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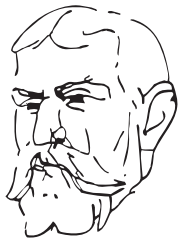

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ORIGINAL ARTICLES

ORIGINAL ARTICLE

STATE OF AUTONOMIC REGULATION AND CEREBROVASCULAR REACTIVITY IN PATIENTS WITH HEADACHE WITH ARTERIAL HYPERTENSION

DOI: 10.36740/WLek202209210

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ABSTRACT

The aim: A comprehensive assessment of the state of the autonomic nervous system and cerebrovascular reactivity of the cerebral blood flow in the patients with the headache accompanied by arterial hypertension (AH) and somatoform autonomic dysfunction (SAD).

Materials and methods: We conducted the clinical, autonomic regulation and Doppler sonography examination of 124 young patients (18-45 years old), including 51 men and 73 women in the conditions of the clinical base of the Kharkiv Medical Academy of Postgraduate Education in 2018-2021. All patients with cephalgias were divided into three groups: with AH stage II (Group I - 41 patients), AH stage I (Group II - 40 patients), SAD (Group III - 43 patients). The control group consisted of 50 patients of the corresponding gender and age

Results: The intensity of cephalalgia in patients with SAD was maximum. The autonomic tone (AT) was changed in 68.5%examined patients. It had a pronounced shift towards sympathicotonia. According to the visual analogue scale the maximum intensity of cephalgias was against the sympathicotonia. In the groups with organic lesions of the cerebral vessels the latent period delay was registered with the progression of the organic pathology. The regularity was revealed - the shortening of the evoked skin sympathetic potentials latency with the severity of cephalalgia, which can be interpreted as an increase in ergotropic effects with the realisation of the pain syndrome. The obtained data on the state of the AT indicate the depletion of the ergotropic processes with the progression of cerebral ischemia with a known increase in parasympathicotonia. In the patients of SAD group the CrCO2 and KrFNTvalues were significantly increased, in AH stage I group they slightly exceeded the standard values , in AH stage II group they were reduced. The reactivity to the orthostatic loads and functional metabolic test in all groups exceeded the control values.

Conclusions: 1. The cephalgic syndrome is one of the main symptoms of the autonomic dysfunction and arterial hypertension; the frequency and intensity of the headache increases with the hyperreactivity of the sympathetic system. 2. The SSP data indicate that the sympathetic activity triggers and maintains the pain syndrome, and can also be realized in the form of arterial hypertension. 3. The dysfunction of the central link of the GSR indicates the instability of the autonomous regulation, the work of the limbic-reticular complex, which is clinically manifested by the changes in the cerebral vascular tone. 4. The cerebrovascular hyperreactivity as a sign of the search for the optimal sanogenetic variant of the cerebral hemodynamics in patients with SAD and AH stage I occurs predominantly due to the vasodilatory component. 5. In the patients with AH stage II the vasoconstrictor reactions are observed with the depletion of the vasodilation reserves, which is a marker of the autoregulation failure.

KEY WORDS: Autonomic nervous system, headache, cerebrovascular reactivity, arterial hypertension, somatoform autonomic dysfunction

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INTRODUCTION

Arterial hypertension (AH) remains one of the predominant causes of the development of acute and chronic forms of the cerebrovascular pathology (CVP), the mortality, the main cause of disability, and deterioration in the quality of the life [1-3]. The disintegration of all levels of the autonomic nervous system (ANS) is one of the pathogenetic links of AH [4,5]. The balance of sympathetic-parasympathetic relationships is disturbed [6], it is clinically manifested by somatoform autonomic dysfunction (SAD), the latter is of a generalized systemic nature with the impaired cerebral blood flow due to inadequate adaptive capabilities against the increased blood pressure. At the same time the hyperactivation of the sympathetic nervous system is of particular importance, which contributes to cardiac and vascular changes with the development of complications of hypertension [7], which clinically leads to an increase in heart rate, an increase in vascular output during the transition to orthostasis, a change in baroreception, and vascular hypersensitivity to various stimulants [8]. The imbalance of autonomic control leads to a rapid depletion of the compensatory capabilities of the vascular system and the narrowing of its homeostatic range with the probable development of the so-called "diseases of adaptation" including cephalgia.

Headache (HA) is considered to be one of the leading symptoms of AH. In the European recommendations on

the diagnosis and treatment of AH special questionnaires for the HA detection during the patients` examination with hypertension are used [9]. The complaints on HA are presented in 44 to 87% of the patients with AH [10], mainly in the presence of the coexisting primary HA, most often, chronic tension headache and migraine [11].

Taking into consideration that the autonomic disorders are observed in the clinical picture of SAD and AH, it is necessary to study autonomic regulations for all levels of the response, state of tone and reactivity of autonomous system, including GSR for the clarification of the degree of adaptation, tactics of therapy and prognosis.

Cerebrovascular reactivity (CVR) is an integral indicator of the adaptive capacities of the cerebral circulation. The Doppler CVR study is informative in the patients with migraine and other types of headaches [12,13]. A combined study of the indicators of the autonomic regulation and CVR may be promising in the patients with the headache associated with an increase in AH.

THE AIM

The aim of the study was a comprehensive assessment of the state of the autonomic nervous system and cerebrovascular reactivity of the cerebral blood flow in the patients with the headache accompanied by hypertension and somatoform autonomic dysfunction.

MATERIALS AND METHODS

124 patients aged 18 to 45 years (56 men, 68 women) with hypertension with the persistent or periodic increase in blood pressure in the conditions of the clinical base of the Kharkiv Medical Academy of Postgraduate Education in 2018-2021 were examined. All patients with cephalgias were divided into three groups: with AH stage II (Group I - 41 patients), AH stage I (Group II - 40 patients), SAD (Group III - 43 patients). The questionnaire was used to identify the signs of the autonomic changes in order to identify the autonomic dysfunctions. The study of the autonomic tone (AT) was performed using the table "24 stigmas" for the rapid diagnosis of AT. The intensity of cephalalgias was studied using the visual analogue scale (VAS), and their characteristics were studied using the questionnaire form for the HA evaluation. The evoked skin sympathetic potentials (SSP) were registered along with the study of the amplitude of the second phase (A_2), as well as the duration of the latent period (LP).

The study of the cerebrovascular reactivity was carried out on the ultrasound scanner Ultima-PA (RADMIR, Ukraine), using the following functional loads and reactivity coefficients: hypercapnic (KrCO2), hyperventilation (KrO2), orthostatic (KrOL), anti-orthostatic (KrAOL), functional nitroglycerin test (KrFNT), functional metabolic test (KrFMT) .

The control group (CG) included 50 clinically healthy male and female volunteers of the corresponding age.

The program Statistica 8.0 was used for the statistical processing with the Wilcoxon as well as the Mann-Whitney U criterion assessment. The differences at $p < 0.05$ were considered statistically significant. The study complies with the requirements of the Helsinki Declaration and is approved by the ethics commission of the Kharkiv Medical Academy of Graduate Education.

RESULTS

All patients underwent a neurological examination with the diagnosis of the type of the headache in accordance with the ICHD-3 (2018). According to the structure HA were distributed between the groups of the patients as follows. Group I: headache associated with arterial hypertension - 22 patients (53.7%), tension headache - 19 patients (46.3%), Group II: tension headache - 16 patients (40.0%), migraine - 13 patients (32.5%), headache associated with arterial hypertension - 11 patients (27.5%); Group III: tension headache - 18 patients (41.9%), mixed headache (tension headache involving pericranial muscle and cervicogenic headache) - 14 patients (32.5%), migraine - 11 patients (25.6%).

In all groups cephalgias were maintained or increased in the presence of the degenerative-dystrophic changes in the cervical spine with muscle tone reactions in the occipital region.

The results obtained in the relation to the intensity of the pain in the studied groups indicate that the average VAS scores were slightly higher in Group II (by 0.27 points) compared to Group I whenever they were present. At the same time in Group III the intensity of cephalalgia was maximum and its average values reached 4.5±0.8 points, and it was more than 1.2 times higher than in Group I ($P< 0.05$).

AT was changed in 85 (68.5%) examined patients, in Group I - 27 (68.4%), in Group II - 31 (77.5%), in Group III - 27 (62.8%). It had a pronounced shift towards sympathicotonia: in Group III SAD - 21 (48.8%) with a minimum in vagotonia (3 - 7.0%), in groups with AH, a similar distribution remained in Group II - 21 (51.2%) versus 6 - (14.6%), however, Group I demonstrated a significant inversion ($P<0.05$) of these indicators with the "leveling" of the number of pathological values of AT: 16 (40.0%) versus 16 (40.0%), which indicates some weakening of ergotropic and an increase in trophotropic effects with a sharp decrease ($P <0.05$) in the normal distribution of AT in the process of the progression of the organic pathology of the brain (Fig. 1).

According to the VAS, the maximum intensity of cephalgias was against the sympathicotonia: 4.2±0.09 points (Group II) and 4.3±0.11 points (Group I), $P<0.05$; 4.5±0.08 points (Group III), $P< 0.05$. (Fig.2).

In the study of the galvanic skin reflex (GSR) according to the registration of SSP in Group III with SAD the average values of the LP duration were 1.29 ± 0.07 s and were minimal. In the groups with organic lesions of the cerebral vessels the LP delay was registered with the progression of the organic pathology: from 1.41±0.07 (Group II) to 1.75±0.09 s (Group I), $P<0.05$.

The regularity was revealed - the shortening of the SSP latency with the severity of cephalalgia, which can be interpreted as an increase in ergotropic effects with the realisation

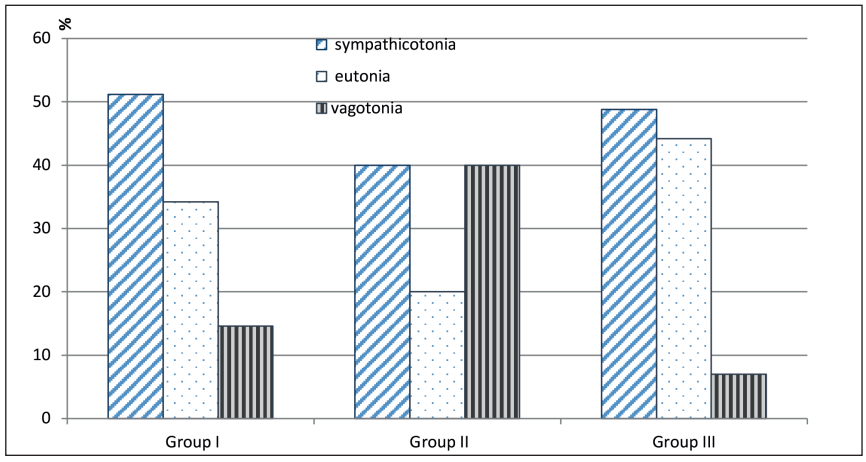

Fig. 1. The relative distribution of AT in the studied groups

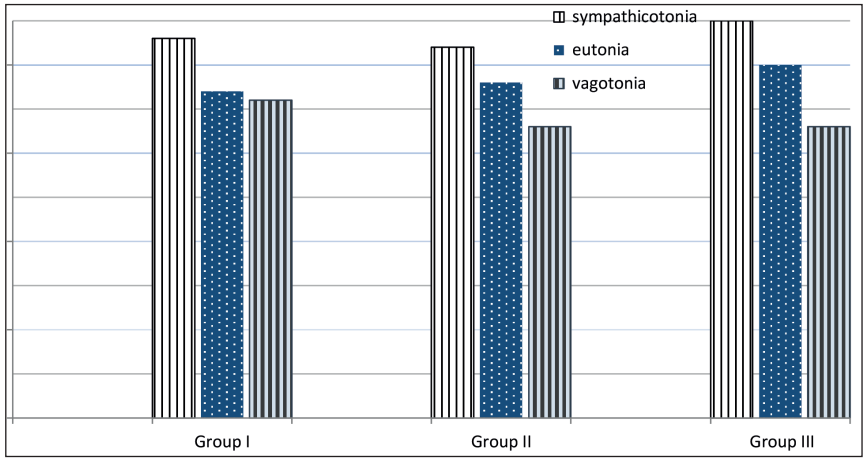

Fig. 2. The intensity of headache in groups depending on the initial autonomic tone (VAS points).

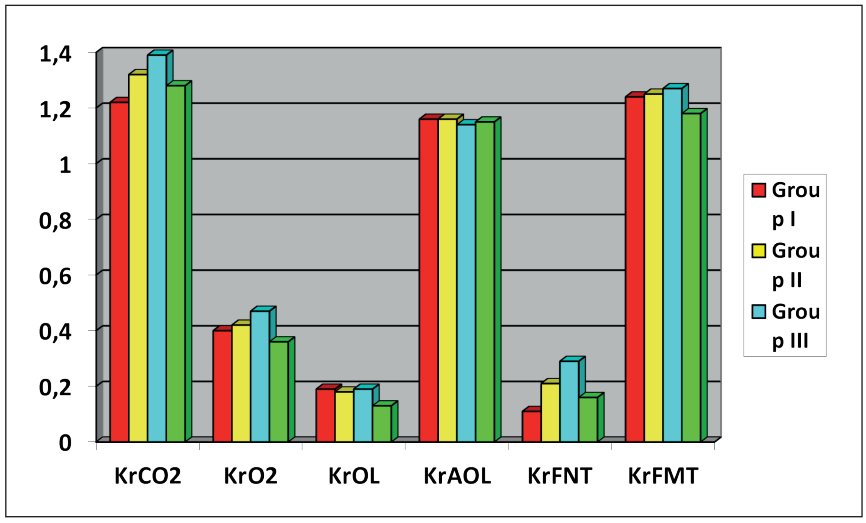

Fig. 3. CVR values in patients with the headache

of the pain syndrome. At the same time, with a low-intensity cephalalgia, the LP lengthened, which is apparently associated with trophotropic inhibition of the development of cephalgia (Table I).

The obtained data on the state of AT indicate the depletion of the ergotropic processes with the progression of cerebral ischemia with a known increase in parasympathicotonia (Table II).

A clear pattern of the decrease in the amplitude of the second phase of GSR - A_2, depending on the depletion of the ergotropic system was revealed (Table III). The average values of A_2 in Groups II and I were below standard values (2.66 ± 0.1 and 2.55 ± 0.2 mV, $p < 0.05$), however, in Group III they were close to the standard and equal to 2.71±0.2 mV.

The significant difference between A_2 indicators by 2 or more times in all examined groups ($p < 0.05$) indicates that, regardless of the etiopathogenesis of vascular lesions, ANS impacts and/or accompanies the pathological process, indicating the state of the body's adaptive capabilities, which may predetermine the prognosis and prospects for therapy.

In the patients of Group III the CrCO2 values were significantly increased compared to the CG (1.39±0.05, CG - 1.28±0.04; $p < 0.05$), in Group II they slightly exceeded the

Table I. The distribution of LP indicators in groups depending on the intensity of cephalgias

Cephalgia (VAS)	SSP latency (sec)		
	Group I	Group II	Group III
High intensivity (4 + points)	1,31±0,06	1,51±0,09	1,21±0,06
Low intensivity (1-3 points)	1,75±0,4*	2,20±0,12*	1,60±0,20*

*p <0,05 compared to average data

Table II. The change in SSP LP depending on the initial AT in groups

Groups	SSP latency (sec)			
	Total	Sympathicotonia	Eutonia	Vagotonia
Group I (n=41)	1,41±0,10	1,24±0,12	1,52±0,14	1,88±0,13*
Group II (n=40)	1,78±0,11	1,52±0,11	1,74±0,12	2,11±0,14*
Group III (n=43)	1,31±0,12	1,17±0,09	1,44±0,05	1,80±0,09*

*p <0,05 compared to average data

Table III. The change in SSP A2 depending on the initial AT in groups

Groups	Amplitude (A_2) SSP (mV)			
	Total	Sympathicotonia	Eutonia	Vagotonia
Group I	2,69±0,2*	3,43±0,3	2,11±0,4	1,55±0,2**
Group II	2,56±0,3*	3,65±0,1	2,17±0,5	1,81±0,3**
Group III	2,73±0,1	3,58±0,2	1,88±0,5	1,61±0,1**

*p <0,05 compared to standart average data
**p <0,05 compared to maximum-minimum

standard values (1.32±0.03), in Group I they were reduced (1.22±0.05). The parameters of CrFNT changed in groups in a similar way: a significant increase in Group III (0.29±0.05, CG - 0.16±0.04; p <0.05), a slight increase in Group II (0.21±0.04) and a decrease in Group III (0.11±0.03, p<0.05), the KrO2 indicators also exceeded the standard ones, but to a lesser extent than the KrCO2 data (0,46±0.07, CG - 0.36±0.03). The reactivity to the orthostatic loads and functional metabolic test in all groups exceeded the control values. The response to the antiorthostatic test was within the standard limits (Fig. 3).

DISCUSSION

It has been found out that HA is a key manifestation of autonomic dysfunctions and arterial hypertension. The HA intensity slightly decreased as the pathological process progressed in the AH groups, while at the same time it was maximum in somatoform dysfunctions. The pathological autonomic tone prevailed in all groups. The frequency and intensity of cephalalgia increased with the presence of sympathicotonia, especially in the SAD and AH stage I groups. At the same time with the growth of structural damage to the CNS (AH stage II) trophotropic (vagal) manifestations intensified, and cephalalgias in all groups were less intense, which can be regarded as a decrease in the adaptive capabilities of the body as a whole.

From the data obtained regarding the shortening of latency during intense headaches, one can assume an increase in ergotropic effects, i.e. sympathetic activity apparently triggers and maintains the pain syndrome, and can also be realized in the form of arterial hypertension.

At the same time, with low-intensity cephalalgia the LP has lengthened, which is apparently associated with trophotropic effects. Thus, the dysfunction of the ANS has a leading influence on the development of HA of various origins.

The involvement of suprasegmental autonomous structures has been registered, i.e. the central link of the GSR with the corresponding central delay in the form of a "spring stretching phenomenon" can be interpreted as instability of autonomous regulation, the work of the limbic-reticular complex, which is clinically manifested by a change in the vascular tone of the brain.

The autoregulatory reserve in case of AH episodic increase (in SAD patients) and AH stage I is characterized by pronounced hyperreactivity in almost all components. In patients with AH stage II there is a decrease in the response to CO2 and FNT, which is associated with the depletion of vasodilation reserves. The changes in the reactivity along the myogenic circuit with AH progression are similar to the data of the metabolic circuit of autoregulation. An increased response to O2-test, orthostatic test and FMT in all groups indicates predominantly vasoconstrictor reactions in patients with HA. It can be assumed that the exhaustion of vasoconstriction reserves in these patients occurs later than similar changes in the vasodilator component.

Our data are also confirmed by the studies of other authors indicating an increase in the sympathetic activity in cephalgias and potentiation of the development of AH [7,8]. In addition, the obtained results correspond to the

hypothesis that the autonomic dysfunctions are an additional factor in the development of some cephalalgias, primarily migraine paroxysms [14]. The identification of this kind of imbalance of tropho- and ergotropic influences can be effectively performed with the help of SSP.

CONCLUSIONS

1. The cephalgic syndrome is one of the main symptoms of the autonomic dysfunction and arterial hypertension; the frequency and intensity of the headache increases with the hyperreactivity of the sympathetic system.
2. The SSP data indicate that the sympathetic activity triggers and maintains the pain syndrome, and can also be realized in the form of arterial hypertension.
3. The dysfunction of the central link of the GSR indicates the instability of the autonomous regulation, the work of the limbic-reticular complex, which is clinically manifested by the changes in the cerebral vascular tone.
4. The cerebrovascular hyperreactivity as a sign of the search for the optimal sanogenetic variant of the cerebral hemodynamics in patients with SAD and AH stage I occurs predominantly due to the vasodilatory component.
5. In the patients with AH stage II the vasoconstrictor reactions are observed with the depletion of the vasodilation reserves, which is a marker of the autoregulation failure.

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Conflict of interest:
The Authors declare no conflict of interest.

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