POINT OF VIEW

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G.A. Usenko, D.V. Vasendin, A.G. Usenko, A.V. Uskov EFFECTIVENESS OF ANTIHYPERTEN-SIVE ARTERIAL THERAPY CONSIDERING EQUILIBRIUM OF CORTICAL PROCESSES IN THE CENTRAL NERVOUS SYSTEM AND PARTS OF THE AUTONOMIC NERVOUS SYSTEM

In the last 20 years, there has been no significant reduction in the level of cardiovascular diseases. At the same time, arterial hypertension and coronary heart disease are leading in the structure of overall morbidity. Various environmental conditions Influence the course of arterial hypertension and coronary heart disease. The latter is able to significantly potentiate emotional stress. In connection with the above, solving issues of effective therapy and secondary prevention play a significant role in the clinical management of patients suffering from cardiovascular diseases. However, in equal conditions, the clinical course of diseases differs in different patients, some individuals have more pronounced changes, while others have less. This may be due to the activity of the Central nervous system, the type of higher nervous activity, and the state of equilibrium of cortical processes. It is assumed that the course of hypertension may have its own characteristics in patients with different characteristics of excitatory or inhibitory processes in the Central nervous system, and the establishment of effective antihypertensive therapy in the process of a differentiated approach to higher nervous activity will contribute to the justification of targeted (targeted) or personalized antihypertensive therapy. The aim of the study was to determine the effectiveness of personalized pharmacotherapy in patients with arterial hypertension with different characteristics of excitatory or inhibitory processes in the Central nervous system. The prevailing type of higher nervous activity (equilibrium of cortical processes) was determined by the reaction to a moving object. The presence and severity of depression were determined using psychological tests by Je. Akhmetzhanov. The quality of life was determined using the «SAN» test (health, activity, mood, score). The effectiveness of antihypertensive therapy was also judged by the value of the hand endurance coefficient (spring dynamometer with a fixed arrow). The coefficient of endurance of the hand was determined by the ratio of the strength of the hand in the 3rd press to the strength in the 1st (× 100%). The activity of the autonomic nervous system was determined by calculating the initial vegetative tone of the body. The results of the study determined the significant effectiveness of personalized pharmacotherapy of arterial hypertension, depending on the prevalence of excitatory (correction of sympathicotonia with highly selective beta-blockers) and inhibitory processes in the Central nervous system (blockade of mineralocorticoid receptors with spironolactone/eplerenone) in comparison with the empirical treatment option. Randomized clinical trials of this new promising approach are appropriate. Keywords: arterial hypertension, personalized antihypertensive therapy, the activity of the Central nervous system.

Introduction. In the last 20 years, there has been no significant reduction in the level of cardiovascular diseases (CVD). At the same time, arterial hypertension (AH) and coronary heart disease (CHD) are leading in the structure of overall morbidity) [1, 6, 11, 12]. Various environmental conditions affect the course of hypertension and CHD [3, 8, 10, 16]. The latter can significantly potentiate psychoemotional stress. In con-

nection with the above, the solution of issues of correction of the peculiarities of the psychoemotional status of patients. effective pharmacotherapy, secondary prevention play a significant role in the clinical management of patients suffering from CVD [5, 7, 9, 17]. However, under equal conditions, some individuals have more pronounced changes, while others have less [13, 14]. The latter is probably related to the activity of the Central nervous system, the type of higher nervous activity (GNI), and the state of equilibrium of cortical processes. It is assumed that the clinical course of hypertension may have its own characteristics in patients with different characteristics of excitatory or inhibitory processes in the Central nervous system, and the establishment of effective antihypertensive therapy in the process of a differentiated approach to GNI will contribute to the justification of targeted (targeted) or personalized antihypertensive therapy (AHT).

Objective: to evaluate the results of treatment of men with hypertension who differ in psychosomatic status, in the coefficient of hand endurance and the coefficient of oxygen utilization by tissues using the "well-being, activity, mood" test; to determine the effectiveness of person-

alized pharmacotherapy in patients with hypertension with different characteristics of excitatory or inhibitory processes in the central nervous system. After establishing patients men features of hypertension (hypertension of stage II) with high and low anxiety level and prevalent type of GNI, a standard empirical AHT (EAT) compared with personalized AHT (PAT), aimed at correction of in patients with sympathicotonia predominance of excitatory processes in the CNS or in other patients with the prevalence of inhibitory processes - the blockade mineralokortikoidna receptors of the reninangiotensin-aldosterone system (RAAS).

Material and methods. Study design: outpatient, single – center, cohort, prospective, controlled, non-randomized, long-term clinical trial (2011-2018). Contingent: patients with AH (n=328,41 patients with high (HA) and low (LA) anxiety on the background of EAT and PAT), engineering and technical workers, aged 44-62 years (average 54±1,8 years) were divided by type of GNI into equal groups with the prevalence of excitatory (sympathotonia) or inhibitory (parasympathotonia and activation of RAAS) processes in the Central nervous system, taking into account anxiety (HA and LA). The

USENKO Gennady Aleksandrovich - doctor of medical Sciences, Professor of Department of hospital therapy of the medical faculty of FSEI HPE 'Novosibirsk state medical Universitv'. MH RF, e-mail: vasendindv@gmail.com; VASENDIN Dmitry Viktorovich - candidate of medical Sciences, associate Professor; associate Professor of technosphere safety Department of FSBEI HE 'Siberian state Universitv of geosystems and technologies', Ministry of science and higher education RF: e-mail: vasendindv@gmail.com; USENKO Andrey Gennadievich - candidate of medical Sciences, the doctor of functional diagnostics office, SBIH Novosibirsk region 'Novosibirsk regional hospital №2 for war veterans', e-mail: h2vv@ mail.ru; USKOV Alexey Vladislavovich head of the FSI 'Military clinical hospital No. 425' of the Ministry of defense RF, e-mail: 425vg_1@mil.ru



examination revealed hypertension in stage II (GB-II, grade 2, risk 3) according to the criteria set out in [11, 12]. The average duration of the disease was 11,6±1,4 years. The control indicators were data from 164 healthy men who were compatible in terms of anthroposocial parameters. The prevailing type of GNI (equilibrium of cortical processes) was determined by the reaction to a moving object [4]. The value of reactive and personal anxiety was determined by the method of Yu.L. Khanin [15]. Persons who scored 32,0±0,6 points are classified as LA, and those who scored 42,8±0,4 points or higher are classified as HA. The study took into account the degree of depression (D, score) on the depression scale of Je.A. Akhmetzhanov [2], which was taken into account in the process of conducting AHT. Quality of life (QOL) was determined using the «SAN» test (health, activity, mood, score) [4]. The effectiveness of AHT was also judged by the value of the coefficient of endurance of the hand (CEH,%) (spring dynamometer with a fixed arrow). CEH, % was determined by the ratio of the hand strength in the 3rd press to the strength in the 1st (x 100%) [4]. The activity of the VNS departments was determined by calculating the initial vegetative tone of the body according to the method of a.m. vane [4]. In individuals with a predominance of excitatory processes, the activity of the sympathetic, and in individuals with inhibitory processes in the Central nervous system the parasympathetic part of the ANS. It was found that a mild degree of neurogenically induced depressiveness (D) was observed only in HA patients with a predominance of braking processes (BP) in the Central nervous system. For the rest of the examined individuals, the values were lower than mild D. In this regard HA ill with the prevalence of excitatory processes was obtained in 96% anxiolytic diazepam 2,5 mg morning and night, and HA ill with the prevalence of TP in the Central nervous system in 96% of the antidepressant tianeptine 12,5 mg in the morning and at night in 4% of cases, sertraline 25 mg /day. The content of cortisol and aldosterone in blood serum was determined by radioimmune method (CEA-IRE-SORIN, France - Italy). The minute volume of blood flow (MVB) was taken into account on the 6-NEG device and by the calculation method. Determination of the coefficient of oxygen utilization by tissues (COUT, %) was performed using the blood gas analyzer «STAT PROFILE. pHOx». AHT included: highly selective beta-blocker metoprolol, 100 (for LA) - 200 (for HA) mg/day, angiotensin converting enzyme (iACE) inhibitor enalapril. 20 mg/day, diuretic hydrochlorothiazide, 12,5-25 mg/day. HA-patients with predominance of excitatory processes in the Central nervous system received hydrochlorothiazide, 25 mg/day, and HT with excitable processes (EP) in the Central nervous system - 12.5 mg/day. Of the iACE, HA patients in 96% took enalapril, 20 mg/day + spironolactone 100-200 mg/ day (in 75%), less often (25%)-hydrochlorothiazide, 25 mg/day, since their blood potassium content was lower than in patients with EP. LA patients with a predominance of inhibitory processes in the Central nervous system received enalapril, 10 mg/day + hydrochlorothiazide, 12,5 mg/ day. A special feature of the appointment of personalized at: sympathicotonia in patients with a predominance of EP, compared with individuals with BP, the activity of the sympathetic part of the ANS and HGNS (cortisol) was high. The latter was blocked by beta-blockers. In individuals with BP, compared with those who had a predominance of excitatory processes in the Central nervous system, against the background of parasympathicotonia, the activity of RAAS (for aldosterone) was high, which was blocked by iACE. All other variants of at are called empirical, or EAT. This approach, taking into account GNI (by temperament), which is consistent with the presented scheme of AHT, made it possible to effectively and at an earlier time reduce the manifestations of left ventricular hypertrophy in patients [9].

The data were processed using variational statistics ($M\pm m$) using the standard software package «Statistica 7.0» and the student's parametric t–test, the Mann-Whitney U-test. The values at p<0.05 were considered statistically significant. The study was performed in compliance with the provisions of the Helsinki Declaration on the examination and treatment of people and approved by the ethics Committee of the Novosibirsk state medical University on 27.10.2009, Protocol No. 19.

The results of the study and their discussion. The study showed that on the background of both variants of AHT quality of life (test SAN) (table 1), the magnitude of CEH (table 2) and COUT, as well as the MVB have HA (LA) healthy and HA (LA) patients, was significantly reduced in sequences from individuals with a prevalence of excitatory processes in the Central nervous system to persons with the prevalence of the brake.

From HA individuals quality of life (for the SAN) and CEH was significantly lower than in lowanxiety, and HA (LA) patients on the background of EAT lower than that of HA (LA) healthy individuals of appropriate state of cortical processes of the CNS. However, against the background of PAT's quality of life (for the SAN) and the magnitude of ICC, IOC and KUCT was the same as in healthy individuals of the appropriate type GNI. Analysis of the data showed that the magnitude of KOUT have HA (LA) individuals was significantly reduced in the sequential series from those with a prevalence of excitatory processes to persons with a prevalence of brake processes in the Central nervous system (fig. 1). Against the background of both variants of AHT, the value of AHT in high-anxiety individuals was significantly lower than in low-anxiety individuals. However, HA (LA) patients on the background of EAT amount COUT was lower than in healthy HA (LA) individuals of the corresponding type of activity of the cortical processes in the CNS, and patients who have used the CAT. the value of COUT did not differ from that in healthy HA (LA) individuals of the appropriate type of HNA.

Fig. 1. The coefficient of oxygen utilization by tissues in high (VOT) and lowanxiety (NT) patients with hypertension with a predominance of excitatory or inhibitory processes in the central nervous system against the background of ET and PAT for the study period 2011-2018.

Thus, if the treatment was aimed at arresting the activity of the RAAS (by aldosterone) in patients with the prevalence of the BP in the Central nervous system, and of sympathicotonia in patients with the prevalence of EP in the Central nervous system, the amount of oxygen utilization by tissues (for COUT) was higher than on the background of EAT, and approached that in healthy HA (LA) individuals of the appropriate type HNA by equilibrium of cortical processes in the CNS. The success of the study is consistent with the results of other studies [9], where the authors reduced the time for remodeling left ventricular hypertrophy using PAT, in contrast to EAT.

The value of MVB (calculated and determined by tetrapolar rheovasography) from healthy HA (LA) and patients with hypertension HA (LA) males was significantly reduced in the sequential series from those with a prevalence of excitatory processes in the Central nervous system to the persons with predominance of inhibitory processes in the CNS (Fig. 2, 3). This decrease was observed both on the background of EAT and on the background of PAT. The peculiarity is that against the background of PAT, in contrast to empirical therapy, the MVB indicators (calculated and hardware) did not

Table 1

Quality of life according to the level of "well-being, activity, mood" (score) on the "SAN" test in patients with ET and PAT for the study period from 2011 to 2018.

		The equilibrium of cortical processes in the central nerv- ous system is shifted towards the predominance of processes			
		excitatory	brake systems		
Highanxiety	EAT	4.2±0.1 41	3.0±0.1 41		
	PAT	5.8±0.1 41	4.3±0.1 41		
	Health	5.7±0.1 41	4.7±0.1 41		
Lowanxiety	EAT	5.0±0.1 41	4.3±0.1 718		
	PAT	6.7±0.1 41	5.8±0.1 41		
	Health	6.8±0.1 41	5.9±0.1 41		

Note. Here and further on, the denominator indicates the number of persons in the group

significantly differ from those in HA (LA) healthy individuals of the corresponding state of equilibrium of cortical processes.

An important component of PAT is that the achievement of the target MVB by PAT was combined with an earlier and more pronounced approximation of the left ventricular mass to that of healthy HA (LA) individuals of equal temperament.

The data obtained by us showed that the utilization of oxygen by tissues decreased in a sequential series from individuals with a predominance of excitatory processes to those with TP in the Central nervous system, both in healthy and in patients. In the background of any at the sympathotonics minute volume of blood flow was higher than parasympathotony. Despite the lower MVB, parasympathotonics with TP in the Central nervous system, in contrast to those with EP in the Central nervous system, have higher anxiety and a tendency to depression. We considered this to be a consequence of a lower level of oxygen utilization by tissues (according to COUT), which also indicated the peculiarities of the course of hypertension depending on the type of HVA.

A review of the scientific literature over the past 20 years shows a great interest of cardiologists and therapists in studying the psychosomatic features of hypertension in conditions of chronic stress [3, 4, 8, 10], as well as the influence of psychosocial factors and stress on the course of AH [13]. However, in various reports, the Coefficient of hand endurance (%) by the ratio of the force in the third press (kg) of the dynamometer spring to the force in the First press (kg) in patients with ET and PAT during the study period from 2011 to 2018.

		The equilibrium of cortical processes in the central nervous system is shifted towards the predominance of processes							
		excitatory			brake systems				
Dynamometer press		I, kg	III, kg	CEH, %	I, kg	III, kg	CEH, %		
Highanxiety	EAT	54.7±0.9 41	42.2±0.9 41	78.1±0.8 41	50.1±0.9 41	37.6±0.7 41	75.0±0.8 41		
	PAT	54.6±0.5 41	53.6±0.5 41	98.2±0.2 41	52.0±0.3 41	50.1±0.4 41	96.4±0.4 41		
	Health	54.7±0.4 41	53.6±0.4 41	98.1±0.3 41	51.7±0.5 41	49.5±0.5 41	95.7±0.3 41		
Lowanxiety	EAT	51.3±0.5 41	45.3±0.5 41	88.3±0.5 41	47.5±0.4 41	39.7±0.4 41	83.5±0.3 41		
	PAT	$53.4 \pm 0.4 \\ 41$	51.9±0.3 41	99.3±0.4 41	49.5±0.3 41	${}^{48.8\pm 0.3}_{41}$	98.6±0.3 41		
	Health	53.3±0.3 41	52.9±0.5 41	99.3±0.1 41	50.6±0.3 41	49.5±0.4 41	97.8±0.2 41		

Note. I, kg – the force of the brush in the 1st fluid of the dynamometer; III, kg-the force of the brush in the 3rd press of the dynamometer

authors investigated anxiety across the entire group of patients, without identifying HA and LA individuals, and without taking into account the type of HNA for the equilibrium of cortical processes. The majority of outpatients with hypertension and CHD showed a predominance of signs of anxiety and depression. However, this was less common in this study compared to previous studies in Russia. In the available literature, such approaches to personalized pharmacotherapy have not been developed.

The observed progress in the treatment of hypertension is associated with the introduction of new antihypertensive drugs, including combined dosage forms. However, the level of mortality and morbidity remains high [6]. The reasons for this are different, including stressful situations, low adherence of patients to treatment [5, 12]. Against the background of our results, we can assume that in the course of empirical therapy, the use of combined drugs contributes to a decrease in the activity of RAAS, but increases the already pronounced prevalence of parasympathicotonia in patients with a predominance of inhibitory processes in the Central nervous system.

It should be noted a certain novelty of the proposed approach to at. It lies in the fact that the correction of sympathicotonia in patients with the prevalence of excitatory processes, and in other patients with a prevalence of brake processes in the Central nervous system activity of the renin-angiotensin-aldosterone system (aldosterone), as well as anxiety from HA individuals combined with the increase of utilization of oxygen by the tissues (cells) to the level of that in healthy individuals of the appropriate type of HNA. With this you can link the decline in the propensity to depression in patients with inhibitory processes in the Central nervous system and tension in the cardiovascular system (for MVB) in patients with a predominance of excitatory processes in the CNS.

In contrast to EAT, in PAT, the values of the studied indicators (anxiety, propensity to depressiveness, COUT, MVB) did not differ from those in healthy individuals of the corresponding type of HNA. The effectiveness of PAT is also evidenced by the fact that the time of remodeling of left ventricular hypertrophy can be reduced in comparison with EAT [9]. It is promising to further study the long-term results of long-term correction of changes in the thickness of the intima-media complex of arteries in patients with hypertension with different CNS activity and HNA type against the background of personalized at.

Conclusion. The differences between the studied indicators of patients with VP and TP on the background of AGT and AGT indicate the feasibility of separation of patients with psychosomatic status and activity of the cortical processes of the CNS and ANS divisions. A greater effectiveness of personalized pharmacotherapy of hypertension was determined depending on the prevalence of excitatory (correction of sympathicotonia with beta-blockers) and inhibitory processes in the central nervous system (block-

Table 2





Fig. 1. The coefficient of oxygen utilization by tissues in high (VOT) and low-anxiety (NT) patients with hypertension with a predominance of excitatory or inhibitory processes in the central nervous system against the background of ET and PAT for the study period 2011-2018.



Fig. 2. Minute volume of blood flow in high (VOT) and low-anxiety (NT) patients with hypertension with predominance of excitatory processes in the central nervous system against the background of ET and PAT during the study period 2011-2018.



Fig. 3. Minute volume of blood flow in high (VOT) and low-anxiety (NT) patients with hypertension with a predominance of inhibitory processes in the Central nervous system against the background of EAT and PAT during the study period 2011-2018.

ade of mineralocorticoid receptors with spironolactone/eplerenone) compared to the empirical treatment option. Randomized clinical trials of this new promising approach are appropriate.

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E.K. Popova, N.S. Arkhipova, E. A. Ignatiev, D.V.Solovieva, I.O. Popov

COMBINATION OF AUTOIMMUNE HEPATI-TIS WITH SYSTEMIC LUPUS ERYTHEMA-TOSUS. CLINICAL OBSERVATION

Abstract: The autoimmune hepatitis (AIH) is a chronic disease of the liver with different clinical phenotypes where significant roles have autoimmune processes of failed self-tolerance mechanism to own hepatocytes. Some other autoimmune diseases such as lupus are also observed with AIH. On the example of clinical observation we present features of course of the AIH with lupus on the background, the challenges of the diagnosis and treatments. During the research we identified a relationship between two autoimmune diseases based on association of autoimmune disorders with major histocompatibility complex.

Keywords: Autoimmune hepatitis, lupus, autoantibodies, liver encephalopathy, immunosuppressive therapy.

POPOVA Elena Kapitonovna - Cand. Sci. Medicine, Associate Professor at the Department of Propedeutic and faculty therapy with endocrinology and exercise therapy, Medical institute, M.K. Ammosov North-Eastern Federal University (NEFU), e-mail: ecapopova@yandex.ru, http://orcid.org/0000-0002-9338-1644; ARKHIPOVA Natalya Spartakovna - Cand. Sci. Medicine, Cardiologist Republican Hospital №1 - National Center of Medicine, http:// orcid.org/0000-0002-6433-3424; IGNATIEV Egor Albertovich - Student of Medical Institute of M.K. Ammosov North-Eastern Federal Universitv (NEFU), https://orcid.org/0000-0001-8815-6824: SOLOVIEVA Diana Vladimirovna - Student of Medical Institute of M.K. Ammosov North-Eastern Federal University https://orcid.org/0000-0003-4496-(NEFU), 6707; POPOV Ivan Olegovich - Postgraduate of Medical Institute of M.K. Ammosov North-Eastern Federal University (NEFU), http://orcid.org/0000-0002-0876-561X.

Autoimmune hepatitis (AIH) is a chronic diffuse liver disease with various clinical phenotypes, laboratory and histological manifestations. The worldwide prevalence of AIH is increasing annually, currently at <30 cases per 100,000 people, regardless of age and ethnicity, with a gender ratio of 4:1 for women over men [7]. The most important issue in the study of this disease is the search for trigger factors and genetic predisposition. In clinical practice, there are also acute problems of early diagnosis and differentiation with other diseases. Thus, most cases are observed among women with increased gamma globulin titers, Immunoglobulin G (IgG), presence of antibodies (Abs) as well as human leukocyte antigen (HLA) DR3 and DR4, morphological signs of periportal hepatitis and a favorable response to immunosuppression [6].

To date, the pathogenesis of AIH remains incompletely understood. It is known that autoimmune processes with impaired tolerance to the liver's own cells are crucial. In clinical practice, timely diagnosis of AIH is difficult, the disease may have a fulminant course, which not infrequently leads to the omission of the possibility of timely therapy in the initial stages of the disease, as well as the development of other autoimmune or immune-mediated pathological diseases. Among them, there is an association of AIH with systemic lupus erythematosus (SLE).

Autoimmune or immune-mediated diseases such as autoimmune thyroiditis, rheumatoid arthritis, type-1 diabetes, systemic lupus erythematosus, Sjögren's syndrome, celiac disease and immune thrombocytopenic purpura may develop at any stage of AIH. SLE is characterized