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MIGRAINE: AN OVERVIEW

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ABSTRACT

A migraine is a severe throbbing pain or a pulsing sensation which is mostly on the one side of head. It can cause significant pain that last for hours to days or it is a primary headache disorder characterize by recurrent headaches that are moderate to severe. There are mainly four stages of migraine attack i.e. Aura, pro-drome, headache and postdrome. Prodrome occurs before two days of headache which includes constipation, increased thirst and urination and frequent yawning. Aura occurs before or in between migraine or occurs by touching sensation or speech disturbance. Post–drome occurs after a migraine attack and is a final phase. In this, person experience confusions, moodiness, dizziness, weakness. It is a complex neurological condition, which is caused by decreased levels of serotonin in brain and mainly affects the whole body. There are six type of medications for the treatment of migraine or migraine associated with vertigo or dizziness. But clinical trial found benefit most from the use of sumatriptans (IMITREX) for treatment of all type of migraine. The other five medications study showed marginal improvement in the treatment of migraine and its associated problems these include: aspirin, dihydroergotamine (DHE), propanolol, amitriptyline and valproate. Ergots like ergotamine are used but are less effective than triptans and dihydroergotamine is more preferred one for i.v administration as it is less hazardous and more effective. In conclusion, migraine can be effectively treated with sumatriptans as this drug can reduce the symptoms or pain of migraine or headache within two hours.

KEYWORDS: Migraine, Vertigo, Dizziness, Headache, Pain.

INTRODUCTION

A migraine is a severe throbbing pain or a pulsing sensation which is mostly on the one side of head. It can cause significant pain that last for hours to days or it is a primary headache disorder characterize by recurrent headaches that are moderate to severe. Migraine is more than "just a headache". It is a complex neurological condition, which can affect the whole body and can result in many symptoms.[1]

Migraine is a common clinical problem characterized by episodic attacks of head pain[2] and associated symptoms such as nausea, sensitivity to light or head movement. It is generally thought of as a headache problem. Migraine is an inherited problem of ion channels in brain. Migraine is a lifelong problem.[3] It starts in childhood and disappears and reappears in new forms throughout an individual's life.

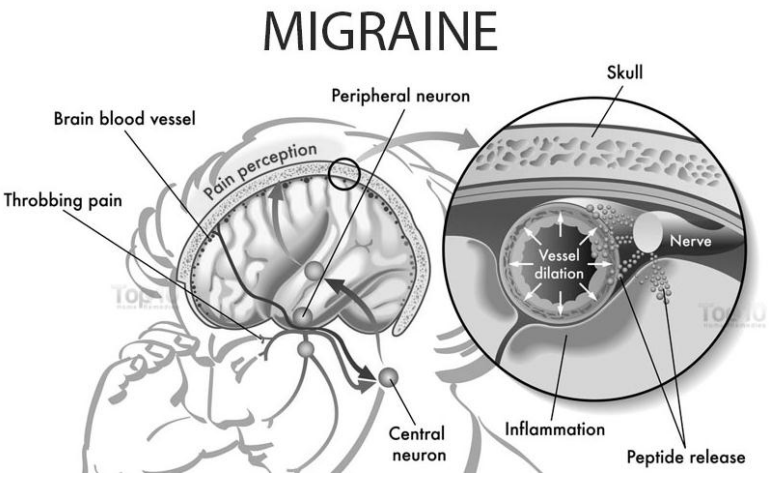


Figure 1: Mechanism of Migraine.

Most individuals exposed to loud noise and light which stimuli the pain within minutes in magraine patients. The strength of stimulus continues to grow and a migraine crisis can occur. Patients have migraine headache or other migraine symptoms may be due to less or lack of adaptability towards strong sensory stimulation. On the basis of prevalence studies of migraine headache in Canada, there is a wide variation in both adult men (1-9%) and in women (3-29%).[4] This is based upon the cause of migraine or the symptoms that arises in migraine i.e. four stages.

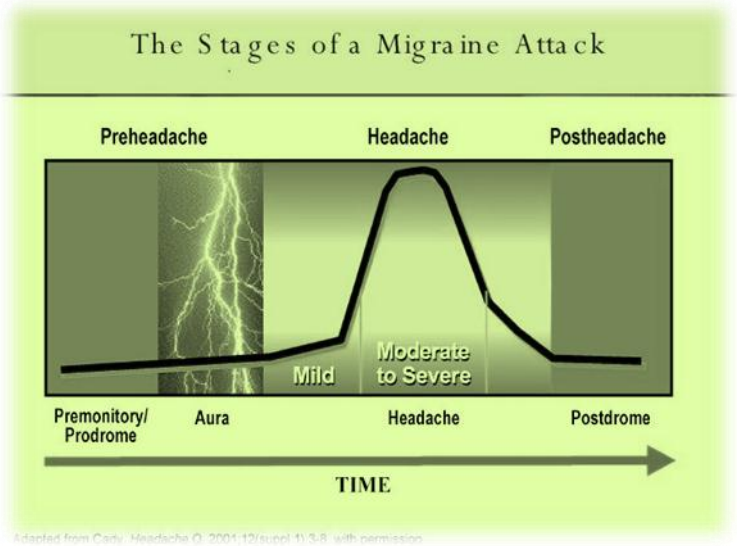
1. Prodrome
2. Aura
3. Headache
4. Post-drome

Prodrome occurs before two days of headache. it is known as warning stage. It includes constipation, increased thirst and urination and frequent yawning. and can last up to 48 hours before attack.[5]

Aura occurs before or in between migraine or occurs by touching sensation or speech disturbance. This part of attack last up to one hour and usually precedes the headache. In this, person feels vision loss, weakness, difficult speaking and numbness.

Headache The main stage of attack. A headache will often be present along with other symptoms such as nausea or vomiting and can last between 4 to 72 hours.[5]

Post – drome occur after a migraine attack and is a final phase. In this person experience, confusions, moodiness, dizziness, weakness. The pain gradually eases or may disappear, but feeling of lethargy or being washout may remain.



Path physiology/ cause of Migraine

It can be caused by changes in the brain stem and its interaction with trigeminal nerve a major pain pathway.[6] Imbalance in brain chemicals includes serotonin which helps to regulate pain in nervous system. During migraine attack serotonin level decreases that cause trigeminal nerve to release substance called neuropeptide which travel to brain's outer covering (mennings) this results in migraine attacks or pain.[6]

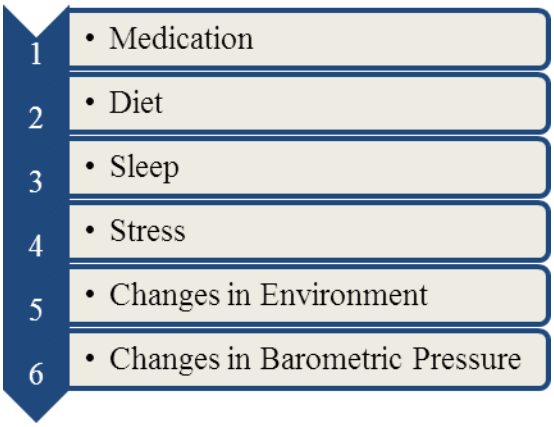


Figure 2: Causes of Migraine.

This is proposed patho physiological mechanism in generation of migraine headache. This evidence indicates that cortical spreading depression (CSD) is most primarily event in trigeminovascular system (TGVS) activation in migraine with Aura and also migraine without aura. Dysfunctional brainstem nuclei involve central control of pain by favoring central trigeminal hyper excitability. Abnormal cortical activity lead to CSD or other triggering factors. The relation between abnormal cortical activity and abnormal brainstem function remain hypothetical and unclear.

There is another theory i.e. vascular theory which suggests that migraine result from the widening of blood vessels around the brain. The chemical serotonin plays an important role in cause of migraine. While the precise cause of migraine is unknown, a number of potential migraine triggers have been identified.

Symptoms of migraine

For most people the main feature of a migraine is a painful headache. However there are other symptoms that can prevent an individual form continuing with daily life and these can occur with or without headache. Following symptoms include.

i) Intense throbbing headache often on one side of head only.
ii) Nausea /vomiting or experience diarrhea.
iii) Increased sensitivity to light, sound, or smells.
iv) Neurological symptoms that include visual disturbances.
v) Other common aura symptoms include: tingling or pins and needles in limbs, paralysis or loss of consciousness. Although normally, last between 4 and 72 hours.[7]

Each migraine sufferer has his or her individual triggers. Migraine can be triggered[5] by.

a. foods such as cheese, tea, coffee, nuts etc).
b. Strong odors such as perfumes.
c. Bright lights.
d. Loud noises.
e. Change in weather.
f. Stress.
g. Sleeping more or less usual.
h. Due to certain medications.

Treatment/ Medications

Many choices of medications for acute and preventive treatment of migraine have grown in response to advance in understanding of migraine patho physiology. Many studies have been done but then also there is urgent need for specific and more potent agents, along with further investigation for withdrawal side effects of migraine.[2]

There are many medicines that are used to treat migraine. Some drugs may help to relive or prevent migraine. Two broad categories of medications includes.

1. Pain relieving medications.
2. Preventive medications.

Pain relieving medications include

Most of the migraine attack treated by the painkillers bought over the counter, such as aspirin (900mg) and ibuprofen (400mg). It is important to take these painkillers at first sign of attacks. As painkillers are soluble and start to work more quickly. These painkillers are taken for 15 days or for a month during migraine attack.

i) **Aspirin**: it may help relieve mild migraine. dose; 900mg for 15days and for a month.

ii) **Triptans**[7]: these block or constrict blood vessels or pathway in brain. Medication include Sumatriptans (IMITREX), Rizatiptans (MAXALT). as these are selective serotonin 5-HT 1B and 1D receptor agonist producing second order brainstem neuronal inhibition, 6mg (sc)injection of sumantriptan appears to be most efficacious dosage. Triptans are considered first-line treatment for acute management of moderate to severe migraine pain. These are combined with NSAIDS or antiemetic drugs.

iii) **Ergots:** Like ergotamine are used but are less effective than Triptans and dihydroergotamine is more preferred one for i.v. administration as it is less hazardous and

more effective. Dihydroergotamine (DHE) is currently widely available ergot alkaloid. 0.5mg to 1mg repeat in 1 hour is usually administered.

Preventive medications include

i) **β-adrenergic blocker:** Propanolol is most commonly used and reduce upto 70% of attacks of patients and recommended as first-line migraine therapy. It is used as a first choice treatment of migraine with aura. In some cases, timolol is also preferred**.**[6]

ii) **Tricyclic depressants:** like Amitriptyline has been used extensively which help in reducing attacks of migraine. Multiple of antidepressants are used in migraine Prophylaxis. Amitriptyline blocks neuronal uptake of serotonin levels which result in various side effects.

iii) **Anticonvulsants:** Valproic acid has some prophylactic effect in migraine. By this medication 50% reduction in attacks of migraine has been noticed. Valproate or divalproex sodium used in treatment of migraine or in epilepsy. A migraine patient with coexisting bipolar disorder favor to get treated with valproate. Topiramate was originally introduced as an anticonvulsant and used in prophylaxis of migraine treatment (100-200 mg), is being studied in chronic migraine prevention.[8]

DRUGS USED TO TREAT MIGRAINE

Migraine is a severe throbbing pain or it is a primary headache disorder characterize by recurrent headaches that are moderate or severe. Therefore, there are many drugs that are used to treat migraine.

Various drugs used in the treatment of migraine are categorized into following categories.[9] All the drugs are categorized on the basis of their mechanism of action.

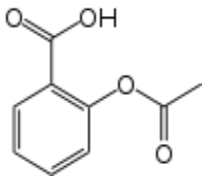
[A] Drugs used as pain killers or pain relieving.

[B] Drugs used as preventive.

[A] Drugs used as pain killers or pain relieving

These include; Aspirin, Triptans, Ergots derivatives.

Aspirin: Aspirin is non-selective and reversibly inhibit both COX-1 and COX-2.[10] Normally COX produces prostaglandins, most of which are pro-inflammatory and thromoboxanes, which promote clotting. The mechanism of aspirin is analgesic, anti inflammatory and anti-pyretic and aspirin relieved pain by acting on central nervous system.



Structure: 2-(acetyl oxy) benzoic acid.

Uses

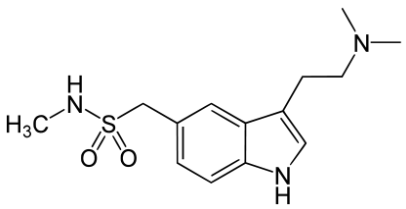
Aspirin, either by itself or in a combined formulation, effectively treats certain types of headache. Aspirin or other analgesic over - the-counter is widely used as effective for treatment of tension headache.[11]

Aspirin considered being a first-line therapy in the treatment of migraine.

Triptans: Their action is contributed to their agonist effects on serotonin 5-HT (1B) and 5-HT (1D) receptors in blood vessels. Triptans[12] have at least two mode of action.

i) Vasoconstriction of pain producing intra cranial vessels by their direct effect on vascular smooth muscles. Sumatriptans have been shown to cause vasoconstriction in humans.
ii) Inhibition of nociceptive neurotransmission with in trigeminocervical complex in the brain stem.

Structure

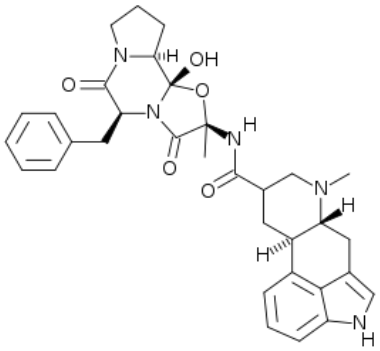


Uses: Triptans are used for the treatment of severe migraine attacks. these are a mild-line treatment suitable for migraine patients with typical attacks. Triptans are effective in reducing the attacks within 30 to 90 minutes in 70-80% patients.[13] Oral Rizatriptans and Nasal zomitriptans are the mostly used for migraine in children's.

Side effects: The most common side effect is recurrence of migraine and after taking Triptans various heart disease or cardiac events can occur.

Ergots: Dihydroergotamine (DHE) is a semi-synthetic form of ergotamine is administered as a nasal spray or injection and has action similar to that of Triptans. It acts as an agonist of

serotonin 5-HT (1d) receptors and causing vasoconstriction of blood vessel. But also interacts with dopamine and adrenergic receptors. Nausea is a common side effect of DHE.[14]



Dihydroergotamine

Uses

It is used to treat acute intractable headache or withdrawal from analgesic. Intravenous injection is considered to very effective for treatment of severe migraine. DHE is also used in the treatment of medication overuse headache.

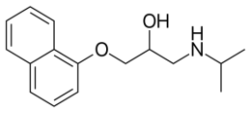
[B] DRUGS USED AS PREVENTIVE

These include

1. β-adrenergic blocker.
2. Tricyclic antidepressant.
3. Anticonvulsant.

These categories are explained as follow.

β-adrenergic blocker: It include propanolol[14] which is a non-selective beta blocker, as it blocks the action of both β1 and β2 adrenergic receptors. It has little intrinsic sympathomimetic activity. Both enantiomers have local anesthetic effect which is mediated by blockade of voltage-gated sodium channels.



(RS)-1-(1-methylethylamino)-3-(1-naphthyloxy)propan-2-ol.

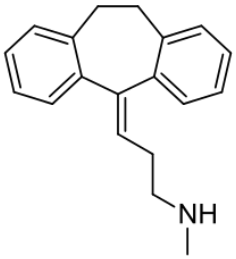
Uses

It is being used in treatment[15] of hypertension and also used to treat anxiety. It is also being used to prevent migraine and cluster headache disorder and in primary exertional headache. It is also used to treat glaucoma and proliferating (excessive sweating) and essential tremors of brain.

Side effects

Due to high penetration across the blood-brain barrier, lipophilic beta blocker causes sleep disturbances, insomnia and vivid dreams and nightmares.

Tricyclic antidepressant: Amitriptyline[16] acts primarily as a serotonin-nor epinephrine reuptake inhibitor, with strong action on serotonin transporter. Therefore does not affect dopamine reuptake, being nearly 1,000 times weaker than on serotonin. It is metabolized to neither nortriptyline- a more potent and selective nor epinephrine reuptake inhibitor.



Amitriptyline

Uses

Amitriptyline is used to treat[17] number of medical conditions like major depression disorder. It is also effective more to antidepressant and it is rarely used as first line drug for depressants. It is also used to prevent migraine and is most widely researched agent for prevention of frequent tension headache.

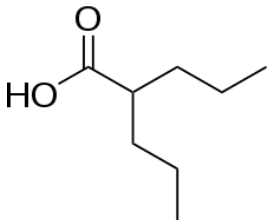
Side effects

Common side effects include dizziness, headache, weight gain, delirium and confusion. Mood disturbance include an anxiety and agitation. Other side effect include impotence, sleep disturbance such as drowsiness, insomnia and nightmares.

Anticonvulsants

These drugs used to treat seizures[18] disorders and but their mechanism is not known but it is recently studied that it is used again a seizure-induced reduction in phosphatidylinositol

(3,4,5)-trisphosphate(PIP_3) as a potential therapeutic mechanism. it is also being effective in blockade of voltage-dependent sodium channels and increased brain levels of (GABA).



2-propylpentanoic acid.

Uses

Valproate[19] (VPA) are medications primarily used to treat epilepsy and bipolar disorder and to prevent migraine headache. It is useful for the prevention of seizures in those with absence seizures, partial seizures, and generalized seizures. It can be given intravenously or by mouth.

Side effects

- nausea
- drowsiness
- dizziness
- weakness
- vomiting
- low body temperature
- Bleeding.

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