



CLINICAL AND DOPPLER CORRELATIONS OF PREVENTIVE MIGRAINE TREATMENT

Kalashnikov V.Y.^{1,2*}, Stoyanov O.M.³, Vastyanov R.S.³, Melnik YuV.⁴, Kuhel Ya.I.³

¹Uzhhorod National University, Uzhhorod, Ukraine

²Kharkiv National Medical University, Kharkiv, Ukraine

³Odessa National Medical University, Odessa, Ukraine

⁴Diagnostic Center "Neuro-CardioLab", Odessa, Ukraine.

*Corresponding Author

Kalashnikov V.Y.

Article History

Received: 09.05.2025

Accepted: 18.06.2026

Published: 10.07.2026

Abstract: - The article presents an analysis of literature data and the results of our own clinical and Doppler examination of 116 young patients with migraine. (18-45 years old), a clinical and neurological examination was performed, an assessment of the intensity of the degree of decrease in the patient's functional activity, a study of the state of cerebral arteries and cerebrovascular reactivity using ultrasound Doppler. Cerebral hemodynamics during a migraine attack is characterized by a pattern vasospasm in migraine without aura and a pattern of impaired perfusion in migraine with aura in the middle cerebral arteries, as well as increased perfusion in the cerebral arteries. For patients with migraine without aura, the characteristic Doppler The pattern is hyperresponsiveness to hypercapnic stress, and for patients with migraine with aura, hyperresponsiveness to hyperventilatory stress, reflecting a hyperconstrictive vascular response. The use of Topiramate for the preventive treatment of migraine in both clinical groups significantly reduces the frequency, duration and intensity of migraine attacks and . Under the influence of the drug, a decrease in the frequency, duration and intensity of attacks was observed. The vascular effect of the drug was manifested in a decrease in the initially increased blood flow velocity in the SMA. The drug contributed to the normalization of cerebrovascular hyperreactivity , mainly to the CO₂ test in patients with migraine with aura and to the photoreactivity test in patients with migraine without aura.

Keywords: migraine, transcranial duplex scanning, cerebral hemodynamics, cerebrovascular reactivity, topiramate.



This is an open access article under the [CC BY-NC](https://creativecommons.org/licenses/by-nc/4.0/) license



Cite this article:

Kalashnikov V.Y., Stoyanov O.M., Vastyanov R.S., Melnik YuV., Kuhel Ya.I., (2026). CLINICAL AND DOPPLER CORRELATIONS OF PREVENTIVE MIGRAINE TREATMENT. *ISAR Journal of Medical and Pharmaceutical Sciences*, 4(7), 1-5.

Introduction

Migraine is one of the most common neurological pathologies in world [1] The high prevalence, steady increase in incidence in young, working-age individuals, as well as the difficulties of diagnosis and therapy determine the great interest in this problem [2,3]. This is due to the high frequency of this disease in the population and the significant impact on disability and loss of working capacity of the population. Migraine is directly related to gender, since the male/female ratio with this pathology is 1:3-4 [4]. Approximately 18.2 and 6.5% of women and men suffer from migraine, respectively, of which the majority (62%) have at least one episode of severe headache per month [5]. The pathogenetic factor of the attack is changes in metabolism and cortical function [6]. Cortical depression causes activation of sensory neurons of the trigeminal complex, increasing their sensitivity to nociceptive irritation of the vessels of the dura mater. [7,8]. Migraine attacks can be triggered by stress, nervous or physical overexertion, sleep disturbances, consumption of certain foods or alcohol, weather factors, use of hormonal contraceptives. [9].

Migraine is a primary neurogenic cerebral dysfunction with the presence of genetically determined brainstem insufficiency, pronounced cortical hyperactivity with periodically occurring hypothalamic dysfunction. [10].

Migraine is manifested by periodically recurring attacks of intense headache of a pulsating nature, which is localized mainly in one half of the head and in most cases is accompanied by nausea, vomiting, photo- and phonophobia, drowsiness. The duration of the attack is from several hours to 2-3 days, the frequency can vary from 1 time per year to 1 time per week. There are two main forms of migraine: without aura - characterized by attacks of headache with specific accompanying symptoms; with aura - characterized by local neurological symptoms that usually precede or accompany the headache [11].

Preventive treatment is performed only for relatively frequent and severe migraine attacks and excludes the use of specific drugs for the treatment of an acute attack [12].

The goals of treatment of patients with migraine are rapid and consistent resolution of the attack without the possibility of relapse, restoration of the ability to function normally, minimizing the use of drugs that alleviate symptoms, optimizing self-care, cost-effectiveness, and the absence/minimum number of side effects [13]. It has been shown that successful preventive treatment of migraine reduces the frequency and severity of cephalgic attacks, helps reduce the amount of analgesics consumed, prevents the transformation of episodic headache into chronic, prevents the development of structural changes in the central nervous system, and improves the quality of life of patients [14].

The main indications for preventive treatment of migraine are the frequency of attacks (more than two per month), their duration (up to 5 or more days with pronounced patient maladaptation), the presence of contraindications to abortive therapy or its ineffectiveness. As a tool for implementing the aforementioned strategy, β -blockers, calcium channel blockers, serotonin antagonists, antidepressants, nonsteroidal anti-inflammatory drugs, and anticonvulsants are used [15].

Among anticonvulsants in the treatment of migraine, valproate, gabapentin and topiramate have found wide application. According to the literature, topiramate deserves special consideration among these drugs. The evidence base allows us to consider topiramate as the drug of choice in pharmacoprophylaxis antimigraine therapy. This is possible to explain multimodal effects of topiramate on the CNS, as well as its impact on the leading mechanisms of migraine pathogenesis [16].

The multiplicity of mechanisms of action of topiramate is reduced to the following factors: blockade of potential-dependent Na^+ channels of the neuronal membrane, which limits the current of sodium ions into the cell; activation of GABA receptors due to the extension of the opening time of Cl^- channels; inhibition of excitatory glutamatergic neurotransmission by selective blockade of AMPA-/kainate receptors; blockade of "fast" potential-dependent L-type Ca^{2+} channels, and inhibition of the activity of the carbonic anhydrase enzyme [17].

Topiramate at a dose of 50-200 mg per day significantly reduces the frequency of migraine attacks in adults, and the effect may persist even after discontinuation of the drug. In 46.3% of patients taking topiramate, the number of migraine attacks decreased by 50%, in 6% the attacks stopped completely. A progressive decrease in the frequency of attacks was found in the period 6 months after the start of taking topiramate [18]. The effectiveness of topiramate was shown in the form of a reduction in the frequency of attacks per month compared to placebo, as well as a reduction in the number of days with migraine attacks compared to baseline. The number of patients who responded to therapy was significantly higher in the topiramate group than in the placebo group. Also, as a result of the studies, it was found that a 3-month course of taking topiramate significantly reduces the frequency of migraine attacks (in general in the group by 2.1 times), and also reduces the duration of the attack and the intensity of the pain syndrome [19]. Topiramate has also been reported to be effective in various pain syndromes other than migraine: cluster headache, SUNCT syndrome, and phantom pain [20]. Thus, the neurochemical mechanisms of action of topiramate are directed at blocking the main factors of migraine pathogenesis.

The method of Transcranial Doppler Sonography (TDS) of the main vessels of the head has long been successfully used for the diagnosis of lesions of the extracranial and intracranial departments of the main arteries [21]. Recently, a fairly large number of works have been published devoted to the study of cerebral hemodynamic disorders in patients with migraine with and without aura, in the period between attacks and during the attack. Their results are very contradictory. Blood flow indicators in the ophthalmic artery and external carotid artery were found to be increased in the ultrasound assessment. In patients with migraine without aura, an increase in blood flow velocity indicators and a decrease in the pulsation index in the arteries of the base of the brain were noted, and in the group of people with migraine with aura, a decrease in velocity indicators and an increase in peripheral resistance indices [22]. There are no data in the available publications on the results of a combined study of cerebral hemodynamics and cerebrovascular reactivity using the TDS method in patients with different types of migraine. paroxysms. In this regard, the issue of using modern diagnostic methods becomes of paramount importance for the study of this pathology.

Objective

Clinical and Doppler study of young patients with migraine on the background of preventive treatment.

Materials and Methods

We conducted a clinical and Doppler examination of 116 young patients (18-45 years old), including 49 men and 67 women. The inclusion criteria for patients in the study were: migraine without aura (group 1 - 61 patients), migraine with aura (group 2 - 65 patients) according to the criteria of the international classification of headache (ICH-3, 2018). The exclusion criteria were the presence of occlusions and hemodynamically significant stenosis of the MAG. All patients underwent a clinical and neurological examination. The intensity of the cephalgic syndrome was assessed using a visual analog scale and a headache diary filled in by the patient himself. The condition of the main arteries of the head and neck, indicators of cerebrovascular reactivity (CVR) were studied using an ultrasound device Ultima PA (RADMYR, Ukraine). The time- averaged maximum blood flow velocity (TAMX) in the middle cerebral (MCA), anterior cerebral (ACA), posterior cerebral (PCA), internal carotid artery (ICA), vertebral arteries (VA), and the common carotid artery (CCA), as well as the reactivity coefficients to hypercapnic (CrCO₂), hyperventilation (CrO₂), orthostatic (CrOL), and antiorthostatic (CrAOL) loads, were studied. The control group consisted of 25 patients of the corresponding sex and age.

Results and Discussion

Pain syndrome during the attack period in patients with migraine was characterized by the following criteria: frontal-ocular-temporal localization of pain was predominant in both clinical groups (85.2% in group 1, 96.3% in group 2). By the nature of pain during the attack, the pulsating type was detected (72.1% of patients in group 1 and 81.8% of patients in group 2), bursting - 8.2% and 5.4%, respectively, a combination of these types - in 16.4% and 12.7%. In 47.5% of patients in group 1 and in 36.3% of patients in group 2, the localization of the pain attack was mainly left-sided, in 34.4% of patients in group 1 and in 39.9% of patients in group 2 - mainly right-sided, in 18.1% of patients in group 1 and in 23.8% of patients in group 2 - alternating sides. Attacks upon awakening were characteristic of 49.1% of patients in group 1 and in 38.1% of patients in group 2, daytime attacks - in 42.6% and 50.9% of cases, respectively, night attacks - in 8.3% and 11.0%. The characteristic accompanying symptoms of migraine attacks were photophobia (73.7% and 88.3%), phonophobia (72.1% and 78.2%), a feeling of pulsation in the head (42.6% and 39.9%), nausea and vomiting (39.3% and 60.0%), dizziness (32.8% and 30.9%). The attacks were stopped after taking combinations of analgesics and antimigraine drugs of the triptan series (spontaneous elimination of the attack during sleep was less common).

The leading subjective symptoms in the inter-attack period in patients with migraine were: general weakness and decreased performance (42.6% in group 1 and 50.9% in group 2), signs of emotional instability combined with irritability and tearfulness in 39.3% and 36.3% of patients, dizziness, mainly of a non-systemic nature - 32.8% and 38.1% of patients, noise in the head - 26.2% and 23.8% of patients, sleep disturbances - 14.7% and 16.3% of patients, memory loss - 11.4% and 14.5% of patients.

In the neurological status of patients with migraine, the following symptoms were noted: increased tendon reflexes - in 62.3% and 65.4% of patients, vegetative stigmata - in 42.6% and 52.7%, respectively, swaying in the Romberg position - in 22.9% and 18.1% of patients, mild oculomotor disorders - in 14.7% and 16.3% of patients, mild asymmetry of facial muscles - in 9.8% and 9.0% of patients.

Hemodynamic patterns in the intracranial arteries were characterized by the presence of vasospastic reactions in the MCA in patients of group 1 (86.2 ± 10.4 cm/s, ($p < 0.05$)). Blood flow in the MCA in patients of group 2 is characterized by a pattern of impaired perfusion.

Patients in group 1 showed hyperreactivity to CO₂ and O₂ loading, while patients in group 2 showed pronounced hyperreactivity to O₂ loading.

The next task of the study was to study the preventive effect of topiramate on the quantitative indicators of migraine paroxysms and hemodynamic patterns in patients with migraine. The drug Topiramat was chosen as a preventive agent. Topiramat was taken as monotherapy, in the 1st week of taking the dosage was 25 mg per day, then the dosage was 50 mg per day, the course of treatment was up to 6 months.

Topiramate therapy has been associated with a reduction in seizure frequency of attacks from 5.8 ± 3.1 to 3.2 ± 2.6 in the 1st group, from 5.2 ± 2.7 to 3.1 ± 1.9 in the 2nd group. The average duration of attacks also decreased - from 43.8 ± 11.7 to 28.4 ± 10.2 in the 1st group, from 57.6 ± 12.2 to 32.8 ± 13.3 in the 2nd group. The most significant decrease in pain intensity according to VAS was: from 6.9 ± 1.6 to 3.4 ± 1.8 ($p < 0.05$) in the 1st group, from 8.2 ± 1.4 to 4.6 ± 1.7 ($p < 0.05$) in the 2nd group.

With normal baseline TAMX data on the background of taking Topiramate practically did not change. In the presence of vasospastic reactions in the background, their regression was noted in MCA in patients of group 1 (TAMX decreased from 84.2 ± 7.4 cm/s to 80.4 ± 4.7 cm/s). In patients of group 2, normalization of reduced MCA velocity indices was observed (from 56.8 ± 5.1 cm/s to 60.4 ± 4.3 cm/s). No significant changes in blood circulation were observed in the VA.

Against the background of course therapy with Topiramate positive dynamics of changed CVR indicators were noted in all clinical groups (1st group - 1.39 ± 0.05 cm/s; 2nd group - 1.37 ± 0.04 ; CG - 1.28 ± 0.04 ; $p < 0.05$) and photoreactive test (1st group - 1.39 ± 0.06 ; 2nd group - 1.32 ± 0.04 ; CG - 1.20 ± 0.04 ; $p < 0.05$).

The greatest tendency towards normalization of initially elevated CVR values was observed during CO₂ loading in patients of group 2 (from 1.37 ± 0.04 to 1.30 ± 0.05), as well as in the photoreactive test in patients of group 1 (from 1.39 ± 0.06 to 1.30 ± 0.04). This effect indicates a reliable effect of Topiramate on the humoral -metabolic circuit of cerebral autoregulation. In this context, as in the situation with blood flow velocity indicators, Topiramate acts as a regulator of certain structural mechanisms of cerebral hemodynamics.

Thus, the conducted studies have proven the presence of both a positive clinical and hemodynamic effect of Topiramate in patients with migraine. Under the influence of the drug, a decrease in the frequency, duration and intensity of attacks was observed. The vascular effect of the drug was manifested in a decrease in the initially increased blood flow velocity in the MCA. The drug contributed to the normalization of cerebrovascular hyperreactivity, mainly to the CO₂ test in patients with migraine with aura and to the photoreactive test in patients with migraine without aura. In our opinion, both the normalization of the changed speed

indicators and the normalization of vascular reactivity to functional loads are associated mainly with the influence on the humoral -metabolic circuit of vascular regulation through the implementation of mechanisms of activation of GABA receptors, inhibition of excitatory glutamatergic neurotransmission and blockade of voltage-gated L-type calcium channels.

Conclusions

1. Cerebral hemodynamics during a migraine attack is characterized by a pattern vasospasm in migraine without aura and a pattern of impaired perfusion in migraine with aura in the middle cerebral arteries, as well as increased perfusion in the cerebral arteries.
2. Hyperreactivity to hypercapnic stress and photoreactive test is a characteristic Doppler pattern in patients with migraine without aura. Hyperreactivity to hyperventilatory stress, reflecting a hyperconstrictor vascular response, dominates in migraine with aura.
3. The use of Topiramate for the preventive treatment of migraine in both clinical groups significantly reduces the frequency, duration, and intensity of migraine attacks, as well as normalizes altered cerebral hemodynamics and cerebrovascular reactivity.

References

1. Lipton, R. B., & Bigal, M. E. (2005). Migraine: epidemiology, impact, and risk factors for progression. *Headache: The Journal of Head and Face Pain*, 45, S3-S13.
2. Ashina, M., Katsarava, Z., Do, T. P., Buse, D. C., Pozo-Rosich, P., Özge, A., ... & Lipton, R. B. (2021). Migraine: epidemiology and systems of care. *The Lancet*, 397(10283), 1485-1495. doi: 10.1016/S0140-6736(20)32160-7.
3. Smith, T. R. (2004). Epidemiology and impact of headache: an overview. *Primary Care: Clinics in Office Practice*, 31(2), 237-241. PMID: 15172504
4. Silberstein, S. (2010). A new frontier for headache. *Frontiers in Neurology*, 1, 135. doi: 10.3389/fneur.2010.00135.
5. Lipton, R. B., Stewart, W. F., Diamond, S., Diamond, M. L., & Reed, M. (2001). Prevalence and burden of migraine in the United States: data from the American Migraine Study II. *Headache: The Journal of Head and Face Pain*, 41(7), 646-657.
6. Olesen, J. (1992). Cerebral blood flow in migraine with aura. *Pathologie-biologie*, 40(4), 318-324.
7. Kellner-Weldon, F., El-Koussy, M., Jung, S., Jossen, M., Klinger-Gratz, P. P., & Wiest, R. (2018). Cerebellar hypoperfusion in migraine attack: incidence and significance. *American Journal of*

- Neuroradiology, 39(3), 435-440. DOI: 10.3174/ajnr.A5508
8. Lucas, C. (2021). Migraine with aura. *Revue neurologique*, 177(7), 779-784. doi: 10.1016/j.neurol.2021.07.010.
9. Goadsby, P. J., Lipton, R. B., & Ferrari, M. D. (2002). Migraine—current understanding and treatment. *New England journal of medicine*, 346(4), 257-270.
10. Ferrari, M. D., Goadsby, P. J., Burstein, R., Kurth, T., Ayata, C., Charles, A., ... & Dodick, D. W. (2022). *Migraine Nat Rev Dis Primers* 8 (1): 2. doi: 10.1038/s41572-021-00328-4.
11. Olesen, J. (2018). Headache classification committee of the international headache society (IHS) the international classification of headache disorders. *Cephalalgia*, 38(1), 1-211.
12. Evers, S. (2008). Treatment of migraine with prophylactic drugs. *Expert opinion on pharmacotherapy*, 9(15), 2565-2573. doi: 10.1517/14656560802377046
13. Ong, J. J. Y., & De Felice, M. (2018). Migraine treatment: current acute medications and their potential mechanisms of action. *Neurotherapeutics*, 15(2), 274-290.
14. Evans, R. W., Loder, E., & Biondi, D. M. (2004). When can successful migraine prophylaxis be discontinued?. *Headache*, 44(10), 1040-1042.
15. Silberstein, S., Tfelt-Hansen, P., Dodick, D. W., Limmroth, V., Lipton, R. B., Pascual, J., ... & Task Force of the International Headache Society Clinical Trials Subcommittee. (2008). Guidelines for controlled trials of prophylactic treatment of chronic migraine in adults. *Cephalalgia*, 28(5), 484-495. doi: 10.1111/j.1468-2982.2008.01555.x
16. Mathew, N. T. (2001). Antiepileptic drugs in migraine prevention. *Headache: The Journal of Head and Face Pain*, 41, 18-25.
17. Silberstein, S. D. (2015). Preventive migraine treatment. *Continuum: Lifelong Learning in Neurology*, 21(4, Headache), 973-989.
18. Ashina, M., Buse, D. C., Ashina, H., Pozo-Rosich, P., Peres, M. F., Lee, M. J., ... & Dodick, D. W. (2021). Migraine: integrated approaches to clinical management and emerging treatments. *The Lancet*, 397(10283), 1505-1518. doi: 10.1016/S0140-6736(20)32342-4.
19. Silberstein, S. D., Lipton, R. B., Dodick, D. W., Freitag, F. G., Ramadan, N., Mathew, N., ... & Topiramate Chronic Migraine Study Group. (2007). Efficacy and safety of topiramate for the treatment of chronic migraine: A randomized, double-blind, placebo-controlled trial. *Headache: The Journal of Head and Face Pain*, 47(2), 170-180. doi: 10.1111/j.1526-4610.2006.00684.x.
20. Rossi, P., Cesarino, F., Faroni, J., Malpezzi, M. G., Sandrini, G., & Nappi, G. (2003). SUNCT syndrome successfully treated with topiramate. *Cephalalgia*, 23(10), 998-1000.
21. Hansen, J. M., & Schankin, C. J. (2019). Cerebral hemodynamics in the different phases of migraine and cluster headache. *Journal of Cerebral Blood Flow & Metabolism*, 39(4), 595-609.
22. Silvestrini, M., Matteis, M., Troisi, E., Cupini, L. M., & Bernardi, G. (1996). Cerebrovascular reactivity in migraine with and without aura. *Headache: The Journal of Head and Face Pain*, 36(1), 37-40.
23. Öztürk, B., & Karadaş, Ö. (2019). Cerebral hemodynamic changes during migraine attacks and after triptan treatments. *Archives of Neuropsychiatry*, 57(3), 192. doi: 10.29399/npa.21650