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ORIGINAL ARTICLE

FEATURES OF CEREBROVASCULAR REACTIVITY IN PATIENTS OF YOUNG AGE WITH MIGRAINE

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ABSTRACT

The aim of the study was to Doppler sonography study of cerebrovascular reactivity in young patients with migraine and comparison of autoregulation patterns between groups of migraine patients with aura and migraine without aura.

Materials and methods: We conducted the clinical Doppler examination of 124 young patients (18-45 years old), including 55 men and 69 women in the conditions of the clinical base of the Kharkiv Medical Academy of Postgraduate Education in 2017-2019. The criteria for involvement of patients in the study were: migraine without aura (group 1-63 patients), migraine with aura (group 2-61 patients) The control group consisted of 45 patients of the corresponding gender and age. The indicators of CVR were studied using the ultrasound device.

Results: A hyperreactive response to tests with CO2 and photoreactivity were more pronounced in the patients with migraine without aura. The patients with migraine with aura showed hyperreactivity in the test with O2, which was an indicator of the tendency to hyperconstriction. The hyperreactivity in the functional nitroglycerin test and the carotid compression test shows the state of the myogenic mechanism of changes in vascular tone. Insignificant hyperreactivity to orthostatic load detected in both groups shows the interest of the neurogenic regulatory link.

Conclusions: 1. The most important hemodynamic patterns in the patients with migraine are excessive perfusion with migraine without aura and difficult perfusion with migraine with aura.

2. For the patients with migraine without aura, a characteristic criterion for autoregulation is the pattern of hyperreactivity hypercapnic load and photostimulation.

3. The most important difference in the autoregulatory response in the patients with migraine with aura compared with migraine without aura is the hyperresponse to hyperventilation load, compression carotid and nitroglycerin tests.

KEY WORDS: migraine, Doppler sonography, cerebral hemodynamics, cerebrovascular reactivity

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INTRODUCTION

Currently, migraine is widespread in the world and can reach 22% in women and 16% in men [1].

The problem of migraine is of interest due to its wide prevalence, growth of the incidence rate in people of young productive age, as well as diagnostic and therapeutic difficulties. Migraine is the primary neurogenic cerebral dysfunction with the presence of genetically determined stem failure, severe cortical hyperactivity with periodically occurring hypothalamus dysfunctions [2-3].

The method of transcranial dopplerography (TCD) of the major vessels of the head has been successfully used to diagnose lesions of extracranial and intracranial sections of the major arteries. Recently, a large number of works have been published on the study of cerebral hemodynamic disorders in patients with migraine with and without aura, during the attack-free period and during the attack [4-6]. Their results are very contradictory. The studies during the attack-free period did not show significant differences in average blood flow velocity in extra- and intracranial arteries in patients with migraine relative to the group of healthy subjects [7]. Cerebrovascular reactivity (CVR) is considered as an integral indicator of the adaptive capabilities of the cerebral circulatory system, the ability of the brain vessels to respond to changing functioning conditions and to optimize blood flow in accordance with these conditions. The use of functional loads in order to assess the reactivity of cerebral vessels makes it possible to objectify the activities of regulatory mechanisms that control cerebral circulation and ensure its functional stability. The use of TCD to assess CVR is informative in patients with migraine. Studies have shown increased reactivity of cerebral arteries to respiratory retention, hyperventilation, visual stimulation, and usage of glyceryl trinitrate (GTN) [8-9]. The study of patients with migraine without aura demonstrated hyperreactivity for hypercapnia, which returned to normal state after preventive treatment [10]. This demonstrates that cerebrovascular reactivity can be a marker of migraine severity. The high sensitivity of cerebral arteries to GTN has also been proven, which draws the particular interest to the mechanisms of nitric oxide (NO) transformation in migraine studies [7]. This theory

Tabl I. Clinical characteristics of migrainous attacks in patients.

	Groupe 1 (n=63)	Groupe 2 (n=61)
Age, years	36,2 ± 5,3	28,9 ± 7,1
Duration of attacks, years	13,8 ± 5,4	10,5 ± 6,1
Frequenc of attacks, days/month	5,8 ± 3,1	5,2 ± 2,7
Average duration of attacks, h	43,8 ± 11,7	57,6 ±12,2
Intensity of the pain syndrome (VAS)	6,9 ± 1,6	8,2 ± 1,4
MIDAS (The degree of decrease in the functional activity of the patient with migraine)	29,3 ± 7,6	33,8 ± 9,1

is supported by the study showing the initiation of the migraine attack by GTN infusion [7].

The combined use of loads reflecting the functioning of various circuits of vascular regulation (humoral metabolic, myogenic, neurogenic) in patients with migraine is of interest.

THE AIM

Was to Doppler sonography study of cerebrovascular reactivity in young patients with migraine and comparison of autoregulation patterns between groups of migraine patients with aura and migraine without aura.

MATERIALS AND METHODS

We conducted the clinical Doppler examination of 124 young patients (18-45 years old), including 55 men and 69 women in the conditions of the clinical base of the Kharkiv Medical Academy of Postgraduate Education in 2017-2019. The criteria for involvement of patients in the study were: migraine without aura (group 1-63 patients), migraine with aura (group 2-61 patients) in accordance with the criteria for the international classification of headache disorders (ICHD-3, 2018) [11]. The exclusion criteria were the presence of occlusions and hemodynamically significant stenoses of brain magistral arteries (BMA). All patients underwent clinical and neurological examinations. The intensity of the cephalgic syndrome was assessed using a visual analogue scale (VAS) and a headache diary filled in by the patient himself. (Tabl.I).

The state of blood flow in cerebral arteries and indicators of cerebrovascular reactivity (CVR) were studied using Ultima PA ultrasound device (RADMIR, Ukraine) and Angiodin transcranial Doppler apparatus (BIOSS, Russia). The study was performed indicators of linear blood flow velocity (BFV) in middle cerebral (MCA), anterior cerebral (ACA), posterior cerebral (PCA) arteries , siphons of internal carotid arteries, intracranial segments of vertebral arteries (VA), basilar arteries (BA), and the reactivity coefficients to hypercapnic (CrCO2) and hyperventilation reactivity (CrO2), orthostatic (CrOL) and antiorthostatic (CrAOL) load, functional nitroglycerin (CrFNT) and functional metabolic (CrFMT) tests, and overshoot coefficient (OC) with carotid compression test and photoreactive coefficient (PRC) for photostimulation. The control group consisted of 45 patients of the corresponding gender and age. Statistical analysis and material processing were performed using the Statistic 6.0 software package. Differences recognized to be statistically significant at $P < 0.05$.

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 AND DISCUSSION

The most indicative were changes in hemodynamics in MCA, which were manifested by the pattern of excessive perfusion and were characterized by an increase in LBV in MCA in the patients of the 1st group (84.2 ± 10.4 cm/s, CG – 61.6 ± 7.3 cm/s, $p < 0.05$) and the pattern of difficult perfusion in the patients of the 2nd group (57.4 ± 6.8 cm/s, CG – 61.6 ± 7.3 cm/s). There is also a slight increase in flow rate indicators in ACA, PCA, VA, BA compared with CG (Fig.1).

The patients of the 1st group showed hyperreactivity to CO_2 and O_2 loads (1.39 ± 0.05 and 1.37 ± 0.04, respectively, CG – 1.28 ± 0.04; $p < 0.05$). The patients of the 2nd group showed pronounced O2 load hyperreactivity (0.51 ± 0.06, CG – 0.36 ± 0.03; $p<0.05$), which indicates the vasoconstrictive nature of vascular reactions. In both clinical groups, a slightly enhanced response to orthostatic load was noted (0.16 ± 0.04 and 0.18 ± 0.03, respectively, CG – 0.13 ± 0.03). Also, in the patients with migraine there was a significant increase in CrFNT indices, more pronounced in the subjects of the 2nd clinical group (0.21 ± 0.03 and 0.26 ± 0.04, respectively; CG – 0.16 ± 0.04; $p < 0.05$). The OC values were increased in both clinical groups, with a significant predominance in the patients of the 2nd group (1.58 ± 0.04; CG –1.4 ± 0.05; $p < 0.05$). In both clinical groups, the PRC values were significantly increased, these changes were more characteristic for the patients of the 1st group (1.39 ± 0.07 and 1.35 ± 0.05, respectively; CG –1.2 ± 0.05; $p < 0.05$). The response to FMT and GA as a whole did not differ from the normative indicators. Figs. 2, 3 show the CVR indices in the patients with migraine.

The most indicative were changes in hemodynamics in MCA, which were manifested by the pattern of excessive perfusion and were characterized by an increase in LBV in MCA in the patients of the 1st group and the pattern of difficult perfusion in the patients of the 2nd group. The studies have led to the conclusion that there are various options for autoregulatory response in the patients with migraine without aura and migraine with aura. Hyperreactivity along all control loops was common for the patients

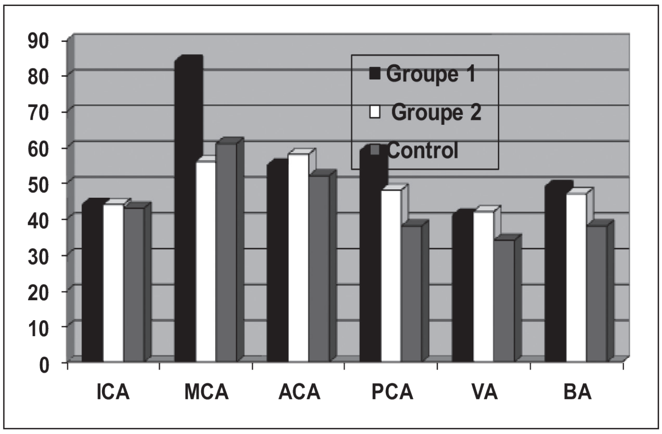

Fig. 1. The indicators of BFV in intracranial arteries in the patients with migraine

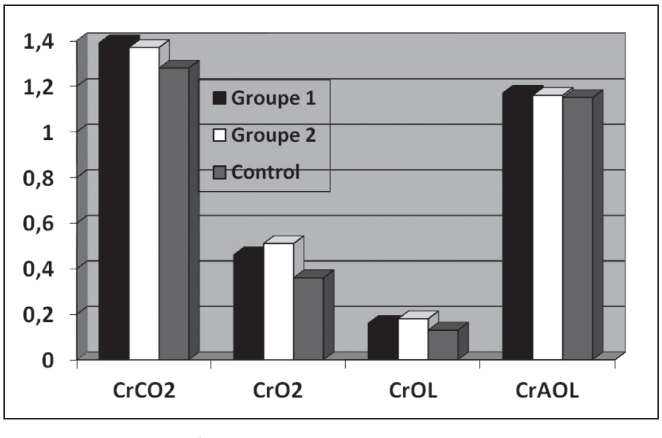

Fig. 2. The indicators of CrCO2, CrO2, CrOL and CrAOL in patients with migraine.

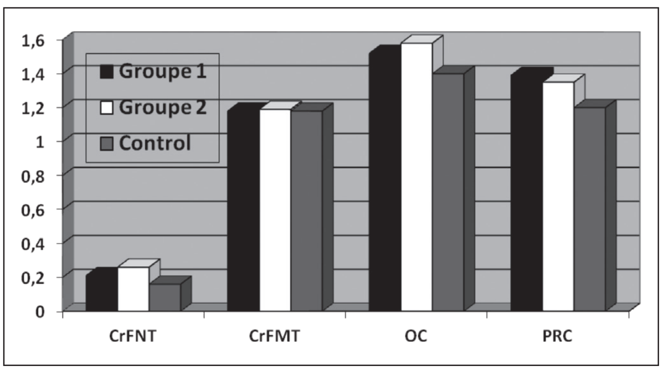

Fig. 3. The indicators of CrFNT, CrFMT, OC and PRC in patients with migrane.

of both groups. The most indicative was hyperreactivity to metabolic loads. A hyperreactive response to tests with CO2 and photoreactivity were more pronounced in the patients with migraine without aura. The patients with migraine with aura showed hyperreactivity in the test with O2, which was an indicator of the tendency to hyperconstriction. The confirmation of this statement was also the hyperreactivity to the carotid compression test (overshoot coefficient), which is the reflection of the hypertonicity of resistive vessels. We also see a similar answer when analyzing nitroglycerin test parameters, which shows the state of the myogenic mechanism of changes in vascular tone. Insignificant hyperreactivity to orthostatic load detected in both groups shows the interest of the neurogenic regulatory link. The neurogenic regulatory loop is not leading in the patients with migraine, but is an indirect reflection of the presence of autonomic imbalance observed in most patients with migraine. Thus, a commonality of responses of the patients of both groups to the majority of presented stimuli is observed, the differences are in the presence of vasoconstrictor reactions and background hypertonicity of resistive vessels in th patients with migraine with aura.

Most previous studies of cerebrovascular reactivity in migraines [8-10]. were differential to patients with migraine with aura and without aura. Also, the studies reflected the state of certain contours of autoregulation (humoral-metabolic, myogenic, neurogenic) and did not give a holistic view of the state of vascular reactivity in a particular patient. For the first time, we have proposed the diagnostic algorithm for Doppler studies in migraine, which allows distinguishing cerebrovascular reactivity patterns, specific for groups of patients with migraine with aura and migraine without aura

CONCLUSIONS

1. The most important hemodynamic patterns in the patients with migraine are excessive perfusion with migraine without aura and difficult perfusion with migraine with aura in the middle and posterior cerebral arteries.
2. For the patients with migraine without aura, a characteristic criterion for autoregulation is the pattern of hyperreactivity to most functional loads, more pronounced with hypercapnic load and photostimulation.
3. The most important difference in the autoregulatory response in the patients with migraine with aura compared with migraine without aura is the reactions associated with hyperconstriction of resistive vessels – a pronounced hyperresponse to hyperventilation load, compression carotid and nitroglycerin tests.
4. The indicators of cerebrovascular reactivity reflect the difference in the hemodynamic mechanisms of the migraine attacks in the patients with migraine with aura and without aura and can be used to clarify the diagnoses and individualize treatment in these patients.

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

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