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Review Article

Migraine: A Comprehensive Review of Pathophysiology Clinical Manifestations, Diagnosis and Treatment

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ABSTRACT

Migraine is a prevalent and disabling neurological disorder characterized by recurrent episodes of unilateral, pulsating headaches that can last from hours to days. These headaches are often accompanied by nausea, vomiting, photophobia, and phonophobia, significantly impacting daily life. Diagnosis is primarily clinical, based on the International Classification of Headache Disorders (ICHD) criteria, though neuroimaging is recommended in atypical cases to rule out secondary causes.Treatment strategies focus on both acute symptom relief and long-term prevention. Acute therapies include NSAIDs, triptans, gepants, and ditans, while preventive treatments involve beta-blockers, antiepileptics, antidepressants, CGRP monoclonal antibodies, and lifestyle modifications. This review explores the pathophysiology, clinical manifestations, diagnostic criteria, and evolving treatment MODALITIES, aiming to enhance the understanding and management of this complex neurological disorder.

INTRODUCTION

The International Headache Society defines migraine as a recurring main headache disease with attacks lasting 4-72 hours. Typically, the headache is unilateral, pulsing, moderate to severe in severity, exacerbated by normal physical activity, and accompanied by nausea, photophobia, and phonophobia.[1] Migraine affects females three times more than males and has a major impact on quality of life, particularly during peak productive years. It is distinguished by bouts of unilateral, throbbing headaches with sensitivity to movement, visual, auditory, and other afferent stimuli. Other symptoms, including as fatigue, irritation, poor attention, and yawning, might occur up to 48 hours before the headache: this is known as the premonitory phase. Most assaults are followed by hours a day of feeling poorly, frequently with fatigue known as the postdrome. Approximately one-third of migraine sufferers experience neurological deficits, including cortical disturbances, known as migraine

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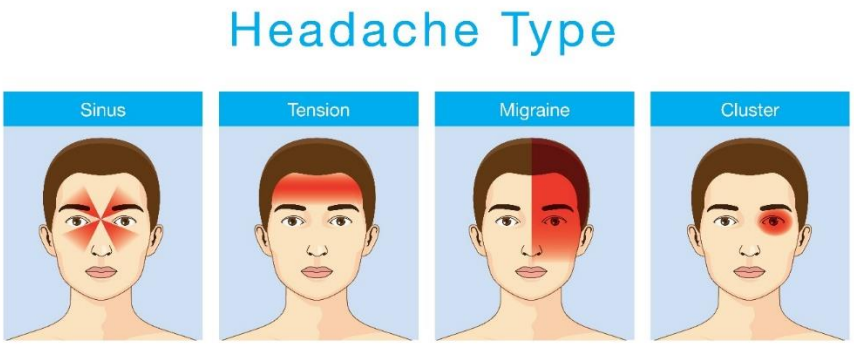
aura. [2] Migraine is currently ranked as the sixth most disabling disorder in the world, and the highest among all neurological disorders. Migraine biology is complex, multifaceted, and certain parts remain unresolved. The underlying feature appears to be a complicated combination of genetic predisposition, behavioral and environmental factors that modify sensory brain processing, leading to greater vulnerability. Migraineurs may interpret normal sensory stimuli as unpleasant.[8]



Chronotype refers to how an individual's circadian clock synchronizes with the 24-hour day. Chronotypes are typically distributed within a population and are influenced by sex, age, genetics, and environment. Some individuals are night owls, while others are early risers ('larks'). Some individuals are night owls, while others are early risers ('larks'). Numerous diseases have been linked to both early and late chronotypes. Early chronotypes have been linked to depression, epilepsy, and paroxysmal brain diseases, with a strong bidirectional correlation with migraine.Late chronotypes are linked to suicide attempts, bipolar disorder, and unidirectional co-morbidity with migraines.[3]

Pathophysiology Of Migraine

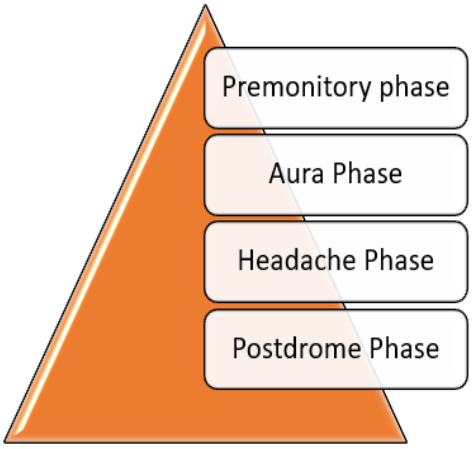


Fig. Phases of Migraine

Premonitory phase

The premonitory phase of migraine contains annoying "prodromal" symptoms that occur hours to days before the actual migraine pain. These symptoms do not include aura, but rather mood changes like irritation, weariness, yawning, concentration difficulties, pallor, nausea, blurred vision, and neck stiffness. Increased sensory symptoms, including photophobia and phonophobia, may occur.Premonitory signs are

present in over two-thirds of the pediatric population, with the most prevalent being common symptoms in children include weariness, irritability, face pallor, and periorbital dark circles.[4]The hypothalamus is assumed to have a crucial role in migraine pathogenesis. Behavioral changes in mood, hunger, and energy suggest hypothalamic involvement during the premenstrual phase. Functional neuroimaging studies indicate hypothalamic involvement during the premonitory phase. Functional magnetic resonance imaging of migraine sufferers during the interictal period revealed increased connection between the hypothalamus and brain regions responsible for pain transmission and autonomic function. The hypothalamus may play a crucial role in amplification of pain during a migraine attack, as evidenced by neuroimaging results.[5]

Neck pain is a typical migraine symptom that can appear in the premonitory phase and persist during the postdrome phase, and it may contribute significantly to migraine-related disability. Although structural disease of the cervical spine is uncommon, the prevalence of neck discomfort suggests that upper cervical nerves may play a role in transmitting migraine pain. The second-order neurons in the brainstem and upper cervical spinal cord receive pain inputs from both the cervical and trigeminal nerves. Stimulating the cervical nerves causes headaches in both healthy and migraine sufferers, while C1 stimulation causes discomfort in the peri-orbital area.[6]

Aura Phase

Up to 25% of migraine sufferers experience the aura, a set of localized neurologic symptoms that precede an acute migraine attack. The aura has played a key role in attempts to explore and eventually understand migraine etiology. The vasogenic theory suggests that the aura is caused by an initial vasoconstrictive phase of a migraine attack. Although this phenomena comprised of an excitatory phase followed by a period of depressed activity, it was dubbed cortical spreading depression. Migraine's aura may be induced by a human version of cortical spreading depression, due to their delayed spread and movement across neurovascular borders. This proposed scenario suggests that blood flow changes during migraine aura are caused by lower metabolic demand in improperly functioning neurons, rather than the underlying cause of the symptoms.[7] The case for the aura as the human equivalent of Leao's cortical spreading depression (CSD) is compelling. Visual aura in humans affects the visual field and spreads at a speed of 3 mm/min from the center to the periphery, indicating the visual cortex.[9] cortical spreading depolarization (CSD) is not limited to migraine aura, but has also been detected in stroke, traumatic brain injury, and seizures. CSD may trigger the trigeminocervical complex, leading to disagreement about whether it can also cause migraines without aura. CSD disrupts ion homeostasis, leading to neuronal dysfunction, hyperemia, and then oligemia. Excess glutamate causes membrane depolarization, leading to a significant current shift and release of vasoactive chemicals such NO and arachidonic acid metabolites. This causes increased cerebral blood flow to meet energy demands and restore balance. During visual aura, functional brain magnetic resonance imaging shows increased blood oxygenation level-dependent signal alterations in the extrastriate cortex (region V3A). Propagates through the occipital cortex correlating with retinal maps of the visual precept.[10]

Headache Phase

The absence of cerebral "oligemia" or changes on functional MRI in migraine without aura prompted researchers to explore alternate explanations for the headache phase of migraine. Migraine's nociceptive component is likely caused by activation of the trigeminocervical complex. The trigeminal nerve's ophthalmic branch innervates the dural and cranial vascular structures in the

anterior and middle fossa, whereas upper cervical roots innervate the posterior fossa. Stimulating these structures causes pain and increased neuronal activity in their respective regions. The meningeal nerves send branches and innervate the pial surface and calvarial bones (by infiltration of calvarial sutures).[11] Migraine headaches are caused by activation of nociceptive receptors on dural and vascular structures, neuropeptide release (e.g., CGRP), activation of thalamicocortical networks, and inhibition of descending cortical pain control pathways.[12] Afferent nerve fibers from the trigeminal ganglion, as well as afferents from the skin and muscles of the neck, synapse on second-order neurons in the trigeminal cervical complex (TCC), explaining upper neck pain. Ascending fibers from the TCC convey signals to different cortical locations after crossing brainstem, thalamic, hypothalamus, and basal ganglia nuclei, resulting in the manifestation of pain.[13]

Vascular Changes:

Imaging investigations in induced migraine have revealed interesting findings about vascular alterations during a migraine attack. Although vasodilation is a common symptom of migraine headaches, there is no direct evidence that it is the cause of pain. It could simply be a result of the same pathophysiological mechanisms that generate headache. Studying vascular changes can improve understanding of migraine pathogenesis, regardless of their relevance to pain.

Exogenous Migraine Triggers:

Migraine triggers include CGRP, PACAP, sildenafil, and prostaglandins I2 and E2. Migraine headaches are an indirect response to exogenous nitric oxide, CGRP, or PACAP, rather than a direct effect. Exogenous delivery of migraine triggers can disrupt a delicate equilibrium, leading to neurochemical alterations and a full-blown migraine attack. Exogenous migraine triggers may cause a compensatory release of neurotransmitters or neuromodulators, such as dopamine, adrenaline, acetylcholine, or adenosine triphosphosphate, leading to the downstream endogenous release of the CGRP, nitric oxide, and PACAP

Central sensitization:

Central sensitization is characterized by symptoms such as photophobia, phonophobia, and allodynia. This occurs when sensory processing pathways in the brain or spinal cord are activated, resulting in altered sensory perception. Traditional pain models view this as a secondary effect of peripheral nociceptive input. This concept contradicts the early onset of sensory sensitivity (photophobia and phonophobia) during migraine attacks, which can begin independently of trigeminal input according to imaging studies. These investigations suggest that migraine attacks are triggered by central sensitization rather than peripheral discomfort.[14]

Postdrome Phase

The locus coeruleus is a brainstem noradrenergic nucleus situated in the dorsal pontine tegmentum. This nucleus is the primary source of norepinephrine for the cerebrum, brainstem, cerebellum, and spinal cord. The nucleus has reciprocal circuits with the neocortex, diencephalon, limbic system, and spinal cord, indicating its vast impact on the neuraxis. During stressful events, the locus coeruleus noradrenergic system is among the first to be activated. It affects a variety of physiological and psychological processes, including pain processing, behavior modification, and stress reactivity. Functional MRI studies reveal activation of the dorsal pons during premonitory and migraine headache stages.[15] Cortical spreading depression may also contribute to reduced regional cerebral blood flow during the postdrome. Cortical spreading depression often suppresses spontaneous and evoked electrical activity for 5-15 minutes. However, under certain pathophysiologic situations, including as hypoglycemia, hypoxia,

and ischemia, cortical spreading depression can occur spontaneously and last for an extended period of time. Impaired astroglial function leads to an increased risk of cortical spreading depression. Cortical spreading depression is preceded by a rapid network of oscillations, indicating temporary hyperexcitement. Neuronal activity is completely suppressed for a few minutes, then fully recovered.[16][17] Symptoms may include fatigue, physical weakness, mood changes, cognitive difficulties, and decreased appetite. The postdromal phase could be explained by prolonged activation of the brainstem and diencephaly during and after pain processing. Functional imaging, including functional MRI (fMRI) and PET, has been increasingly used in migraine and other pain states and has alluded to areas of brain activation that are thought to be key structures in the initiation and propagation of the headache and pain states.[18]

General systemic symptoms	Symptoms
Neuropsychiatric symptoms	Mood changes, concentration trouble, sleep disturbance (insomnia and hypersomnolence)
Sensory symptoms	Head soreness, photophobia, phonophobia, speech disturbance
Gastrointestinal symptoms	Nausea, flatulence, constipation, vomiting, anorexia, food craving, abdominal pain, diarrhoea
General systemic symptoms	Tiredness, urination, fluid retention

Symptoms Associated with Migraine

Nausea in Migraine and Related Conditions-

According to the International Classification of Headache Disorders, Third Edition (ICHD-3), nausea is one of the canonical migraine symptoms. Ictal and interictal nausea have a significant influence on quality of life and economic costs , and are the second most troublesome migraine symptom, recorded in 28% of patients, trailing only photophobia. Up to half of adults with episodic migraine have nausea in more than half of their headache episodes, and the attacks are accompanied by more headache symptoms and have a greater impact than patients with less frequent nausea.[19,20,21]

Cyclical Vomiting Syndrome-

It is generally established that migraine and cyclic vomiting syndrome share similar related symptoms and triggers, as described by patients. Both nausea and cyclic vomiting syndrome patients have reduced connection between the sensorimotor network and the insula, which controls viscero-sensory processing and may be modulated by the endocannabinoid system. Cannabis can act as both a pro- and antiemetic, causing cannabis hyperemesis syndrome, which is related to cyclic vomiting sickness and is treated by cannabis discontinuation. Surprisingly, the care of cyclic vomiting syndrome relies primarily on therapies utilized for migraines.[22,23]

Motion Sickness-

Motion sickness and migraine may have a similar pathogenesis, as people with motion sickness have a strong migrainous biology , and around half of migraineurs have motion nausea, compared to 20% of those with non-migrainous headaches. Patients with "migrainous vertigo" improved their severe motion sickness after taking rizatriptan . Nociceptive stimulation in the trigeminal area can increase nausea during motion sickness generated by optokinetic stimulation, although nausea does not increase in response to extra-trigeminal nociceptive inputs. A migraine history has also been connected with developing post-operative nausea, and having motion sickness and being a female are independent risk factors for post-operative vomiting.[24]

Diagnosis Of Migraine [25]

The third edition of the International Classification of Headache Disorders (ICHD-3) divides migraine into three types: without aura, with aura, and chronic migraine. Accurate diagnosis requires

careful consideration of each individual's clinical characteristics.

Migraine Without Aura

Migraine without aura is characterized by recurring headache bouts lasting 4–72 hours. An attack typically has a unilateral location, pulsing character, moderate to severe pain intensity, and worsens with ordinary physical activity.

Migraine With Aura

Aura is experienced by roughly one-third of migraine sufferers, either during all or some attacks. Aura refers to brief neurological symptoms that occur before or during a migraine attack.

Family history of migraines

Migraine has a strong genetic component and is more common in individuals with directly affected first-degree relatives than in the general population. Family history is generally positive in migraine patients, but may be under-reported.

Medical history

The medical history is the mainstay of migraine diagnosis. Additional investigations, such as neuroimaging, blood samples, or lumbar puncture, may be necessary to confirm or rule out secondary causes of headache. A physical examination is typically sufficient to confirm diagnosis. A complete medical history should include the following: age at headache onset, duration, frequency, pain characteristics (location, quality, severity, aggravating and relieving factors), accompanying symptoms (e.g., photophobia, phonophobia, nausea and vomiting), aura symptoms (if present), and history of acute and preventive medication use. All are required for applying the ICHD-3 criterion.

Diagnostic Criteria.

The International Headache Society published the ICHD-3 criteria , which outline clinical symptoms for diagnosing migraine and its various variants. To prioritize specificity over sensitivity, probable migraine is defined as "migraine-like attacks missing one of the features required to fulfil all criteria for a type or subtype of migraine." Additional criteria are provided for this diagnosis. ICHD-3 diagnostic criteria for primary headache disorders[26]

Migraine Without Aura

1.At least five attacks meet the criteria.

2.Headache bouts lasting 4-72 hours when untreated or poorly treated

3.Headache exhibits at least two of the following four characteristics:

-unilateral location

- pulsing quality.

- Moderate to severe pain intensity

-Avoidance or aggravation of routine physical activities, such as walking or climbing stairs.

4.At least one of the following occurs during the headache:

- nausea or vomiting

- Photophobia and Phonophobia

5. Not better explained by another ICHD-3 diagnosis.

Migraine With Aura

1.At least two attacks that meet criteria two and three.

2.One or more of the following completely reversible aura symptoms:

-Visual, sensory, speech/language, motor, brainstem, and retinal.

3.At least three of the six characteristics listed below:

-At least one aura symptom appears progressively over ≥5 minutes.

-two or more aura symptoms appear in succession.

Aura symptoms typically last 5-60 minutes and are unilateral.

Symptoms of an aura include at least one positive symptom and a headache within 60 minutes.

4. Not better explained by another ICHD-3 diagnosis.

Chronic Migraines

1. Headache (migraine-like or tension-type) lasting ≥15 days per month for
more than 3 months, meeting criterion 2 and 3.
2. Attacks occur in individuals who have experienced at least five attacks that meet the criteria for migraine without or with aura.
3.n ≥8 days/month for more than 3 months, meeting any of the following criteria:
-Criteria 3 and 4 for migraine without aura.
-Criteria 2 and 3 for migraine with aura - Patient reports migraine at onset and relief by triptan or ergot derivatives.
4. Not better explained by another ICHD-3 diagnosis.

Overuse Of Medication Causes Headache

1. Individuals with a pre-existing headache who experience headaches on atleast 15 days each month disorder.
2. Regular abuse for more than three months of one or more medicines that can be used for acute and/or symptomatic therapy of headache (consistent ingestion of one or more Non-opioid analgesics on ≥15 days/month for ≥3 months, or any other acute Medication or combination of drugs used for at least 10 days each month for at least 3 months.
3. Not better explained by another ICHD-3 diagnosis.

Potential trigger factors related to the occurrence of migraine attacks [27]

Stress	**Stress in general, private (emotional) stress, work stress**
Sleep	Excessive sleep, poor sleep, restless sleep
Environmental factors	Bright lights, loud noise, odours
Lifestyle habits	Physical activity, missed meals
Dietary– drink	Dehydration
Dietary– alcohol	Alcohol, beer, red wine, white wine, sparkling wine, spirits
Dietary– caffeine	Caffeine (coffee and other drinks containing caffeine)
Dietary– food	Chocolate, nitrates, MSG (monosodium glutamate), citrus fruits, artificial sweetener, nuts, cheese
Nicotine	Nicotine (smoking)
Hormonal factors	Menstruation
Tiredness, neck pain	Tiredness, neck pain
Meteorological factors	Humidity mean (relative), pressure change (atmospheric), temperature mean (air)

Health Treatments for Migraine

Supplements

Supplements include vitamins, minerals, and herbal treatments. Despite limited FDA regulation, the usage of migraine medications is increasing . Despite being advertised as safe, there is limited data on their safety during pregnancy and lactation.

- Magnesium can help manage and avoid acute migraine attacks, according to studies. Magnesium is the second most abundant intracellular cation in the body. It contributes significantly to glucose metabolism, nucleic acid production synthesis, muscular action, and membrane stabilization.Approximately 67% of magnesium is stored in human bodies into the bones and the remainder intracellularly. Serum levels are not a reliable estimate of total body reserves, as only 1%-2% are available extracellularly. Low magnesium levels in serum and intracellular concentrations in cells and the brain have been associated to migraines, both ictal and interictal .In emergency departments, IV magnesium is often used alongside other medications to treat intense migraines. One study found that administering 1 g of IV magnesium reduced pain intensity by.50% in almost half of patients with low serum ionized magnesium levels. Magnesium should be avoided during renal failure. It is secreted in urine and can be hazardous in renal failure, leading to arrhythmias, hypotension, disorientation, coma, and death.[28]
- Riboflavin (vitamin B2) is a crucial cofactor for enzymes involved in energy production in mitochondria via the Kreb's cycle and electron transport chain. It is one of the safest and most affordable migraine prevention treatments.

Riboflavin is used to address mitochondrial abnormalities in the brain, which can lead to decreased energy production and imbalanced cortical excitability. A pharmacogenetic study found that migraine patients with non-H mitochondrial DNA haplotypes responded well to treatment.[29]

- Co-enzyme Q 10 is a cofactor in the mitochondrial electron transport chain. Its action, as an antioxidant and anti inflammatory by reducing production of H2O2 and matrix metalloproteinases, is believed to be the likely antimigraine mechanism. Co-Q10 is available over the counter and is well tolerated.[30]
- Melatonin, an endogenous hormone secreted by the pineal gland, regulates the circadian rhythm. It is used for various clinical conditions, but has recently been proposed for migraine prevention due to its anti-inflammatory effects against calcitonin gene-related peptide and other proinflammatory mediators in vitro, proregulatory effect in the circadian rhythm, and low melatonin levels in serum and urine due to hypothalama.[31]

- **Behavioural Interventions**

migraine is a chronic disabling neurologic condition that is often comorbid with various psychiatric conditions such as depression and anxiety and triggered by stress, several behavioral treatments were extended in the management of migraine with the primary aim of prevention. Most of the interventions described below have been extensively studied in clinical trials and often used an adjunct to with pharmacotherapy. However, studies have also shown that they are effective even without preventive medications/supplements.

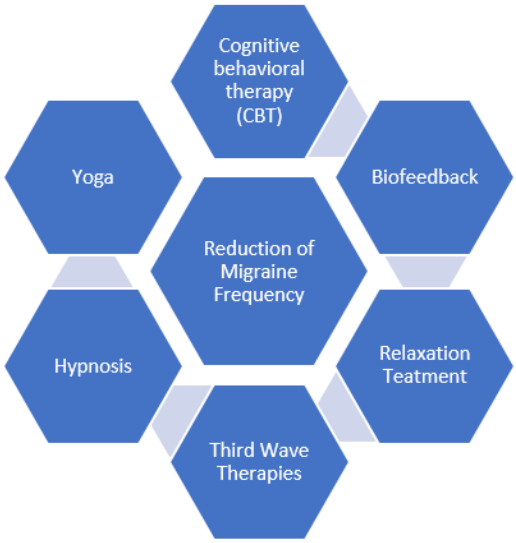


Fig. Reduction of Migraine Frequency

i. Cognitive behavioral therapy (CBT)

Cognitive behavioral therapy (CBT) is a psychotherapeutic approach developed by Aaron Beck to treat mental health disorders. It is based on the idea that our thoughts influence our feelings and behaviors . CBT challenges dysfunctional thoughts (e.g., "My headache will never get better," "I will never be able to perform," and "My wife will leave me") and uses behavioral techniques (e.g., problem-solving).[32]

ii. Biofeedback

Biofeedback is a behavioral method that manipulates information from external devices to generate desired physiological responses . The objective is to teach patients how to manage physiological parameters including heart rate, respiration, and muscular tension using relaxation techniques. Once mastered, behavioral approaches can be applied in illness circumstances without the need for sensors or external equipment. Biofeedback is available in several modalities, including blood volume pulse (BVP) feedback,

thermal biofeedback, and electromyography (EMG) feedback. Responses can be given as auditory or visual visuals.[33]

iii. Relaxation treatment

Relaxation treatment, frequently combined with cognitive behavioral therapy, reduces sympathetic activity and central pain processing. Migraine prophylaxis involves relaxation strategies such as autogenic training, progressive muscle RT (PMRT), diaphragmatic breathing, guided imagery, meditation, and hypnosis. PMRT is a common strategy that involves alternately activating and relaxing fewer muscles throughout successive sessions.[34]

iv. Third Wave Therapies

Meditation is a mental method that helps improve focus, self-awareness, and emotional management. Scientific study distinguishes between two meditational approaches based on attention focus: concentrative and mindfulness (MM).[35]

v. Hypnosis

Hypnosis is a condition of heightened attention, less peripheral awareness, and increased responsiveness to suggestions. Hypnotherapy is the therapeutic use of hypnosis. Hypnosis has been used to treat pain since the 18th century , and its effectiveness for therapeutic purposes has been supported by recommendations from The National Institute of Health Technology Assessment Panel and the American Psychological Association.[36]

vi. **Yoga**

Yoga is a mind-body intervention that addresses many physical and mental health issues. Yoga is based on Indian philosophy and incorporates physical postures (known as "asanas" in Hatha Yoga), breathing methods (pranayama), and meditation. Yoga schools differ dependent on whether they prioritize spiritual or physical activities. A session typically lasts between one and two hours. This secular intervention aims to improve physical flexibility, coordination, and strength while also promoting mental calm and awareness.[37]

vii. Alcohol and Smoking

Alcohol triggers migraine episodes in 75% of patients, perhaps due to an inflammatory mechanism. Additional processes may include vasodilation, dehydration, toxicity, histamine, tyramine, sulfites, flavonoids, and 5-HT release. At this stage, red wine is the most indexed. However, all forms of alcohol may be trigger factors. Smoking and nicotine use have a direct impact on the central nervous system, leading to debate about their role in migraine development. Smoking can trigger migraine episodes. Smoking more than 5 cigarettes per day may cause migraines. Former smokers should consider quitting.[38]

Treatment For Migraine

Acute therapies are classed as first-line, second-line, and third-line. Medication selection at each step was based on effectiveness, tolerability, safety, cost, and availability.

- First-line medicine. [39,40]

Over-the-counter analgesics are often used to treat acute migraines globally. Non-steroidal anti-inflammatory medicines (NSAIDs) with established effectiveness, particularly acetylsalicylic acid, ibuprofen, and diclofenac potassium, are recommended as first-line treatments. Paracetamol is less effective and should only be used for persons who are intolerant to NSAIDs.

- Second-line medicine. [41,42]

Patients with insufficient headache relief from over-the-counter analgesics may benefit from a triptan medication. Triptans have shown efficacy, however availability and access varies by country. Triptans work best when taken early in an episode, while the headache is still moderate. There is no evidence supporting the use of triptans during the aura phase of a migraine episode. If one triptan is useless, another may still give relief. Sumatriptan

can be administered subcutaneously in cases when other triptans have failed, patients achieve peak headache severity quickly, or oral triptans are not effective due to vomiting.

- Third-line medicine. [43,44]

If triptans do not provide appropriate therapeutic response after three consecutive episodes or are contraindicated, there are few options. However, ditans and gepants are now in short supply. Lasmiditan is the sole ditan authorized for acute migraine therapy, while ubrogepant and rimegepant are the only gepants approved. Data from randomized controlled studies indicate that lasmiditan is equivalent to triptans in terms of effectiveness (56-58). However, it is associated with transitory driving impairment, which may limit its usage. Individuals using lasmiditan may struggle to self-assess their driving skills and should avoid operating machines for a least 8 h after intake.

Drug Class	Drug	Dosage and Route	Contraindication
First Line Medication			
NSAIDs	Acetylsalicylic acid	900–1,000 mg oral	Gastrointestinal bleeding, heart failure
	Ibuprofen	400–600 mg oral	
	Diclofenac potassium	50 mg oral (soluble)	
Other simple analgesics (if NSAIDs are contraindicated)	Paracetamol	1,000 mg oral	Hepatic disease, renal failure
Antiemetics (when necessary)	Domperidone	10 mg oral or suppository	Gastrointestinal bleeding, epilepsy, renal failure, cardiac arrhythmia
	Metoclopramide	10 mg oral	Parkinson disease, epilepsy, mechanical ileus
Second-line medication			
Triptans	Sumatriptan	50 or 100 mg oral or 6 mg subcutaneous or 10 or 20 mg intranasal	Cardiovascular or cerebrovascular disease, uncontrolled hypertension, hemiplegic migraine, migraine with brainstem aura
	Zolmitriptan	2.5 or 5 mg oral or 5 mg intranasal	
	Almotriptan	12.5 mg oral	
	Eletriptan	20, 40 or 80 mg oral	
	Frovatriptan	2.5 mg oral	
	Naratriptan	2.5 mg oral	
	Rizatriptan	10 mg oral tablet (5 mg if treated with propranolol) or 10 mg mouth-dispersible wafers	

Third-line medication			
Gepants	Ubrogepant	50, 100 mg oral	Co-administration with strong CYP3A4 inhibitors
	Rimegepant	75 mg oral	Hypersensitivity, hepatic impairnment
Ditans	Lasmiditan	50, 100 or 200 mg oral	Pregnancy, concomitant use with drugs that are P-glycoprotein substrates

CONCLUSION

In this review, we have discussed the pathophysiology and Treatment of migraine. Migraine is a multifactorial chronic neurological condition that varies in frequency, severity and its effect on the quality of life. The pathophysiology stresses the presence of different triggers that initiate a headache attack or increase the frequency of the attacks. Treatment options should consider not only the symptoms, diagnosis, and co-existing or comorbid conditions of the patient, but also the desires, wishes and aspirations of the patient.

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