World Journal of Pharmaceutical Science and Research

www.wjpsronline.com

Review Article

ISSN: 2583-6579
SJIF Impact Factor: 6.916
Year - 2026
Volume: 5; Issue: 6
Page: 957-980

MIGRAINE: CURRENT CONCEPT AND CLINICAL MANAGEMENT

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Article Received: 28 April 2026 | | ***Article Revised: 18 May 2026*** | | ***Article Accepted: 08 June 2026***

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DOI: https://doi.org/10.5281/zenodo.20689099

How to cite this Article: Shubham Kumar Pathak, Dr. Meenakshi Tyagi (2026) MIGRAINE: CURRENT CONCEPT AND CLINICAL MANAGEMENT. World Journal of Pharmaceutical Science and Research, 5(6), 957-980.

ABSTRACT

Migraine is a chronic and persistent neurovascular illness characterized by repeated attacks of moderate to severe headaches, often accompanied by nausea, vomiting, photophobia, and phonophobia. It is acknowledged as one of the most common neurological disorders in the world, having significant consequences for the affected individuals' quality of life, everyday activities, and socioeconomic productivity. According to the World Health Organization, migraine is one of the top causes of disability, especially among young adults and women. Migraine's precise pathogenesis is complex and multifaceted, involving trigeminovascular system activation, cortical spreading depression, inflammatory neuropeptide release, and neurotransmitter dysregulation such as serotonin and calcitonin gene-related peptide (CGRP). Migraines are caused by a variety of genetic, environmental, hormonal, nutritional, and psychological variables. Migraine is usually characterized as migraine with or without aura, although various different subtypes have been identified, including chronic migraine, vestibular migraine, and hemiplegic migraine. The diagnosis is primarily clinical, based on criteria defined by the International Classification of Headache Disorders (ICHD). Migraine treatment includes both acute and preventative measures. Nonsteroidal anti-inflammatory drugs (NSAIDs), triptans, ergot derivatives, beta-blockers, antidepressants, calcium channel blockers, and antiepileptic medications are examples of conventional pharmacological therapy. In recent years, there have been significant advances in migraine management with the introduction of CGRP antagonists, monoclonal antibodies, gepants, ditans, and neuromodulation approaches. Non-pharmacological therapies such as lifestyle change, stress management, dietary regulation, sleep hygiene, yoga, and cognitive behavioral therapy can also help reduce the frequency and intensity of migraines. The current study examines current ideas about migraine pathophysiology, classification, clinical symptoms, diagnosis, and modern therapeutic approaches. New medicines and recent advancements in clinical management have received special attention, as they have the potential to improve treatment outcomes and patient quality of life.

KEYWORDS: Migraine, Neurovascular Disorder, CGRP, Triptans, Headache, Clinical Management, Preventive Therapy, Neuromodulation.

1. INTRODUCTION

Migraine is a chronic, burdensome neurologic illness characterized by repeated bouts of moderate to severe headaches, which are frequently accompanied by nausea, vomiting, photophobia, and phonophobia. The headache is usually unilateral, pounding, and can continue between 4 and 72 hours, having a significant impact on the patient's physical, psychological, and social health. Migraine is increasingly recognized as a complicated neurovascular condition rather than a simple vascular headache disorder,[1,2] characterized by anomalies in neuronal excitability, vascular control, and inflammatory pathways.

Migraine is a major public health concern worldwide because to its high prevalence and impairment load. Migraine is one of the leading causes of disability, particularly among people under the age of 50.[3] Epidemiological studies estimate that migraine affects between 12 and 15% of the world's population. Women are impacted roughly three times more than men due to hormonal effects and genetic predisposition.[4] The disease usually begins in adolescence or early adulthood and can last throughout life with different frequency and severity of attacks.[5]

Burden and Epidemiology of Migraine Worldwide

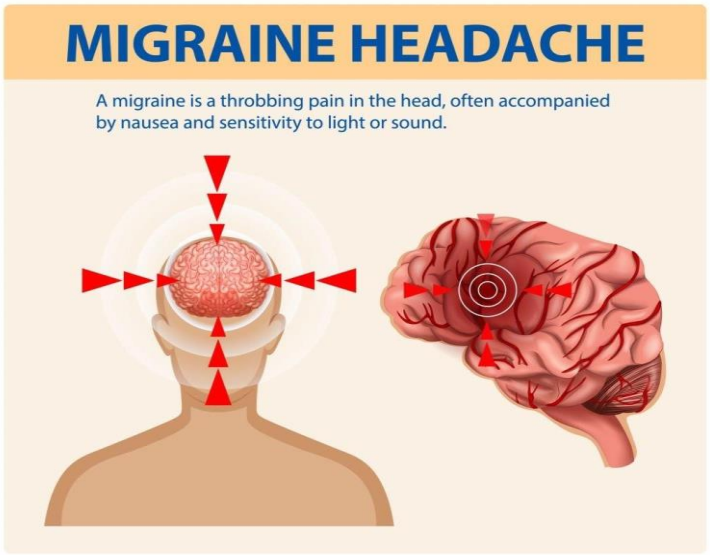

Figure 1: Migraine.

Migraine is a significant contributor to health-care costs, work absenteeism, lost productivity, and a lower quality of life. Recurrent migraine attacks have an influence on academic achievement, occupational functioning, and social functioning. In severe circumstances, chronic migraine can produce anxiety, depression, sleep difficulties, and drug overuse headaches.[6] Migraine is especially prevalent in developing nations, where underdiagnosis and insufficient treatment remain major difficulties.[7]

Pathophysiological Mechanisms of Migraines

The exact pathogenesis of migraine is complicated and not entirely understood. Earlier vascular theories stated that cerebral dilatation was the fundamental cause of migraine discomfort. Migraine is now thought to be primarily a neuronal malfunction and trigeminovascular system activation condition.[8]

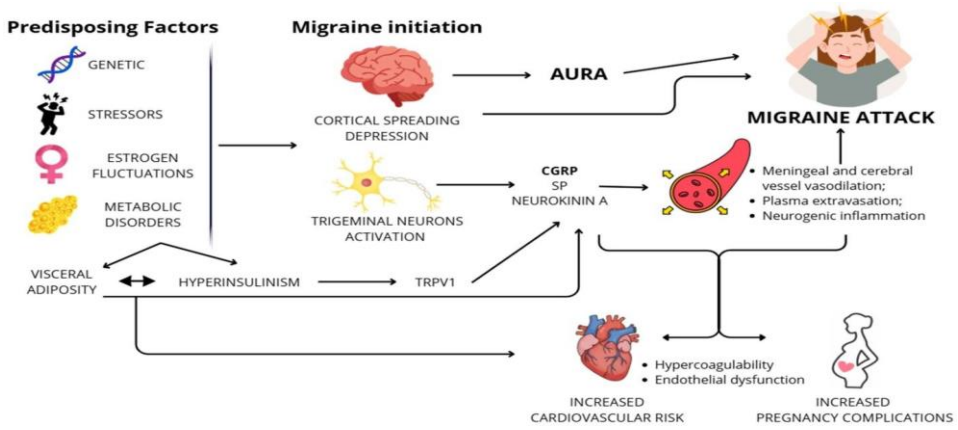

Figure 2: Pathophysiological Mechanisms of Migraines.

Vasoactive neuropeptides, such as calcitonin gene-related peptide (CGRP), substance P, and neurokinin A, are released when trigeminal nerve sensory fibers are activated. These mediators cause vasodilation, extravasation of plasma proteins, neurogenic inflammation, and transfer of pain signals to central nervous system tissues.[9] CGRP has emerged as one of the most prominent therapeutic targets in migraine treatment due to its critical role in pain transmission and vascular regulation.[10]

Another significant mechanism associated with migraine is cortical spreading depression (CSD), which is characterized by a slowly propagating wave of neuronal depolarization followed by cortical activity suppression. CSD is hypothesized to play a role in migraine auras and the activation of trigeminal nociceptive pathways.[11] Abnormalities in serotoninergic neurotransmission, ion channel failure, mitochondrial abnormalities, and hereditary susceptibility have all been implicated in migraine pathophysiology.[12]

Risk and Precipitation Factors

Migraine attacks are frequently caused by a range of endogenous and external trigger events. The most prevalent source is thought to be emotional stress, followed by sleep disruptions, fasting, hormonal variations, weather changes, strong light exposure, loud noises, and nutritional variables.[13] Certain foods and beverages, such as chocolate, aged cheese, processed meat, alcohol, monosodium glutamate, and caffeine-containing goods, might cause migraine headaches in sensitive people.[14]

Women's migraines are also heavily influenced by hormonal changes that occur during menstruation, pregnancy, and menopause. Genetic predisposition is also crucial, as familial aggregation and inherited sensitivity have been identified in many migraine patients.[15]

Classification of Migraine Headache

According to the International Classification of Headache Disorders (ICHD-3), migraine is classified into many types.

The most common variety is migraine without aura, which is described as repeated headache attacks that are not preceded by any neurological symptoms. Migraine with aura is distinguished by brief neurological symptoms such as visual disturbances, sensory disturbances, speech difficulties, or motor weakness preceding the onset of headache.[16]

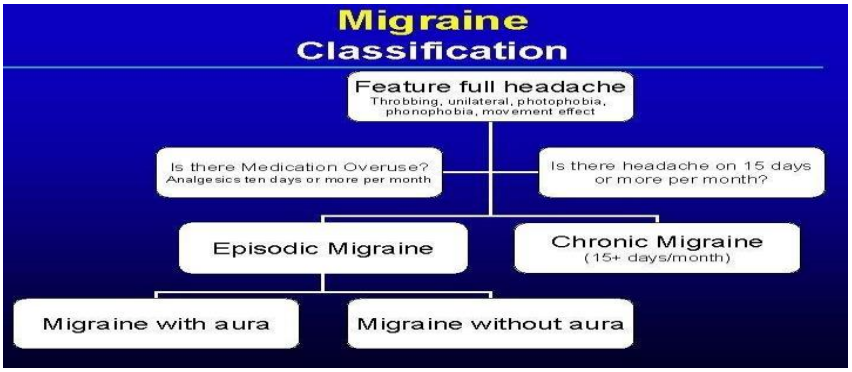

Figure 3: Classification of migraine headache.

Chronic migraine, vestibular migraine, menstrual migraine, retinal migraine, and hemiplegic migraine are other acknowledged clinical types. Chronic migraine is characterized as headaches on ≥15 days per month for at least 3 months, with migraines on ≥8 days per month.[17]

Diagnosis and Clinical Management

According to the ICHD diagnostic criteria,[16] the migraine diagnosis is primarily clinical and is based on the patient's comprehensive history, symptom features, attack duration, and concomitant manifestations. Neuroimaging investigations, such as computed tomography (CT) and magnetic resonance imaging (MRI), are typically used in unusual cases or suspected secondary headache diseases.[18]

Migraine treatment involves both acute and preventative treatments. The goal of acute treatment is to stop migraine attacks and alleviate related symptoms, whereas preventive therapy aims to reduce attack frequency, intensity, and recurrence.[19] Nonsteroidal anti-inflammatory medications (NSAIDs), triptans, ergot alkaloids, beta blockers, calcium channel blockers, antidepressants, and antiepileptic pharmaceuticals are all examples of conventional pharmacological agents.[20]

Recent advancements in migraine therapy include the introduction of CGRP monoclonal antibodies, gepants, ditans, and neuromodulation devices, all of which have improved efficacy and safety profiles in individuals with refractory migraine.[21] Lifestyle adjustment, sleep hygiene, regular exercise, yoga, stress management, and cognitive behavioral therapy are all essential non-pharmacological treatments for long-term migraine control.[22]

Scope and Objectives of Review

As migraines become more widespread and cause greater impairment, we must continue to advance our understanding of migraine etiology and therapy. The current study aims to provide a complete overview of migraine, focusing on current concepts, epidemiology, pathophysiology, classification, clinical symptoms, diagnosis, and recent improvements in clinical therapy. Emerging therapeutic approaches and current treatment tactics have received special attention as they have the potential to improve patient outcomes and quality of life.

2. Classification of the Migraine

Migraine is a complicated neurovascular disease that can emerge in a range of clinical forms depending on the underlying neurological symptoms as well as the frequency, length, and intensity of episodes. The International Classification of Headache Disorders (ICHD-3) divides migraine into seven subtypes: migraine without aura,

migraine with aura, chronic migraine, vestibular migraine, hemiplegic migraine, retinal migraine, and menstrual migraine.[22] Correct migraine classification is critical for effective diagnosis, treatment planning, and complication prevention.

Figure 4: Classes.

2.1 Migraines without aura (MO)

The most frequent type of migraine is migraine without aura, which accounts for roughly 70- 80% of all migraine cases. It is distinguished by recurring headache bouts lasting 4–72 hours. The headache is typically unilateral, pulsing, moderate to severe in severity, and exacerbated by normal physical activity like walking or climbing stairs.[22]

Other possible symptoms include nausea, vomiting, photophobia, and phonophobia. Migraine attacks can be caused by a variety of causes, including emotional stress, fasting, hormonal imbalance, sleep disruptions, weather changes, and eating patterns.[23] The primary mechanisms implicated in migraine pathophysiology include trigeminovascular system activation and the release of inflammatory neuropeptides such as calcitonin gene-related peptide (CGRP).[24]

2.2 Migraine with aura

Migraine with aura is characterized by transitory focused neurologic symptoms that often occur before the headache. Aura symptoms are present in roughly one-third of migraine patients.[25] The most common type is a visual aura, which includes flashing lights, zigzag lines, blurred vision, scintillating scotomas, and transitory visual field abnormalities.[26]

Sensory symptoms (numbness or tingling sensations) and speech problems may also be present. Aura symptoms normally appear gradually over 5 to 20 minutes and persist no longer than an hour. Cortical spreading depression is a self-propagating pulse of neuronal depolarization followed by suppression of cortical activity, and it is assumed to be the primary mechanism producing migraine aura.[27]

2.3 Chronic Migraine

Chronic migraine is a disabling neurological illness defined by headaches occurring on 15 or more days per month for more than three months, with migraines occurring on at least 8 days each month.[27] Chronic migraine usually results from episodic migraines caused by drug overuse, obesity, stress, depression, anxiety, or sleep difficulties.[28]

Persistent activation of pain pathways and central sensitization are likely to play key roles in the evolution of chronic migraine.[29] Many chronic migraine patients experience a lower quality of life, poorer social functioning, and an increased healthcare burden.

2.4 Hemiplegic Migraine

Hemiplegic migraine is an uncommon form in which the aura is accompanied by temporary unilateral motor weakness.[30] Patients may experience one-sided paralysis or weakness, as well as visual and sensory disturbances, speech difficulties, and severe headaches.

It is further classified as familial hemiplegic migraine and sporadic hemiplegic migraine depending on genetic inheritance patterns. Disease development has been linked to mutations that impair neuronal ion channels and neurotransmitter regulation.[31]

2.5 Migraine vestibular

Vestibular migraine is defined as recurrent vertigo, dizziness, imbalance, and motion sensitivity accompanied by migraine symptoms.[32] Vestibular symptoms can occur with or without headaches. Common manifestations include nausea, vomiting, photophobia, and phonophobia.

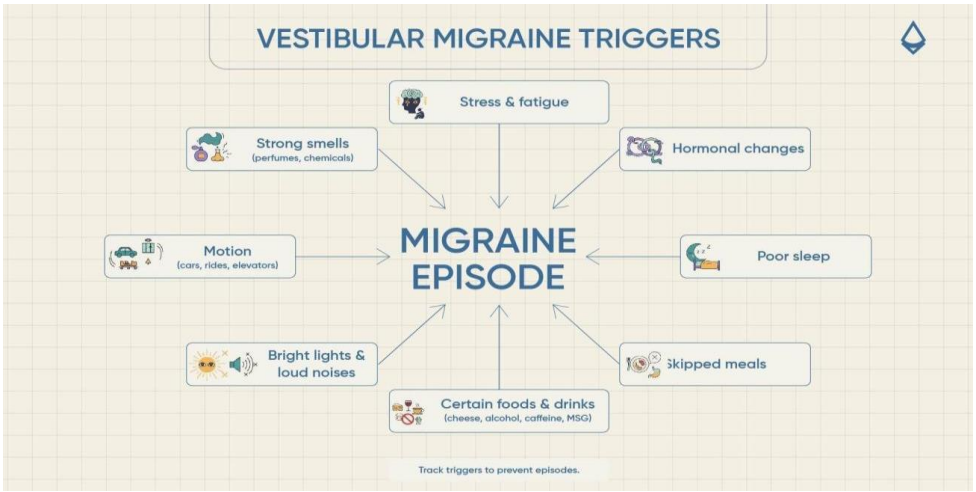

Figure 5: Migraine vestibular.

The pathogenesis involves aberrant connections between vestibular circuits and trigeminovascular processes.[33]

Vestibular migraine affects many people's daily lives and is sometimes misdiagnosed as inner ear diseases.

2.6 Menstrual Migraine

Menstrual migraine is intimately linked to hormonal changes, specifically a drop in estrogen levels during the menstrual cycle.[34] These migraine attacks typically occur two days before or three days after menstruation begins. Menstrual migraines are typically more intense, persist longer, and are less responsive to treatment than non-menstrual migraines.

2.7 Retinal Aura Migraine

Retinal migraine is an uncommon migraine subtype distinguished by transitory monocular visual abnormalities such as momentary blindness, scintillations, or scotomas, followed by headache.[35] The symptoms are totally reversible and are thought to be caused by retinal vasospasm or vascular dysfunction.

2.8 Migraine Status

Status migrainosus is a serious consequence characterized by migraine attacks that continue unabated for more than 72 hours after therapy.[36] Patients frequently have extreme nausea, dehydration, vomiting, and profound impairment, necessitating emergency treatment and hospitalization.

2.9 Clinical Relevance of the Classification of Migraines

The classification of migraine helps clinicians make accurate diagnoses, assess disease severity, choose tailored treatment approaches, and avoid disease progression. Recent developments in migraine research have resulted in the development of targeted medicines such as CGRP antagonists, monoclonal antibodies, and neuromodulation techniques, all of which have significantly improved patient outcomes.[37]

3. The Pathophysiology of Migraine

Migraine is thought to be a multifactorial neurovascular disease involving complex combinations of neuronal dysfunction, vascular abnormalities, inflammatory mediators, hereditary vulnerability, and central nervous system sensitization. Previous models viewed migraine as a vascular condition, but recent research has demonstrated that the pathophysiology of migraine is mostly neuronal, with secondary vascular changes.[38] Trigemino-vascular system activation, cortical spreading depression, neurogenic inflammation, and the production of vasoactive neuropeptides such as calcitonin gene-related peptide (CGRP) are all important factors in migraine pathophysiology.[39]

3.1 Activation of the Trigeminovascular System

The trigeminovascular system is regarded to be the primary mechanism in the development of migraine pain. It is composed of trigeminal nerve fibers that innervate the cerebral blood vessels, meninges, and dura mater. During a migraine attack, trigeminal sensory neurons fire and release neuropeptides such as CGRP, substance P, and neurokinin A.[40]

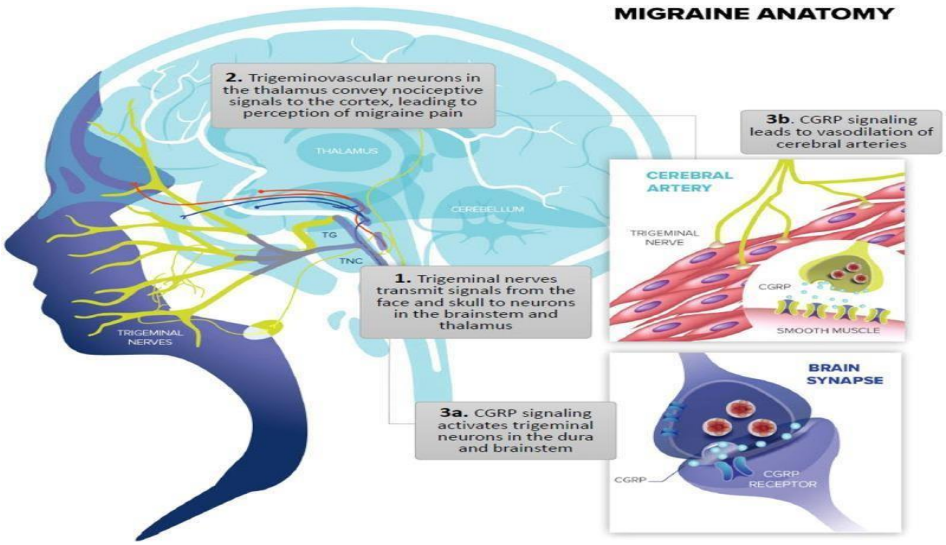

Figure 6: Activation of the Trigeminovascular System.

These inflammatory mediators cause dilatation of cerebral blood vessels, extravasation of plasma proteins, and sterile neurogenic inflammation. The characteristic throbbing headache of migraine is caused by chronic activation of pain-sensitive meningeal structures, which transfer pain signals to higher brain areas.[41]

CGRP has recently been proven to have a key role in migraine etiology. CGRP levels are elevated during acute migraine attacks, and inhibiting CGRP activity dramatically reduces migraine symptoms.[42]

3.2 Cortical Spreading Depression

Cortical spreading depression (CSD) is a slow-moving wave of neuronal and glial depolarization followed by long-term suppression of cortical activity.[43] This condition is significantly linked to migraine aura and is hypothesized to cause activation of trigeminal nociceptive pathways.

CSD causes transitory ionic imbalances, glutamate release, changes in cerebral blood flow, and the generation of inflammatory mediators. These alterations activate meningeal nociceptors, which are important in the development of migraine pain.[44] Experimental evidence supports the importance of CSD in the development of visual aura symptoms such as flashing lights, blurred vision, and zigzag patterns, which are prevalent prior to the start of migraine headache.

3.3 Neurogenic Inflammation

Another major factor in migraine development is neurogenic inflammation. Activation of trigeminal nerve endings causes the production of inflammatory neuropeptides, which increase vascular permeability and stimulate mast cell degranulation.[45]

Inflammatory mediators include prostaglandins, nitric oxide, serotonin, histamine, and cytokines activate pain receptors and enhance nociceptive transmission.[46] Neurogenic inflammation persists, causing peripheral sensitization and increasing the severity and duration of migraines.

3.4 Central and Peripheral Sensitization

Peripheral sensitization refers to the enhanced sensitivity of nociceptive neurons to inflammatory mediators. This procedure improves pain perception during regular physiological actions such as coughing, bending, and moving.[47]

Central sensitization is caused by the persistent stimulation of second-order neurons in the trigeminal nucleus caudalis and higher pain-processing areas. This can cause cutaneous allodynia, hyperalgesia, and enhanced sensitivity to light, sound, and scent in patients.[48] Central sensitization is especially important in the progression of chronic migraine.

3.5 Neurotransmitters: Their Role

Several neurotransmitters are involved in migraine pathophysiology, with serotonin (5- hydroxytryptamine, 5-HT) being the most extensively researched. Lower serotonin levels during migraine attacks are associated with vasodilation and activation of trigeminal pathways.[49]

Dopamine has been linked to migraine symptoms including nausea, vomiting, yawning, and hypotension. Glutamate-mediated excitatory neurotransmission triggers cortical spreading depression and hyperexcitability.[50]

3.6 Genetic Effects on Migraine

Genetic predisposition plays a significant impact in migraine susceptibility. Migraine with aura and hemiplegic migraine are particularly common in persons with a familial history of migraine.[51]

Familial hemiplegic migraine has been connected to ion transport channel mutations and neurotransmitter modulation. Migraine development is heavily influenced by genes related with calcium channels, sodium-potassium ATPase pumps,

and neural excitability.[52]

3.7 Migraine and Vascular Theory

The classical vascular theory stated that aura symptoms are caused by cerebral vasoconstriction, whereas headache pain is caused by extracranial vasodilation.[53] While recent notions emphasize neural pathways, vascular alterations are still recognized as essential factors to migraine pathogenesis.

Changes in cerebral blood flow, endothelial dysfunction, and vascular hypersensitivity may all play a role in migraine beginning and progression.[54]

3.8 Role of Calcitonin Gene-Related Peptide (CGRP)

CGRP is currently recognized as one of the most critical neuropeptides in the pathogenesis of migraine. It is extensively distributed in trigeminal sensory fibers and has potent vasodilatory properties.[55]

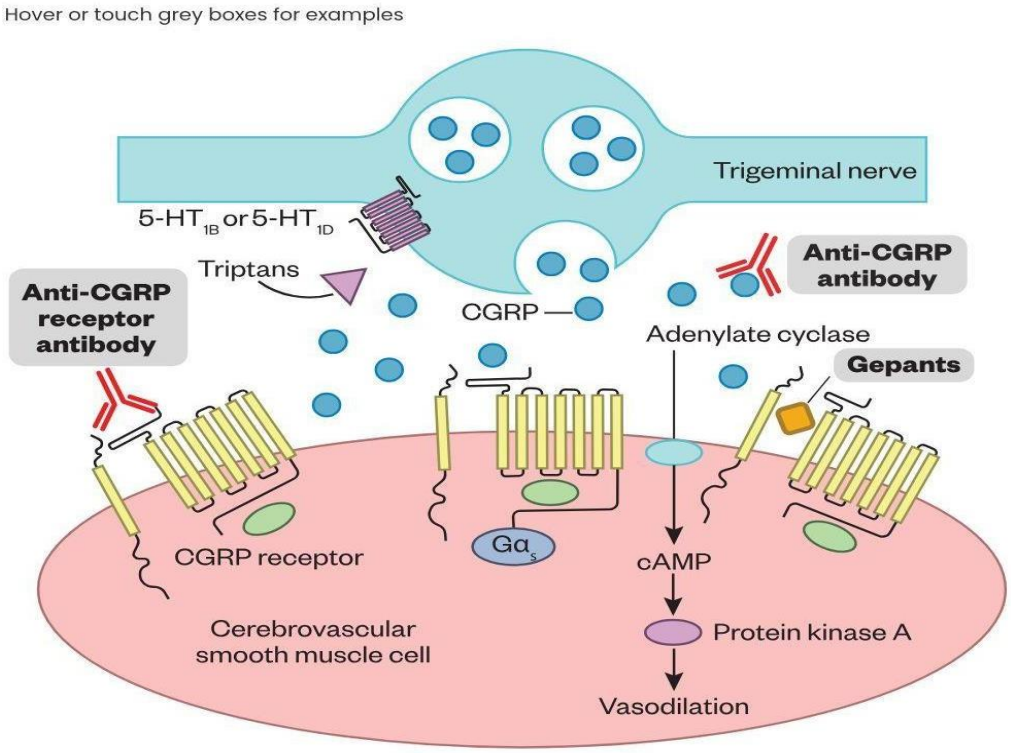

Figure 7: Role of Calcitonin Gene-Related Peptide (CGRP).

CGRP production during migraine attacks induces vasodilation, inflammation, and the transmission of nociceptive signals. The development of CGRP antagonists and monoclonal antibodies has transformed modern migraine management, providing more tailored therapeutic choices with better efficacy and safety profiles.[56]

3.9 Pathophysiological mechanisms underlying migraine symptoms

Migraine's multifactorial clinical picture can be described by the complex combination of neuronal hyperexcitability, inflammation, neurotransmitter imbalance, and vascular dysfunction. Photophobia and phonophobia are caused by abnormal sensory processing, while activation of brainstem autonomic centers produces nausea and vomiting.[57]

The understanding of migraine pathophysiology has tremendously aided the development of new pharmacological treatments that target particular molecular pathways implicated in migraine production.

4. MIGRAINE ETIOLOGY AND RISK FACTORS

A complex neurological condition, migraines are influenced by environmental, nutritional, hormonal, genetic, and psychological variables. Although the exact cause of migraine is unknown, current research indicates that it results from aberrant neuronal excitability that stimulates inflammatory mediators and trigeminovascular pathways.[58] Many endogenous and external triggers play a role in the onset and course of migraine attacks in vulnerable individuals.

4.1 Genetics

A significant contributing factor to migraine vulnerability is genetic predisposition. According to epidemiological research, individuals with a favorable family history are far more likely than the general population to get migraines.[59]

Twin studies have provided additional evidence that migraine, particularly migraine with aura, has a genetic basis.

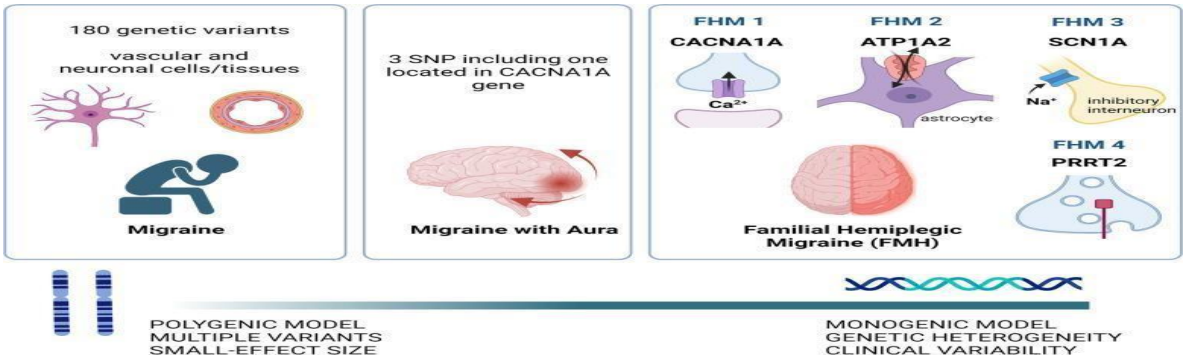

Figure 8: MIGRAINE ETIOLOGY AND RISK FACTORS.

Numerous genes that control ion transport, neurotransmitter release, and neural excitability have been connected to the pathophysiology of migraines. Familial hemiplegic migraine is closely linked to mutations in the genes CACNA1A, ATP1A2, and SCN1A.[60] Migraine susceptibility may also be influenced by genetic changes in the serotoninergic and dopaminergic pathways.

4.2 The role of hormones

One of the most significant risk factors for migraine, particularly in women, is believed to be changes in hormones. Variations in estrogen levels during menstruation, pregnancy, menopause, and oral contraceptive usage have a significant impact on the incidence and intensity of migraines.[61]

A sharp drop in estrogen levels during the late luteal phase of the menstrual cycle is frequently the cause of menstrual migraines. Some women's migraine symptoms have been reported to improve during pregnancy, but others may experience worsening episodes as a result of hormonal instability.[62]

4.3 Environmental causes

For those who are predisposed, environmental variables frequently trigger migraine attacks. Migraine pathways can be triggered by bright lights, loud noises, strong odors, weather variations, high altitudes, and exposure to heat or cold.[63]

Seasonal variations and variations in barometric pressure have also been linked to migraines. Long screen time and irregular sleep patterns are examples of contemporary environmental factors that are becoming more widely acknowledged as migraine causes.[64]

4.4 Nutritional Elements

Migraine attacks are known to be triggered by a variety of dietary variables. Chocolate, cheese, processed meat, coffee, alcohol, monosodium glutamate (MSG), and artificial sweeteners are common food triggers.[65]

Fasting and skipping meals can trigger migraine pathways and cause hypoglycemia, which can lead to headache attacks. Another frequent trigger that is linked to an increase in migraine frequency and intensity is dehydration.[66]

4.5 Emotional and Psychological Elements

Psychological stress is the most common cause of migraines. The onset of migraines has been linked to emotional disorders such anxiety, despair, rage, and mental exhaustion.[67]

Stress-induced activation of the autonomic nervous system and the hypothalamic-pituitary- adrenal axis may encourage the release of neurotransmitters and inflammatory mediators involved in migraine etiology.[68] Migraine incidence is also strongly associated with sleep problems, such as insomnia and excessive sleep.

4.6 Age and Gender

Although it affects people of all ages, migraines are more common in women than in men. Hormonal factors play a major role in the higher prevalence in women.[69] Migraines typically start in adolescence and are most prevalent between the ages of 25 and 55.

Children's migraine symptoms can differ from those of adults and frequently include vomiting, abdominal pain, and bilateral headaches.[70]

4.7 Obesity and lifestyle variables

One significant risk factor for the development of chronic migraine is obesity. Both the frequency and severity of migraine attacks are linked to a greater body mass index.[71]

Migraine symptoms can be exacerbated by a sedentary lifestyle, inactivity, smoking, excessive coffee consumption, and alcohol consumption. Thus, it is believed that regular exercise and good lifestyle modifications can help avoid migraines.[72]

4.8 Excessive Medication Use

Medication-overuse headache, which can lead to chronic migraine, is linked to frequent use of analgesics and antimigraine medications.[73] Over time, repeated use of opioids, triptans, nonsteroidal anti-inflammatory medications (NSAIDs), and combination analgesics may alter how pain is processed and decrease the efficacy of treatment.

4.9 Co-occurring disorders

Numerous comorbid conditions, such as depression, anxiety, epilepsy, hypertension, obesity, cardiovascular illnesses, and sleep difficulties, are frequently linked to migraine.[74] These illnesses may make migraine treatment more difficult and have a detrimental effect on the **patient's quality of life.**

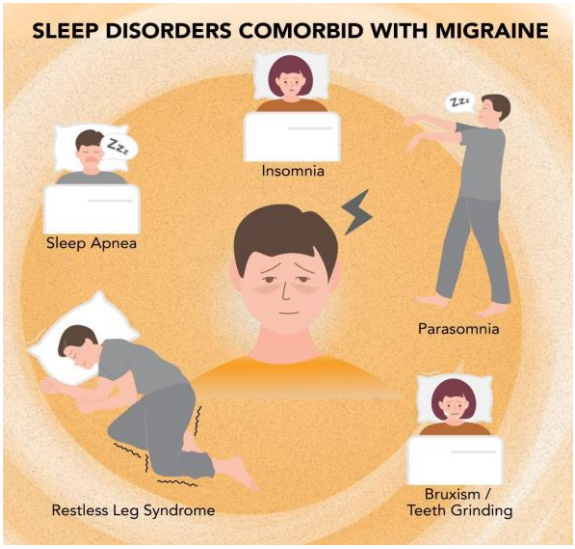

Figure 9: Co-occurring disorders.

Additionally, recent research points to a link between migraine with aura and a higher risk of ischemic stroke, particularly in young women and smokers.[75]

4.10 Triggers' Clinical Significance

Identification of migraine triggers and risk factors is necessary for effective illness management and prevention. Maintaining a headache journal, changing one's lifestyle, reducing stress, controlling one's nutrition, and practicing good sleep hygiene can all greatly lower migraine frequency and enhance treatment response.[76]

The development of individualized treatment plans and preventative measures in clinical practice has been substantially aided by the thorough understanding of migraine causation.

5. MIGRAINE: CLINICAL FEATURES AND DIAGNOSIS

Migraine is characterized by recurrent episodes of headache in association with various neurological, gastrointestinal and autonomic symptoms. The clinical presentation may vary greatly between individuals depending upon migraine subtype, severity, duration and associated comorbidities.[77] Accurate diagnosis of migraine is important as it helps to differentiate migraine from other primary and secondary headache disorders and to provide appropriate therapeutic management.

5.1 Clinical Features of Migraine

Migraine attacks generally happen in distinct phases including prodrome, aura, headache phase and postdrome. The patient does not go through every stage in every attack but it is important to know these stages for early recognition and treatment.[78]

5.1.1 Prodromal Phase

The prodromal phase may occur several hours or even a day or two before the headache starts. This stage includes subtle neurological and systemic symptoms such as mood changes, irritability, fatigue, food cravings, neck stiffness, excessive yawning, difficulty concentrating and increased urination.[79]

These symptoms are believed to be due to hypothalamic activation and altered neurotransmitter activity prior to the onset of migraine.

5.1.2 Phase Aura

About one-third of migraine sufferers experience aura symptoms before the headache. An aura is defined as focal, reversible, neurologic disturbances that develop gradually and usually last less than 60 minutes.[80]

The most common manifestation is visual aura that includes flashing lights, scintillating scotomas, zigzag lines, blurred vision and temporary visual field defects. Sensory aura includes tingling, numbness, and paresthesia, but speech disturbances and motor weakness are less common.[81]

5.1.3 Headache phase

The headache phase is the most disabling part of the migraine. Migraine headaches are usually unilateral, throbbing, of moderate to severe intensity, and exacerbated by routine physical activity.[82] If untreated, the duration of headache is usually 4 to 72 hours.

Associated symptoms are commonly:

- Nausea & vomiting
- Photophobia
- Fear of sound Phonophobia
- Osmophobia
- Dizziness
- Impaired vision

Attacks are often accompanied by increased sensitivity to sensory stimuli, and many patients prefer to rest in dark, quiet surroundings.[83]

5.1.4 Postdromal Stage

Postdromal symptoms are common after the resolution of the headache and include fatigue, weakness, difficulty concentrating, mood changes, dizziness and lingering head pain.[84] This phase can last from several hours to one day after the headache is gone.

5.2 Diagnosis of Migraine

The diagnosis of migraine is clinical and based on criteria established by the International Classification of Headache Disorders (ICHD-3).[85] There is no specific laboratory test for migraine and so a detailed history and a thorough neurological examination of the patient is essential.

Migraine without aura: Criteria for diagnosis

Migraine without aura is diagnosed according to ICHD-3 if the patient has had at least 5 attacks fulfilling the following criteria:

- Headache lasting 4 to 72 hours
- Unilateral situation

- Pulsating quality factor
- Intensity of moderate to severe
- Effort exacerbation
- Nausea, vomiting, photophobia, or phonophobia[85]
- Diagnostic Criteria for Migraine With Aura

Migraine with aura is diagnosed if at least two attacks are characterized by reversible aura symptoms, such as visual, sensory, speech or motor disturbances, that develop gradually over 5– 20 minutes and last less than 60 minutes.[86]

5.3 Physical and Neurological Examination

In patients with migraine the physical examination is usually normal between attacks. Neurological examination is mainly done to exclude secondary causes of headache such as brain tumors, meningitis, stroke, or intracranial hemorrhage.[87]

- Neurological abnormalities including persistent weakness, altered consciousness, seizures, papilledema or focal deficits, require immediate further investigation.

5.4 Differential diagnoses

Several neurological and systemic disorders may simulate migraine symptoms. Important differential diagnoses are:

- Tension headache
- Cluster headache
- Sinusitis
- Temporal arteritis (arteritis, temporal)
- Intracranial neoplasms
- meningitis
- Headache and hypertension
- Subarachnoid haemorrhage[88]

Careful history and assessment of red flags can differentiate migraine from serious secondary headaches.

5.5 Red Flag Symptoms in Migraine

Some clinical features, known as “red flag signs”, may suggest possible secondary headache disorders and require urgent evaluation. *These include*.

- Thunderclap headache (sudden onset severe headache)
- Patient over 50 years old with new headache
- Neck stiffness or fever
- Headache, progressive deterioration
- Neurological deficits
- Headache with cancer or immunosuppression
- Altered mental status[89]

Awareness of such symptoms is important to avoid a delayed diagnosis of life-threatening conditions.

5.6 Laboratory and Imaging Tests

Routine laboratory tests are generally not indicated for uncomplicated migraine. However, neuroimaging techniques such as CT and MRI may be indicated in atypical presentations or in cases of suspected secondary pathology.[90]

Electroencephalography (EEG) may be used in some patients presenting with seizure-like symptoms. Lumbar puncture is indicated if there is suspicion of meningitis or subarachnoid hemorrhage.

5.7 Evaluation of migraine severity and disability

Various standardized tools for assessing the severity and disability related to migraine exist. Commonly used scales are:

- Migraine Disability Assessment (MIDAS) Score
- Headache Impact Test (HIT-6) Scale
- Visual Analogue Scale (VAS)[91]

They enable clinicians to assess the burden of disease, monitor response to treatment and improve personalized patient care.

5.8 The Importance of Early Diagnosis

Early diagnosis and appropriate management of migraine reduces the disease burden, improves the quality of life and prevents progression to chronic migraine.[92] Raising awareness of the symptoms and triggers of migraine also contributes to better patient outcomes and adherence to therapy.

6. CURRENT MIGRAINE MANAGEMENT STRATEGIES

A greater understanding of migraine biology and advancements in both pharmaceutical and non- pharmacological therapy have led to significant changes in migraine management during the past few decades. In addition to relieving acute headache attacks, contemporary migraine management aims to reduce attacks, enhance quality of life, lessen disability, and avoid the onset of chronic migraine.[93]

Acute symptomatic treatment, preventive medication, lifestyle changes, behavioral interventions, neuromodulation techniques, and particular biological therapies such monoclonal antibodies and calcitonin gene-related peptide (CGRP) antagonists are among the available therapeutic alternatives.[94]

6.1 Migraine Management Goals

The primary objectives of migraine treatment are:

- Quick alleviation of headaches and related problems
- Resume your regular daily activities
- reduction in the number and intensity of attacks
- Preventing medication-related headaches
- Enhancing the quality of life for patients It is possible to lessen drug side effects.[95]

The frequency, intensity, accompanying symptoms, co-occurring disorders, and response to treatment should all be taken into consideration when managing a patient.

6.2 Acute (Abortive) Migraine Treatment

The headache and associated symptoms of a migraine attack are treated with acute treatment. A better therapeutic success is linked to early treatment in the early stages of migraine.[96]

6.2.1 NSAIDs, or non-steroidal anti-inflammatory drugs

Initially, mild to moderate migraine attacks are treated with NSAIDs. These medications reduce prostaglandin-mediated inflammation and discomfort by inhibiting cyclooxygenase enzymes.[97]

Typical NSAIDs consist of:

- Naproxen with Ibuprofen
- Diclofenac sodium
- Aspirin ____Ketorolac

NSAIDs work well to lessen the severity of headaches and their accompanying symptoms. However, long-term use might result in medication-overuse headaches, renal toxicity, and gastrointestinal discomfort.[98]

6.2.2 Triptans

The best medications for treating moderate to severe migraine attacks are thought to be triptans, which are selective serotonin 5-HT1B/1D receptor agonists.[99] They prevent the transmission of trigeminal pain, suppress the production of neuropeptides, and cause cranial vasoconstriction.

Typical triptans include:

- Imitrex, or sumatriptan
- Zolmitriptan Rizatriptan
- Naratriptan Eletriptan

Triptans provide quick relief from headaches and are particularly helpful when nausea, photophobia, and phonophobia are present.[100]

6.2.3 Antiemetic Drugs

Antiemetics are frequently used to treat severe nausea and vomiting in migraineurs. These substances promote stomach emptying and enhance oral drug absorption.[101]

Antiemetics that are frequently recommended include

- Metoclopramide (10)
- Domperidone
- Compazine, or prochlorperazine
- Chlorpromazine

6.2.4 Alkaloids of Ergot

Due to their vasoconstrictive properties, ergotamine and dihydroergotamine were once used to treat migraines. However, because of side effects and the availability of safer substitutes like triptans, their use has decreased.[102]

6.3 Preventive (Prophylactic) Therapy

Patients who experience frequent, severe, protracted, or incapacitating migraine attacks may consider migraine preventative treatment. Reducing the frequency, duration, and intensity of attacks is the aim.[103].

6.3.1 Beta-adrenergic inhibitors

The most popular migraine preventive medication is beta blockers. These alter vascular tone and reduce neuronal excitability.[104]

Typical agents include

Timolol, Metoprolol, and Propranolol

They are especially helpful for people who have anxiety or high blood pressure.

6.3.2 Anticonvulsants

Antiepileptic medications lessen migraine-related cortical hyperexcitability and normalize neuronal activity.[105]

Typical agents are as follows:

- Topiramate
- Valproate
- Gabapentin

One of the best medications for prophylaxis in the prevention of persistent migraines is topiramate.

6.3.3 Depression medications

Serotonin-norepinephrine reuptake inhibitors and tricyclic antidepressants are helpful in preventing migraines,[106] particularly in patients who already have depression or sleep difficulties.

Drugs that are frequently used include:

- Amitryptiline
- Nortriptyline with Venlafaxine

6.3.4 Blockers of Calcium Channels

Calcium channel blockers reduce vascular instability and neural excitability. For the prevention of migraines, verapamil and flunarizine are commonly used.[107]

6.4 CGRP-focused treatments

CGRP is a key mediator in the pathophysiology of migraines, according to recent developments in migraine research. Because of this discovery, CGRP antagonists and monoclonal antibodies particularly designed to prevent migraines have been developed.[108]

The CGRP monoclonal antibodies that are currently authorized include:

- Erenumab
- Eptinezumab, Galcanezumab, and Fremanezumab

These medications have comparatively good safety profiles and have been demonstrated to be beneficial in lowering monthly migraine days.[109]

6.5 Neuromodulation Treatment

Neuromodulation techniques have shown promise as non-pharmacological migraine therapies. These methods use electrical or magnetic stimulation to alter neural activity.[110]

Here are a few instances:

- TMS, or transcranial magnetic stimulation
- stimulation of the vagus nerve
- Stimulation of the occipital nerve
- External trigeminal nerve stimulation

Patients who do not gain sufficiently from traditional therapy can benefit most from neuromodulation.

6.6 Modifications to Behavior and Lifestyle

Changing one's lifestyle is essential for managing and preventing migraines. The frequency of migraine attacks can be decreased by identifying and avoiding migraine triggers.[111]

The following are suggestions for an important lifestyle:

1. A consistent sleep schedule
2. Adequate hydration
3. Controlling tension
4. Regular exercise
5. A balanced diet
6. Reducing alcohol and caffeine intake

Behavioral therapies that have also shown promise in managing migraines include yoga, biofeedback, relaxation training, and cognitive behavioral therapy (CBT).[112]

6.7 A novel approach

For the treatment of migraine, several therapeutic strategies are being researched. Gepants (small molecule CGRP receptor antagonists) and ditans (5-HT1F receptor agonists) are two more recent groups of migraine drugs that have better tolerance and less cardiovascular damage.[113]

Future migraine treatments are anticipated to be further revolutionized by gene-targeted therapeutics, precision medicine, and customized medication.

6.8 Issues with Migraine Management

The therapy of migraines is still hampered by a number of problems, including underdiagnosis, poor treatment compliance, medication misuse, adverse drug responses, and the high cost of healthcare.[114]

To enhance migraine outcomes, interdisciplinary approaches, tailored therapy, early diagnosis, and increased awareness are all necessary.

7. CONCLUSION

Migraine is a very common and incapacitating neurological condition that has a substantial impact on people's physical, mental, social, and financial well-being all over the world. Recurrent episodes of moderate to severe headaches, together with a variety of neurological and autonomic symptoms like nausea, vomiting, photophobia, phonophobia, and sensory abnormalities, are the hallmark of the illness. Trigeminovascular activation, cortical spreading depression, neurogenic inflammation, neurotransmitter imbalance, and calcitonin gene-related peptide (CGRP) pathways have all been shown to play significant roles in the development and progression of migraine.[115]

More precise diagnosis and customized treatment strategies have been made possible by the division of migraine into several clinical subtypes, including migraine with aura, migraine without aura, chronic migraine, vestibular migraine, and hemiplegic migraine. Comprehensive migraine management solutions have benefited from the identification of genetic predisposition, hormonal impacts, environmental triggers, dietary habits, psychological stress, and lifestyle factors.[116]

The International Classification of Headache Disorders' (ICHD-3) established diagnostic criteria and a thorough patient history continue to be the mainstays of clinical migraine diagnosis. To distinguish migraine from severe secondary headache diseases and stop the disease from getting worse, early diagnosis and awareness of warning signals are crucial.[117]

A multidisciplinary, patient-centered strategy incorporating both pharmaceutical and non- pharmacological therapy is emphasized in current migraine care strategies. NSAIDs, triptans, antiemetics, and ergot derivatives are examples of conventional acute therapies that are still crucial for symptomatic relief. Beta-blockers, antiepileptic medications, antidepressants, and calcium channel blockers are examples of preventive treatments that have demonstrated significant effectiveness in lowering migraine frequency and intensity.[118]

The development of CGRP antagonists and monoclonal antibodies, in particular, has transformed migraine prevention and offered highly focused treatment options with better safety and efficacy profiles. Furthermore, behavioral therapies like cognitive behavioral therapy, stress management, yoga, and lifestyle changes, as well as neuromodulation techniques, have become important supplemental methods for long-term migraine control.[119]

In many groups, migraine is still underdiagnosed and undertreated despite significant treatment advancements. Optimal illness management is nevertheless hampered by issues such pharmaceutical overuse, poor treatment adherence, healthcare accessibility, and socioeconomic load. Therefore, improving clinical outcomes and quality of life for migraineurs requires more public awareness, early clinical intervention, patient education, and continued research into new treatment targets.[120]

In summary, migraine is a complicated neurovascular condition that necessitates a thorough comprehension of its etiology, clinical symptoms, diagnostic methods, and contemporary treatment techniques. Future migraine treatment options should be safer and more effective thanks to ongoing developments in pharmacology, neuroscience, and personalized medicine.

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