v. 4, n. 9, 2024

International Journal of Health Science

BEHAVIORAL AND PHARMACOLOGICAL MEASURES IN THE TREATMENT OF MIGRAINE

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Abstract: The objective of this review is to understand the effects on the quality of life of individuals who have migraines, the eating habits that influence attacks and the drug treatment of this disease. An integrative, descriptive literature review was carried out in the following databases: SCIELO, PUBMED, LILACS, MEDLINE and SCOPUS. The descriptors used were: "migraine disorders" and "headache". With filtering of articles in Portuguese, English and Spanish from the last 5 years, duplicate studies and those that did not address the subject were excluded. Migraine is highly prevalent in the population and, as it affects quality of life, it is considered a debilitating disease. Patients with acute crises often seek emergency services, in addition to being hospitalized and medicated. Treatment generally includes a combination of behavioral and pharmacological measures. Among them, respectively, adequate nutrition and the use of anti-inflammatories. Therefore, there is a need for more in-depth studies and qualification of doctors regarding the disease, as some symptoms and behaviors reported by patients are not yet fully understood.
Keywords: migraine, headache, attacks, diet, triggers.

INTRODUCTION

Migraine can be defined as an abnormal neurovascular reaction in a genetically vulnerable organism, demonstrating a clinical condition with recurrent episodes of headache and linked manifestations that generally depend on the presence of triggering factors, whether endogenous (genetic) or exogenous (environmental). Amery's theory of hypoxia has become increasingly important to the international scientific community as an explanation of the pathophysiology of migraine. As a consequence of widespread depression, hypoxia can present several triggering factors, such as physical and/

or emotional stress, hormonal changes (for example: menstruation), food, altered sleep pattern, alcoholic beverages, hypoglycemia, among others. that cause this condition, which can give rise to several events with neuronal, vascular, humoral and autonomic effects.

Migraine is the most common cause of moderate to severe recurrent headache, usually occurring during puberty or early adulthood, fluctuating in frequency and severity in subsequent years and decreasing after the age of 50. Many potential migraine triggers have been identified. include the following: drinking red wine; skipping meals; excessive afferent stimuli (for example: bright lights, strong odors); climate change; sleep deprivation; stress; hormonal factors, especially menstruation; c and certain foods (food triggers vary from person to person). Often, a prodrome (the feeling that the migraine is starting) announces the attacks. The prodrome may include mood changes, neck pain, food cravings, loss of appetite, nausea, or a combination.

The aura precedes attacks in about 25% of patients. Other very common symptoms of migraine: sensitivity to light, smells, noise; nausea, vomiting; visual symptoms, such as bright and dark spots and zigzag lines that precede or accompany pain attacks; tingling and numbness in the body (migraine auras); dizziness, sensitivity to movement or feeling sick when traveling by car, bus, boat.

Diagnosis of migraine is based on characteristic symptoms and a normal physical examination, including a complete neurological examination.

The headache varies from moderate to severe and attacks last from 4 hours to several days, generally disappearing with sleep. Daily physical activity often aggravates migraines; This effect, combined with photophobia and sonophobia, encourages most patients to lie down in a dark, quiet room during attacks. Serious crises can be disabling, disrupting family life and working conditions. Patients with episodic migraines may develop chronic migraines. These patients have headaches ≥ 15 days/month.

Migraine is a primary episodic and chronic headache. The pain is usually unilateral, pulsating, worsens with exertion and is accompanied by symptoms such as nausea and sensitivity to light, sound or odors. The diagnosis is clinical. Treatment includes triptans, dihydroergotamine, antiemetics and analgesics. Prevention regimens include lifestyle modifications (for example: sleeping habits or diet) and drugs (for example: beta-blockers, amitriptyline, tipiramate, divalproex, monoclonal antibodies).

The positive impact of the use of Topiramate (beta-blocker) and Botulinum Toxin in the prophylactic treatment of migraine and, to a lesser extent, therapy with Valproic Acid, Neuroleptics, Amitriptyline, Ca Blockers, Tizanidine, Dichloroergotamine, IRSS, was identified in several studies. NSAIDs and Lisinopril showed significant benefit. The Brazilian Headache Society in 2002 recommended in a consensus the use of biofeedback, relaxation techniques, cognitive behavioral therapy, diet, acupuncture, psychotherapy and physiotherapy as non-pharmacological prophylactic treatments. (SANVITO, 1993; SILBERSTEIN, 2023; STEFANE, 2012)

METHODOLOGY

Aiming for a broad understanding of the topic, it was decided to carry out an integrative review of the literature, since, through this type of study, it is possible to simultaneously analyze experimental and non-experimental studies on the phenomenon addressed.

The inclusion criteria were articles between January 1, 2002 and December 31, 2023, which involved the effects of migraine on

patients' quality of life and how this would be seen through triggers or attacks. Articles that contained an overview of the disease and its pathophysiology were evaluated, as well as the medications used in each situation. As exclusion criteria, there were duplicate articles that did not fit the subject.

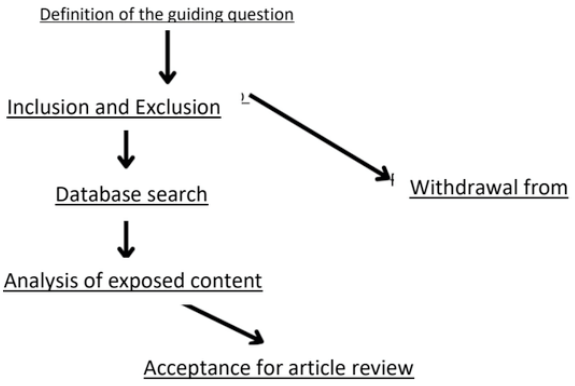

Fig.1. Flowchart of selection steps

Source: own authorship

To search for standardized descriptors, the DeCS (Health Sciences Descriptors) was used, defining "migraine disorders" and "headache" as descriptors. The bibliographic databases chosen to carry out this study were: Scientific Electronic Library On-line (SciELO), Latin American and Caribbean Literature in Health Sciences (LILACS), PUBMED, Health Information from the National Library of Medicine (MEDLINE) and SCOPUS.

40 studies were selected for analysis, of which 18 comprised this article as they met the inclusion criteria mentioned above. The selection of studies for analysis included articles in Portuguese and English published between 2002 and 2021, with the majority, 64.28% (14), being from the last ten years.

RESULTS AND DISCUSSIONS

OVERVIEW

Migraine or migraine is a neurological, genetic and chronic disease whose main characteristic is throbbing pain on one or both sides of the head. This illness can be aggravated by physical activity, photophobia, phonophobia and also by odors. Migraine is most commonly presented as recurrent attacks of disabling headaches, nausea and intolerance to all sensory stimuli. Most of the triggers associated with migraines are related to metabolic disorders. According to research, fasting; changes in sleep pattern; changes in the secretion of ovarian hormones, especially during menstruation; physical exercise; alcohol; and climate change can lead to disease. (DODICK, 2022). Any psychological or physiological stress can be considered a triggering factor. Hormonal changes are another potential metabolic denominator. Even changes in oxidative stress caused by psychological or physiological stress can be triggering factors. (DODICK, 2022). It has also been reported that hypoxia can increase the prevalence of headaches, as data indicates that people living at high altitudes have a higher incidence of migraines.

It has now become common knowledge that migraine is a disease that affects the entire cerebral hemisphere, being promoted by the association of genetic factors and environmental triggers. Migraine symptoms typically occur periodically and are most common in women during their childbearing years. The disease is classified as chronic when its signs last for 15 days or more. Patients with chronic migraine reported excessive and periodic use of medications and, as a consequence, developed significant comorbidities, such as depression, sleep disorders, anxiety and cognitive decline. Migraines are the most common causes of

moderate, severe and recurrent headaches.

Updated information about migraine indicates an activation of the intracranial network that culminates in the sensitization of the trigeminovascular system, release of inflammatory markers and the beginning of a meningeal inflammatory reaction that is perceived as headache. Genetic factors may play an important role in deciding an individual's susceptibility to migraine. Active myofascial trigger points are prevalent in patients with migraines, a myofascial trigger point is defined as a hyperirritable point in skeletal muscle that is associated with a hypersensitive palpable nodule in a taut band. It is unclear whether myofascial trigger points contribute to increased migraine burden in terms of frequency and intensity.

Therefore, from this perspective, it is essential that every doctor working in urgent and emergency services, such as emergency care units and emergency rooms, is able to receive these patients, since the number of people affected is high and, on the day to day for neurologists, this is one of the most prevalent complaints.

PATHOPHYSIOLOGY

Migraine is divided into four phases including (Premonitory, Aura, Headache and Prodromal). These phases may occur sequentially or may overlap significantly.

The pathophysiology of migraine involves the modulation of pain originating in disrupted neural networks in the head. (GOADSBY et al., 2017). Studies have shown that the brainstem and diencephalic nuclei control the trigeminovascular system, which comprises efferent neurons that supply vascular networks and afferent neurons that provide information to the trigeminal nucleus caudalis. (GOADSBY et al., 2017), (AKERMAN et al., 2011). The headache is perceived as meningeal inflammation and vasodilation due to the activation of these networks. (MD et al., 2009), (GOADSBY et al., 2009).

Neurotransmitters, such as serotonin, also play critical roles in the pathophysiology and treatment of migraine. Therapies for migraine treatment have been adapted to modulate serotonin receptors. Modulation is directed to amplify the serotonin signal, leading to pain relief via vasoconstriction of blood vessels and inhibition of peptides.

PREMONITORY PHASE

This phase begins before the typical migraine headache. Symptoms include irritability, binge eating, mood swings, fatigue, stiff neck, and phonophobia. (GIFFIN et al., 2003).

Hunger, bright light or sleep deprivation can trigger migraines in migraineurs or may indicate premonitory symptoms.

AURA PHASE

This phase is observed in one third of migraine patients. Depolarization of the cortex and the creation of a transient wave are the main pathological mechanisms associated with the aura phase, also known as cortical spreading depression (CSD). (CHARLES, 2013).

The headache phase is marked by unilateral, pulsating pain of moderate to extreme intensity. (OLESEN, 2018)

THALAMOCORTICAL CIRCUITS, THALAMIC CIRCUITS AND MIGRAINE

Changes in brain functionality have been reported during the premonitory phase. Electrophysiological studies have reported increased blood flow, particularly in circuits connecting the thalamus-cortex.

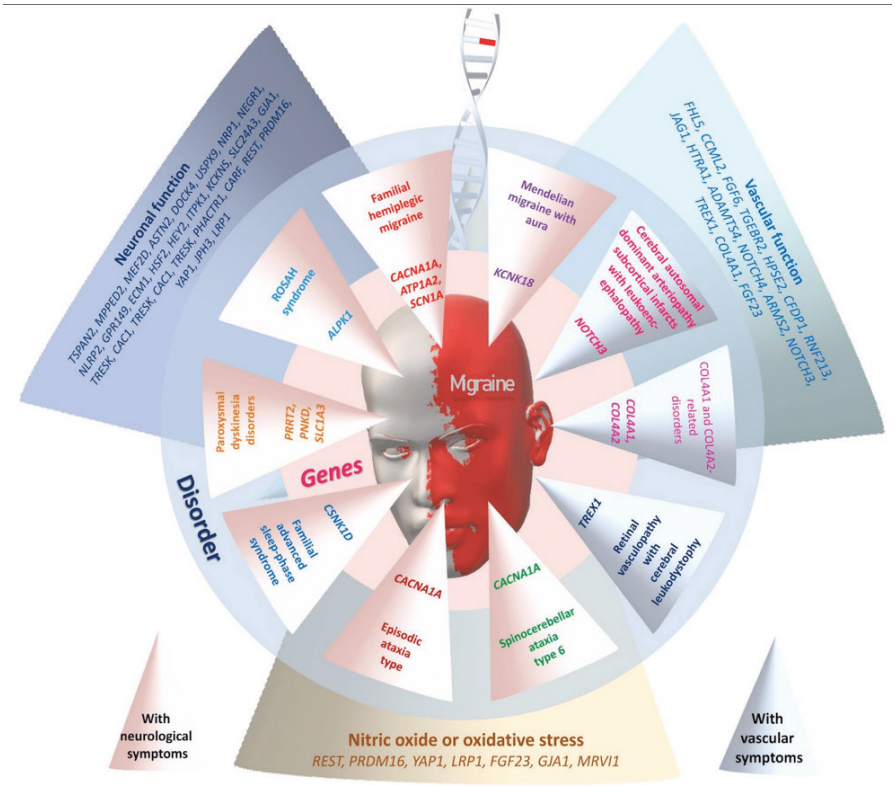

Fig. 3. Genes associated with the development of migraine and associated disorders

Source: Science Direct (2021).

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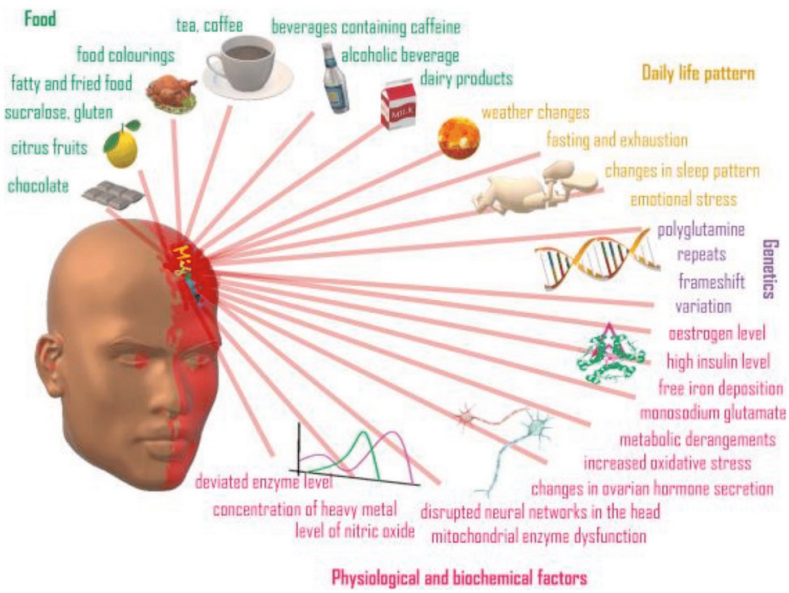

Fig. 2. Factors that trigger migraines

Source: ScienceDirect (2021).

Available on the website: https://www.sciencedirect.com/science/article/pii/S0753332221003425?via%3Dihub#bib1

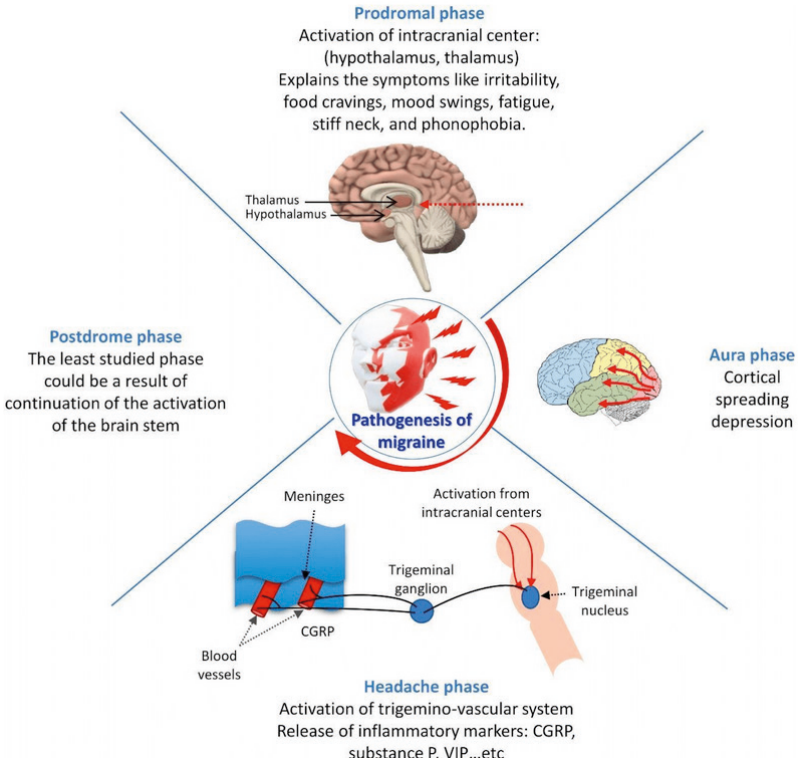

Fig. 4. The mechanisms of the different phases of migraine. An overlap of the different phases is possible.

Source: Science Direct (2021).

Available on the website: https://www.sciencedirect.com/science/article/pii/S0753332221003425?via%3Dihub#bib1

POSTDROMIC PHASE

This phase is the least studied in the literature. It is mostly ignored and unreported by patients. However, sometimes it is a distinct phase of the disease or a continuation of the same pathology. Patients may report symptoms such as tiredness, muscle weakness, mood changes, difficulty concentrating and reduced appetite.

METABOLIC DYSFUNCTION AND TRIGGERING FACTORS

Most of the triggers associated with migraine are associated with metabolic disorders. Fast; changes in sleep pattern; changes in the secretion of ovarian hormones, especially during menstruation; physical exercise; alcohol; and climate change can lead to migraines. (MD *et al.*, 2014).

Any psychological or physiological stress can be considered a triggering factor. Hormonal changes are another potential metabolic denominator. Even changes in oxidative stress caused by psychological or physiological stress can be a triggering factor. (M.D. et al., 2015). It has also been reported that hypoxia may increase the prevalence of headaches, as people living at high altitudes have a higher incidence of migraines. (KHAN, *et al*, 2021).

Metabolic abnormalities, such as oxidative stress in peripheral tissues, glucose metabolism, and mitochondrial enzyme dysfunction, are also associated with migraine. (KHAN, et al, 2021). Patients suffering from metabolic syndrome have a higher prevalence of migraines.

METABOLISM AND DIETS

Patients suffering from metabolic syndrome have a higher prevalence of migraines. Insulin levels are higher in migraine patients and almost 11.1% of patients suffer from insulin resistance. (KHAN, et al, 2021). The association between metabolic syndrome and a migraine attack and its severity needs more evidence to establish a meaningful correlation.

The human brain depends on glucose as its main source of energy, as little glycogen is stored in the brain, which can predispose the brain to hypoglycemia. The association between hypoglycemic drugs and migraines has been known for almost a century. Similarities in the symptoms of the conditions also indicate an association between them. Symptoms such as cold hands and feet, low blood pressure, fatigue, tremors, pale skin, and slurred speech are common in hypoglycemic and migraine patients. All of these symptoms are caused by insufficient glucose in the brain, which releases catecholamines as a result of sympathetic activation. (MD *et al.*, 2009).

The clinical manifestations of migraine are influenced by eating behaviors and dietary elements. Several dietary triggers for migraines have been identified, leading to the definition of strategies such as elimination diets, ketogenic diets, and whole-grain diets, primarily to help prevent migraines.

Researchers have attempted to develop lifestyle modification strategies to prevent and treat headaches. (WELCH, 2002). Along these lines, the role of dietary triggers has been recognized (GAZERANI, 2020), leading to diet therapy strategies for headaches, including migraines (GAZERANI, 2020), (GAZERANI, 2020). There are long lists of possible dietary triggers, but controversy has remained in the field. 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 (AKERMAN et al, 2011), (MD et al., 2009), (GOADSBY et al., 2009). Food diaries and specific serological tests have been used to identify triggers in individual patients.

ELIMINATION DIET

Elimination diets require the identification of provocative dietary ingredients and their subsequent elimination. Identifying trigger elements of the diet can be taken on a personal approach, where an individual notice a high frequency of headaches or migraines after exposure to a food trigger and, consequently, avoids it. It is important to distinguish between a food allergy and a food trigger for migraine. A complete food diary noting the presence or absence of migraines for evaluation by doctors may be useful from a practical point of view (AKERMAN et al., 2011).

As defining an association between food and migraine is a challenge, it was proposed to establish a limit (AKERMAN et al., 2011). According to the literature, a food can be considered a trigger if the headache occurs in ≥50% of cases within one day of exposure (GAZERANI, 2020). Multiple triggers may be present in a patient, and identifying a single trigger may be difficult, especially because some factors may potentiate each other. Additionally, some foods are complex and contain many ingredients; therefore, it is difficult to identify a specific ingredient as the trigger. The disadvantage of an elimination diet is the long-term negative effect of malnutrition - a form of malnutrition - which is characterized as inadequate intake of protein, energy and micronutrients and can result in disorders including psychological problems or infections. (GAZERANI, 2020), (GAZERANI, 2020).

MIGRAINE DIETS

The idea of migraine-specific diets was developed in parallel with elimination diets.

A recent literature review (GAZERANI, 2020) found that ketogenic, high-folate, low-fat, modified Atkins, and high-omega-3, low-omega-6 diets demonstrated beneficial effects. The Mediterranean diet was also mentioned, but with less data available (GAZERANI, 2020). The ketogenic and modified Atkins diets have been proposed to promote neuroprotection, improve mitochondrial function, compensate for serotonergic dysfunction, decrease CGRP levels, and suppress neuroinflammation (GAZERANI, 2020). Ketogenic diets lead to an increase in ketone bodies, which have recently been considered beneficial in preventing migraines (GAZERANI, 2020). A balance between omega-6 and omega-3 fatty acid intake has also been suggested to reduce inflammatory responses, increase platelet function, and regulate vascular tone. Therefore, a dietary strategy reducing omega-6 and increasing omega-3 fatty acid intake may be beneficial for migraine (GAZERANI, 2020).

Sodium levels have been shown to be higher in the cerebrospinal fluid of migraine patients than in controls, particularly during a headache attack (GAZERANI, 2020). Therefore, sodium intake must be tailored to specific patient populations.

EPIGENETIC DIET

In 2011, Hardy and Tollefsbol introduced the term "epigenetic diet" (GAZERANI, 2020) to explain that environmental factors, such as dietary components, can interfere with the epigenetic profile of affected patients and, therefore, can be beneficial for disease prevention. Adding certain dietary compounds with specific mechanisms of action can potentially interfere with the pathogenesis of disease (GAZERANI, 2020) (for example: cancer (GAZERANI, 2020)). These types of diets target specific cellular structures (for example: mitochondria) and molecules (for example: DNA). In theory, for migraine, such an intervention would mean that a dietary component could block mechanisms underlying migraine or promote prevention mechanisms. This assumption raised a question about the existence and potential benefits of an epigenetic diet for migraine (GAZERANI, 2020). This hypothesis was formed mainly after recent advanced studies on the pathogenesis of migraine focusing on epigenetics (GAZERANI, 2020), where aberrant DNA methylation was associated with the occurrence of migraine (GAZERANI, 2020).

Folate, which is involved in DNA methylation and has previously been shown to be beneficial in migraine, has drawn more attention in the context of an epigenetic migraine diet. Recently, it has been proposed that defining a diet that can target DNA methylation - for example, a high-folate diet - could potentially provide a future direction for epigenetic dietary studies related to migraine (GAZERANI, 2020). Further investigations are needed to provide evidence on potential dietary components that may interfere with migraine epigenetics (GAZERANI, 2020). Furthermore, migraine comorbidities such as depression and epilepsy must be taken into consideration. Another important point is that, currently, several chemicals targeting the epigenome have been accepted as epigenetic drugs (GAZERANI, 2020). For example, valproate has long been used to treat epilepsy and has been shown to be effective in several migraine patients. However, epigenetic drugs are different from epigenetic diets. For example, ketosis has been reported to alter cellular functions through epigenetic mechanisms. On the other hand, the ketogenic diet has been considered a quick and effective

migraine diet.

TREATMENT STRATEGIES

The main goal of migraine treatment is to reduce the severity and duration of the migraine attack. Other goals include restoring functional capacity, reducing the use of rescue medications, and promoting overall management with no or minimal side effects. Current therapies for migraine include acetaminophen, triptans, (WELCH, 2002), nonsteroidal anti-inflammatory drugs (NSAIDs), dihydroergotamine, non-opioid analgesics, NSAID-triptan combinations and antiemetics. (WELCH, 2002). Drugs such as acetaminophen, butorphanol, and tramadol show some effectiveness; however, the disadvantages of NSAIDs outweigh their benefits and therefore their use is less recommended.

A key component of migraine therapy involves over-the-counter medications, which are considered first-line therapy by most migraine sufferers. Medications such as naproxen, ibuprofen, paracetamol and aspirin form the first line of treatment for a migraine attack. (MD *et al.*, 2015).

PARACETAMOL

It is a non-opioid analgesic and antipyretic that relieves pain and treats fever. It is used to treat mild and moderate forms of migraine as a single agent. (MD *et al.*, 2015).

NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS)

NAPROXEN

Naproxen is used to treat inflammation, pain and fever (AKERMAN et al., 2011). Naproxen therapy is used for early treatment of migraine.

IBUPROFEN

Ibuprofen has analgesic, antipyretic and anti-inflammatory effects for the treatment of migraines (KHAN et al., 2021). This drug inhibits COX-1 and COX-2 (KHAN et al., 2021), which play important roles in the synthesis of prostaglandins.

ASPIRIN

Aspirin is used to treat chronic headache, both in combination and alone (KHAN et al., 2021). Aspirin inhibits COX enzymes (KHAN et al., 2021), which hinders the synthesis of thromboxane.

TAMONIFEN, ASPIRIN AND CAFFEINE

Acetaminophen, aspirin, and caffeine are used together as triple therapy to treat chronic migraines. The combined effect is analgesic and has been observed in many studies (KHAN et al., 2021). Migraine and tension-type headache are indications for the use of these drugs as triple therapy. (MD et al., 2015). The effectiveness of combining these medications is greater than the effectiveness of an individual medication.

MELATONIN

Melatonin is a hormone involved in the regulation of circadian rhythms that is released by the pineal gland. Melatonin acts on hypothalamic receptors to promote sleep (KHAN et al., 2021). It is used as a short-term treatment for insomnia and migraine prevention.

ACUTE MIGRAINE: TREATMENT STRATEGIES

TRIPTANS

In acute attacks of moderate to severe migraine (with or without aura), triptans are the most efficient "first-line therapy", especially in patients whose pain is not relieved by analgesics/NSAIDs, (KHAN et al., 2021). Triptans are selective serotonin agonists. Triptan binding to neurogenic and central serotonin receptors (5-HT1D) inhibits the release of Substance P and CGRP and blocks pain signals to the brain by inhibiting nociceptors (KHAN et al., 2021). Thus, triptans can potentially reverse several steps of trigeminovascular activation in migraine.

SUMATRIPTAN

The subcutaneous formulation has the fastest onset of action; therefore, it is preferable in patients with severe headache. Furthermore, in patients who cannot tolerate oral tablets due to excessive nausea/vomiting, the subcutaneous preparation is the drug of choice.

ZOLMITRIPTAN

ALMOTRIPTAN

FROVATRIPTAN, NARATRIPTAN

ELETRIPTAN, RIZATRIPTAN

PREVENTIVE MEASURES

Preventive therapy is an important factor in migraine treatment. The frequency of attacks can be reduced with the use of preventive pharmacological agents. Furthermore, this approach improves quality of life in migraine patients and reduces the cost of effective treatment. Various agents, including beta blockers, antidepressants, and anticonvulsant agents such as topiramate sodium, botulinum toxin A, and flunarizine, are common migraine preventative treatments (KHAN *et al.*, 2021).

Preventative treatment is used to minimize the duration, frequency, and intensity of attacks. Additional benefits include improving response to acute procedures, improving a patient's functional potential, and reducing disability.

An examination of the natural history of these patients may also help prevent migraines. (KHAN, *et al*, 2021).

CONCLUSION

Migraine causes disability, damaging people's quality of life. Several important factors can determine the onset of a migraine, including internal and external factors. Treatment begins with the correct diagnosis. Acute crisis requires early and effective medications. Preventive strategies to reduce migraine attacks include behavioral and physical therapies, lifestyle modifications, management of comorbidities, diets and pharmacological treatment. Prophylaxis may be indicated if the patient is having three or more migraines per month or are difficult to control.

Migraine is considered a primarily neurogenic disease, with excessive cortical excitability and mediated by genetic factors that promote instability of neuronal membranes. Along these lines, a balance must be taken into consideration, between avoiding the trigger and coping strategies, according to the needs of each patient. It is crucial to consider age, sex and influence of diet headache.

Therefore, it is essential that all doctors working in health services are attentive and able to care for these patients, since it is highly prevalent and debilitating in the population.

REFERENCES

AKERMAN, Simon *et al.* Mecanismos diencefálicos e do tronco cerebral na enxaqueca. **Nature Reviews Neuroscience,** 2011. Disponível em: https://www.nature.com/articles/nrn3057. Acesso em: 24 jun. 2023.

CHARLES, A. Document details - Migraine: A brain state. **Scopus preview,** 2013. Disponível em: https://www.scopus.com/record/display.uri?eid=2-s2.0-84877708795&origin=inward&txGid=d086e65baefede83e9ca05146377ad97. Acesso em: 26 jun. 2023.

DODICK, David W. Migraine. **National Library of medicine,** 2018. Disponível em: https://pubmed.ncbi.nlm.nih.gov/29523342/. Acesso em: 22 nov. 2022.

GAZERANI, Parisa. Enxaqueca e Dieta. **Nutrients,** 2020. Disponível em: https://www.mdpi.com/2072-6643/12/6/1658#B11-nutrients-12-01658. Acesso em: 10 dez. 2023.

GIFFIN, N.j. *et al.* Document details - Premonitory symptoms in migraine: An electronic diary study. **Scopus preview,** 2003. Disponível em: https://www.scopus.com/record/display.uri?eid=2-s2.0-0037465769&origin=inward&txGid=e5d606c8674a4adf0fbecdf688dcfb62. Acesso em: 26 jun. 2023.

GOADSBY, Peter J. *et al.* Pathophysiology of Migraine: A Disorder of Sensory Processing. **American Physiological Society,** 2017. Disponível em: https://journals.physiology.org/doi/full/10.1152/physrev.00034.2015. Acesso em: 24 jun. 2023.

GOADSBY, P.j. *et al.* Neurobiology of migraine. **ELSEVIER,** 2009. Disponível em: https://www.sciencedirect.com/science/article/abs/pii/S0306452209003303. Acesso em: 24 jun. 2023.

GOADSBY, P.j. *et al.* Neurobiology of migraine. **ELSEVIER,** 2009. Disponível em: https://www.sciencedirect.com/science/article/abs/pii/S0306452209003303. Acesso em: 24 jun. 2023.

KHAN, Johra Khan *et al.* Genetics, pathophysiology, diagnosis, treatment, management, and prevention of migraine. **ScienceDirect,** 2021. Disponível em: https://www.sciencedirect.com/science/article/pii/S0753332221003425?via%3Dihub#bib1. Acesso em: 10 dez. 2023.

MD, Andrew Charles *et al.* Advances in the basic and clinical science of migraine. **Annals of NEUROLOGY,** 2009. Disponível em: https://onlinelibrary.wiley.com/doi/10.1002/ana.21691. Acesso em: 24 jun. 2023.

MD, Jelena M. Pavlovic *et al.* Trigger Factors and Premonitory Features of Migraine Attacks: Summary of Studies. **HEADACHE - The Journal of Head and Face Pain,** 2014. Disponível em: https://headachejournal.onlinelibrary.wiley.com/doi/10.1111/head.12468. Acesso em: 26 jun. 2023.

M.D., Alessandro Pingitore *et al.* Exercise and oxidative stress: Potential effects of antioxidant dietary strategies in sports. **ELSEVIER,** 2015. Disponível em: https://www.sciencedirect.com/science/article/abs/pii/S0899900715000738. Acesso em: 26 jun. 2023.

MD, Michael J. Marmura *et al.* The Acute Treatment of Migraine in Adults: The American Headache Society Evidence Assessment of Migraine Pharmacotherapies. **HEADACHE - The Journal of Head and Face Pain,** 2015. Disponível em: https://headachejournal.onlinelibrary.wiley.com/doi/10.1111/head.12499. Acesso em: 26 jun. 2023.

OLESEN, J. Headache Classification Committee of the International Headache Society (IHS) The International Classification of Headache Disorders, 3rd edition. **Scopus preview,** 2018. Disponível em: https://www.scopus.com/record/display.uri?eid=2-s2.0-85062180659&origin=inward&txGid=59cc44bd6550c21a5bf449d5b9e73296. Acesso em: 26 jun. 2023.

SANVITO, Wilson *et al.* Tratamento profilático da enxaqueca: Estudo prospectivo aberto com a flunarizina em 100 pacientes. **Arq Neuropsiquiatrico**, 1993, v. 51, n. 1, p. 31-35

STEFANE, Thais *et al.* Influência de tratamentos para enxaqueca na qualidade de vida: revisão integrativa de literatura**. Revista Brasileira de Enfermagem**, 2012, v. 65, n. 2.

SILBERSTEIN, Stephen . Enxaqueca. **Manual MSD,** 2023. Disponível em: https://www.msdmanuals.com/pt-br/profissional/dist%C3%BArbios-neurol%C3%B3gicos/cefaleia/enxaqueca. Acesso em: 11 jan. 2024.

WELCH, K.m.a.; GOADSBY, P.j.. Chronic daily headache: Nosology and pathophysiology. **Scopus Preview,** 2002. Disponível em: https://www.scopus.com/record/display.uri?eid=2-s2.0-0036263758&origin=inward&txGid=11e5ca72e84b7507ccdc2845cd08ca70. Acesso em: 26 jun. 2023.