# Migraine Across the Ages: A Comprehensive Review of Pathophysiology, Diagnosis, and Management Strategies

**Dr A Geethalakshmi[1*], Dr Mamatha GC[1], Himadri Priya Gogoi[2], Rahul Prasad[3], Rohan Debnath[4], Salunkhe Samruddhi Santosh[5], Satyam Kumar Pandey[6], Sharma Sameer Rajkumar[7]**

[1*]Professor & HOD, Department of Pharmaceutics, Harsha College of Pharmacy, Nelamangala, Bangalore
[1] Principal, Harsha College of Pharmacy, Nelamangala, Bangalore
[2]Assistant Professor, Department of Pharmaceutics, Harsha College of Pharmacy, Nelamangala, Bangalore
[3,4,5,6,7] Department of Pharmaceutics, Harsha College of Pharmacy, Nelamangala, Bangalore

**Corresponding Author***
Dr. A Geethalakshmi
Professor & HOD
Dept. of Pharmaceutics Harsha College of Pharmacy Nelamangala, Bangalore
Mail ID: geelak74@gmail.com
Mob No. 9901418806

**ABSTRACT:**

Migraine is a widespread and disabling neurological condition that poses a substantial burden on global health, particularly among people aged 15 to 39. It is defined by repeated episodes of pulsating or throbbing head pain, often unilateral, and commonly accompanied by nausea, light and sound sensitivity, and in some cases, visual or sensory auras. The underlying pathophysiology is complex, involving disruptions in the trigeminovascular system and multiple brainstem circuits. This review offers an in-depth analysis of migraine classification, symptoms, mechanisms, diagnostic methods, and emerging treatment approaches. Migraine is generally categorized into two main types: with aura and without aura, each presenting distinct clinical features. Accurate diagnosis is supported by validated tools like the ID-Migraine™ screener, Migraine Disability Assessment (MIDAS), and the Visual Aura Rating Scale (VARS).

The review also highlights advancements in drug delivery systems designed to improve patient adherence and therapeutic outcomes. These include sublingual tablets, nasal sprays, buccal films, and inhalable particles. Additionally, the shift toward personalized medicine—leveraging monoclonal antibodies and genomic profiling—offers potential for more effective, individualized migraine management.

**Keywords:** Migraine, Aura, Triptans, Neuromodulation, Personalized medicine.

## 1. INTRODUCTION

A migraine is a neurological condition characterized by recurring, intense headaches, typically on one side of the head. It is often accompanied by symptoms such as nausea, vomiting, and heightened sensitivity to light, sound, or smells. Some individuals experience visual disturbances known as auras before the headache begins. Migraines can last from a few hours to several days and impact daily functioning.

Migraine is the third most prevalent and seventh leading cause of disability worldwide[1]. It is a widespread condition globally, associated with significant health challenges and economic costs. The direct financial burden of migraines correlates with the intensity of pain and disability, increasing sharply with the use of prescription drugs. However, the indirect costs especially those linked to work-related disability are even greater. Individuals with migraines frequently miss work (absenteeism) or experience reduced productivity while at work (presenteeism).

A chronic migraine sufferer experiences headaches at least 15 days a month for at least three months, with at least eight of those migraines meeting the migraine headache criteria[2].

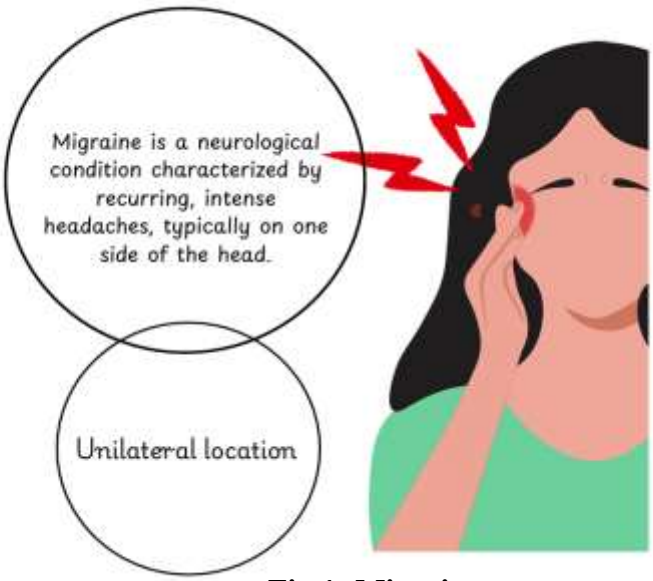



**Fig.1- Migraine**

Research indicates that effectively treating individuals with severe migraines could substantially reduce the overall economic impact. Migraine management includes both preventive and acute treatments, using a combination of medications and lifestyle modifications. By closely monitoring headache patterns and lifestyle influences, around 50–75% of people with migraines can pinpoint specific triggers. Recognizing and avoiding these triggers is a key part of treatment aimed at reducing migraine frequency. Common triggers include certain foods and drinks, emotional stress or its aftermath, and hormonal changes like those during menstruation or pregnancy[3].

### 1.1. Prevalence

Between 1990 and 2021, migraine prevalence among individuals aged 15 to 39 raise dramatically on a global scale. There were 425.6 million probable migraine cases reported in 1990; by 2021, that figure is predicted to increase to 593.8 million. Over the past 30 years, the prevalence of migraine in the general population has remained relatively stable, ranging from 11.7% to 14.7% overall, 17.1% to 19.2% in women, and 5.6% to 7.2% in males, according to the reviewed study. The prevalence of Chronic Migraine is 0.8% in adolescents and 0.91% in adults (1.3% in women and 0.5% in males)[4].

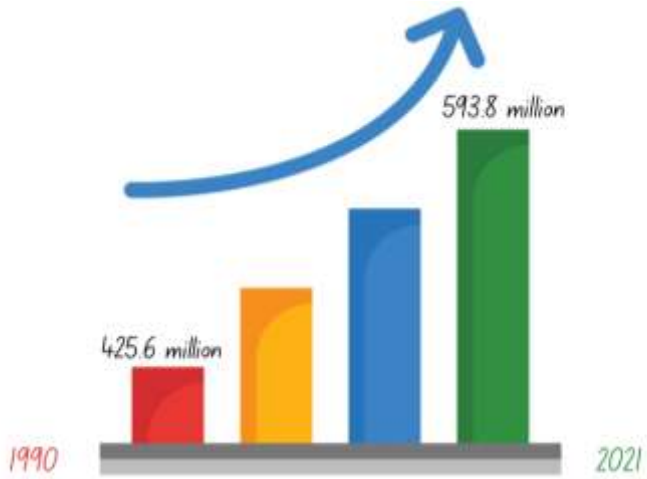



**Fig. 2-Prevalence**

### 1.2. Types of migraine


There are two principal forms of migraine, the first of which is migraine with aura, formerly known as classical migraine, in which a migraine episode is preceded by sensory and other neurological symptoms[5].

### 1.2.1 Migraine without aura

Recurrent headache bouts lasting four to seventy-two hours are the hallmark of migraine without aura. A unilateral location, pulsing nature, moderate to severe pain intensity, and intensification by ordinary physical activity are typical characteristics of an attack. Bilateral pain, however, is not unusual; according to population-based research, approximately 40% of migraineurs experience bilateral pain during attacks[5].

### 1.2.2. Migraine with aura

Aura is experienced by about one-third of migraineurs, either during all or some of their attacks. Transient localised neurological symptoms known as aura typically occur prior to, but occasionally concurrent with, the headache phase of a migraine attack. Aura typically appears visually as fortification spectra in over 90% of afflicted people[6].

## 2. PATHOPHYSIOLOGY OF MIGRAINE

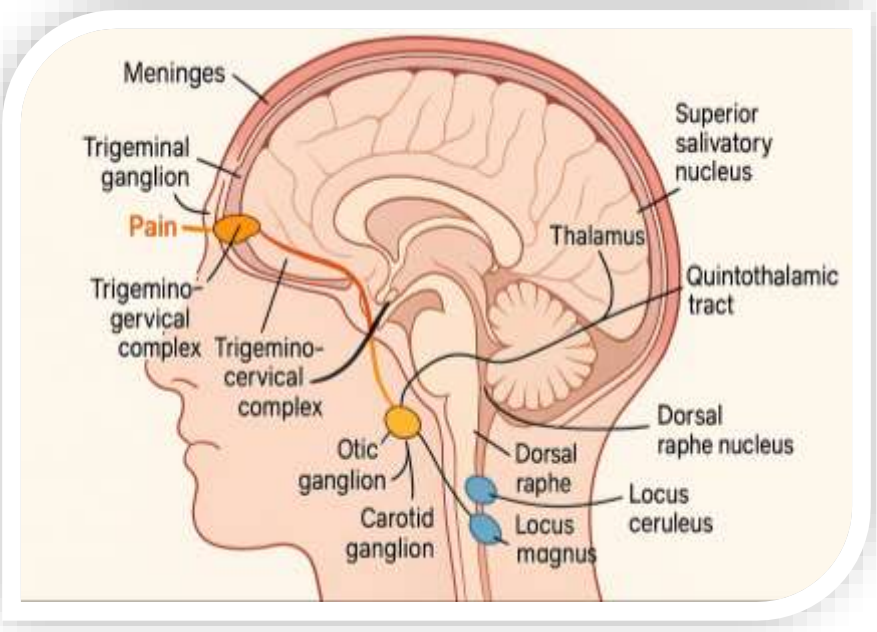



**Fig.3. Pathophysiology**

Migraine involves primarily, alteration of pathways in the brain stem, which are involved in regulation of sensory signals. The main routes of pain transmission include involvement of the meningeal blood vessels linked with the trigeminal ganglion and providing connections to the second order neurons of the trigeminocervical complex. These neurons, in turn, pass through the quintothalamic tract and, after crossing in the brain stem, form synapses with neurons in the thalamus. A reflex arc exists between neurons of the superior salivatory nucleus situated in pons which sends cranial parasympathetic out flow through pterygopalatine, otic and carotid ganglia. This trigeminal–autonomic reflex in present in normal person and is particularly elevated in patients with trigeminal autonomic cephalgias like cluster headache and paroxysmal hemicrainia, and is possibly implicated in migraine. Brain imaging studies have shown that the

trigeminovascular nociceptive input is modulated by important nuclei that include the dorsal raphe nucleus, locus ceruleus, and nucleus raphe magnus[7].

## 3. SIGNS AND SYMPTOMS OF MIGRAINE

### 3.1 Sign of migraine

#### 3.1.1 Throbbing or Pulsating Headache

- Typically, on one side of the head (unilateral), but can occur on both sides.

#### 3.1.2 Aura (in some patients)

- Visual disturbances: flashes of light, zigzag lines, or blind spots.
- Sensory symptoms: tingling in arms or face.
- Occurs in about 25% of migraine sufferers.

#### 3.1.3 Sensitivity to Light (Photophobia) and Sound (Phonophobia)

- Many people with migraines need a dark, quiet room during an attack.

#### 3.1.4 Nausea and/or Vomiting

- Often accompanies the headache phase.

#### 3.1.5 Neck Stiffness or Pain Before Headache

A common early warning sign (prodrome phase) [8,9,10].

### 3.2 Symptoms of Migraine

**3.2.1 Headache:** Typically, unilateral (one side of the head), throbbing or pulsating pain that worsens with physical activity. The pain can last between 4 to 72 hours if untreated**.**

**3.2.2 Nausea and Vomiting:** Often accompanies the headache phase, with nausea occurring in about 80% of cases and vomiting in 50%

**3.2.3 Sensitivity to Light (Photophobia) and Sound (Phonophobia)**: Individuals may seek relief in dark, quiet environments.

**3.2.4 Aura:** In approximately 25% of cases, individuals experience neurological symptoms before or during the headache phase, such as:

a. Visual disturbances like flashing lights, zigzag lines, or blind spots.
b. Sensory changes, including tingling or numbness, typically on one side of the body.

c. Speech or language difficulties.
d. Muscle weakness.

### 3.2.5 Phases of a Migraine Attack

**a. Prodrome (Pre-headache phase)**:
- Occurs 24 to 48 hours before the headache.
- Symptoms may include mood changes, neck stiffness, increased yawning, fatigue, and food cravings**.**

**b. Aura (if present):**
- Neurological symptoms that precede or accompany the headache.
- Typically lasts less than 60 minutes and is fully reversible

**c. Headache (Attack phase):**
- Severe, throbbing pain often on one side of the head.
- Accompanied by nausea, vomiting, and sensitivity to light and sound.

**d. Postdrome (post-headache phase):**
- Occurs after the headache subsides.
- Symptoms may include fatigue, difficulty concentrating and mood changes [10,11].

## 4. DIAGNOSIS

### 4.1 Diagnosis criteria:

- **Migraine without Aura**

The criteria listed below must be fulfilled in order to diagnose a migraine without aura:

1. A minimum of five attacks that meet the requirement 2 & 4
2. 4–72-hour headache episodes that are either untreated or do not respond to treatment.
3. At least two of the following must be present in Headache characteristics: One-sidedness, pulsating sensation, moderate to severe intensity, or aversion to regular physical activities (such as walking or climbing stairs)
4. At least one of the following symptoms occurs with a headache: nausea and/or vomiting Phono phobia and photophobia
5. Could not be explained by another ICHD-3 diagnosis.

- **Migraine with Aura**

The following factors apply to migraine with aura:

1. A minimum of two assaults that meet criteria 2 and 3.
2. Aura symptoms that are completely reversible and suggest brainstem and/or localised cerebral cortical dysfunction.
3. At least three of the following six qualities:

a. It takes at least five minutes for at least one aura symptom to spread.
b. Each aura symptom manifests in turn.
c. Aura symptoms vary in duration from five to sixty minutes.
d. At least one unilateral aura symptom.
e. Positive aura symptoms include at least one visual or sensory abnormality.
f. Either within 60 minutes of the aura or concurrently, a headache develops.
4. No alternative ICHD-3 diagnosis might better explain [12-15].

**4.2 Diagnostic instruments:**

**4.2.1 ID-Migraine™:**

A brief, self-administered device comprising three questions surveying incapacity, queasiness, and photophobia. Approved in essential care settings, it demonstrates[16].
Sensitivity: ~81%
Specificity: ~75%
Positive Prescient Esteem: ~93%
This instrument helps in distinguishing patients who may advantage from advance symptomatic assessment[17].

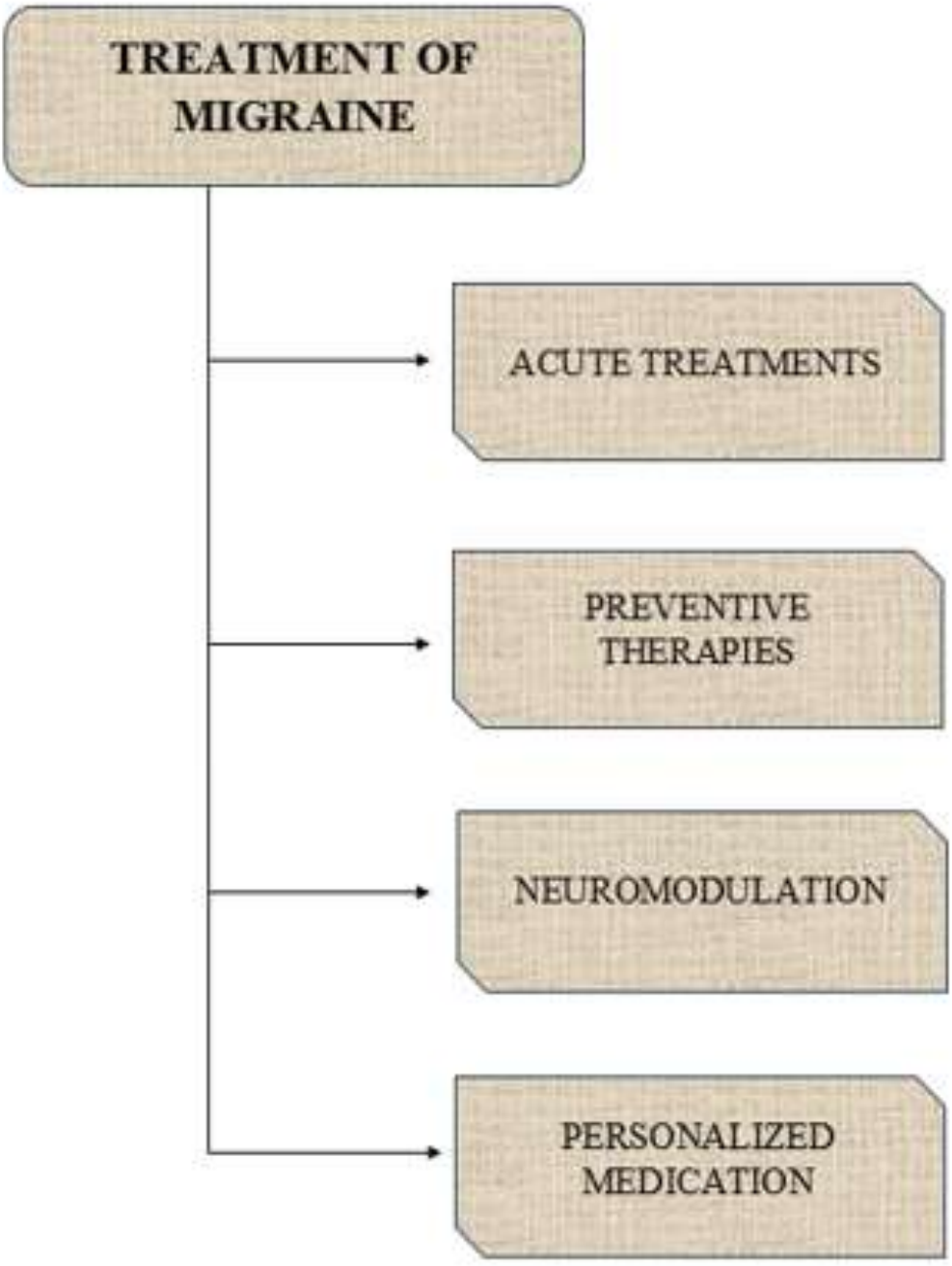
**4.2.2 Migraine Disability Assessment Test (MIDAS):**

Over a three-month period, the Migraine Disability Assessment Test (MIDAS) evaluates how migraines affect day-to-day functioning. Disability is ranked from Grade I (little or no disability) to Grade IV (severe)[18].

**4.2.3 Visual Aura Rating Scale (VARS):**

The purpose of the Visual Aura Rating Scale (VARS) is to diagnose migraine with aura by looking at visual symptoms.
A score of ≥5 indicates the presence of migraine aura[19].

## 5. TREATMENT OF MIGRAINE:




### 5.1. Acute Treatments:

**NSAIDs:**

NSAIDs includes Ibuprofen (Advil®, Motrin®) and naproxen sodium (Aleve®, Anaprox®), flurbiprofen, diclofenac potassium (Cataflam®, diclofenac sodium, Voltaren®, Zipsor®), nabumetone, mefenamic acid, and other medications. When treating acute migraine attacks, NSAIDs are the recommended first-line medication, particularly in emergency rooms.

According to the American Headache Society's guidelines, ibuprofen, an NSAID, is an effective painkiller that can be used to treat acute migraine[20].

**Triptans:**

Triptans, which are commonly used to treat migraines, mainly work by activating serotonin (5-HT1) receptors. Examples of these drugs include sumatriptan, zolmitriptan, rizatriptan, naratriptan, eletriptan, almotriptan, and frovatriptan. The mechanism of action triggers a number of physiological reactions that are essential for reducing migraine symptoms. Triptans have a strong affinity for and selective binding to particular subtypes of serotonin receptors when administered. Interestingly, the 5-HT1B and 5-HT1D subtypes of these receptors are primarily found in the cerebral blood vessels. Previously dilated cerebral blood vessels narrow as a result of vasoconstriction brought on by stimulation of these receptors. In order to lessen the severe headache pain that comes with migraine attacks, this vasoconstrictive activity is essential. Additionally, triptans play a key role in reducing neurogenic inflammation by inhibiting calcitonin gene-related peptide (CGRP) and other pro-inflammatory neuropeptides. This peptide plays a crucial role in the brain's ability to transmit pain signals[21].

**CGRP antagonist:**

The use of CGRPs such as Rimegepant (Nurtec ODT), Ubrogepant (Ubrelvy), Atogepant (Qulipta), and Zavegepant (Zavzpret) in migraine pathophysiology is supported by evidence that CGRP concentrations increase in the cerebral circulation during true migraine attacks. CGRP levels in saliva have been found to be higher in acute migraine, and they correlate with pain and triptan-induced attack termination. The peripheral projections of the trigeminal system are implicated in neurogenic vasodilation, sensitization, and inflammation, whereas central release can cause hyperalgesia. Trigeminal nerve activity causes antidromic release of CGRP[22].

**Ditans (5-HT1F receptor agonists):**

The serotoninergic receptor 5HT1B-1D is active, it causes vasoconstriction, neurogenic inflammation blocking, and a reduction in cephalalgic symptoms. These effects pose a concern to patients with cardiovascular and/or cerebrovascular illnesses. "Ditans" are novel molecules that were just developed. These compounds are selective agonists for the 5-HT1F receptor and have minimal affinity for the 5-HT1B-1D receptor subtypes, resulting in a better tolerability profile than triptans and less involvement in vasoconstrictive mechanisms[23].

**5.2. Preventive Therapies:**

**Pharmacological:**

**a. Beta-blockers**

It was by accident that beta-blockers were found to be effective in preventing migraines when individuals with migraines who were taking them for heart problems or high blood pressure noticed a notable decrease in the frequency of their attacks. Beta-blockers have undergone the

most research and are the most often used medication for the prevention of migraines. Propranolol and metoprolol are two of the beta-blockers that have been well studied in the prevention of migraines and are widely acknowledged to be beneficial. Although these two medications have been used in a variety of trials at varying dosages, their meta-analysis indicates that 200 mg/day of metoprolol and 160 mg/day of propranolol can be regarded as useful preventative dosages.

Since non-selective medications like propranolol, moderately β1-selective drugs like metoprolol, and highly β1-selective drugs like bisoprolol are all effective prophylactics, β1-adrenoceptor selectivity does not seem to be a major factor in determining prophylactic efficacy. Therefore, it doesn't seem that concurrent blocking of β2-adrenoceptors is necessary for migraine prevention to be effective.

Propranolol and pindolol are two beta-blockers that have a strong affinity for 5-HT receptors, including 5-HT1A, 5-HT1B/D, and 5-HT2 receptors, which are either candidate for acute migraine treatment[24].

**b. Anti-epileptic Drugs**

Anti-epileptic medications are used to treat migraines in advance. Double-blind, placebo-controlled trials have demonstrated the effectiveness of valproic acid and its sodium counterpart, divalproex, in avoiding migraines. More thorough research is required to validate the effectiveness of gabapentin and lamotrigine, which have also been suggested for the prevention of migraines. Anti-epileptic medications work primarily by blocking the sodium channel, which causes a depolarization and stops the high, numerous action potentials that are normally triggered by convulsive seizures.

Sodium valproate and other anticonvulsive medications have been used more frequently recently with positive outcomes in the prevention of migraines. By influencing the GABA system or membrane ion channels, these medications lessen the firing response of neurons. Through an unclear mechanism, gabapentin stimulates GABA release. Gabapentin may be helpful in treating chronic migraines because it suppresses the brain production of L-glutamate[25].

**c. Antidepressants**

There are several distinct pharmacological classes with various modes of action that make up antidepressants. For migraines, only tricyclic antidepressants (TCAs) have demonstrated effectiveness.

The effectiveness of the TCAs amitriptyline and clomipramine as well as the selective serotonin reuptake inhibitors (SSRIs) fluoxetine and fluvoxamine has been examined in a total of 16 controlled trials[26]**.**

**d. CGRP-targeted Therapies:**

Both central and peripheral neurons contain the CGRP receptor.

People who have migraines may experience acute headaches and delayed migraine-like symptoms as a result of exogenous CGRP. As a result, CGRP has emerged as a key target for migraine treatments aimed at preventing and treating acute attacks. CGRP receptor antagonists

regulate thalamic activity in response to trigeminal nociceptive input. A reduction in CGRP release is one possible mechanism of action of triptans, which are 5-HT receptor agonists. While CGRP mAbs are large-molecule CGRP receptor or ligand antagonists, the gepants, rimegepant and ubergepant, are small-molecule CGRP receptor antagonists. By preventing CGRP from being released at any point along the migraine pathway, CGRP antagonists prevent migraines by inhibiting vasodilation and neurogenic inflammation.

Three CGRP mAbs-erenumab, fremanezumab, and galcanezumab were authorized by the FDA in 2018 to prevent adult migraines. All of them are given monthly subcutaneously (SC), with fremanezumab receiving an extra quarterly dosage schedule. Injection-site responses brought on by the SC administration are the most frequent side effects[27].

**Non-pharmacological:**

**a. Nutraceuticals**

Nutraceuticals are described as food or dietary supplements that provide medicinal or health advantages. The use of this type of non-pharmacological therapy in migraine patients is increasing and is probably underappreciated. The most widely used nutraceuticals with some evidence of preventing migraines include magnesium, coenzyme, butterbur root extract (Petasites hybridus), feverfew (Tanacetum parthenium), riboflavin (vitamin B2), and butterbur root extract[28].

**b. Dietary modification**

Diet has a significant role in migraine management. Therefore, it is important to take into account the elements of the diet and how they may provoke migraine attacks.

Dietary lifestyle modification can be influenced by a number of factors, such as avoiding hunger and fasting, eating regular meals, sticking to frequent meals (five or six small meals per day), avoiding certain foods, consuming slow-digesting foods that provide a stable blood glucose level, cooking instead of consuming processed or fast food, remembering to drink enough water and stay hydrated, and eating a low-fat diet[29].

**c. Behavioural treatment, lifestyle modification and Biofeedback**

Migraine prevention can be achieved with behavioral treatment, which includes biofeedback, cognitive therapy, stress management, and relaxation techniques. Numerous techniques can be used, including muscle relaxation (tension and relaxation cannot coexist), mindfulness-based stress reduction and cognitive therapy, biofeedback-assisted relaxation, and desensitization by visualizing anxiety stimuli.

Group or private sessions are available for behavioral interventions. Treatment teams of several specialists may instruct the necessary skills over the phone[29].

**d. Acupuncture**

One component of traditional Chinese medicine is acupuncture.

The effectiveness of acupuncture in treating migraine and chronic pain is supported by a number of studies. While acupuncture has been shown to be beneficial for both chronic and episodic migraines. There are few adverse effects and acupuncture is a safe technique.

However, acupuncture should be used with caution and discussed with a physician for pregnant migraine patients for migraine management[29].

### 5.3. Neuromodulation:

Neuromodulation involves the targeted use of electrical, magnetic, or chemical stimuli to modify nerve activity in the central or peripheral nervous system. This non-invasive, reversible, and adjustable approach is increasingly recognized for its effectiveness and safety in treating migraines compared to conventional medications. Non-invasive methods, such as vagus nerve stimulation (nVNS) and single-pulse transcranial magnetic stimulation, are gaining traction among clinicians and patients due to their proven benefits. These techniques offer significant advantages, especially for vulnerable groups like pregnant women or those who cannot tolerate or respond to medications. In some cases, non-pharmacological neuromodulation may also be cost-effective[30].

### 5.4. Personalized medication:

The potential for personalized pharmacological polypharmacy, tailored to a patient's unique biochemical profile and the therapeutic needs arising from comorbidities, appears to conflict with certain biotechnological drugs, many of which remain under investigation. These include monoclonal antibodies, antagonist, and agonist molecules critical to migraine pathophysiology. Unlike traditional drugs, these agents are not subject to enzymatic metabolism or membrane transporter interactions, enabling them to circumvent challenges posed by individual biochemical variability and adverse drug interactions common in polytherapy. A key pathogenetic mechanism under exploration for these drugs involves trigeminal neuron activation, which triggers the release of neuropeptides such as CGRP, substance P, PACAP, and nitric oxide. These induce peripheral vasodilation of meningeal blood vessels and reflex parasympathetic activation. Currently, therapeutic agents targeting CGRP-induced vasodilation are in use and under study. For acute migraine treatment, two drug classes-gepants and ditans have been developed, while monoclonal antibodies targeting CGRP are employed for prophylaxis[31].

## 6. CURRENT RESEARCH ON MIGRAINE TREATMENT

Research on treating migraine is still being conducted, with the goal of creating new and better therapies. These are a few recent study topics.

**Table no. 1: Current research on Migraine treatment**

| SL NO. | DRUG | TECHNOLOGY | FORMULATION | STUDY OUTCOME |
|---|---|---|---|---|
| 1 | Rizatriptan Benzoate (Singh MK *etal.*,2022) | Wet granulation technique | Sublingual tablet | The study used a $2^3$ factorial design and wet granulation to successfully create a fast-dissolving sublingual tablet of rizatriptan benzoate. It was shown that sepitrap 80 greatly increased drug permeability and was a more potent bioenhancer than sodium lauryl sulfate. The improved formulation (S-3) demonstrated high in vitro (77.28%) and ex vivo (82.28%) penetration within 90 minutes, as well as quick disintegration (9 seconds) and full drug release (10 minutes). The resilience of the formulation was validated by stability studies. All things considered, the method showed improved permeability and bioavailability of a BCS Class III medication for efficient migraine treatment[32]. |
| 2. | Zolmitriptan (Chettupalli AK, Katta etal.,2025) | Rotary melting sonication method | Intranasal | The study effectively created a liposomal intranasal gel formulation of zolmitriptan to improve its therapeutic efficacy and bioavailability for the treatment of acute migraines. High drug entrapment (up to 99.12%), regulated particle size, and prolonged drug release (up to 99.38%) were all proven by the optimized liposomal gel using a central composite design. The formulation's bioavailability and penetration were noticeably better than those of the drug solution and control gels. The formulation's safety and non-irritating properties were validated by histopathological investigation, and in |

| | | | | |
|---|---|---|---|---|
| | | | | vitro release followed a non-Fickian pattern. In terms of migraine treatment, the liposomal gel presents a viable, efficient, and well-tolerated substitute[33]. |
| 3 | Zolmitriptan (Abou Youssef NA etal., 2025 | Conventional thin film hydration method | Niosomal transdermal patches | In comparison to traditional ZOL, the study showed that transdermal ZOL-nanoformulation (niosomes) greatly enhanced zolmitriptan's effectiveness and brain receptor delivery. It controlled epigenetically changed chronification genes, lowered trigeminal neuronal activation, and successfully decreased migraine symptoms and important pain markers. It also resisted the hypercoagulable state and platelet activation brought on by migraines, which makes it a viable substitute for migraine treatment[34]. |
| 4. | Rizatriptan (Suhagiya K *eta*l.,2023 | Cold technique | In situ gel | The study focused on formulating an in-situ nasal gel of Rizatriptan (RZT) to enhance its bioavailability and therapeutic effectiveness for migraine treatment. Carbopol 934P and HPMC K4M were evaluated for optimizing gel viscosity and mucoadhesive properties, with HPMC K4M proving more suitable due to better compatibility. The formulations maintained physiological nasal pH and exhibited high drug content (over 97%). Gelation occurred rapidly (within 1.3 to 8.6 seconds), corresponding with increased viscosity and mucoadhesion. Statistical analysis confirmed significant correlations between formulation components and performance. Intranasal delivery notably improved RZT brain concentration (Cmax 340.27 ng) and AUC compared to oral administration, indicating enhanced bioavailability and faster onset, |

| | | | | |
|---|---|---|---|---|
| | | | | positioning the gel as a promising treatment option for migraines[35]. |
| 5 | Propranolol Hydrochloride (Joshua JM *etal.,* 2017) | Solvent casting technique | Oral thin films | The study focused on developing oral thin films of Propranolol hydrochloride for migraine prevention, aiming to bypass first-pass metabolism and improve bioavailability. Out of six formulations (F1–F6), F4 emerged as the most effective, exhibiting a rapid disintegration time of 47 seconds and 93% drug release within 20 minutes. Compatibility between the drug and excipients was verified through FT-IR and DSC analyses. SEM images of F4 revealed a smooth surface with minimal porosity. Stability testing confirmed F4 remained stable at both room and refrigerated temperatures. Additionally, ex vivo permeation through goat oral mucosa showed 91% drug absorption, establishing F4 as the most promising formulation[36]. |
| 6 | Rizatriptan benzoate (Upadhyay J *etal.,* 2024) | Direct compression | Mouth Dissolving Tablet | This study focused on improving the safety, effectiveness, and quick onset of action of Rizatriptan Benzoate for migraine relief by formulating orally disintegrating tablets (ODTs) through direct compression. A $3^2$ factorial design was used to assess eight formulations incorporating various superdisintegrants. The optimized tablet |

| | | | | |
|---|---|---|---|---|
| | | | | exhibited rapid disintegration within 15–30 seconds and achieved 99.60% drug release in just 2 minutes and 15 seconds. A simple, accurate, and cost-effective UV spectrophotometric method was developed at 225 nm for drug estimation. Method validation confirmed its accuracy, linearity, sensitivity, and suitability for routine quality control[37]. |
| 7 | Rimegepant (Suruse PB *etal.*,2023) | Solvent casting method | FAST DISSOLVING FILMS | This study successfully formulated fast-dissolving Rimegepant films for quick migraine relief using a $3^2$ full factorial design and the solvent casting method, incorporating HPMC E100 and honey. The optimized films exhibited favorable physicochemical characteristics, such as rapid disintegration within 6.9–11.2 seconds, uniform drug content ranging from 83.2% to 99.6%, and efficient drug release between 64.7% and 90.8% within 6 minutes. Additionally, the films showed strong tensile properties and good folding endurance. These findings suggest that Rimegepant fast-dissolving films could be a convenient and effective alternative to traditional oral dosage forms, enhancing patient comfort and compliance. Further in vivo evaluation is needed to confirm their clinical performance[38]. |

| | | | | |
|---|---|---|---|---|
| 8 | Zolmitriptan (Kumria R *etal.*,2018) | Solvent casting method | Buccal Bioadhesive Films | This study focused on optimizing a chitosan-based buccal bioadhesive film for efficient zolmitriptan delivery in migraine management using a $3^2$ factorial design. Films were produced via solvent casting with different concentrations of chitosan and polyvinyl alcohol and assessed for swelling index, drug release, and mucoadhesive strength. The results indicated that chitosan increased swelling and mucoadhesion but decreased drug release, whereas polyvinyl alcohol showed the reverse effects. The formulation F7 demonstrated the most favorable properties for buccal use and exhibited a high drug flux of $63.93 \pm 12.51$ μg/cm²/h in ex vivo testing. These results highlight the potential of F7 for both acute and preventive migraine treatment, although in vivo studies are necessary for further validation[39]. |
| 9 | Frovatriptan succinate monohydrate (Singh H *etal*.,2018) | Solvent casting method | Sublingual flim | The study successfully formulated Frovatriptan succinate monohydrate (FSM) sublingual films using the solvent casting method with HPMC E15, mannitol, glycerine, and low levels of mucoadhesive polymers like chitosan or CMCNa. The optimized films demonstrated strong physicochemical characteristics, such as folding endurance above 300 and rapid disintegration within 2 minutes. These drug-loaded films achieved high dissolution rates (89.9% in 5 minutes) and improved permeability, facilitating rapid systemic absorption by avoiding first-pass metabolism. Pharmacodynamic studies confirmed their effective antimigraine properties. Overall, FSM sublingual films offer a |

| | | | | |
|---|---|---|---|---|
| | | | | promising and efficient alternative for migraine treatment[40]. |
| 10 | Rizatriptan benzoate (Faghihi H *etal.*,2021) | spray freeze drying | Inhalable microparticles | The study successfully prepared inhalable Rizatriptan benzoate microparticles via spray freeze drying using sugars (mannitol or trehalose) combined with amino acids (leucine, phenylalanine, or serine). These microparticles exhibited appropriate particle size, morphology, thermal stability, and excellent aerosolization properties. Notably, the formulation containing trehalose and phenylalanine achieved the highest fine particle fraction (61.1%), reflecting improved dispersion and reduced agglomeration. The results indicate that Rizatriptan can be effectively engineered into breathable microparticles, presenting a promising pulmonary delivery approach for fast and effective migraine treatment[41]. |

## CONCLUSION

Migraine is a chronic neurological disorder that is seen increasingly among those aged 15 to 39 on a worldwide scale. Includes migraine with aura and migraine without aura, types of migraine. The pathophysiology comprises spastic contraction of cranial arteries. Diagnostic tools and clinical criteria are involved for accurate diagnosis for management. NSAIDs, triptans, Neurological and personalized medicine are used in the treatment along with the preventive therapies that include pharmacological and non-pharmacological approaches in the management of migraine. Future research should focus on improving or bridging the gap to improve the patient outcomes and quality of life.

**Reference:**


1. Ramasamy B, Karri M, Venkat S, Andhuvan G. Clinical profile and triggers of migraine: an Indian perspective. Int J Res Med Sci. 2019 Apr;7(4):1050-4.
2. Mungoven TJ, Henderson LA, Meylakh N. Chronic migraine pathophysiology and treatment: a review of current perspectives. Frontiers in Pain Research. 2021 Aug 25;2:705276
3. Friedman DI, De Ver Dye T. Migraine and the environment. Headache: The Journal of Head and Face Pain. 2009 Jun;49(6):941-52.
4. Chen, Zf., Kong, Xm., Yang, Ch. *et al.* Global, regional, and national burden and trends of migraine among youths and young adults aged 15–39 years from 1990 to 2021: findings from the global burden of disease study 2021. *J Headache Pain* **25**, 131 (2024). https://doi.org/10.1186/s10194-024-01832-0
5. Gupta J, Gaurkar SS. Migraine: an underestimated neurological condition affecting billions. Cureus. 2022 Aug 24;14(8).
6. Eigenbrodt AK, Ashina H, Khan S, Diener HC, Mitsikostas DD, Sinclair AJ, Pozo-Rosich P, Martelletti P, Ducros A, Lantéri-Minet M, Braschinsky M. Diagnosis and management of migraine in ten steps. Nature Reviews Neurology. 2021 Aug;17(8):501-14.
7. Khan J, Al Asoom LI, Al Sunni A, Rafique N, Latif R, Al Saif S, Almandil NB, Almohazey D, AbdulAzeez S, Borgio JF. Genetics, pathophysiology, diagnosis, treatment, management, and prevention of migraine. Biomedicine & pharmacotherapy. 2021 Jul 1;139:111557.
8. Pleș H, Florian IA, Timis TL, Covache-Busuioc RA, Glavan LA, Dumitrascu DI, Popa AA, Bordeianu A, Ciurea AV. Migraine: advances in the Pathogenesis and treatment. Neurology international. 2023 Sep;15(3):1052-105
9. Puledda F, Silva EM, Suwanlaong K, Goadsby PJ. Migraine: from pathophysiology to treatment. Journal of Neurology. 2023 Jul;270(7):3654-66.
10. Frimpong-Manson K, Ortiz YT, McMahon LR, Wilkerson JL. Advances in understanding migraine pathophysiology: a bench to bedside review of research insights and therapeutics. Frontiers in Molecular Neuroscience. 2024 Feb 28;17:1355281.
11. Lipton RB, Lanteri-Minet M, Leroux E, Manack Adams A, Contreras-De Lama J, Reed ML, Fanning KM, Buse DC. Pre-and post-headache phases of migraine: multi-country results from the CaMEO–International Study. The Journal of Headache and Pain. 2023 Nov 8;24(1):151.
12. Weatherall MW. The diagnosis and treatment of chronic migraine. Therapeutic advances in chronic disease. 2015 May;6(3):115-23.
13. Eigenbrodt AK, Ashina H, Khan S, Diener HC, Mitsikostas DD, Sinclair AJ, Pozo-Rosich P, Martelletti P, Ducros A, Lantéri-Minet M, Braschinsky M. Diagnosis and management of migraine in ten steps. Nature Reviews Neurology. 2021 Aug;17(8):501-14.
14. https://emedicine.medscape.com/article/1142556-overview?form=fpf
15. Tzankova V, Becker WJ, Chan TL. Diagnosis and acute management of migraine. Cmaj. 2023 Jan 30;195(4):E153-8.

16. Lipton RB, Dodick D, Sadovsky RE, Kolodner K, Endicott J, Hettiarachchi J, Harrison W. A self-administered screener for migraine in primary care: the ID migraine™ validation study. Neurology. 2003 Aug 12;61(3):375-82.
17. Peng KP, Wang SJ. Migraine diagnosis: screening items, instruments, and scales. Acta Anaesthesiologica Taiwanica. 2012 Jun 1;50(2):69-73.
18. Eckardt NA. Functional evolutionary genetics and plant adaptation: linking phenotype and genotype.
19. Peng KP, Wang SJ. Migraine diagnosis: screening items, instruments, and scales. Acta Anaesthesiologica Taiwanica. 2012 Jun 1;50(2):69-73.
20. Dogruyol S, Gur ST, Akbas I, Kocak MB, Kocak AO, Ceylan M, Tekyol D. Intravenous ibuprofen versus sodium valproate in acute migraine attacks in the emergency department: A randomized clinical trial. The American Journal of Emergency Medicine. 2022 May 1;55:126-32.
21. Borkowska A, Kiełb A, Mich A, Kaźmierczak A, Sornek P, Izdebska W, Pawlak I, Ciesielski R, Stanek J, Perkowska K. The use of triptans as an effective form of migraine treatment–review. Quality in Sport. 2025 Jan 11;37:56600-.
22. Edvinsson L. CGRP receptor antagonists and antibodies against CGRP and its receptor in migraine treatment. British journal of clinical pharmacology. 2015 Aug;80(2):193-9.
23. Capi M, De Angelis V, De Bernardini D, De Luca O, Cipolla F, Lionetto L, Simmaco M, Martelletti P. CGRP receptor antagonists and 5-HT1F receptor agonist in the treatment of migraine. Journal of clinical medicine. 2021 Apr 1;10(7):1429.
24. Diener HC, Limmroth V. Prevention of migraine: beta-blockers and amine agonists: efficacy. FRONTIERS IN HEADACHE RESEARCH. 2004 Jan 1;12:59-66.
25. Pini LA, Lupo L. Anti-epileptic drugs in the preventive treatment of migraine headache: a brief review. The Journal of Headache and Pain. 2001 Jun;2:13-9.
26. Silberstein SD, Goadsby PJ. Migraine: preventive treatment. Cephalalgia. 2002 Sep;22(7):491-512.
27. Peters GL. Migraine overview and summary of current and emerging treatment options. Am J Manag Care. 2019 Jan 1;25(2 Suppl):S23-34.
28. Puledda F, Shields K. Non-pharmacological approaches for migraine. Neurotherapeutics. 2018 Apr;15(2):336-45.
29. Haghdoost F, Togha M. Migraine management: Non-pharmacological points for patients and health care professionals. Open Medicine. 2022 Nov 23;17(1):1869-82.
30. Tiwari V, Agrawal S, TIWARI V. Migraine and neuromodulation: a literature review. Cureus. 2022 Nov 7;14(11
31. Pomes LM, Guglielmetti M, Bertamino E, Simmaco M, Borro M, Martelletti P. Optimising migraine treatment: from drug-drug interactions to personalized medicine. The journal of headache and pain. 2019 Dec;20:1-2.
32. Singh MK, Mazumder R, Padhi S, Singh DK. Formulation development and optimization of bioenhanced sublingual tablets of rizatriptan benzoate to combat migraine. Indian J Pharm Educ Res. 2022 Apr 1;56(2):200-15.
33. Chettupalli AK, Katta S, Fateh MV, Haque MA, Kothapally D, Damarasingu P, Padmasri B, Archana P. Design, optimization, and characterization of zolmitriptan loaded

liposomal gels for intranasal delivery for acute migraine therapy. Intelligent Pharmacy. 2025 Feb 1;3(1):11-25.

34. Abou Youssef NA, Labib GS, Kassem AA, El-Mezayen NS. Zolmitriptan niosomal transdermal patches: combating migraine via epigenetic and endocannabinoid pathways and reversal of migraine hypercoagulability. Drug Delivery and Translational Research. 2025 Jun;15(6):2179-99.
35. Suhagiya K, Borkhataria CH, Gohil S, Manek RA, Patel KA, Patel NK, Patel DV. Development of mucoadhesive in-situ nasal gel formulation for enhanced bioavailability and efficacy of rizatriptan in migraine treatment. Results in Chemistry. 2023 Dec 1;6:101010.
36. Joshua JM, Hari R, Jyothish FK, Surendran SA. Formulation of propranolol hydrochloride oral thin films for migraine prophylaxis. Int J Pharm Sci Rev Res. 2017 Jan;42(1):232-41.
37. Upadhyay J, Sonaji AV, Naaz F. Formulation & Evaluation of Anti Migrane Mouth Dissolving Tablet.
38. Suruse PB, Deshmukh AP, Barde LG, Devhare LD, Maurya VK, Deva V, Priya NS. Rimegepant embedded fast dissolving films: A novel approach for enhanced migraine relief. Journal of Survey in Fisheries Sciences. 2023;10(1):2071-84.
39. Kumria R, Al-Dhubiab BE, Shah J, Nair AB. Formulation and evaluation of chitosan-based buccal bioadhesive films of zolmitriptan. Journal of Pharmaceutical Innovation. 2018 Jun;13:133-43.
40. Singh H, Singla YP, Narang RS, Pandita D, Singh S, Narang JK. Frovatriptan loaded hydroxy propyl methyl cellulose/treated chitosan based composite fast dissolving sublingual films for management of migraine. Journal of Drug Delivery Science and Technology. 2018 Oct 1;47:230-9.
41. Faghihi H, Darabi M, Mirmoeini M, Vatanara A. Formulation and evaluation of inhalable microparticles of Rizatriptan Benzoate processed by spray freeze-drying. Journal of Drug Delivery Science and Technology. 2021 Apr 1;62:102356.