

Features of cerebral hemodynamics in patients with chronic migraine

Matlyuba Sanoeva^{1*}, Munisakhon Gulova¹, Mekhriniso Avezova¹, Farruh Saidvaliev²

¹Bukhara State Medical Institute, Uzbekistan

²Tashkent Medical Academy, Uzbekistan

*Corresponding author: Matlyuba Sanoeva DSc, professor, Bukhara State Medical Institute, Uzbekistan; E-mail: matlyubadoct@bsmi.uz

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Abstract

According World Health Organization (2012), migraine is one of the top 40 serious conditions cause disability in the world, as well as stroke, meningitis, epilepsy, and, according to some data, cause a significant economic burden to society and the state as a whole. The purpose was to study the clinical, pathophysiological and hemodynamic features of the course of chronic migraine. 82 patients with chronic migraine were studied, aged 12 to 47 years; the average age was $31,9 \pm 3,8$ years. For comparison, 85 patients with simple migraine (migraine without aura) were selected, aged 14 to 42 years, and their average age was $29,2 \pm 2,6$ years. The following analysis were carried out: clinical, neurological, electroencephalographic, and hemodynamic studies, the ID-migraine questionnaire, MIDAS scale (with the determination of migraine severity), EEG, and cerebral vascular ultrasound. Clinical and neurological, bioelectric and hemodynamic features of chronic migraines have been identified – prolonged migraine paroxysms, intense headaches, reduced performance, daily work activity lead to deterioration of the condition and form psychopathological manifestations, reduce the quality of life; EEG parameters can be objective indicators of the development of acute and chronic vascular complications, determining organic brain damage; migraine paroxysms are the background for the violation of the quality abilities of the cerebral vessels, and the frequency and duration of attacks change the normal physiology of the cerebral blood supply to the brain, being a predictor of acute and chronic brain ischemia.

Keyword: migraine, chronic migraine, ID-migraine questionnaire, MIDAS scale, EEG, ultrasonic dopplerography

Relevance

According World Health Organization (2012), migraine is one of the top 40 serious conditions [Sacco S. et al, 2013] that cause disability in the world population, as well as stroke, meningitis, epilepsy, and, according to some data, cause a significant economic burden to society and the state as a whole [Berg J. et al, 2005; Burch R. C et al, 2015].

By studying the problem of migraine, we were convinced of the complexity of etiopathogenesis and the presence of various theories regarding the formation of its complicated forms. One of the theory is a biochemical one, which states the hypoactive

cell membrane due to decreased level of serotonin in the blood, which cause pulsating headache. The predominance of migraine attacks in women says the opposite – changes in the level estrogens in plasma increases the content of serotonin [Ripa P. et al, 2014].

Summing up the complex pathophysiological concept, it is necessary to take into account that migraine is a significant disease for humanity, accompanied by serious complications such as disorders of the functioning of cerebral integrative vascular and neuronal mechanisms that lead to the interaction of the adaptive and antinociceptive systems with the development of inflammatory reaction of the vascular wall, perivascular edema and ischemic cascade of focal and/or diffuse localization of hypoxic nature of the lesion and, accordingly, have set the goal to study the clinical, pathophysiological and hemodynamic features of chronic migraine in patients.

Material and Methods

We studied 82 patients with chronic migraine, aged 12 to 47 years; the average age was $31,9 \pm 3,8$ years. As a comparison group, we selected 85 patients with simple migraine, aged 14 to 42 years; the average age was $29,2 \pm 2,6$ years. The following examinations were carried out: clinical, neurological, electroencephalographic, hemodynamic studies, ID-migraine questionnaire, the MIDAS scale (with the definition of migraine severity), EEG, and cerebral vascular ultrasound.

Results

The analysis of cause-and-effect factors of chronic migraine confirmed the polyethologicity and polymorphism of its pathogenesis, and exogenous and endogenous factors had a great influence in the formation of attacks. Attention was drawn to the fact that exogenous factors prevailed in uncomplicated forms, while endogenous factors prevailed in chronic migraines.

Patients due to intolerance to light and sound became anxious, agitated, aggressive, lost appetite, hyperosmia was observed – they could not stand the smell of food, spices and perfumes, which increased the headache. The attacks led to a sharp decrease in performance and daily activity, which were the main symptom of patients with chronic migraines prevailing group with uncomplicated migraines 2 times ($p < 0.05$), in the majority (53.5%) of patients, it lasted for 3-5 days. After relief of

migraine paroxysm-patients noted General lethargy, a feeling of heaviness and fatigue throughout the body, as well as drowsiness.

The combination of photo-and phonophobia prevailed in chronic migraines, as opposed to the simple form of migraine ($P<0.05$). Phonophobia was the predominant symptom of chronic migraine, in contrast to photophobia ($P<0.05$), which was apparently associated with the excitatory action of nociceptors, causing cortical depression. As the study shows, the ID-migraine questionnaire was a companion for patients and signs of it became the primary diagnostic marker for the differential diagnosis of chronic migraine from other types of headaches, the criteria of which were nausea, vomiting, phonophobia, photophobia and decreased performance.

Along with qualitative and quantitative assessment of headache, we analyzed its nature and localization [Sanoeva M. Zh. et al, 2019].

The typical localization of hemicrania did not differ statistically from pain with diffuse distribution, but the fronto-parietal localization prevailed by 25% ($P<0.05$). By nature, throbbing headache prevailed by 33% of the compressing headache ($P<0.05$), and by 71.5% of the bursting headache ($P<0.001$) (Fig.1).

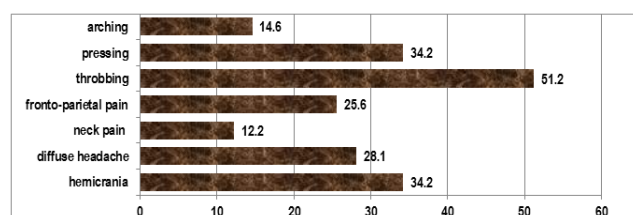


Figure 1: the Nature and localization of headaches in chronic migraine.

In order to assess the functional state of the bioelectric potentials of the central nervous system, the total bioelectric activity of the brain was studied. The EEG of an adult is individual, it reflects to a certain extent his personal characteristics and pathological conditions of both cerebral and somatic genesis. The results of EEG study with an assessment of the functional activity of the surface layers and distant influences of the deep structures of the brain were studied.

In chronic migraine, there was a decrease in the amplitude of the alpha rhythm, the predominance of slow waves over fast ones, and the appearance of single pathological waves without zonal differences. Paroxysmal activity in the background curve was recorded regardless of the presence of migraine attacks, while patients with "Migraine with aura" were 1.7 times less than "Migraine without aura" ($P<0.05$), accounting for 8 (11.9%) and 17 (20.7%) of the subjects, respectively. The rhythmic photostimulation test showed the appearance of photoparoxysmal activity in 12 (14.6%) patients, which was 2.0 times less than in the background curve ($P<0.01$). the same difference was observed in the hyperventilation test ($P<0.05$), which represented bilateral flashes with high-amplitude alpha, theta, and delta waves, with their predominant localization in the temporal, Antero-frontal and parietal regions. On the basis

of spectral analysis in chronic migraine was observed proportional of fast and slow waves activity, mainly in bilateral localization. When comparing groups of patients with simple migraine, there was a significant increase in alpha activity in the central-parietal region of the left hemisphere with spread to the anterior parts of both hemispheres, in chronic migraine, theta activity increased in the central-parietal and occipital regions of the hemispheres, while beta activity was significantly increased than the other waves. The appearance of paroxysmal activity in simple migraines was 2.8 times less than in chronic migraines ($P<0.01$).

Consequently, mild regulatory changes in bioelectric activity were typical in patients with simple migraine, while a significantly disorganized, desynchronous type of EEG with the appearance of pathological waves was observed in chronic migraine. Similar features for these groups were polymorphic activity and a sign of "perverse zonal diversity", which indicated a decrease in the functional activity of neurons in a state of adaptive tension, due to reactive angiodystonia and cortical stimulation by the nociceptive action of migraine paroxysms.

Based on the identified changes in brain biopotentials, we developed a predictive system that allowed us to identify individuals with an increased risk of vascular deficit (HRVD) (acute or chronic) based on the Framingham scale [Sorokina N. D., 2018; Sanoeva M. J., 2020], and to determine the criteria (predictors) of the pathological pattern in patients with chronic migraine. In the presence of an organized type of EEG (I-type), the risk of developing brain ischemia is HRVD=0 (the criterion is a pronounced α -rhythm organized by the bilateral regions, with a frequency of 8-13 Hz); in the presence of light changes-hypersynchronous type II-there is a low risk of vascular deficiency, the risk level HRVD=1.0 (the criterion is the appearance in one or more areas of the brain of slow theta (4-8 Hz) and delta activity (0.3-4 Hz) with an amplitude of up to 30 mV, fast asynchronous oscillations against a fairly regular alpha rhythm); the average risk level HRVD=3.0 is observed with moderate changes in bioelectric activity, desynchronous type III EEG (the criterion is diffusely expressed disorganization of all rhythms, the appearance of a non-dominant curve, at a low amplitude level no higher than 30-35 mV, alpha activity is irregular, beta activity is unstable, and the characteristic appearance of low-amplitude slow activity). Pronounced disorganized type IV EEG, refers to a high risk of brain ischemia HRVD=5.0 (the criterion is the absence of zonal differences in bioelectric rhythms in the presence of gross irregular pathological components: β -rhythm-13-25 Hz, β -rhythm-4-8 Hz). The presence of a gross disorganized - V type refers to a very high risk of developing brain ischemia HRVD=5.0+ (the criterion is the appearance of gross irregular pathological components with a clear zoning of the lesion: the presence of theta (4-8 Hz) and Delta (0.3 - 4 Hz) rhythms). 29.9% were at high risk (HRVD=5.0) and 23.9% of patients with chronic migraines were at very high risk (HRVD=5.0+). 40.5% of patients with simple migraine were assigned to a low risk group (HRVD=1.0) for developing vascular deficits (table 1).

EEG types	Group
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	Simple migraine (n=42)		Chronic migraine (n=67)	
	abs	%	abs	%
I	17	40,5	6	9,0**
II	18	40,5	11	16,4**
III	4	9,5	14	20,9**
IV	2	4,8	20	29,9***
V	1	2,4	16	23,9***

Table 1: Prognostic system of acute cerebrovascular treatment for migraines.

Note: differences regarding simple migraines are significant (*- $P<0.05$, ** - $P<0.01$, *** - $P<0.001$)

Studies show that migraine attacks, depending on the clinical severity and course, duration and frequency of attacks of the disease can become a risk of developing acute and chronic blood flow disorders in the brain.

Dopplerographic indicators for chronic migraine showed a 15-18% decrease in blood flow in the extra cranial parts of the common carotid artery (CCA) compared to the simple form of migraine, without significant asymmetry of the sides. When analyzing data in a statistical decrease of the index of Pourcelot (30%), Stewart (by 40-45%) and Gosling (15-20%) in the studied vessels confirmed the deterioration in peripheral resistance, tone and viscoelasticity, increased hypo perfusion of the brain, and this reduction held steady in the interictal period ($p<0.001$), meanwhile, the linear velocity of blood flow (LVB) reduction was mainly isolated reduction in Vmin. Long-term headaches were accompanied by a hemodynamically significant decrease in LVB for the main trunks (CCA, ICA (internal carotid artery)) (up to 30%), but such changes did not correlate with EEG results, which was apparently associated with compensatory brain perfusion by collaterals. In 16 (34.8%) patients, there was a decrease in blood flow for middle cerebral artery (MCA), anterior cerebral artery (ACA) and posterior cerebral artery (PCA), mainly due to Vmax. In 15 (32.6%) there was an increase in Vmin, with the relative preservation of Vmax for ACA and PCA, of which 10 (21.7%) showed an increase in both Vmax and Vmin, 5 (10.9%) had an isolated increase in Vmax, while in all cases peripheral circulatory resistance and vascular tonic properties were low (<0.57), which confirmed the prevalence of vascular dystonia of the hypotonic type.

Signs of vertebrobasilar insufficiency were observed in 4 (8.7%) patients, which correlated with the basilar type of chronic migraine, venous dyscirculation mainly along the main artery (a.basilaris) was detected in 28 (60.9%) of the examined patients, and a decrease in blood flow along the anterior cerebellar artery was observed in 2 (4.35%) patients.

Vascular dystonia by hypotonic type correlated with a state of lethargy, rapid fatigue, drowsiness and a sharp decrease in performance in the post-seizure period.

The systolic and diastolic components of the blood flow rate in the CCA were inferior to 28% in chronic migraine, compared to the simple form of migraine. Also, the relatively low indicator of the average blood flow rate (Vmed) in the CCA in 29 (35.4%) patients with chronic migraine, while in the simple form of migraine, it did not change statistically in relation to the physiological norm ($p<0.01$). The decrease in LVB was accompanied by a significant decrease in the peripheral resistance index of Pourcelot (Ri) to 21%, while the index of spectral expansion increased by 1.4 times, with the appearance of moderate blood flow turbulence. There was a simultaneous increase in the tone of the external carotid artery (ECA) ($N=0.68-0.74$) – due to an isolated decrease in Vmin in 12 (14.6%) patients due to a decrease in Vmax and Vmin. Statistically significant changes in blood flow in the extracranial parts of the vertebral artery (VA) were not observed.

The obtained results predetermined the study of autoregulatory abilities of brain vessels, which became the subject of predicting acute and chronic brain ischemias in migraines. The Overshoot coefficient (CO) was determined by pressing the CCA and registering blood flow in the middle cerebral artery (MCA) of the ipsilateral side, the normal value of which was $N=1.23-1.54$ (table. 2).

Group		V1 mm / sec	V2 mm / sec	Redu ced blood flow %	V3 mm / sec	Incre ased blood flow %	OC
Simple migraine	Dex	84,5	53,6	36,6	106,6	49,7	1,26
	Sin	91,1	51,1	43,9	112,6	54,1	1,24
Chronic migraine	Dex	76,2*	55,6	27,0*	74,8*	25,7*	0,98**
	Sin	79,2*	57,4*	27,5*	78,6*	27,0*	0,99**

Table 2: Comparative analysis of the Overshoot coefficient.

Note: differences regarding simple migraines are significant (*- $P<0.05$, ** - $P<0.01$, *** - $P<0.001$)

As can be seen from table. 2 in chronic migraine after CCA compression, the blood flow rate in the ipsilateral MCA decreased by 1.4 times (25.0-28%), significantly differing from the comparison group (35-45%) ($P<0.05$), after stopping pressure, the blood flow increased by only 25-30%, statistically inferior to the simple form (50-55%), which showed a decrease in the reactivity of the cerebral arteries due to their hypotension. OC had a significant difference compared to the group of patients with simple migraine, yielding 20-22% in chronic migraine ($p<0.05$).

Thus, the observed signs – the decrease in the indices of resistivity of Pourcelot (Ri) <0.57 ($N=0.57-0.67$), pulsation of Gosling (Pi) to 50%, making <1.05 ($N=1.05-1.17$), determining the tone, reactive abilities and resistance (peripheral and circulatory) of the vascular wall and decrease of the coefficient Overshoot 20-30%, amounting $CO<1.23$ ($N=1.23-1.54$) that defines the reserve capacity of the brain and the state of autoregulation of cerebral vessels, and the presence of venous

discirculation at the same time, prove the reduction of adaptive-compensatory mechanisms thus, being signs of predicting acute and chronic brain ischemia, referred to as cerebrovascular complications, which have a direct correlation with bioelectric, clinical and neurological dysfunctions.

Conclusions

- Our results prove the prevalence of organized EEG type in simple migraine and disorganized type in chronic migraine, determining organic brain damage, which can be used to control and select differentiated adequate therapy for various variants of the clinical course of migraine.
- Migraine paroxysms are the background for impaired quality abilities of cerebral vessels, and the frequency and duration of attacks change the normal physiology of blood supply to the brain, being a predictor of acute and chronic brain ischemia, referred as cerebrovascular complications.

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