 was detected in 63% of patients with chronic viral hepatitis and in 41% of healthy respondents.

Symptoms of autonomic dysfunction were observed even more often, than the symptoms of fatigue. Increased anxiety, anxiety and fear, mood swings were detected in patients with chronic viral hepatitis in more than 90% of cases. Deterioration of health because of the changing weather was detected in 80% of patients. On the poor tolerance of heat and stuffiness 76% of patients with CVH complained. Diagnostics with ADSC revealed autonomic dysfunction syndrome in 76% of patients with chronic viral hepatitis. With IHS "Omega" detection rate of autonomic dysfunction increased to 87%, which shows the great potential of this approach in comparison with ADSC.

In 57% of patients with chronic viral hepatitis was diagnosed autonomic dysfunction syndrome. At the same time 91% of patients with asthenia syndrome are accompanied by autonomic-dysfunction.

In a clinical study, AHI allowed us to divide all patients with chronic viral hepatitis autonomic regulation level into the following groups: patients with normal or satisfactory regulation (AHI 100-80%) - 3% of patients with functional regulation voltage (AHI 80-60%) - 5 % patients with overexertion or poor regulation (AHI 60-40%) - 16% of patients with depletion of the regulatory system - 76%.

In addition, using IHS "Omega" equilibrium states of autonomic regulation (eutonia) is generally considered the norm, can also be divided into groups based on the integral indicator of autonomic homeostasis and make a full assessment of eutonia (Table. 1).

Table 1: Autonomic tone in patients with CVH depending on the level of autonomic regulation

IT, cond. Units	(AHI 100-80)		(AHI 80-60)		(AHI 60-40)		(AHI 40-0)	
	n	%	n	%	n	%	n	%
Expressed sympathicotonia (ID > 500)	–	–	–	–	–	–	72	50,4
Moderate sympathicotonia (ID 200-500)	–	–	1	25	2	22	55	38,5
Vegetative balance (ID 50-199)	–	–	3	75	7	78	16	11,2
Moderate vagotonia (ID 25 -50)	2	100	–	–	–	–	–	–
Expressed vagotonia (ID < 25)	–	–	–	–	–	–	–	–

Note: IT - tension index of autonomic regulation; AHI – autonomic homeostasis index.

In patients with chronic viral hepatitis eutonia (MI 50-199 cond. Units) in 11.6% of the rate of vegetative homeostasis abnormalities reflect autonomic regulation (AHI 80-60%), 26.9% of patients showed significant changes in autonomic regulation (AHI 60 -40%), in 61.5% of patients defined by the expression violations in the autonomic regulation (AHI 40-0%).

HRV analysis using IHS "Omega" in CVH patients with mild degree of jaundice showed greater severity of autonomic imbalance compared with the group of patients with chronic viral hepatitis without jaundice (Table. 2).

Table 2: Average autonomic homeostasis index in CVH patients' groups according to the clinical form of the disease

Indicator units.	Norm	CHV patients' groups	
		Anicteric form, M±m	Icteric form, M±m
Mode, c	0,7–0,9	0,76±0,01	0,71±0,01**
Mode amplitude, %	30–50	60,1±2,3	68,3±1,9*
Variation range from	0,15–0,45	0,13±0,01	0,10±0,01**
Index vegetative balance, cond. u.	35–145	613,7±54,0	812,4±52,4*
Vegetative index rate, cond. u	0,25–0,6	0,19±0,01	0,16±0,01*
Adequacy of the suspension control processes, cond. u	15–50	81,3±4,2	98,5±3,8**
Tension index, cond. u.	10–100	427,3±44,2	595,9±45,7*
Index of autonomic homeostasis, %	60–100	22,2±2,1	13,4±1,4**

Note: The significance of the difference between the two groups: * p<0,05; ** p<0,01.

Using the SF-36 questionnaire it was found that some exponents, if the quality of life of patients with chronic viral hepatitis groups with FAA differed from that of the group of patients with chronic viral hepatitis without ABC (Table. 3).

Table 3: Averages of MOS SF-36 questionnaire results in CVH patients groups with ABC and without it and a group of healthy people without ABC

Averages	Groups		
	Patients with chronic viral hepatitis with ABC	Patients with chronic viral hepatitis without ABC	PH without ABC
Physical functioning	64,8±1,0	74,7±1,8***	95,9±0,7***
Role functioning	57,2±2,1	60,0±2,1	66,5±4,7
Physical pain	39,5±1,4	48,3±2,4**	69,1±3,0***
General health	27,6±1,2	44,0±2,2***	73,9±1,8***
The viability	33,6±1,2	42,1±1,8***	57,4±2,4*
Social functioning	63,4±1,5	67,8±1,8	77,1±3,2***
Emotional functioning	86,7±2,1	86,2±2,1	84,6±2,9
Psychological health	44,7±1,0	50,7±1,5***	63,2±2,3***
The physical component of health	36,5±0,5	41,3±0,7***	51,1±0,8***
Mental health component	41,8 ±0,5	43,2±0,7*	45,8±1,2**

Note: The significance of the difference between the two groups: * p<0,05; ** p<0,01; *** p<0,001.

Despite the fact that the correlation between the average scores of the rating scale and asthenia ADSC was weak ($r = 0,23$; $p < 0,05$), the average correlation between an indicator of fatigue rating scale - "general fatigue" and the average score ADSC ($r = 0,41$; $p < 0,05$) was found. The correlation between the average force ADSC average score and a score of his being - truth degree the following statements: "I feel tired" ($r = 0,35$; $p < 0,05$), «I feel rested» ($r = 0,40$; $p < 0,05$) and "I get tired fast" ($r = 0,36$; $p < 0,05$) was observed. Also, the indicator of "general fatigue" had contact with the index of regulatory systems tension ($r = 0,39$; $p < 0,05$), while the relationship between the average of the rating scale fatigue and stress index was weak ($r = 0,26$; $p < 0,05$).

The total score and ADSC indicator "mental health component" of quality of life questionnaire SF-36 had an average negative correlation ($r = -0,40$, $p < 0,05$), while the connection with the indicator "physical health component" of the same questionnaire was weak ($r = -0,18$, $p < 0,05$). Between the total score of MFI-20 and "physical health component" is set correlation of medium strength ($r = -0,44$; $p < 0,05$), but with "a mental health component of the" correlation was weak ($r = -0,11$; $p < 0,05$).

The correlation is established between the index of hepatocellular failure according to Child-Pugh with a total score of ADSC ($r = 0,43$) and the index of regulatory systems tension (IHS "Omega") ($r = 0,48$) at $p < 0,05$. The total score of the scale MFI-20 at the same time had little connection with the indicator of hepatocellular failure according to Child-Pugh ($r = -0,12$; $p < 0,05$).

CONCLUSIONS

Based on statistical data analysis ECG and correlation analysis revealed the following correlations:

- The state of severity in patients with autonomic indices circuit detection of autonomic disorders and heart rate variability;
- The severity of fatigue (one of the symptoms of asthenia) with heart rate variability;
- Asthenia and autonomic dysfunction with the quality of life of patients.

Identified correlations indicate that:

- It is possible to increase the probability of detection of autonomic dysfunction in patients with chronic viral hepatitis in the early stages.
- The variability of heart rate can be used as a marker of fatigue in patients with chronic hepatitis.
- The suggested approach to the diagnosis of the syndrome in patients asthenic vegetative CVH provides a fairly objective data on the influence of asthenic vegetative syndrome on the quality of life of chronic viral hepatitis patients.
- There is an opportunity to use this approach for diagnostic evaluation of the effectiveness of correctional treatment asthenic vegetative syndrome.

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