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THE ROLE OF ACTIVATION OF THE SYMPATHETIC NERVOUS SYSTEM IN THE PATHOGENESIS OF ARTERIAL HYPERTENSION AND THE CHOICE OF A METHOD FOR THE TREATMENT OF ARTERIAL HYPERTENSION

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SUMMARY

The basis for the successful treatment of any disease is a clear understanding of its cause, the mechanisms of its development, and their relationship to symptoms. The article considers one of the links in the pathogenesis of arterial hypertension – an increase in the activity of the sympathetic nervous system, describes the main methods for detecting hypersympathicotonia, approaches to the selection of drug therapy.

Key words: *arterial hypertension, sympathetic nervous system, hypersympathicotonia, beta-blockers, heart rate variability.*

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Despite of undoubted successes in the treatment of arterial hypertension (AH), this disease remains for many years the undisputed leader among the causes of morbidity and mortality throughout the world. Indeed, about half of all cases of complications of cardiovascular diseases occur in hypertension, the contribution of hypertension to the risk of fatal and nonfatal stroke, heart failure, myocardial infarction is high [1].

Another distinct trend in the modern world has been a significant decrease in the age of debut of AH – more and more young people have an elevated level of blood pressure (BP). In the Russian Federation, the number of young and middle-aged patients with identified hypertension is 44% (the results of the ESSE study) [2]. This category of patients often identify "AH in the workplace". And the leading role in the development of hypertension in this category of patients is the hyperactivation of the sympathetic link of the autonomic nervous system (sympathetic hyperactivation) as a natural, physiological response of the body to functioning under conditions of constant stress. In the future, stress is fixed, an increase in heart rate (HR), blood pressure is formed, the process of pathological activation of the renin-angiotensin-aldosterone system (RAAS) started, remodeling of blood vessels, hearts, involvement in the pathological process of other target organs – the brain, kidneys and etc. The result is the development of heart failure and death of the patient [3].

Is the role of the sympathetic nervous system in the pathogenesis of hypertension proved? Certainly yes. Then it is logical to assume that a decrease in the activation of the sympathetic nervous system (SNS) should lead to the normalization of blood pressure. It is this hypothesis that was remarkably confirmed by the method of radiofrequency denervation of the renal arteries in resistant hypertension. However, in this case the success of therapy is not equal to 100%. A significant number of patients who received radiofrequency denervation of the renal arteries as therapy for hypertension did not receive the proper effect-an elevated level of blood pressure persisted [4]. Does this mean that the hypothesis about the role of activation of the sympathetic nervous system

(SNS) is not sustainable? No. And here the primary degree of hyperactivation of the sympathetic nervous system (SNS) comes to the fore. hus, in further studies of this problem it will be advisable, when choosing the method of AH therapy, to take into account the degree of activation of the SNS.

What are the ways to assess the degree of SNS activity?

The simplest and most obvious, coming from the obvious effects of stimulating the SNS - high heart rate.

Indeed, in modern recommendations for the diagnosis and treatment of hypertension, this indicator is specified– heart rate more than 80 beats per minute [5]. How accurate and objective is it? The indicator is highly dependent on compliance with measurement rules. Its main advantage is that it is simple to define. In conditions of real polyclinic practice, there is nothing easier than to determine heart rate and take this into account when choosing a method of treatment.

The second obvious way is to determine the concentration of catecholamines in the blood. Indeed, in a stressful situation, there is a more than 10-fold increase in the level of adrenaline and noradrenaline - the main mediator of nerve impulse transmission in the SNS. Consequently, a persistent increase in serum norepinephrine concentrations may be an important biochemical marker of increased SNS activity, but remember the synthesis of epinephrine and norepinephrine by adrenal cells, and not only in postganglionic neuronal outgrowths.

Since the concentration of norepinephrine in blood plasma is influenced not only by the hormone synthesis in SNS structures, it is more important from the clinical point of view to estimate the concentration of noradrenaline is to determine its release from synaptic endings using tritiated norepinephrine. It is believed that such an assessment will be most accurate and, therefore, the most promising in terms of the quality of detection of hypersympathicotonia.

It is possible to assess the state of the SNS and with the help of functional samples. However, a sample with an isometric load, as well as an orthostatic test with baroreflex evaluation, are more applicable to assessing the hypnosis of the SNS. The calculation of the Valsalva coefficient, performed when carrying out the test of the same name, makes it possible to evaluate the interaction of the sympathetic and parasympathetic parts of the nervous system.

It is difficult to overestimate the importance of microneurography in assessing the degree of SNS activity. This method shows not only the level of local activation of the SNS, but also the severity of systemic sympathetic activity.

Promising is the one-photon emission tomography method with metaiodobenzylguanidine, which makes it possible to identify sympathetic nerve endings, to evaluate the metabolism of noradrenaline in the synaptic gap, and indirectly to estimate the density of beta-1 receptors [6].

But the most promising from a clinical point of view, in our opinion, is the method for assessing heart rate variability (HRV) – a quantitative statistical analysis of the duration of RR intervals over a short (5 minutes) or 24 hours continuous recording of an electrocardiogram.

During ECG analysis, the following calculation is performed:

SDNN is the standard deviation of NN (RR) intervals. It is used to assess the overall variability of heart rhythm.

SDANN is the standard deviation of the average values of NN intervals computed over 5-minute intervals throughout the record.

SDNNi is the average of the standard deviations of NN intervals computed over 5-minute intervals throughout the record.

RMSSD is the square root of the mean sum of squared differences between adjacent NN intervals.

NN 50 is the number of pairs of neighboring NN intervals that differ by more than 50 m / s over the entire record.

pNN 50 is the value of NN 50 divided by the total number of NN intervals.

As an example, we give the results of daily monitoring of the 57 y.o. patient's ECG on a background of chronic stress (Figure 1). The results of the time analysis in this patient reflect chronic sympathetic hyperactivity: mean heart rate 95.74 beats per minute, SDNN 107.3 ms, RMSSD18.9 ms, narrow base of the differential histogram, pronounced displacement of the interval histogram polygons to the left (450 and 600 ms). With parallel monitoring of 24-hour BP monitoring, AH of the 2nd degree was revealed.

The study of heart rate variability in the frequency range allows one to analyze the intensity of oscillations of different frequencies

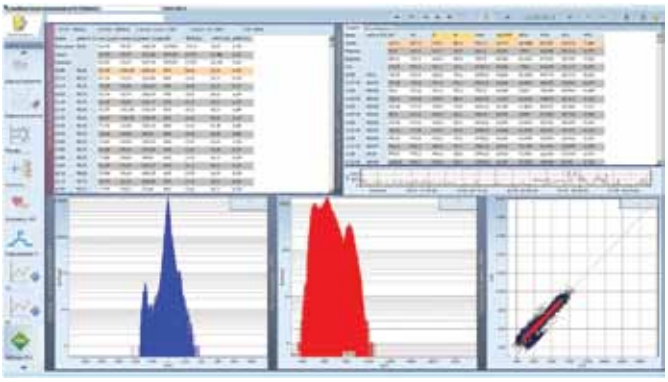

Figure 1. Results of a temporary analysis of heart rate variability (HRV) in a 57 y.o. patient with chronic stress

in the overall spectrum. With respect to the powers of various spectral components, one can judge the dominance of one or another physiological mechanism for regulating the heart rhythm

Most often, the spectrum is constructed by the method of fast Fourier transform. There are four frequency ranges:

HF – high-frequency (0,15-0,4 Hz). The parasympathetic system activity marker.

LF – low-frequency (0.04-0.15 Hz). It is often treated as a SNS marker.

VLF – very low-frequency (0,003-0,04 Hz). VLF, as well as the ULF-ultra-low frequency (<0.003 Hz) component, are most likely to reflect the activity of the sympathetic subcortical center of regulation. And the evaluation of the ULF-component is possible

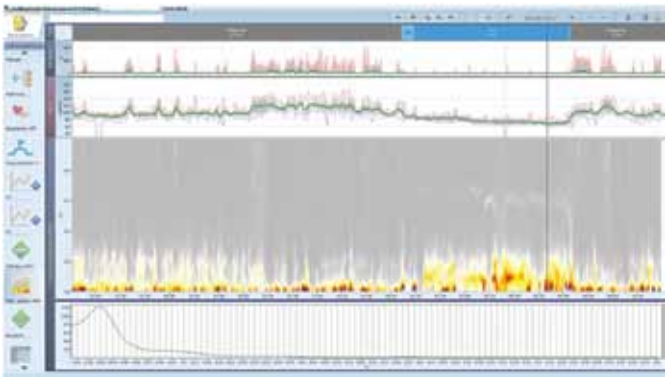

Figure 2. Results of spectral analysis in a 57 y.o. patient with chronic stress

only with a 24-hour ECG study.

Figure 2 shows the results of a spectral analysis of a patient already familiar to us with AH and chronic stress. Obviously, the lack of activity of the high-frequency spectrum, which indicates

a decrease in activity of the parasympathetic nervous system, marked activity of the SNS.

The therapy of beta-adrenoblockers (bisoprolol) in such patients allows to correct the activity of the autonomic nervous system: in patients receiving bisoprolol, in comparison with nebivolol and carvedilol [8], a significant increase in activity in the high-frequency range (parasympathetic regulation) and a decrease in blood pressure were noted, which again confirmed the relevance of the results of previous studies on the effect of beta-adrenoblokatorami therapy on blood pressure level and heart rate variability (HRV)in patients with mild to moderate AH. In addition, the use of bisoprolol in patients with severe heart failure also leads to significant correction of the state of the autonomic nervous system (ANS): patients who received 5 mg of bisoprolol per day, after 2 months of therapy, showed a statistically significant increase in activity in the high-frequency part of the spectrum, a significant increase in rMSSD and pNN50 (increased activity of the parasympathetic department of the ANS) [9], which significantly changes the prognosis in such patients.

CONCLUSIONS

Hypersympathicotonia, of course, plays one of the leading roles in the pathogenesis of hypertension. Early and reliable detection of hypersympathicotonia in patients with both debutting hypertension and resistant hypertension is possible to select the optimal methods for correcting elevated blood pressure and therapy for target organ damage. Evaluation of heart rate variability with daily monitoring of ECG can be recommended as one of the optimal methods for assessing hypersympathicotonia.

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