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A review on recent advancement and pharmacological management of migraine

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Abstract

Modern theories suggest that the primary disorder in migraine takes place within the CNS and that this inspires adjustments in blood vessels within pain-producing intracranial meningeal systems that deliver upward push to headache pain. Migraine is now concept of as a neurovascular ailment it has been proposed that genetic abnormalities may be answerable for changing the response threshold to migraine particular trigger elements in the mind of a migraine compared to a normal individual. the exact nature of the principal disorder that is produced in migraine continues to be not clear and can contain spreading despair-like phenomena and activation of mind stem monoaminergic nuclei that are a part of the primary autonomic, vascular and ache control facilities. it is commonly notion that local vasodilatation of intracranial extracerebral blood vessels and a consequent stimulation of surrounding trigeminal sensory nervous ache pathways is a key mechanism underlying the era of headache ache related to migraine. This activation of the Trigemino-vascular device' is idea to reason the release of vasoactive sensory neuropeptides, mainly CGRP, that boom the ache reaction. The activated trigeminal nerves deliver nociceptive records to significant neurons within the mind stem trigeminal sensory nuclei that in turn relay the ache alerts to better facilities in which headache pain is perceived. it's been hypothesized that these significant neurons may become sensitized as a migraine assault progresses. The 'triptan' anti-migraine marketers (e.g. sumatriptan, rizatriptan, zolmitriptan naratriptan) are serotonergic agonists which have been proven to act selectively via inflicting vasoconstriction through 5-HT_{1B} receptors which are expressed in human intracranial arteries and by way of inhibiting nociceptive transmission via an movement at five-HT_{1D} receptors on peripheral trigeminal sensory nerve terminals within the meninges and crucial terminals in brain stem sensory nuclei. these 3 complementary web sites of movement underlie the clinical effectiveness of the 5-HT_{1B/1D} agonists towards migraine headache pain and its related signs and symptoms

Keywords: Migraine; Headache; Chronic; Inherited; Neurology; CNS; Brain

1. Introduction

Migraine is a public fitness problem of great impact on both the affected person and society. the overall migraine prevalence in western international locations is 6–eight% in guys and 15–25% in ladies. it's been calculated that approximately five% of the general population have at least 18 days pharmacology of migraine in keeping with, and that at the least 1% this is, extra than 2.5 million humans in North America have as a minimum in the future of migraine per week. severe migraine is rated as one of the maximum disorders.[1] Migraine is a common chronic headache ailment characterized by recurrent attacks lasting 4–72 hours, of a pulsating high-quality, slight or intense intensity irritated via routine bodily hobby and related to nausea, vomiting, photophobia or photophobia.[2] Older patients with migraine. show reduced gray rely volumes when in comparison with each healthful controls and sufferers with a records of Migraine. even though the medical significance of reduced grey count number remains uncertain, in older sufferers who're hu already susceptible to decreased gray matter, early and powerful treatment. [3]

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continual migraine is the most not unusual type of continual daily headache visible by headache specialists.17 globally, approximately 2% of the populace reports chronic migraine; occurrence is 2.5- to six.5-fold better in girls(1.7% than in men (0.6%–zero.7%) An inherited neurological sickness, is one of the main reasons of disability in the quarter [4] whilst range of migraine attacks tends to decrease around the 5th To 6th a long time of existence, there are nonetheless a large number of sufferers>sixty five years of age complete precept migraine or have new-onset migraine about three% of people with episodic migraine development to chronic circumstance in keeping with 12 months [5]

1.1. What's migraine ?

An inherited neurological ailment, is one of the leading causes of incapacity within the international. even as quantity of migraine assaults tends to decrease across the 5th to sixth many years of life, there are nonetheless a tremendous number of patients>65 years of age whole precept migraine or have new-onset migraine. about 3% of human beings with episodic migraine progress to persistent situation according to 12 months [6]

1.2. Types of migraine

- Migraine without aura
- Migraine with aura
- Childhood periodic syndrome
- Retinal migraine [5]

1.3. Common Symptoms in Migraine

- Severe headache
- Ringing in ears
- Nausea
- Irritability
- Vomiting
- Neck or shoulder pain[6]

1.4. How migraine work?

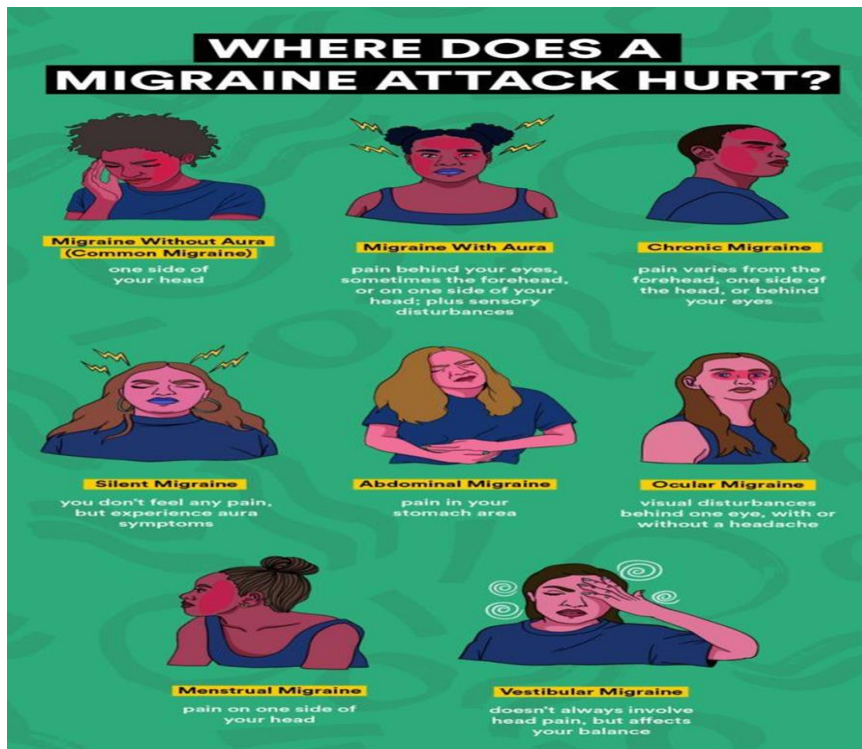


Figure 1 Types of migraine

- Migraine originated deep within brain.
- Electrical impulses obtained in other raging of mind.
- Changes in nerve cellular actively and blood flow may also result in visual Disturbance chemical substances in mind comes in blood vessels dilation and irritation in keeping with tissue.
- The irritation irritates the trigeminal nerve ensuing excessive throbbing [7]

2. Pathophysiology of migraine

A migraine attack can be divided into phases on the premise Of its temporal courting to headache: the premonitory segment (precedes headache) the aura segment (right now Precedes or accompanies headache), the headache phased the postdrome phase (after decision of headache).[8]the precise pathophysiology of migraine is uncertain. it has been counseled that the characteristic pathophysiology of migraine Is the cortical spreading despair (CSD) of neural impulses from a focal point of vasoconstriction observed by using vasodilation. however, it's miles not going that vasoconstriction observed by way of vasodilation (spreading despair) or vasodilation on my own money owed for the nearby edema and focal tenderness often observed in migraine patients [9]

2.1. Phases involve in pathophysiology of migraine

premonitory section of migraine can begin as early as 3 days earlier than a migraine assault. This permits about seventy five% of patients to correctly are expecting a migraine prevalence for as much as 12 h earlier than its onset The maximum connections to common premonitory signs include fatigue, Impaired attention, neck stiffness, photophobia, yawning and food craving puppy studies of brought about and spontaneous attacks [10] provided evidence for hypothalamic activation inside the premonitory section. Activation of this region and its critical to the limbic

gadget may provide an explanation for symptoms at some point of the premonitory segment, together with yawning, polyuria, food craving and mood adjustments and the truth That migraine is typically induced by changes in homoeostasis (e.g., adjustments in sleep-wake cycles and overlooked meals). moreover, structural and useful imaging studies have tested variations in Thalamic and thalamocortical activities in patients with migraine and controls at some stage in migraine attacks research have shown that the thalamus is a key mediator of cutaneous allodia and exacerbation of headache via mild [11]

2.2. Aura phase

about one-third of migraines revel in brief neurological deficits, the migraine air of mystery, within the context of their Migraine attacks The ICHD-3 defines the migraine aura as one or extra transient, absolutely reversible neurological deficits, of which at least one has to have a unilateral neighborhood-ization, that broaden over 5 min extra and of which every deficit lasts between 5 and 60 min. distinct prospective Diary study paintings has proven that 26% of sufferers have as a minimum one of three auras that lasts longer than an hour This draws interest to the polythetic problem, because investigations of air of secrecy lasting over an hour could be a huge waste Of sources. 5 percent of auras are over 4 h [12] so perhaps that is a beneficial cut-off. at the same time as a visible aura, which may display nice (fortification spectra), terrible (scotoma), or both phenomena, is discovered in over ninety% of the instances, and the maximum common deficit, sensory, motor, speech ,mind stem and retinal aura signs and symptoms may occur. charisma signs and symptoms may also precede the headache section however may additionally last nicely into the headache section or maybe provoke throughout the Headache segment. In contrast to the not unusual notion that the aura and headache levels comply with a sequential order, current studies have confirmed that the overlap of these stages is very common place rather than being the exception.[13]

2.3. Headache phase

inside the modern-day edition of the ICHD-3, migraine is defined as Headache assaults lasting 4 seventy two h that are followed via Nausea, photophobia and photophobia, or both. the pinnacle ache is characterized as unilateral, pulsating, of slight or severe intensity and annoyed via physical hobby; of these characteristics suffice to fulfil the diagnostic standards as compared with preceding editions, ICHD-3 distinguishes chronic migraine, which occurs on 15 or extra days in line with Month, from episodic migraine in a greater realistic style constructing on the appendix definition [14]

2.4. Postdrome phase

They may additionally initiate during the head pain section, or maybe even appear after the headache section has ended. Migraine usually relate symptoms of the postdrome segment to the drugs that efficaciously abolished Their headache, indicating that these signs appear or Reappear after the headache phase has ended whilst they seem to play a negligible

role all through the headache phase but, a met analysis of a clinical trial software revealed that postdrome symptoms are visible in the placebo Arm maximum prominently while ache is relievedthe headache phase but, a metanalysis of a clinical trial software revealed that postdrome symptoms are visible in the placebo Arm maximum prominently while ache is relieved [15]

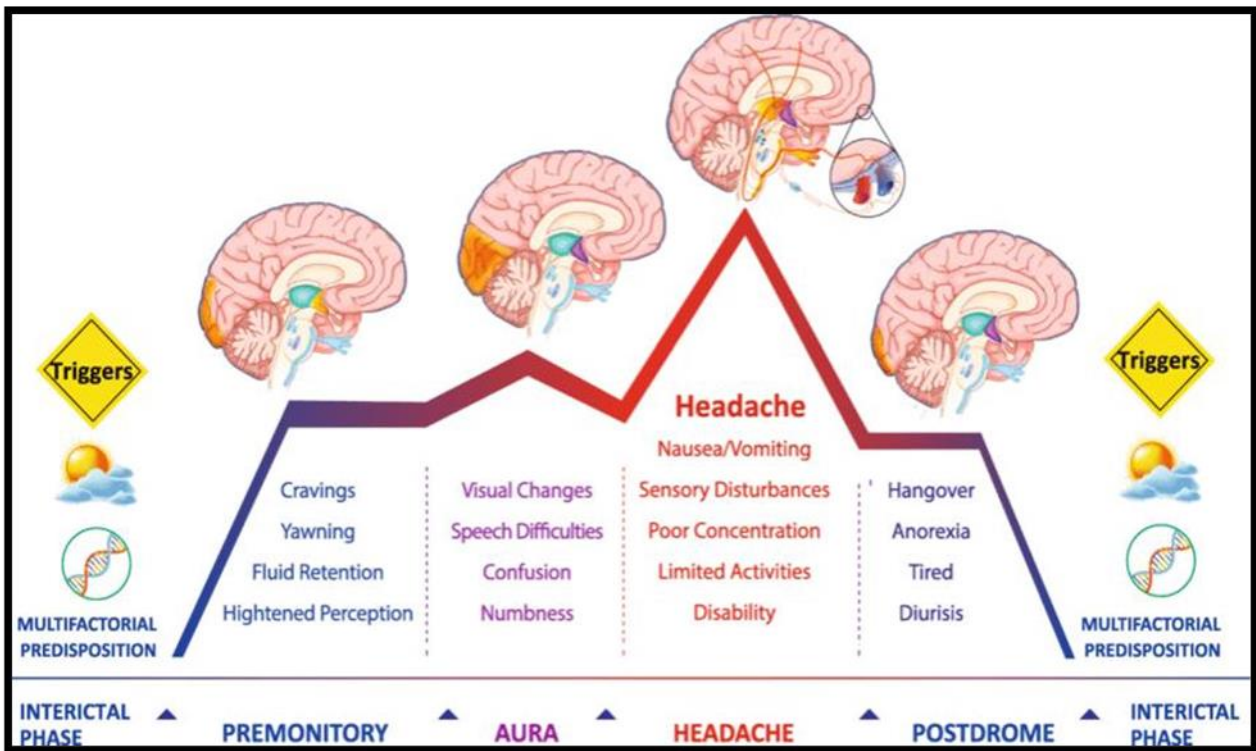


Figure 2 Phases of migraine

3. Mechanism of Migraine

3.1. Cortical spreading

Initiation: Migraine assaults frequently start with a wave of neuronal hyperactivity located by a length of inhibition, referred to as cortical spreading despair (CSD). This occasion movements slowly at some stage in the mind’s cortex and might motive air of thriller, a common pre-migraine symptom that includes seen disturbances and sensory modifications. results: CSD is idea to reason adjustments within the thoughts’s blood waft, as well as activation of pain pathways, specifically in regions just like the trigeminal nerve, which performs a primary function in migraine pain.[16]

3.2. Activation of the Trigeminal vascular system

The trigeminal vascular tool (TVS) consists of sensory neurons that innervate massive cerebral vessels, the dura mater (the outer masking of the thoughts), and pain-sensitive structures within the head.

procedure: - The CSD triggers the release of neurotransmitters consisting of calcitoninegene related peptide (CGRP), substance P, and different molecules from trigeminal nerve endings. those compounds purpose vasodilation (widening of blood vessels) and contamination inside the meninges, which contributes to the throbbing headache function of migraines.[17]

3.3. Neurogenic infection

the discharge of inflammatory mediators, like CGRP, results in the dilation of blood vessels and stepped forward vascular permeability. This reasons an inflammatory response known as neurogenic infection. quit end result: This inflammation sensitizes the trigeminal system and amplifies ache signals sent to the brainstem, in addition intensifying the headache phase of a migraine[18]

3.4. Fundamental Sensitization

extended or recurrent activation of ache pathways can lead to primary sensitization, in which neurons within the brainstem end up hypersensitive to stimuli.[19]

Genetic predisposition performs a role within the susceptibility to migraines. Mutations in certain ion channels and transporters have been associated with familial sorts of migraines. Environmental triggers which include strain, hormonal modifications, meals, and sensory stimuli can precipitate migraines in genetically inclined people.[17]

4. Treatment of migraine

4.1. Pharmacological treatment

- Analgesics: (OTC) medicinal drugs like aspirin, ibuprofen, and acetaminophen are usually used for slight to slight migraines.
- Triptans: these are a class of pharmaceuticals especially designed for migraines, along with sumatriptan and rizatriptan. Triptans work by way of stimulating serotonin receptors, decreasing irritation, and narrowing blood vessels over-the-counter mind. [19]
- Ergots: Ergotamine and dihydroergotamine (DHE) are used less often however may be effective in certain cases. They paintings similarly over the counter to triptans but are frequently utilized in extra severe assaults.
- Anti-nausea medicinal drugs: pills like metoclopramide or domperidone can assist with migraine related nausea. [18]]
- CGRP (Calcitonin Gene-associated Peptide) Inhibitors: more moderen drugs like Ubrogepant and Rimegepant goal CGRP, a protein worried in migraine pathways, and are used for acute relief.
- Antidepressants: Tricyclic Antidepressants (e.g., amitriptyline) or serotonin- norepinephrine reuptake inhibitors (SNRIs) may be powerful.
- Anticonvulsants: tablets like topiramate and valproate were found to lessen migraine frequency.
- CGRP Monoclonal Antibodies: - pills like erenumab and galcanezumab are newer alternatives specifically evolved for migraine prevention.
- Botox Injections: OnabotulinumtoxinA is approved for persistent migraine prevention, specifically in individuals who suffer from common migraines [19]

5. Novel Advanced Treatment of Migraine

Preventive migraine treatments are a valuable tool inside the Clinician's arsenal, Mainly for sufferers with better Migraine frequency contributing to Disability. That is specially real if the frequency of migraine and subsequent Common dosing with acute abortive remedies may additionally place sufferers prone to Medication overuse headache. Further, Preventive remedies have the Advantage of enhancing reaction to acute therapy [20]

Calcitonin Gene-associated Peptide Monoclonal Antibodies CGRP mABs are big molecules which are metabolized in the reticuloendothelial System. This metabolic pathway is beneficial for older patients as it avoids Interaction with most different medications. As a end result, the hepatic enzyme Induction or inhibition visible with gepants are left out With CGRP mAB use. Those treatments also are most often Dosed month-to-month or quarterly, which may also Resource with remedy compliance. There are four FDA-accredited CGRP mABs For the Prevention of migraine: erenumab, fremanezumab, galcanezumab, and Eptinezumab. All scientific trials so far comparing CGRP mABs have met their Primary endpoints. Erenumab, fremanezumab, and galcanezumab are Administered thru a self-administered subcutaneous injection.[20]

Herbal treatments: Ayurveda uses herbs like Ashwagandha, Brahmi, and Ginger, regarded for their and strain-lowering houses, to address migraine ache and decrease frequency. additionally, Vacha(Acoruscalamus) is used to relieve symptoms like nausea and vomiting

5.1. Panchratta remedy

This detoxifying technique gets rid of toxins and balances the body's doshas, assisting reduce migraine occurrences. Panchakarma consists of treatment options like oil massages and herbal steam bath Nasya therapy: This includes the utility of natural oils through the nostrils to detoxify and clean the sinuses, which facilitates save you migraine complications

5.2. Shirodhara remedy

A specialized remedy where warm oil is poured over the brow to calm the apprehensive device, imparting relief from migraines,[21]

6. Conclusion

pace of progress in the understanding of migraine is accelerating rapidly, and the direct translation of the results of basic migraine research into new treatments that specifically target migraine mechanisms is particularly gratifying. Improved understanding of genetic factors underlying migraine has the potential to tailor therapies to individuals with different genetic backgrounds. Characterization of the premonitory phase of a migraine attack and its underlying mechanisms provides an opportunity to treat a migraine attack at its very earliest stages, and could reveal new therapeutic targets, such as the hypothalamus. Neuromodulation approaches could enable physicians to specifically target novel central and peripheral migraine mechanisms, such as alterations in thalamocortical circuits, contributions of cervical nerve roots to migraine headache. The recognition of the key roles for neuropeptides, including CGRP and PACAP, and the development of therapies targeting these peptides or their receptors represent a promising new approach to migraine treatment. Now is a crucial time to maintain the momentum that has been established by recent basic and clinical research, and push forward towards safe, efficacious, and individualize.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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