IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.53
Volume 4, Issue 2, September 2024

A Review on Migraine Treatment and Physiology

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Abstract: *A multitude of peripheral and central nervous system areas and networks are involved in the complicated neurobiology of migraine, a frequent and highly incapacitating neurological condition. The pathophysiology of migraines has been better understood in recent years, which has made it easier to translate that understanding into innovative treatments. These treatments are now being made available to patients worldwide and are significantly altering the clinical approach to the condition. The first section of this review will present a current summary of migraine pathophysiology by examining the structure and function of the primary illness-affected regions and emphasizing how these contribute to the wide range of symptoms that define the disease and attacks. In addition to giving a brief summary of recent research supporting established migraine treatments, the second section of the paper will address the novel therapeutic agents that have been developed for the treatment of migraine. These agents include molecules that target the calcitonin gene-related peptide serotonin,5-HT1F receptor agonists, and on-invasive neuromodulation*

Keywords: Migraine, Pathophysiology, Treatment, Diagnosis

I. INTRODUCTION

A recurrent syndrome of headache associated with other symptoms of neurologic dysfunction in varying admixtures" or "an episodic headache associated with certain features, such as sensitivity to light, sound, or movement" are two definitions of migraine. There are two types of migraines: refractory migraines, which are defined as "having failed all on a thorough anamnesis and physical examination. Usually, testing is not necessary. Pharmacological and nonpharmacological therapies form the basis of treatment. The purpose of pharmaceutical available preventatives and suffering from at least 8 debilitating headache days per month for at least 6 consecutive months," and resistant migraines, which are defined as "having failed at least 3 classes of migraine preventatives and suffer from at least 8 debilitating headache days per month for at least 3 consecutive months without improvement."[1,2] Among all neurological disorders, migraines rank highest and are currently the sixth most debilitating disorder worldwide. The biology of migraine is intricate, multifaceted, and yet unclear in certain areas. The fundamental characteristic appears to be a complicated genetic tendency that is likely accompanied by behavioural and environmental factors. These factors modify the way the brain processes sensory information, making an individual more susceptible to sensory stimuli. As a result, migraineurs experience ordinarily normal sensory stimuli as uncomfortable. A headache disorder is one of the most prevalent nervous system disorders, characterized by persistent headaches. A handful of primary headache disorders, including migraine, tension-type headache, and cluster headache, are characterized by the unpleasant and incapacitating headache itself. The most common, prevalent, incapacitating, and essentially curable of these is the migraine headache, which is yet underdiagnosed and undertreated. A frequent chronic headache illness, migraine is characterized by recurring attacks that last between four and seventy-two hours, have a throbbing quality, can be moderately or severely intense, are increased by regular physical activity, and are linked to phonophobia, photophobia, and nausea. In primary care, migraines are the most common neurological condition. The results of the most recent Global Burden Disease survey show that migraines rank second globally and first among young women in terms of causes of disability. Chronic migraine affects 2% of the world's population and is a very burdensome condition for sufferers, their families, and society as a whole. Migraine is a common ailment, affecting 18% of women and 6% of men. The diagnosis is mostly dependent interventions is to both treat and prevent headaches. [3,4]

Types of Migraine:

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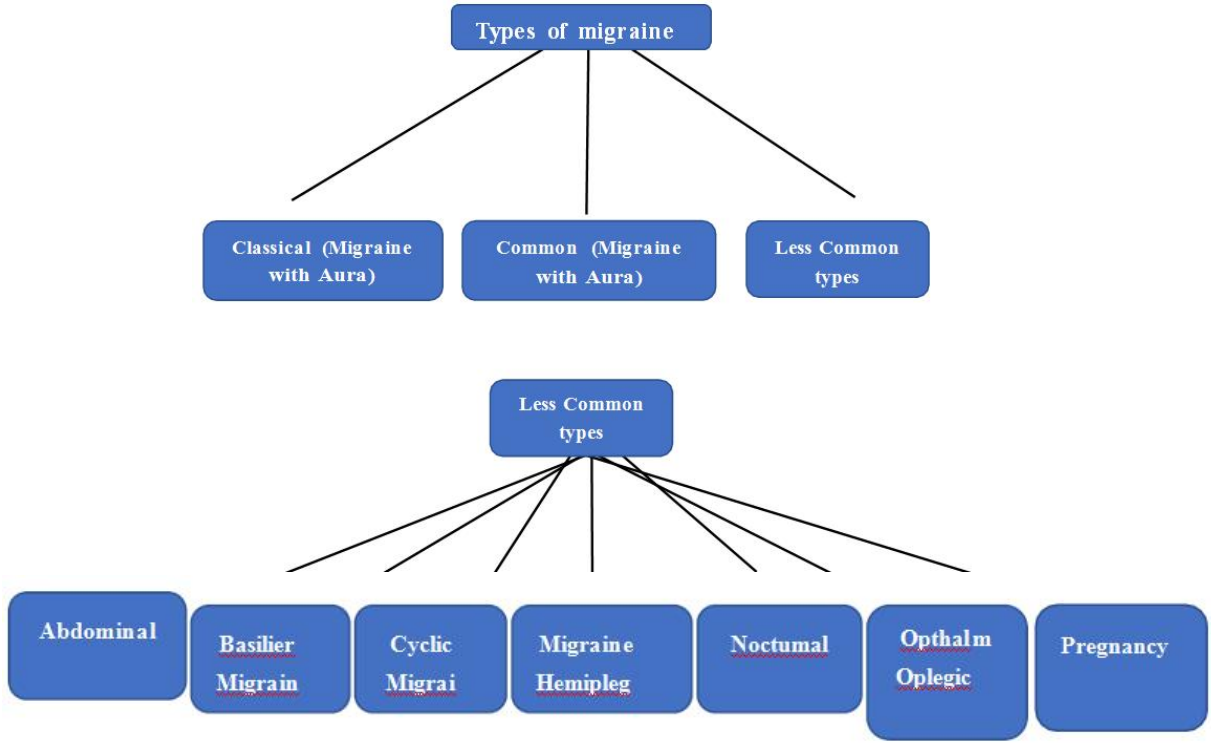
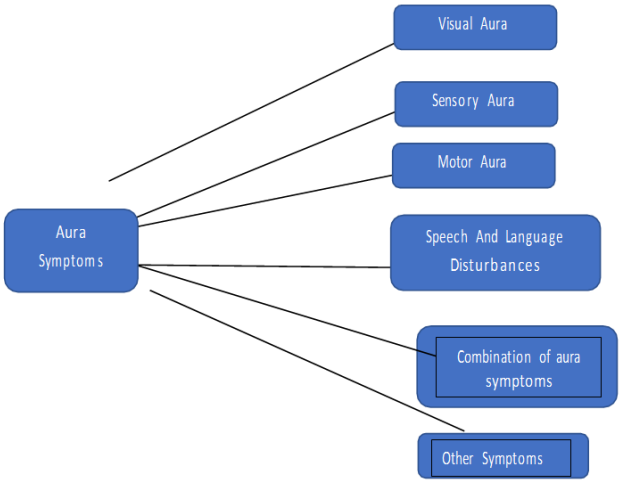


Classical migraine:

aura-producing migraines, or classical migraines Less than 20% of migraineurs suffer aura, which is the medical word for the pain's onset. These might be characterized as the zigzag or spot patterns that appear before the eyes and are linked to blurry vision. Usually, these symptoms disappear after an hour, and a headache takes their place[6]. One or more symptoms of a totally reversible aura that point to brain malfunction. At least one symptom of the aura appears progressively over more than four minutes or in the sequence of two or more symptoms. No aura symptom persists for longer than sixty minutes. A headache may start before or with the aura, and it usually follows it with a free period of fewer than sixty minutes. Aura-producing migraineurs typically also experience aura-free migraines. Usually, the aura lasts for less than an hour in total. When an aura persists for more than an hour but less than a week, it is referred to as "complicated migraine" or "migraine with prolonged aura."[5]



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2. Common migraine:

When a common migraine occurs, headaches often start suddenly. Children were primarily affected by this. At least two of the following apply to headaches:

- Unilateral location
- Pulsating quality
- Moderate or severe intensity (inhibits or prohibits daily activities)
- Aggravation by walking stairs or similar routine physical activity

3. Less common types:

Abdominal migraine

- Also known as periodic syndrome
- Abdominal pain lasting for 1-72 hours along with nausea, vomiting, flushing or pallor.

Basilar migraine

- Pain arises from brain stem.
- Symptoms like dizziness, double vision, tingling on both sides of body are seen in this type.

Cyclic migraine

- Long lasting attacks (10 or more /month)
- Careful monitoring of blood level and thyroid functioning is needed.

Hemiplegic migraine

- plegic migraine
- Severe type of migraine causes temporary motor paralysis.
- Sensory disturbances on one side of the body followed by headache.

Nocturnal migraine

- Attacks during early in the morning or middle in the night often awaken patients from sleep.

Ophthalmoplegic migraine

- The pain usually surrounds eyeball and lasts from a few days to few months.
- It is caused by the weakness of the muscles surrounding the eye.

Pregnancy related migraine

- Migraine attacks from the 3rd month of pregnancy till delivery due to hormonal stability.
- Non-medical treatment was effective in this case.

Pathophysiology:

Based on clinical symptoms, the pathophysiology of migraine can be divided in to three phases:

- The trigger phase characterised by neuronal hyperexcitability,
- The aura phase possibly involving cortical spreading depression and finally,
- The headache phase due to cranial vasodilatation precipitated by activation and sensitization of the trigeminal system at the peripheral and central levels

Exploring each phase of migraine reveals unique mechanisms and divulges novel therapeutic targets. Sensory fibres innervating the cranial vessels arise from trigeminal ganglion neurons that contain neuropeptides. Trigeminovascular inputs from dural meningeal vessels pass sthrough the trigeminal ganglion and synapse on second order neurons. [6]

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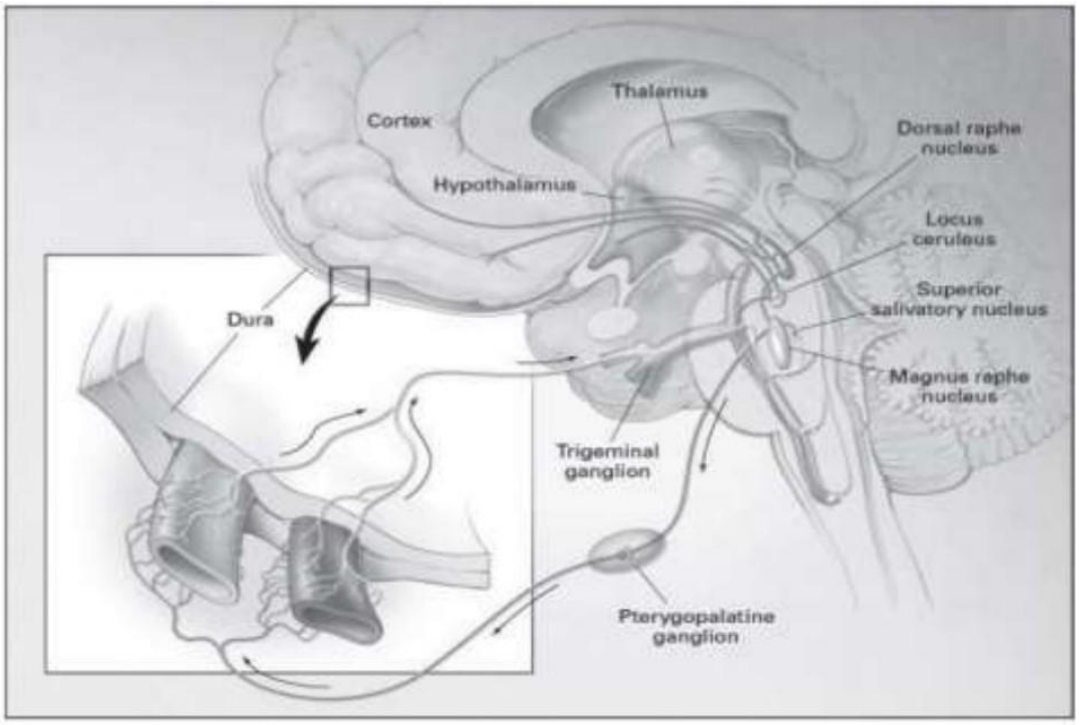

Fig 1. Pathophysiology of Migraine

Trigemino vascular inputs from dual meningeal vessels pass through the trigeminal ganglion and synapse on second order neurons. These neurons project to the quintothalamic tract and synapse with neurons in the thalamus. There is also a reflex connection between neurons in the pons in the superior salivatory nucleus, which results in a cranial parasympathetic output, which is partially mediated by the ganglion of the pterygopalatine (sphenopalatine) ganglion. [7]

Treatment:

Pain relieving medications:

- Pain relievers: Acetaminophen with Ibuprofen For mild migraines, acetaminophen, aspirin, and caffeine may be helpful, but not for severe ones. These can cause rebound headaches, gastrointestinal bleeding, and ulcers if taken over an extended length of time.
- Triptans: The medications zolmitriptan, almotriptan, frovatriptan, eletriptan, and sumatriptan. Sumatriptan and naproxen sodium (treximet) together have been shown to be more effective at reducing migraine symptoms than either drug alone.
- Ergot: Ergotamine and caffeine combinations (migrergot, cafergot) are less costly than triptans, but they are also less effective. When pain persists for longer than 48 hours, they are most beneficial. Compared to ergotamine, dihydroergotamine is more efficient and has less negative effects. It is also offered as an injectable and as a nasal spray.
- Anti-Nausea: When using medication for nausea, it is frequently taken in combination with other medications. Medication prescriptions for prochlorperazine and metoclopramide are common.
- Opiates: When persons cannot take ergots or triptans, narcotics, especially codeine, are frequently used to relieve migraine headache pain.
- Butalbital Combinations: Sometimes, aspirin or acetaminophen is used with the sedative butalbital in medications to treat migraine attacks. Codeine or caffeine are also included in some mixtures.

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Preventive Medications

- Cardiovascular drugs: Anti-hypertensive drugs such as candesartan and lisinopril help lessen migraine frequency and intensity. blockers, as well as calcium channel blockers such as verapamil.
- Anti-depressants: Tricyclic antidepressants, such as protriptyline, nortriptyline, and amitriptyline, work best to prevent migraines and other types of headaches. They function by altering serotonin and other neurotransmitter levels.
- Anti-seizure drugs: Migraine frequency is decreased with gabapentin, topiramate, and divalproex.
- Cyproheptadine: Serotonin activity is the unique effect of these anti-histamines. Children may receive it from doctors as a preventative strategy.
- Botulinum Toxin: It is applied to the management of persistent migraines. The muscles of the neck and forehead are injected. The course of treatment usually needs to be repeated every three months once it is found to be effective.

Home remedies:

- Muscle relaxation exercises
- Sleep enough
- Relax and take rest
- Maintain headache dairy and act accordingly

Symptoms of migraine:

Before the headache:

According to a 2023 review of migraine, around 77% of people Trusted Source with migraine experience symptoms that start hours or days before the headache. At this stage, a person might experience a “prodrome,” which may involve emotional changes, specifically depression and irritability. A prodrome can also include yawning, dizziness, thirst, frequent urination, and sensitivity to light and sound. Sometimes an aura can occur. This involves physical or sensory symptoms, such as flashing lights in the field of vision.

During the headache:

Symptoms may include nausea, vomiting, neck pain, dizziness, and nasal congestion in addition to a mild to severe throbbing or pulsating headache.

Resolution:

Exhaustion and irritation may persist for several days following the headache. This is referred to as the "hangover from migraines." It's referred to as the postdrome period officially. Other common features of migraine are:

- head pain that worsens during physical activity or straining
- an inability to perform regular activities due to the pain
- increased sensitivity to light and sound that can sometimes be relieved by lying quietly in a darkened room

Other symptoms may include sweating, feeling unusually hot or cold, a stomachache, and diarrhoea.

Causes and Triggers of Migraine:

There Are Various Emotional Triggers, That Include:

- Stress
- Depression
- Anxiety
- Excitement

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Certain Dietary Factors Can Trigger Migraine, Including:

- Alcohol
- Caffeine
- Chocolate
- Nuts
- Cheese
- Citrus Fruits
- Foods Containing the Additives Tyramine And Monosodium Glutamate (Mgs)

Some People May Find Certain Medications A Triggering Factor, Such As:

- Sleeping Pills
- Hormone Replacement Therapy (HRT)
- Some Birth Control Pills.

Various Environmental Factors Can Potentially Trigger Migraine, Including:

- Flickering Screens
- Strong Smells
- Second hand Smoke
- Loud Noises
- Humidity
- Stuffy Rooms
- Temperature Changes
- Bright Lights

Some Other Possible Triggers Include:

- Tiredness
- A Lack of Sleep
- Shoulder and Neck Tension
- Poor Posture
- Physical Overexertion
- Low Blood Sugar
- Irregular Mealtimes
- Dehydration

Risk Factors:

- Depression
- Bipolar Disorder
- Fibromyalgia
- Irritable Bowel Syndrome
- Overactive Bladder
- Sleep Disorders
- Obsessive-Compulsive Disorder
- Anxiety

Identifying and avoiding triggers:

A trigger can occasionally cause a migraine attack. A person may keep a journal in which they document their feelings as well as what they did, ate, and drank before to the onset of symptoms in an effort to pinpoint a trigger.

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- low blood sugar
- physical overexertion
- stress
- certain foods, such as chocolate and any that contain tyramine or MSG
- certain medications, including HRT and some birth control pills
- bright lights and flickering screens

The following strategies may help reduce the frequency of migraine episodes:

- getting enough sleep
- reducing stress
- drinking plenty of water
- having healthy posture
- avoiding known dietary triggers
- getting regular physical exercise

If making these changes does not ease the severity and frequency of migraine episodes, a healthcare professional may suggest medication or other options.

Diagnosis:

The International Headache Society recommends the "5, 4, 3, 2, 1" criteria to diagnose migraine without aura. These numbers stand for:

- having 5 or more episodes, each lasting 4 hours to 3 days
- having a headache with at least 2 of the following qualities:
- occurring on one side
- pulsating
- causing moderate-to-severe pain aggravated by activity

having at least 1 additional symptom, such as:

- nausea
- vomiting
- sensitivity to light
- sensitivity to sound

A healthcare professional may recommend imaging or other tests to exclude other causes of the symptoms, such as a tumour, meningitis, or a stroke.

II. CONCLUSION

The complex and multifactorial nature of migraine is reflected in the presence of a variety of risk factors and triggers agents. Furthermore, there is extensive evidence to indicate that various biological factors, especially hormones, genetic factors, and metabolic disorders, in addition to psychiatric and psychological factors are risk factors for migraine. Migraine is common cause of headache, early diagnosis and prompt treatment of migraine enhances the quality of life; prevent conversion of episodic migraine to chronic migraine. As there is growing interest in pathophysiology, new crematorium targeting the different pathways are being discovered. Genetic makeups play a significant role in defining an individual's susceptibility to migraine. In these patients, 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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