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Review Article

Migraine – A Malady: A Short Review

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Abstract: Migraine is a mysterious disorder and much misunderstood condition characterized by pulsating headache, restricted to one side, in the form of attacks lasting from 4-48 hrs. Family, friends and work colleagues often find it difficult to understand how people who suffer from migraine can be fine in one minute and then have a deliberating headache the next. It is a complex neurological condition, which can effect the whole body and can result in many symptoms, sometimes without a headache at all. Two types of migraines are seen generally classical migraine – a migraine with an aura or warning and common migraine – a migraine without an aura. The pharmacological treatment of migraine may be acute or preventive. Frequent severe and long lasting migraine attacks require prophylaxis. The better knowledge about migraine pathophysiology led us to discuss new treatment options. Migraine can be diagnosed by the symptoms like intense headache, relentless, throbbing pain, inability to carry out daily activities etc. The majority of migraineurs who seek medical attention consult primary care physicians. Therefore, it is important for the generalist to be conversant with the diagnosis, prevention and treatment of migraine. However there are many ways to help in managing the condition and lessen its impact ultimately reducing the disruption caused to everyday life.
Keywords: Migraine, pulsating headache, classical migraine

INTRODUCTION

In general, a migraine is a very bad headache that tends to come back. It may occur as often as several times a week or only once every few years. It can last anywhere from a few hours to 3 days. The pain usually begins in the morning, on one side of the head. (In fact, the word migraine is derived from a Greek word that means "half-head.") Less frequently, the entire head is swallowed up by pain. The amount of pain can vary. Some migraines can be fairly mild, while others seem to be almost unbearable. Obviously, the worse the pain, the more trouble you have carrying out daily activities, whether it's going to work or simply getting out of bed. Of course, different people have different abilities to put up with pain. For some people, even a mild migraine can force them to lie down; others are able to work through a more severe migraine. Multiple threads of research over the last 15 years have led to the concept that migraine is generated from a hyperexcitable brain[1]. In fact, most people who think they suffer from sinus headaches may actually have migraine headaches. Other symptoms may include nausea and abdominal pain. You might vomit or have diarrhoea. That's why migraine is often known as a "sick headache." In addition, you may be very sensitive to bright lights, noises, and even smells when you have a migraine. Moving around, especially making rapid movements of the head can make your headache feel worse. An in-depth analysis of current thoughts on the pathophysiology of migraine is beyond the scope of this article; however, suffice it to say that the previous concept of migraine being a primary vascular phenomenon is untenable. The importance of serotonergic circuitry in the brainstem in the pathogenesis of migraine is now clear. Its perturbation can lead to not only intracranial and extracranial vasoconstriction and dilation, but also activation of pain receptors of the so-called trigeminovascular system. This knowledge will prove useful in comprehending the rationale behind migraine pharmacotherapy discussed below.

EPIDEMIOLOGY

Headache is a painful and common symptom. A number of primary headache disorders have been characterized, including tension-type headache, migraine and cluster headache, and overall these disorders account for approximately 95% of all headache complaints [2].

Worldwide, migraines affect nearly 15% or approximately one billion people. It is more common in women at 19% than men at 11%. In the United States, about 6% of men and 18% of women get a migraine in a given year, with a lifetime risk of about 18% and 43% respectively. In Europe, migraines affect 12–28% of

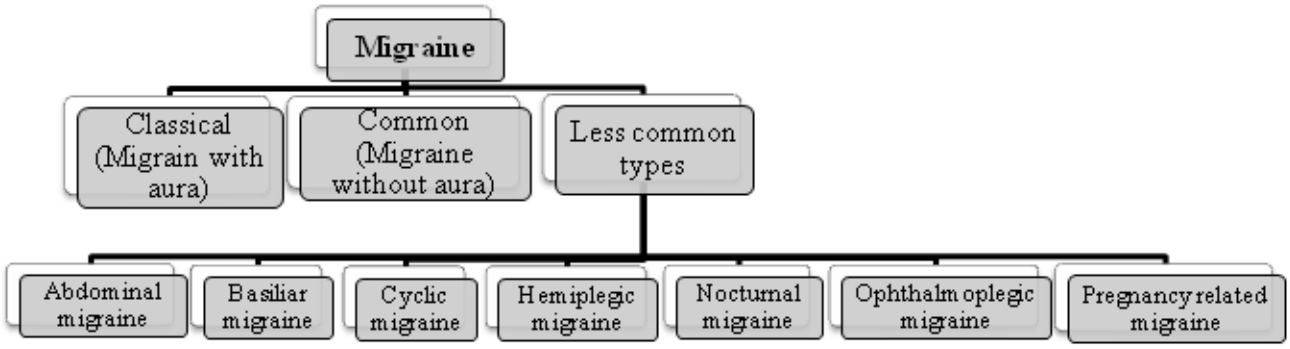
people at some point in their lives with about 6–15% of adult men and 14–35% of adult women getting at least one yearly[3].Rates of migraines are slightly lower in Asia and Africa than in Western countries. Chronic migraines occur in approximately 1.4 to 2.2% of the population.

There is scarcity of Indian data on the epidemiology of migraine. The prevalence of migraine is 17.6% in females and 6% in males in the US. In an urban headache clinic 47% of the patients were found to have migraine without aura and 4% migraine with aura. Indian data for the incidence of migraine with aura seem to be lower when compared with data from other parts or the world [4].

AETIOLOGY

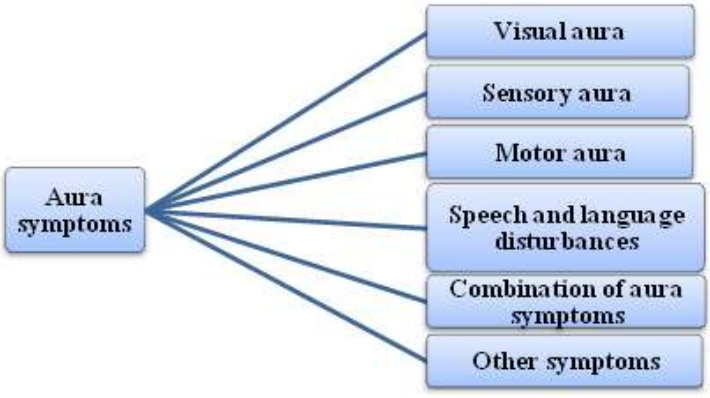
- Environmental triggers like Loud noises, bright lights, certain odours and perfumes
- Allergic reactions and allergies
- Psychological triggers like emotional stress
- Irregular sleep or changes in sleep pattern
- Alcohol consumption
- Physical triggers like birth control pills, menstrual cycle fluctuations,
- Food additives like monosodium glutamate (MSG), aspartame, phenylethylamine, nitrates, and tyramine. Also chocolates, citrus fruits, nuts, peanut butter, meat that has been cured or processed, large amount of aspartame (Nutra sweet) are some other examples for food triggers.
- Medication triggers includes vasodilators like glyceryl trinitrate(GTN), isosorbide dinitrate, Hormones (oral contraceptives, estrogens, clomiphene, danazol), Anti-hypertensives (nifedipine, captopril, prazosin, reserpine, minoxidil), H_2 blockers (cimetidine, ranitidine), Antibiotics (trimethoprim-sulfa, griseofulvin) and Selective Serotonin Reuptake Inhibitors like escitalopram, fluoxetine[5].

TYPES OF MIGRAINE



Classical migraine:

Classical migraine (migraine with aura) less number of migraine patients (20%) experiences the aura, which is the term of sign of occurrence of the pain. These can be described as the spots or the zigzag lines before the eyes associated with blurred vision. These symptoms go away usually within one hour and are replaced by a headache[6]. One or more fully reversible aura symptoms indicating brain dysfunction. At least one aura symptom develops gradually over more than 4 minutes or 2 or more symptoms occur in succession. No single aura symptom lasts more than 60 minutes. Headache follows aura with a free interval of less than 60 minutes (it may also begin before or with the aura). Most migraineurs with aura also have migraine without aura. Total duration of the aura is usually less than 1 hour. If the aura lasts more than 1 hour but less than 1 week, then it is ‘‘migraine with prolonged aura’’ (also termed ‘‘complicated migraine’’).



Common migraine:

Headaches begin without warnings in common migraine. This was mostly seen in children.

Headache has at least two of the following characteristics:

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

Less common types:

1. Abdominal migraine
   - Also known as periodic syndrome
   - Abdominal pain lasting for 1-72 hours along with nausea, vomiting, flushing or pallor.
2. Basiliar migraine
   - Pain arises from brain stem.
   - Symptoms like dizziness, double vision, tingling on both sides of body are seen in this type.
3. Cyclic migraine
   - Long lasting attacks (10 or more /month)
   - Careful monitoring of blood level and thyroid functioning is needed.
4. Hemiplegic migraine
   - Severe type of migraine causes temporary motor paralysis.
   - Sensory disturbances on one side of the body followed by headache.
5. Nocturnal migraine
   - Attacks during early in the morning or middle in the night often awaken patients from sleep.
6. 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.
7. 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 [16]:

(i) The trigger phase characterised by neuronal hyperexcitability,
(ii) The aura phase possibly involving cortical spreading depression and finally,
(iii) 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.

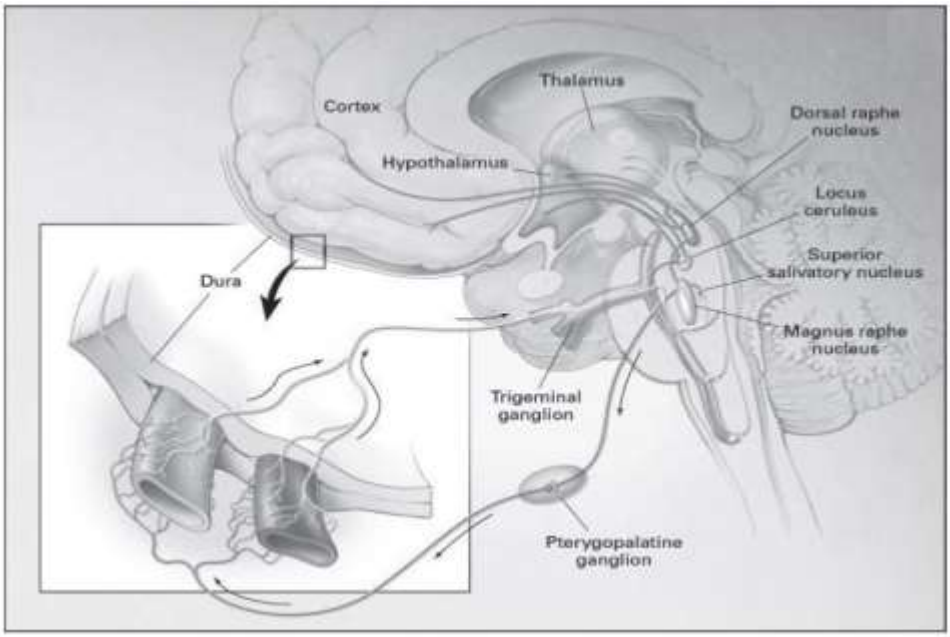


Fig-1: Pathophysiology of Migraine

Sensory fibres innervating the cranial vessels arise from trigeminal ganglion neurons that contain neuropeptides. Trigeminovascular inputs from dural 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 outflow that is in part mediated through the pterygopalatine (sphenopalatine) ganglion.

Several lines of evidence, including studies using positron emission tomography, indicate that brainstem structures, rather than cortical structures, are activated during a migraine attack. This activation remained unaffected after the resolution of the headache by sumatriptan treatment, suggesting that brainstem activation is a fundamental part of migraine. In addition, certain genetic abnormalities may be responsible for altering the response threshold to migraine-specific triggers in the brain, e.g. mutations of the P/Q-type calcium channel gene that plays an important role in familial hemiplegic migraine. The subsequent events following the trigger phase leading to the symptoms observed during the aura and headache phases can be explained on the basis of neurovascular involvement.

Up to 15-30% of migraine sufferers experience aura symptoms that last for 5 to 60 min before the onset of headache and may involve cortical spreading depression[7]. Cortical spreading depression is a wave of transient intense spike activity that spreads along the cortex slowly at rates between 2 and 6 mm min-1, possibly leading to a long-lasting neuronal inhibition. With the advent of non-invasive methods, including magnetic resonance imaging and magnetoencephalography[8], it has been shown that a wave of cortical spreading depression is followed by a decrease in regional cerebral blood flow. Most clinicians believe that the migraine aura is due to a neuronal dysfunction, probably resulting from cortical spreading depression[9], rather than ischemia.

Clinical and experimental considerations suggest that the pathogenesis of the migraine headache is intimately linked to the trigeminal innervations, which when activated possibly following cortical spreading depression, causes dilatation of cranial blood vessels, including arteriovenous anastomotic shunts[10]. The involvement of shunt vessels in migraine has once again attracted attention because patients with right to left cardiac shunts have been reported to have a high incidence of migraine headaches that are substantially reduced after shunt repair. Moreover, it is well known that patients with cranial arteriovenous malformations have a high incidence of migraine, which is reduced after correction of malformations [11-14]. Thus, migraine pain is due to activation of the nociceptors in intracranial structures, in concert with a reduction in the function of endogenous pain-control pathways. This nociceptive information from the cranial blood vessels is conveyed to central neurons in the trigeminal sensory nucleus that, in turn, relay the pain signals to higher centres, where headache is perceived. In addition, trigeminal pathways may get sensitized as well as release CGRP, thus reinforcing vasodilatation relaying the nociceptive impulses to the central nervous system[15].

TREATMENT

A. Pain relieving medications
B. Preventive medications
C. Home remedies

A. Pain relieving medications

1. Pain relievers – Ibuprofen, Acetaminophen
Combination of acetaminophen, aspirin and caffeine may ease moderate pain but are not effective for severe migraines. If taken for long periods, these can lead to ulcers, gastro intestinal bleeding and rebound headaches.

2. Triptans – Sumatriptan, Rizotriptan, Almotriptan, Zolmitriptan, Frovatriptan and eletriptan. Combination of sumatriptan and naproxen sodium (treximet) has proved effective in relieving migraine symptoms than individual medications.

3. Ergot – Combination of ergotamine and caffeine (migrergot, cafergot) are less expensive and also less effective than Triptans. They are most effective where pain lasts for more than 48hrs. Dihydroergotamine is more effective and has fewer side effects than ergotamine. It is also available as nasal spray and in injection form.

4. Anti-Nausea - Medication for nausea is appropriate and usually combined with other drugs. Metoclopromide or prochlorperazine are frequently prescribed medications.

5. Opiates - Narcotics, particularly codeine are sometimes used to treat migraine headache pain when people can't take ergots or Triptans.

6. Butalbital Combinations - Medications that combine the sedative Butalbital with aspirin/acetaminophen are sometimes used to treat migraine attacks. Some combinations also include caffeine or codeine.

B.Preventive Medications

1. Cardiovascular drugs - Anti-hypertensive medications like lisinopril, candesartan are useful in decreasing the frequency and severity of migraines. β-blockers and calcium channel blockers like verapamil are also used.

2. Anti-depressants - Tricyclic antidepressants like amitriptyline, nortriptyline and protriptyline are most effective in preventing certain headaches including migraines. They act by affecting the level of serotonin and other brain chemicals.

3. Anti-seizure drugs – Divalproex and topirmate and gaba-pentene reduce the frequency of migraines.

4. Cyproheptadine - These anti histamines specifically affect the serotonin activity. Physicians sometimes give it to children as a preventive measure.

5. Botulinum Toxin - It is used as treatment for chronic migraines. Injections are made in the muscles of forehead and the neck. When this is shown to be effective, the treatment typically needs to be repeated every 3 months.

C. Home remedies

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

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