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MIGRAINE, A MODERN VIEW OF THE PROBLEM

Introduction: Migraine is a common primary headache that has been known and studied for over 3,000 years. Current research shows that migraines can be caused by a variety of factors, including genetic predisposition, hormonal changes, stress, and certain foods. Current treatments for migraines include drug therapy, preventive treatment, and non-drug treatments such as cognitive behavioral therapy and lifestyle modification. It is important to note that the approach to migraine treatment should be individual and take into account the characteristics of each patient.

Keywords: migraine, primary headache, genetic predisposition, hormonal changes, stress, modern treatment method, drug therapy, preventive treatment, non-drug methods.

Migraine is a paroxysmal condition of the autonomic nervous system, the most common and characteristic symptom of which are episodic or regular severe and painful attacks of headache [1]. An increase in the frequency of this disease (women experience migraine attacks 2-3 times more often than men, but the pain intensity is usually higher in the latter) [4], a decrease in the age of migraine patients (the peak incidence occurs in the period from 25 to 34 years) [3] require a special approach to the development of new diagnostic and treatment methods.

Migraine as a disease has been described since ancient times. Scientists, writers, artists, musicians, military leaders and rulers of the world suffered from migraines, the literature describes the clinical symptoms at the time of the attack in many famous people [9], which proves the existence and development of the disease regardless of the position, race, time and location of patients. The first description of migraine appeared in the 2nd century AD, it was made by Areteus of Cappadocia (the discoverer of migraine), who in his book "On Acute and Chronic diseases" he described his own observations [9]. He compiled the first classification of headaches: in his opinion, cephalgia is short-term headaches, and he called cephalgia chronic headaches, migraine described as a "heterocrania" ("other head"), in which deaths were observed, which were later attributed to subarachnoid hemorrhages. Modern studies have confirmed that there really are migraine strokes of ischemic and hemorrhagic origin, and they can be fatal if untimely diagnosed.

The famous ancient Greek physician Galen (II century A.D.)

changed the name "heterocrania" to "hemicrania", which means "half of the head" in Greek, and described one of the important distinguishing features of the disease — the localization of pain in half (hemi) of the head (krania). The modern name "migraine" is obviously a corruption of Galen's term [9]. The Greek physician Aeginatus was the first to point out the factors that provoke migraine attacks: noise, screaming, bright lights, strong-smelling substances, drinking wine, etc.

Periodic headaches, according to their description Scientists find migraine-like symptoms in documents dating back to ancient Babylon and in letters from the Sumerian civilization, and according to the writings of the ancient Greek historian Herodotus (490-425 BC), in ancient Egypt, among

people who practiced healing and specialized in the treatment of various diseases, there were priests who treated only headaches.

In 1860, the German physician A. Gubler (1821-1879) was the first to describe ophthalmoplegic migraine. In the works of the English physician Thomas Willis (T. Willis, 1622-1675), you can find a detailed description of the clinical manifestations of migraine and a description of it as a family disease.

Over the past decade, the understanding of the pathophysiology of migraine has undergone significant changes, due to the introduction of new technologies in the study of epidemiology, genetics, pathogenesis and treatment of the disease (Amelin A.V. et al., 2001). In this regard, an integrated approach to the diagnosis and treatment of migraine becomes especially relevant, taking into account clinical, psychological, neurophysiological and biochemical parameters (Gavrilov E.L., 2004).

According to modern literature, if both parents had migraine attacks, the risk of the disease in the offspring reaches 60-90%. If the seizures migraines were observed in the mother, the risk of the disease is 72%, if the father has 30% [3, 7]. The results of molecular biological studies in patients with familial hemiplegic migraine have shown that chromosome 19p13 is responsible for the appearance of this form of migraine. Mutations of the CACNA1A gene localized on chromosome 19p131 determine the condition of cerebral specific calcium channels of the P/Q type, responsible for the occurrence of this form of migraine and a number of other diseases called channelopathies, such as hyperkalemic and hypokalemic periodic paralysis, and paramyotonia. Eilenburg syndrome, episodic ataxia with myocemia, episodic ataxia with cerebellar atrophy, CADASIL syndrome (cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy) [8, 19]. It has been established that migraine and these diseases also combine the paroxysmal course and the absence of symptoms during the inter-onset period. Moreover, in patients Migraine cephalgias occur with channelopathies significantly more often than in the general population. The metabolic disorder of major neurotransmitters found in migraine patients is associated with genetically determined disorders of mitochondrial phosphorylation. This assumption was based on clinical observations indicating that virtually all patients with MELAS syndrome (mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke-like episodes — mitochondrial myopathy with encephalopathy, lactic acidosis, and stroke-like episodes) suffer from migraines, and migraine cases are often observed in the immediate family of patients with MELAS syndrome [10]. Thus, there are various evidences of the involvement of genetic factors in the origin of migraine, but their significance and role remain unclear. Undoubtedly, migraines can be the result of more than one genetic defect. It is likely that new genetic studies will significantly expand the understanding of the etiology of migraine, improve the diagnosis and treatment of this disease. According to statistics, migraines affect almost 10% of the inhabitants of civilized countries. In a study conducted in France in 1988 on Based on a representative sample of the population over the age of 15, it was found that the prevalence of migraines was 8.1%, with people aged 30 to 49 years most often affected. In 50-60% of cases, migraine turns out to be inherited in an autosomal dominant type, while in 2/3 of cases it is transmitted through the maternal line [5]. It is believed that the genes that transmit a predisposition to migraine are part of chromosome 19 in some patients. In fact, the features of neurohumoral response to changes in homeostasis leading to the development of migraines are inherited.

In fact, migraine is not just a headache: it is a critically painful condition characterized by pulsating spasms mainly on one side of the head, sensitivity to light and sound, nausea and even vomiting,

which requires further careful study of the etiology and pathogenesis of development, based on the study of the genetic background.

In some studies, migraine has been associated with clinically "mute" brain damage, predominantly white matter. In a meta-analysis of neuroimaging studies, the relative risk of white matter damage in migraine patients was 3,9 (2,3–6,7). In a large cross-sectional magnetic resonance imaging study, M. Kruit et al. The neuroimaging characteristics of three groups of patients were compared: those with migraine with aura, those with migraine without aura, and healthy individuals in the control group, strictly randomized by gender and age. The authors found no significant differences between patients with migraine and those in the control group in the observed cases of heart attacks (8.1 and 5.0%, respectively). Meanwhile, an analysis of the subgroups identified by the principle of localization of neuroimaging data showed that patients with migraine had a higher incidence of "silent" heart attacks in the posterior cerebral basin (5.4 and 0.7%, respectively), that is, higher in 7.71 times. This frequency was 13.7 times higher in patients with migraine with aura compared to those without a history of migraine. In patients with migraine with a frequency of attacks of 1 or more times per month, this representation was 9.3 times higher. The highest risk of detecting neuroimaging changes was in patients with migraine with aura with a frequency of attacks of 1 time or more per month (15.8 times) compared with those in the control group. Convincing evidence of the relationship between migraine and cerebral infarction concerns cases verified using angiography, computed tomography, positron emission tomography, magnetic resonance imaging, and triplex scanning of brain vessels, which provides an opportunity to determine the true cause of degenerative changes in the brain in conjunction with genetic and biochemical blood tests.

Thus, detailed descriptions of migraine symptoms appeared long before our era, many centuries ago. In this regard, modern science has managed to add little to the work of scientists of the past, who were distinguished by their unique ability to observe and correctly evaluate the results of their research.

The end of the 19th — beginning of the 20th century is characterized by a surge of activity in the study of migraines. Suffice it to say that in his monograph on migraine, Flatau cites over 470 papers on this problem. This work is an unsurpassed example of describing the manifestations of the disease and deep discussions about the mechanisms of its development. The outstanding French neurologist Charcot put forward the concept of complicated migraine, which he observed, which remains relevant to this day [13]. The modern period of migraine research began with a lively discussion about which forms of headache should be attributed to migraines. Leving believed that this disease is not always manifested by sharp unilateral pain. He assumed, and this has only now been confirmed, that migraine attacks can also be expressed by bilateral headaches. The same opinion was shared by world-renowned scientists Govers and Quincke. Thus, one of the main symptoms of migraine, unilateral pain, lost its relevance, and other symptoms that were previously considered secondary were brought to the fore for diagnosis. Detailed descriptions of the visual aura have appeared, which, although it has long been known, is crucial. No importance was attached to the diagnosis. Some doctors believed that migraines should be considered only those headaches that begin with characteristic visual symptoms — blindness or hemianopia, and only later headache and vomiting join these symptoms. This statement is supported, with some modifications, by some modern clinicians. However, Flatau disputed this hypothesis, believing that visual symptoms cannot be considered the main ones for migraines [4]. The famous German neurologist Oppenheim expressed It is believed that the most important, and often the only symptoms of migraine are the frequency of headaches and vomiting. The literature provides interesting facts about the origin and pathogenesis of migraine. So, J. Olesen et al. (1981) found that during a migraine aura, a wave of oligemia begins in the occipital region of the brain

and spreads only to the central sulcus at a rate of 2-3 mm per minute, which corresponds to the rate of spread of cortical neuronal depression, described as early as 1944 by A. Leao [2, 8]. The data obtained called into question the vasoconstrictor origin of oligemia and formed the basis for the claim that brain hypoperfusion observed during aura is secondary and is initiated by depolarization of cortical neurons [7]. Later, it was shown that experimentally modeled cortical depolarization in animals increases the spontaneous activity of neurons in the spinal nucleus of the trigeminal nerve, involved in the pathogenesis of migraine. These clinical and experimental data have confirmed the position of most scientists that spreading cortical depression may be not only the cause, the development of aura symptoms, but also a factor triggering an attack of migraine headache.

The modern theory of migraine is called trigeminovascular and combines the neuronal and vascular mechanisms of migraine formation [4, 7]. It is based on a violation of the mechanisms of interaction between the extra- and intracranial vessels, the trigeminal nerve and the central nervous system, resulting in the development of aseptic neurogenic inflammation of the meningeal vessels. Moreover, the trigeminal nerve plays a key role in this process, which is the initiator of neurogenic inflammation and the conductor of pain information from the meninges. Moreover, the first participants. The ascending nociceptive flow is formed by the neurons of the Gasser node and the sensory nucleus of the trigeminal nerve [16]. Anatomical and experimental neurophysiological studies reveal a close relationship between the sensory nuclei of the trigeminal nerve and the parasympathetic fibers of the facial nerve and the nuclei of the vagus nerve. The axons of the neurons of the upper salivary nucleus have synaptic contacts with the neurons of the pterygoid ganglion, the projections of which end at the cerebral vessels and dura mater. Activation of trigeminal neurons. This complex leads to parasympathetic vasodilation of the dura mater vessels and impaired gastric motility, causing nausea and vomiting during a migraine attack. A migraine attack begins due to activation of the trigeminovascular complex against the background of reduced endogenous pain control [6]. Neurophysiological and biochemical studies have revealed signs of functional insufficiency of the endogenous antinociceptive system in patients with migraine, correlating with low levels of enkephalins in the blood and cerebrospinal fluid. There is reason to believe that migraine patients have a genetically determined defect in the metabolism of endogenous opioids and serotonin. For the first time, a possible connection between migraine and impaired metabolism of endogenous serotonin was suggested in the late 60s by A.M. Ostfeld and H.G. Wolff. Later, it was discovered that fluctuations in plasma serotonin levels correlate with the dynamics of a migraine attack, and the "serotonin" hypothesis of migraine was formulated. Later, the "serotonin" hypothesis was confirmed in the clinic.

To achieve better results in relieving migraine attacks, a stratified approach is used, according to which first-line therapy is determined depending on the intensity of migraine symptoms (severity of headache and concomitant symptoms, including disability). Treatment of a migraine attack with eletriptan at a dose of 40 mg proved to be highly effective in reducing not only the intensity of headache and concomitant symptoms within 1 hour after taking the drug, but also rapid recovery of working capacity.

Sumatriptan is the gold standard of migraine therapy. The efficacy and safety of sumatriptan have been studied in 300,000 attacks (more than 60,000 patients) in clinical trials and in 200 million attacks in clinical practice over 15 years of its use. Patient satisfaction with this drug is 63% and significantly exceeds satisfaction with drugs of other classes that are used to relieve migraines (Pascual J., 2007). Sumatriptan is more effective in patients with a slow onset of headache. Research on sumatriptan

generics (amigrenin, sumamigren), conducted in our country, confirmed its high effectiveness (Wein A.M., Artemenko A.R., 2002; Tabeeva G.R., Azimova Yu.E., 2007).

In recent years, modern diagnostic methods and the development of various medicines for migraine have appeared, and therefore qualitatively new opportunities for studying this problem. Nowadays, more than 80% of people suffer from headaches of various types, but not all consider it a disease and turn to doctors [4, 7]. It is known that not all primary headaches can be associated with migraines, and there are many types of secondary headaches that are often difficult to treat. It was mentioned above that the ancient Roman physician Celsus said that migraines are a lifelong, fatal disease. As we now know, it's not a lifetime sentence at all. In addition, some researchers claim that migraine attacks are a kind of compensatory mechanism that protects the brain from harsh external and internal stimuli precisely when it needs rest. Today, many scientific papers prove that timely diagnosis and correct appropriate treatment can reduce the frequency and intensity of migraine headaches, meaning migraines can be managed. It has been shown that a migraine attack in humans can be induced by drugs that deplete the serotonin content in the central nervous system (reserpine) or activate vascular serotonin receptors (methachlorophenylpiperazine). It was noted that intravenous administration of serotonin relieves a migraine headache attack that develops spontaneously or is induced by reserpine administration. pain. Modern effective means of relieving a migraine attack are agonists of serotonin 5HT1 receptors, and some means for the prevention of migraine are antagonists of 5HT2 receptors.

Pharmacological prophylaxis of migraine includes: antiepileptic drugs (sodium valproate, topiramate), beta-blockers (propranolol, metoprolol), calcium channel blockers (flunarizine, verapamil), antidepressants (amitriptyline), as well as riboflavin, magnesium preparations, and recently attention has been paid to combined nonsteroidal drugs. Among the variety of means for the prevention of migraine, the choice of a specific drug is based on improving metabolism, microcirculation, and reducing the inflammatory factor of the brain [5, 8]. And when in migraine complications, preference is given to drugs with neurotrophic and modulatory properties that improve the plasticity of nervous tissue and normalize metabolic processes, in the central nervous system and peripheral nervous system. Of the preventive and therapeutic agents, drugs with higher efficacy and good tolerance not only for migraines, but also for comorbid diseases have priority. At the same time therapeutic the dose should be adequate for both diseases. Very often, a combination of hypertension and thyroid disease is observed in the migraine clinic. breast injury, head injury, vascular malformations. In the treatment and prevention of these comorbid conditions, it is important to identify the predominance of a particular disease in a timely manner, as well as to understand the aggravating factors for a particular case. All of this may lead to a preventive approach in relation to both migraine complications, comorbid conditions, and recurrent migraine attacks.

According to the observations of some authors, the first signs of the disease appear during puberty [1, 4]. It occurs 3-4 times more often in women than in men. In men, migraine attacks in women are often associated with the menstrual cycle. In most cases, migraines occur in young people, up to 30 years old [2]. Many cases of migraine are observed in children (there are even cases of the disease at the age of five). By old age, the disease subsides. The circumstances of a person's life largely determine the intensity and frequency of headaches. A prosperous, peaceful life reduces the frequency of seizures, and stress, physical and emotional overload provoke migraines. A simple migraine occurs in three stages. Usually for several hours or even days before the start of the pain phase, performance and mood deteriorate, and harbinger symptoms appear: pallor, indifference, drowsiness, yawning, and nausea. With the so-called visual migraine, flashes, flashes, and zigzag stripes appear in front of the eyes immediately before the attack. Then there is an acute headache that lasts from a few minutes to

15-20 hours. Usually, during an attack, a person cannot stand bright lights, loud noises, loses his appetite, nausea increases, and sometimes vomiting occurs., the face turns red, chest pain appears, chills. After the attack, the third stage begins — prolonged sleep. Doctors also note other clinical manifestations of migraine, for example, impaired motor activity of the extremities: with pain in the right side of the head, various motor and sensory disturbances occur in the left leg or arm, and vice versa. It is believed that in the first stage of migraine, the blood vessels of the head constrict and blood flow decreases. Then, in the painful phase, the carotid artery expands [2]. Such psychophysiological traits as increased excitability and emotional lability, touchiness, ambition, intolerance to the mistakes of others, love of perfection, initiative, ambition are associated with migraines. According to long-term observations of scientists, strong,

strong-willed, active people suffer from this disease. Migraines often coexist with hysteria, epilepsy, and allergies. Migraine sufferers are usually stubborn, self-centered, easily irritated, and internally tense. At the same time, they are conscientious, even prone to meticulousness and excessive detail. They often experience unreasonable anxiety, dissatisfaction, and frustration [10].

Summarizing the study of the history of the origin of migraine and the analysis of data from the literature review, we can conclude that headache, as a state of nociceptive chain reaction, has always been at the peak of relevance and has been an interesting and studied problem of civilization. Interest in this problem has persisted for centuries, not only because it is common in the population and is a primary headache, but also because of the polymorphism of symptoms, the difficulty of correcting the intensity of headaches, and the frequent complications associated with vascular system of the brain, as well as degenerative changes in brain matter. The long-standing study of this pathology has not yet led to a consensus on the pathogenesis of the disease, the prevention and treatment of simple and complicated forms of migraine, as well as migraine with aura. The presence of structural changes in the brain substance in patients with migraine, according to instrumental studies, makes it possible to predict the disease and provide timely assistance to victims of migraine, depending on the type of clinical manifestations.

An often erroneous approach to diagnosis and treatment migraines in its complicated forms, the lack of an analysis of the origin and insufficient collection of anamnesis of the disease in young patients with strokes and epilepsy lead not only to an elongation of the incidence period and the formation of persistent foci of necrosis in the brain, but also to the development of disability in patients of working age, as well as to frequent deaths due to the use of inappropriate means. Clinicians, and especially neurologists and intensive care physicians, should once again to reflect on the origin of acute vascular conditions of the brain in young patients, conduct a thorough analysis of examinations and reconsider the choice of treatment tactics for complicated forms of migraine. The development of preventive and curative measures, depending on the types of migraine and its complications, may be a breakthrough in the prevention of disability and maladaptation of people of working age with simple and complicated forms of migraine.

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