SKRZYPEK, Jakub, NIEWIADOMSKA Jagoda, BONDOS, Borys, STĘPIEŃ, Aleksandra, PALUCH, Alicja, NIEKRA, Aleksandra, FUSSEK, Łukasz, KOCHAN, Robert, WIECZOREK, Ewelina and LEE, Kacper. Episodic and chronic migraine - treatment and risk factors - A literature review. Journal of Education, Health and Sport. 2024;75:56459 eISSN 2450-3118.
https://dx.doi.org/10.12775/JEHS.2024.75.56459
https://apcz.umk.pl/JEHS/article/view/56459

The journal has had 20 points in Ministry of Higher Education and Science of Poland parametric evaluation. Annex to the announcement of the Minister of Higher Education and Science of 05.01.2024. No. 32553.
Has a Journal's Unique Identifier: 201398. Scientific disciplines assigned: Economics and finance (Field of social sciences); Management and Quality Sciences (Field of social sciences).
Punkty Ministerialne z 2019 - aktualny rok 20 punktów. Załącznik do komunikatu Ministra Szkolnictwa Wyższego i Nauki z dnia 05.01.2024 r. Lp. 32553. Posiada Unikatowy Identyfikator Czasopisma: 201398.
Przypisane dyscypliny naukowe: Ekonomia i finanse (Dziedzina nauk społecznych); Nauki o zarządzaniu i jakości (Dziedzina nauk społecznych).

The authors declare that there is no conflict of interests regarding the publication of this paper.
Received: 26.11.2024. Revised: 16.12.2024. Accepted: 17.12.2024. Published: 20.12.2024.

Episodic and chronic migraine - treatment and risk factors - A literature review

Authors:

Jakub Skrzypek [JS]
jakub.skrzypek.00@gmail.com
https://orcid.org/0009-0004-1155-5818
Medical University of Lublin, Poland
al. Racławickie 1, 20-059 Lublin, Poland

Jagoda Niewiadomska [JN]
malwatexass@wp.pl
https://orcid.org/0009-0003-2219-984X
Medical University of Lublin, Poland
al. Racławickie 1, 20-059 Lublin, Poland

Borys Bondos [BB]
borysb97@gmail.com
https://orcid.org/0009-0005-7971-4691
Medical University of Lublin, Poland
al. Racławickie 1, 20-059 Lublin, Poland

Aleksandra Stępień [AS]
stepienaleksandra00@gmail.com
https://orcid.org/0009-0004-9258-2294
Medical University of Lublin, Poland
al. Racławickie 1, 20-059 Lublin, Poland

Alicja Paluch [AP]
alapal123op@gmail.com
https://orcid.org/0000-0001-8233-3885
Medical University of Lublin, Poland
al. Racławickie 1, 20-059 Lublin, Poland

Aleksandra Niekra [AN]
ola.niekra@gmail.com
https://orcid.org/0009-0007-0116-4882
Medical University of Lublin, Poland
al. Racławickie 1, 20-059 Lublin, Poland

Łukasz Fussek [ŁF]
lukaszfussek@gmail.com
https://orcid.org/0009-0008-2185-399X
Medical University of Lublin, Poland
al. Racławickie 1, 20-059 Lublin, Poland

Robert Kochan [RK]
robkochan2211@gmail.com
https://orcid.org/0009-0002-9796-9231
Medical University of Lublin, Poland
al. Racławickie 1, 20-059 Lublin, Poland

Ewelina Wieczorek [EW]
ewelinawieczorek1255@gmail.com
https://orcid.org/0009-0009-3763-0384
Medical University of Lublin, Poland
al. Racławickie 1, 20-059 Lublin, Poland

Kacper Lee [KL]
liosek17@gmail.com
https://orcid.org/0009-0005-4474-6140
Medical University of Lublin, Poland
al. Racławickie 1, 20-059 Lublin, Poland

Abstract

Introduction and objective

Migraine is a chronic paroxysmal neurological disease characterised by attacks of moderate to severe headache and accompanying symptoms such as hypersensitivity to light and sound and gastrointestinal disturbances such as nausea and vomiting, among others. In some people, an attack of pain is preceded by a migraine aura - visual disturbances, numbness, tingling and even muscle weakness. Treatment includes medications taken as a temporary measure (at the onset of an attack) and as a prophylactic measure. The aim of this study is to systemasise information about chronic migraine and to raise awareness about this disease among health care workers and patients

Brief description of the state of knowledge

Migraine is a recurrent, usually unilateral, throbbing headache. A migraine usually lasts between 4 and 72 hours. It is characterised by varying degrees of severity and frequency of occurrence. The pain is exacerbated by emotion or physical exertion. There is photophobia,

hypersensitivity to sounds (phonophobia) and odours (osmophobia), and nausea and vomiting occur. Sometimes before a migraine episode occurs, a so-called aura - occurring in 10% of migraine cases may appear, in the form of paresthesias, visual field loss, appearance of gloom, paresis, aphasia. Chronic migraine is a headache that occurs for at least 15 days per month, at least 8 of which are days when the headache has the characteristics of migraine pain as described below or is relieved by prescription anti-migraine medication. There are many triggers for migraine, which include genetic, environmental and personal factors. Chronic migraine severely reduces the quality of life of affected patients; therefore it is important to raise awareness of currently available methods for its diagnosis and treatment

Summary

Early recognition and treatment of migraine improves the quality of life of patients therefore any action to increase publin knowledge and awareness on the disease is important.

Keywords

Migraine, migraine risk factors, migraine treatment, chronic migraine, migraine pharmacotherapy

Introduction and description of current knowledge

Migraine is by far the most frequent neurological problem in primary care. Migraine is ranked second among causes of disability worldwide and first among young women, as reported in the latest Global Burden Disease survey. Migraine is a highly prevalent disorder, as it affects 18% of women and 6% of men, while chronic migraine affects 2% of the global population and is extremely burdening for patients and their families. [1] Chronic migraine is described by frequent headache attacks with at least 15 headache days per month. Patients with chronic migraine usually have a history of episodic migraine and their headache intensity tends to increase over time.[2]

Migraine is occasionally mistaken for other types of headaches, such as tension headache. Migraine patients may not receive a correct diagnosis and appropriate treatment.[3] As there are currently no dedicated diagnostic tests or biomarkers available, the diagnosis of most primary headache disorders is still exclusively based on clinical assessment, which complicates the diagnosis process. [4] The clinical symptoms of migraine in childhood differs

from those in adulthood. Childhood migraine is marked by shorter attacks and less often one-sided pain. Accompanying manifestations include mild light intolerance and rarely noise intolerance for example, while emesis and craniofacial autonomic features are significantly more frequent in comparison to the adult patients. [5] Most patients have a family history of migraine. [6]

The genesis of migraine headache

The theories describing the probable pathomechanism of migraine headache include the following: the vascular theory, the neuronal theory, the inflammation of the
neural tissue, biochemical theory, central sensitisation theory and genetic origin. The vascular theory assumes that migraine symptoms are caused by vasoconstriction (vasoconstriction of the occipital region during the visual aura) and then their relaxation/dilatation which is accompanied by hyperperfusion and perivascular oedema to be the cause of severe pain. The neural theory identifies the source of migraine headaches as a disturbance in the bioelectrical activity of the brain. A different hypothesis is that sterile inflammation of the nerve tissue (neuroinflammation) is the reason for migraine. An increase in the release of inflammatory factors by the meningeal vessels stimulates the sensory nerves, especially the trigeminal nerve, which may be the origin of the migraine.[7] It remains a challenge to understand the mechanisms of migraine because migraine is not a static disorder, and even in its episodic form migraine continues to be an 'evolving' chronic condition. [5] The biochemical theory is mainly founded on disorders of serotonergic transmission. There is also a hypothesis of autonomic system disturbances (sympathetic insufficiency) in migraine patients. It would explain the symptoms occurring in patients with migraine (vasomotor and heart rhythm disturbances, nausea, vomiting and diarrhoea).[7] Genetic factors may determinate vulnerability to migraine, while various environmental factors may play a role in the progression of a migraine attack. [5]

Migraine risk factors

A number of factors are involved in the progression of migraine. The power of the proof is higher for some of the factors than for others, though this may reflect the strength of the methodologies, study design and sampling size of the studies undertaken, and not necessary the strength of the correlation. The factors are mainly divided in groups such as suboptimal treatment, comorbidities, lifestyle and external factors and demographic factors.

Non-optimal treatment of episodic migraine in the acute phase is related to an increased risk of progression to chronic migraine. Continuing suboptimal acute therapy may lead to a

change in dosage or the use of another acute drug, possibly resulting in increased drug misuse and risk of subsequent progression of the disease. [8] It should also be noted that the patients who did not think they could control their headache or thought their headache was due to chance or fate were more likely to inadequately manage their headache, resulting in worse overall disability. These factors emphasise the necessity of being educated on how best to effectively manage and cope with migraine. There is a high need for healthcare professionals to educate patients in that matter of migraine headache.[9]

A number of common neurological and psychiatric disorders show co-existence with migraine. Depression and anxiety are both associated with an elevated migraine risk, which is even greater when both disorders co-occur in a patient. About 45-65% of patients with depressive disorders fulfil the criteria for anxiety disorders and inversely, 30-65% of patients with anxiety disorders also have depression. Migraine doubles the risks of ischaemic stroke, which is most evident in migraine with aura. Migraine may enhance individual vulnerability to ischaemic stroke in acute cerebral ischaemia. Migraine may be a stroke risk factor or may be an symptom of underlying structural anomalies. Lifetime frequency of migraine is elevated in patients with epilepsy. Co-occurrence is especially common in haemiplegic migraine, with epilepsy present in ∼40% of patients with haemiplegic migraine. Migraine aura-triggered attacks may also develop during or directly after an attack of migraine with aura, which has not been reported for migraine without aura [10].

Metabolic associated comorbidities are highly common in the advanced disease states, including obesity and metabolic syndrome. Studies showed an elevated risk of metabolic syndrome in overweight individuals (body mass index [BMI] 25 to < 30 kg/m2) and an even greater risk of metabolic syndrome in obese individuals (BMI ≥ 30 kg/m2) in comparison to normal weight individuals. [8]

Scientists have been trying to design lifestyle modification strategies for the prevention and treatment of headaches. The roles of dietary factors have been recognized, which has resulted in the formulation of diet therapy strategies for headaches, including migraine. The involvement of dietary associations in the pathogenesis of headache has been acknowledged and, on this basis, an eradication diet strategy has been implemented in this area. It is widely assumed that migraines are diet-sensitive and that some dietary ingredients trigger migraine attacks. There are long listings of possible dietary triggers, but there is still controversy in this area. Chocolate, citrus fruits, nuts, ice cream, tomatoes, onions, dairy products, alcoholic beverages, coffee, caffeine, monosodium glutamate (MSG), histamine, tyramine,

phenylethylamine, nitrites, aspartame, sucralose and gluten have been noted in the literature. [11]

One of the contributing factors to migraine conversion is sleep disorders, which can function as a trigger and/or consolidating factor in these migraine patients.[12] These disturbances often coexist, which has resulted in the hypothesis of an associated not just coincidental occurrence. More recent biochemical and functional imaging research has now identified central nervous system structures and neurotransmitters that are involved in the migraine pathophysiology and also relevant to the control of normal sleep architecture, implying a possible causative role, in the pathogenesis of both disorders, of the dysregulation in these common nervous system tracts. [13] The hypothalamus is a key controller of homeostatic mechanisms, to include sleep and wakefulness cycles, which are regulated diurnally. Considering circadian character of several forms of attacks, the clinical association with sleep disorders and the neuroimaging data confirming abnormal hypothalamic activation in several primary headache disorders may be an answer in clinical diagnosis. [14] Some research confirms the evidence that migraine patients have worse sleep quality than non-migraine patients, that self-reported bad sleep quality is related to an increased rate of attacks or migraine chronicity and that preventative migraine therapy can increase sleep quality. [13]

Gut dysbiosis appears to play a key role among the factors linked to migraine occurrence. In fact, it has been proven that the gut is able to modify central nervous system activity through the gut-brain axis. The microbiological components and their inheritance in genetics are impacted by the lifestyle, eating patterns and other factors external to the body, such as the surroundings. [15] Accordingly, the gut can be seen as some kind of brain, as it is producing a variety of neurotransmitters such as serotonin and histamine. [16] A number of studies have found that low brain serotonin is strongly related to migraine. In detail, migraineurs have greater levels of brain serotonin levels throughout an acute pain attack in comparison to periods in-between attacks. [17] Furthermore, it was revealed that patients with chronic migraine showed elevated histamine levels than healthy individuals, both during and between migraine attacks. [18] In fact, numerous studies in both animal models and clinical trials have shown changes in the gut microbiota of migraine patients compared to healthy individuals. Thus, it is essential to understanding whether particular nutritional strategies or lifestyle modifications can be a relevant and an innovative complementary therapy in the treatment of migraine. [15]

Pharmacological treatment of acute migraine

When treating migraine, the most important principle is that treatment should be initiated at an early stage and, if treatment fails, patients should be presented with a further alternative within a very short period of time.[19] One of the possibilities is the preventive therapy. Adequate oral medication is beneficial in the preventive therapy of episodic migraine. The different classes of drugs that have been shown to be helpful in the oral preventive treatment of migraine are mainly, but not only, antihypertensive drugs, antidepressants and antiepileptics.[20] A reduction in headache frequencies of more than 50 percent with the antihypertensive and antidepressant drugs was recorded in about half to two-thirds of people when they were taking as part of initial preventive therapy. [21]

When dealing with an acute migraine attack, patients get to choose from various therapeutical options too.

Sumatriptan was authorised in 1992 by the US Food and Drug Administration (FDA). Since then, triptans have been the prominent choice for the treatment of acute migraines. The effectiveness of triptans in the treatment of migraine has been validated, as, however, how migraine arises has not been fully clarified, nor has the exact mode of action been explained. It is presumed that the following mechanisms may play an important role: the constriction of pathologically dilated intracranial blood vessels by triptans and the restoration of normal blood flow, and the blocking of the release of pro-inflammatory neurotransmitters at the level of the nerve endings in the perivascular space. Currently, there is a modern generation of triptans group, which include drugs such as rizatriptan, zolmitriptan, naratriptan or eletriptan. [22]

Ergot alkaloids, like ergotamine (approved in 1976), have been in use since the 1970s for the symptoms treatment of acute migraine. Dihydroergotamine (DHE) is recommended for the acute treatment of migraine headaches with or without aura and for the acute treatment of cluster headache episodes. DHE is associated with a high binding affinity to the 5-HT1Dα and 5-HT1Dβ receptors . It has been proposed that two theories explain the effectiveness of 5-HT1D receptor agonists in migraine: (i) activation of 5-HT1D receptors localised on intracranial blood vessels and consequent vasoconstriction of blood vessels, although this has little significance for therapeutic effect, and (ii) activation of 5-HT1D receptors on trigeminal sensory nerve endings, which results in the inhibition of the production of proinflammatory neuropeptides.[23]

Ditans are part of a new class of drugs which target the 5-HT1F receptor for the therapy of acute migraine. One of this class, lasmiditan, a high selective 5-HT1F agonist, was authorised in 2019. Ditans are structurally different from triptans in that triptans have an indexole group structure that highly resembles the 5-HT receptor, whereas ditans substitute this indole group with a pyridine-piperidine scaffold. Tryptans bond non-selectively to 5-HT1B and 5-HT1D receptors and with variable binding affinity to 5-HT1F receptors, resulting in direct vasoconstriction.[24]

From the late 1980s, research has revealed that CGRP is considerably implicated in the pathophysiology of migraine. [22] CGRP can cause migraine in patients, and inhibition of the canonical CGRP receptor is successful in the treatment of acute migraine. [25] Two gepants, ubrogepant and rimegepant, have been FDA endorsed for acute migraine treatment. As gepants do not vasoconstrict the cranial arteries, they can be used as first-line therapy for migraine in patients at higher risk of
cardiovascular incidents or in those with proven cardiovascular disease. [22]

Migraine is characterised by inflammation as well. Thus, the use of anti-inflammatory drugs to suppress the inflammatory cascade can help to relieve migraine headaches and to prevent their reoccurrence, and anti-inflammatory drugs may also provide advantages by easing inflammation [26]

Pharmacological treatment of chronic migraine

Botulinum toxin is a compound protein that is produced by a Gram-positive and anaerobic bacterium known as Clostridium botulinum. It was originally proposed as a hypothesis that the pain-relieving mechanism of this toxin is due to muscle relaxation with subsequent hypotension. A number of mechanisms have been suggested for the function of BoNT-A, including the inhibition of exocytosis of neurochemicals and proteins of the motor and sensorimotor systems, the reduction of proinflammatory cell exocytosis, neurotransmitters and nervous system excitatory neuropeptides such as substance P, CGRP and glutamate. [27] It has now become a first-choice therapy for many disorders, this includes dystonia, spasticity, hyperhidrosis and some types of bladder disorders. In the therapy of migraine, botulinum toxin is injected intramuscularly into numerous areas of the head and back of the neck, with repeated administration on a regular basis. It is believed that botulinum toxin has the potential to prevent migraine by disrupting SNAP-25, one of the proteins of the SNARE complex, by impairing

synaptic vesicle assembly and the releasing of neurotransmitters related to pain susceptibility. [22]

Another group of drugs used in therapy of chronic migraine are antagonists of β-adrenoceptors. Propranolol is one of the most frequently used drugs for migraine prevention, and numerous clinical studies have been consistently proving its efficiency in decreasing the frequency of migraine attacks since the 1970s [22]

It has been suggested that propranolol decreases central hyperexcitability by suppressing β1 -adrenoreceptor-mediated norepinephrine releasing, hence decreasing central catecholaminergic hyperexcitability. In a further addition, propranolol suppresses NO generation by blocking inducible NOS, as well to inhibit kainate-induced afferents and act in synergy with NMDA blockers to diminish neuronal activity and have membrane stabilising qualities. One latest study demonstrated a considerable decline in the frequency, intensity and length of migraine headaches. [28]

Non-pharmacological treatment of migraine

The currently existing oral pharmacological treatments for migraine may be badly tolerated by certain patients. Uncomfortable side-effects and less-than-expected efficiency can lead to low compliance with treatment and other complaints such as headache chronicity and medication misuse. However, a variety of new therapeutic approaches for the treatment of migraine have become available in recent years, as well as new technical approaches that hold great promise as areas for development. [29]

Cognitive behavioural therapy (CBT) is a therapeutic treatment that uses cognitive modifiers to help manage mental disorders and psychological distress. The latest practice guidelines emphasise CBT as a selective psychotherapy for issues that range from depression, anxiety and personality disorders to chronic pain, addiction and relationship pain. Migraine sufferers are turning increasingly to supplementary and integrative health approaches [30] As patients tend to prefer CBT treatment for different reasons, a number of behavioural methods of migraine reduction have been used, particularly during pregnancy or when the choice of pharmacotherapy for patients is restricted, for instance because of low efficacy or lack of persistence of pharmacotherapy, or in association with pharmacological treatment. [31] CBT addresses the cognitive mechanisms involved in the development and retention of psychopathology, especially of emotional pain and dysphoria, which are primarily conducted

during sessions, which requires therapists to co-ordinate their interventions to most effectively help patients. [32] CBT therapy allows patients to elaborate prevention and self-care strategies, such as identifying their triggers, modification of maladaptive, related thoughts, feelings and behaviours related to the headache, and the physiological autoregulation strategies. The behavioural therapies for migraine headaches, which include behavioural cognitive therapy, stress relaxation and biofeedback, have shown effectiveness in decreasing the incidence of migraine attacks and migraine-associated disorders. [30]

A surgical therapy of chronic migraine headaches

According to the inflammation theory of migraine origin, chronic inflammation of some cranial nerves leads to a string of inflammation that causes migraines of the type without aura. For attacks located anteriorly, two nerves would be engaged (on each side): the supraorbital and suprascapular nerves. The neurolysis of these nerves would allow to obtain successful outcomes in a high percentage of cases. These nerves are typically irritated mechanically by the spasm of the adjacent facial muscles: the supraspinatus tiltator muscle and the supraspinatus depressor muscle. The operative approach is based therefore on neurolysis of the two nerves with concurrent sectioning of these muscles. The operation is carried out using regional anaesthesia with sedation. According to this paper, a decrease of monthly migraine attacks has been observed among the patients who have undergoned the surgery. [33]

Summary

Early recognition and treatment of migraine attacks allows the right therapy to be chosen for the patient. Despite the unclear origin of this disease, we now have, as a health service, a multitude of therapeutic options available to patients. This is why it is so important to identify the symptoms, manage the patient appropriately and treat the disease with the means at our disposal. It is important for health care professionals to promote the current state of knowledge about migraine and its treatments. This will significantly improve the quality of life for many sick patients.

Disclosure

Authors contribution:

Conceptualisation: Jakub Skrzypek [JS], Aleksandra Stępień [AS], Robert Kochan [RK]

Methodology: Jagoda Niewiadomska [JN], Alicja Paluch [AP], Aleksandra Niekra [AN]

Formal analysis:Jakub Skrzypek [JS], Borys Bondos [BB], Alicja Paluch [AP], Ewelina Wieczorek [EW]
Investigation: Aleksandra Stępień [AS], Jakub Skrzypek [JS], Łukasz Fussek [ŁF], Kacper Lee [KL]
Writing - Rough Preparation: Borys Bondos [BB], Łukasz Fussek [ŁF], Ewelina Wieczorek [EW]
Writing - Review and Editing: Borys Bondos [BB], Robert Kochan [RK], Kacper Lee [KL]
Visualisation: Jagoda Niewiadomska [JN], Jakub Skrzypek [JS], Aleksandra Niekra [AN]

All authors have read and agreed with the published version of the manuscript.

Conflicts of Interest: The authors declare no conflicts of interest.

Funding Statement: No external funding was received to perform this review.

Board Statement: Not applicable – this review included an analysis of the available literature.

Statement of Informed Consent: Not applicable.

Bibliography:

1. Aguilar-Shea AL, Membrilla Md JA, Diaz-de-Teran J. Migraine review for general practice. Aten Primaria. 2022 Feb;54(2):102208. doi: 10.1016/j.aprim.2021.102208. Epub 2021 Nov 16. PMID: 34798397; PMCID: PMC8605054.
2. Su M, Yu S. Chronic migraine: A process of dysmodulation and sensitization. Mol Pain. 2018 Jan-Dec;14:1744806918767697. doi: 10.1177/1744806918767697. Epub 2018 Apr 12. PMID: 29642749; PMCID: PMC5900816.
3. Peters GL. Migraine overview and summary of current and emerging treatment options. Am J Manag Care. 2019 Jan;25(2 Suppl):S23-S34. PMID: 30681821.
4. Onan D, Younis S, Wellsgatnik WD, Farham F, Andruškevičius S, Abashidze A, Jusupova A, Romanenko Y, Grosu O, Moldokulova MZ, Mursalova U, Saidkhodjaeva S, Martelletti P, Ashina S. Debate: differences and similarities between tension-type headache and migraine. J

Headache Pain. 2023 Jul 21;24(1):92. doi: 10.1186/s10194-023-01614-0. PMID: 37474899; PMCID: PMC10360340.

5. Andreou AP, Edvinsson L. Mechanisms of migraine as a chronic evolutive condition. J Headache Pain. 2019 Dec 23;20(1):117. doi: 10.1186/s10194-019-1066-0. PMID: 31870279; PMCID: PMC6929435.

6. Youssef PE, Mack KJ. Episodic and chronic migraine in children. Dev Med Child Neurol. 2020 Jan;62(1):34-41. doi: 10.1111/dmcn.14338. Epub 2019 Aug 28. PMID: 31463934.

7. Wachowska K, Bliźniewska-Kowalska K, Sławek J, Adamczyk-Sowa M, Szulc A, Maes M, Kuan-Pin S, Gałecki P. Common pathomechanism of migraine and depression. Psychiatr Pol. 2023 Apr 30;57(2):405-419. English, Polish. doi: 10.12740/PP/OnlineFirst/143982. Epub 2023 Apr 30. PMID: 36371736.

8. Lipton RB, Buse DC, Nahas SJ, Tietjen GE, Martin VT, Löf E, Brevig T, Cady R, Diener HC. Risk factors for migraine disease progression: a narrative review for a patient-centered approach. J Neurol. 2023 Dec;270(12):5692-5710. doi: 10.1007/s00415-023-11880-2. Epub 2023 Aug 24. PMID: 37615752; PMCID: PMC10632231.

9. Peters GL. Migraine overview and summary of current and emerging treatment options. Am J Manag Care. 2019 Jan;25(2 Suppl):S23-S34. PMID: 30681821.

10. Pelzer N, de Boer I, van den Maagdenberg AMJM, Terwindt GM. Neurological and psychiatric comorbidities of migraine: Concepts and future perspectives. Cephalalgia. 2023 Jun;43(6):3331024231180564. doi: 10.1177/03331024231180564. PMID: 37293935.

11. Gazerani P. Migraine and Diet. Nutrients. 2020 Jun 3;12(6):1658. doi: 10.3390/nu12061658. PMID: 32503158; PMCID: PMC7352457.

12. Garrigós-Pedrón M, Segura-Ortí E, Gracia-Naya M, La Touche R. Predictive factors of sleep quality in patients with chronic migraine. Neurologia (Engl Ed). 2022 Mar;37(2):101-109. English, Spanish. doi: 10.1016/j.nrl.2018.11.004. Epub 2019 Mar 8. PMID: 30857790.

13. Tiseo C, Vacca A, Felbush A, Filimonova T, Gai A, Glazyrina T, Hubalek IA, Marchenko Y, Overeem LH, Piroso S, Tkachev A, Martelletti P, Sacco S; European Headache Federation School of Advanced Studies (EHF-SAS). Migraine and sleep disorders: a systematic review. J Headache Pain. 2020 Oct 27;21(1):126. doi: 10.1186/s10194-020-01192-5. PMID: 33109076; PMCID: PMC7590682.

14. Holland PR, Barloese M, Fahrenkrug J. PACAP in hypothalamic regulation of sleep and circadian rhythm: importance for headache. J Headache Pain. 2018 Mar 5;19(1):20. doi: 10.1186/s10194-018-0844-4. PMID: 29508090; PMCID: PMC5838029.

15. Di Lauro M, Guerriero C, Cornali K, Albanese M, Costacurta M, Mercuri NB, Di Daniele N, Noce A. Linking Migraine to Gut Dysbiosis and Chronic Non-Communicable Diseases. Nutrients. 2023 Oct 11;15(20):4327. doi: 10.3390/nu15204327. PMID: 37892403; PMCID: PMC10609600.

16. Ochoa-Repáraz J, Kasper LH. The Second Brain: Is the Gut Microbiota a Link Between Obesity and Central Nervous System Disorders? Curr Obes Rep. 2016 Mar;5(1):51-64. doi: 10.1007/s13679-016-0191-1. PMID: 26865085; PMCID: PMC4798912.

17. Deen M, Christensen CE, Hougaard A, Hansen HD, Knudsen GM, Ashina M. Serotonergic mechanisms in the migraine brain - a systematic review. Cephalalgia. 2017 Mar;37(3):251-264. doi: 10.1177/0333102416640501. Epub 2016 Jul 11. PMID: 27013238.

18. Heatley RV, Denburg JA, Bayer N, Bienenstock J. Increased plasma histamine levels in migraine patients. Clin Allergy. 1982 Mar;12(2):145-9. doi: 10.1111/j.1365-2222.1982.tb01633.x. PMID: 6176358.

19. Pozo-Rosich P, Carmo M, Muñiz A, Armada B, Moya-Alarcón C, Pascual J. Migraine treatment: quo vadis? Real-world data study (2015-2022) in Spain. BMC Neurol. 2024 Apr 2;24(1):107. doi: 10.1186/s12883-024-03600-8. PMID: 38566063; PMCID: PMC10985889.

20. Ranganathan LN, Ramamurthy G, Kanthimathinathan S. Preventive Oral Treatment of Episodic Migraine: An Overview. Neurol India. 2021 Mar-Apr;69(Supplement):S51-S58. doi: 10.4103/0028-3886.315985. PMID: 34003148.

21. Goadsby PJ, Lipton RB, Ferrari MD. Migraine--current understanding and treatment. N Engl J Med. 2002 Jan 24;346(4):257-70. doi: 10.1056/NEJMra010917. PMID: 11807151.

22. Zobdeh F, Ben Kraiem A, Attwood MM, Chubarev VN, Tarasov VV, Schiöth HB, Mwinyi J. Pharmacological treatment of migraine: Drug classes, mechanisms of action, clinical trials and new treatments. Br J Pharmacol. 2021 Dec;178(23):4588-4607. doi: 10.1111/bph.15657. Epub 2021 Sep 26. PMID: 34379793.

23. Silberstein SD, Kori SH. Dihydroergotamine: a review of formulation approaches for the acute treatment of migraine. CNS Drugs. 2013 May;27(5):385-94. doi: 10.1007/s40263-013-0061-2. PMID: 23620146.

24. Goadsby PJ, Classey JD. Evidence for serotonin (5-HT)1B, 5-HT1D and 5-HT1F receptor inhibitory effects on trigeminal neurons with craniovascular input. Neuroscience. 2003;122(2):491-8. doi: 10.1016/s0306-4522(03)00570-0. PMID: 14614913.

25. Younis S, Christensen CE, Toft NM, Søborg T, Amin FM, Hougaard A, Ashina M. Investigation of distinct molecular pathways in migraine induction using calcitonin gene-

related peptide and sildenafil. Cephalalgia. 2019 Dec;39(14):1776-1788. doi: 10.1177/0333102419882474. Epub 2019 Nov 4. PMID: 31684759.

26. Khazaei M, Hosseini Nejad Mir N, Yadranji Aghdam F, Taheri M, Ghafouri-Fard S. Effectiveness of intravenous dexamethasone, metoclopramide, ketorolac, and chlorpromazine for pain relief and prevention of recurrence in the migraine headache: a prospective double-blind randomized clinical trial. Neurol Sci. 2019 May;40(5):1029-1033. doi: 10.1007/s10072-019-03766-x. Epub 2019 Feb 19. PMID: 30783794.

27. Shaterian N, Shaterian N, Ghanaatpisheh A, Abbasi F, Daniali S, Jahromi MJ, Sanie MS, Abdoli A. Botox (OnabotulinumtoxinA) for Treatment of Migraine Symptoms: A Systematic Review. Pain Res Manag. 2022 Mar 31;2022:3284446. doi: 10.1155/2022/3284446. PMID: 35401888; PMCID: PMC8989603.

28. Dakhale GN, Sharma VS, Thakre MN, Kalikar M. Low-dose sodium valproate versus low-dose propranolol in prophylaxis of common migraine headache: A randomized, prospective, parallel, open-label study. Indian J Pharmacol. 2019 Jul-Aug;51(4):255-262. doi: 10.4103/ijp.IJP_457_18. PMID: 31571712; PMCID: PMC6759533.

29. Puledda F, Shields K. Non-Pharmacological Approaches for Migraine. Neurotherapeutics. 2018 Apr;15(2):336-345. doi: 10.1007/s13311-018-0623-6. PMID: 29616493; PMCID: PMC5935652.

30. Bae JY, Sung HK, Kwon NY, Go HY, Kim TJ, Shin SM, Lee S. Cognitive Behavioral Therapy for Migraine Headache: A Systematic Review and Meta-Analysis. Medicina (Kaunas). 2021 Dec 28;58(1):44. doi: 10.3390/medicina58010044. PMID: 35056352; PMCID: PMC8777662.

31. Peng W, Lauche R, Frawley J, Sibbritt D, Adams J. Utilization of complementary and alternative medicine and conventional medicine for headache or migraine during pregnancy: A cross-sectional survey of 1,835 pregnant women. Complement Ther Med. 2018 Dec;41:192-195. doi: 10.1016/j.ctim.2018.09.027. Epub 2018 Sep 29. PMID: 30477838.

32. Rapoff MA, Connelly M, Bickel JL, Powers SW, Hershey AD, Allen JR, Karlson CW, Litzenburg CC, Belmont JM. Headstrong intervention for pediatric migraine headache: a randomized clinical trial. J Headache Pain. 2014 Feb 28;15(1):12. doi: 10.1186/1129-2377-15-12. PMID: 24580721; PMCID: PMC3996073.

33. Raposio G, Antonini A, Gualdi A, Raposio E. Frontal site surgery for chronic migraine therapy. Acta Biomed. 2023 Dec 5;94(6):e2023253. doi: 10.23750/abm.v94i6.14777. PMID: 38054685; PMCID: PMC10734223.