

REVIEW ARTICLE

Headache, Primary Headaches and Their Treatment

¹Rita Upadhyay, ²Mayank Chansoria, ³Mamta Mahobia, ⁴Neha Vyas

ABSTRACT

Introduction: Headache is a symptom which may be associated with a variety of clinical conditions whether the underlying disorder be organic, psychologic or psychophysiologic. Headache disorders can be classified as primary, secondary and specific types of headache.

Patients usually present with primary headache in primary health care settings. More than one type of primary headache may be present in one patient and each headache has to be treated separately. Migraine is the most common severe primary headache disorder.

Conclusion: Every presentation of headache requires care to exclude organic disease, and every presentation provides the opportunity to relieve suffering.

Keywords: Headache, Migraine, Prophylactic therapy.

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INTRODUCTION

Headache is a symptom which may be associated with a variety of clinical conditions, whether the underlying disorder be organic, psychologic or psychophysiologic. Headache disorders can be classified as primary, secondary, and specific types of headache. An underlying pathology is not present in primary headache. Examples include migraine, tension-type, and cluster headache. Secondary headache disorders are associated with an underlying pathological condition and include any head pain of infectious, neoplastic, vascular, or drug-induced origin.¹ Depending on the severity of the headache, there are two types of treatments: (1) Acute treatment refers to medication, i.e., taken to relieve the pain instantly and (2) preventive treatment refers to the medicines which are taken in regular basis to prevent future attacks of

headache for all types of headaches like chronic daily headache (CDH), tension type headache, etc. Short-term treatments done by analgesics, such as aspirin, acetaminophen, triptans, etc. Anti-depressants, verapamil, etc., are used for preventive treatment. Physical therapies like acupuncture, etc., and a healthy lifestyle can also help. Patients usually present with primary headache in primary health care centers. More than one type of primary headache may be present in one patient and each headache has to be treated separately.² Patients rarely present with secondary headache. In primary headache, findings on neurological examination are usually normal and investigations are not helpful for diagnosis.^{3,4} For evaluation of headache, patient's history is most important.^{4,5} Patients may suffer from more than one type of headache. Migraine is the most common severe primary headache disorder.^{6,7} A migraine headache is characteristically unilateral pulsating builds up over minutes to hours moderate to severe in intensity associated with nausea and/or vomiting and/or sensitivity to light and/or sensitivity to sound disabling aggravated by routine physical activity.² Aura is important in classification of migraine. A typical aura comprises fully reversible visual and/or sensory and/or dysphasic speech symptoms. Symptoms may be positive, such as flickering lights, spots, zigzag lines, tingling and negative, such as visual loss, and numbness. Evolution over 5 minutes with gradual resolution around 60 minutes is characteristic symptom.² Different aura symptoms may occur in succession. A transient ischaemic attack should be considered if the aura has a very rapid onset, there is simultaneous rather than sequential occurrence. Prolonged aura should raise the possibility of a secondary cause.^{8,9} Aura may occur without headache. Chronic migraine is classified as migraine occurring on 15 or more days per month for more than 3 months daily. One to two per month is median frequency.¹⁰ In chronic migraine the headache may have features more typical of tension-type headache. Headaches with reliable triggers and patterns, such as perimenstrual exacerbation with relief during pregnancy are likely to be migrainous. It is also typical to notice relief of the headache after sleep.^{2,11}

MIGRAINE TREATMENT

Pharmacological and other data point to the involvement of neurotransmitter 5-hydroxytryptamine (5-HT). It is

¹Senior Resident, ^{2,3}Associate Professor, ⁴Consultant

¹⁻³Department of Anesthesia, Neta Ji Subhash Chandra Bose Medical College, Jabalpur, Madhya Pradesh, India

⁴Department of Anesthesia, Sukh Sagar Medical College, Jabalpur Madhya Pradesh, India

Corresponding Author: Rita Upadhyay, Senior Resident Department of Anesthesia, Neta Ji Subhash Chandra Bose Medical College, Jabalpur, Madhya Pradesh, India, e-mail: ritaupadhyay10@yahoo.com

also known as serotonin in migraine.¹² Methysergide was introduced as first drug which prevented migraine. Its mechanism was found to antagonize peripheral actions of 5-HT. Antagonists of 5-HT_{1B}, 5-HT_{1D} and 5-HT_{1F} receptors are triptans and they are less potent at 5-HT_{1A} receptor. A growing body of data indicates that antimigraine efficacy of the triptans relates to their ability to stimulate 5-HT_{1B/1D} receptors, which are located on both blood vessels and nerve terminals. It has now been shown that selective 5-HT_{1F} receptor activation, which has purely neural effect, can terminate acute migraine. Dopaminergic stimulation induces most of migraine's symptoms. There is dopamine receptor hypersensitivity in patients suffering from migraine, as demonstrated by induction of yawning, nausea, vomiting, hypotension, and other symptoms of a migraine attack by dopaminergic agonists at doses that do not affect non-migraineurs. Dopamine receptor antagonists are effective in treatment of migraine, especially when used with other antimigraine agents and given intravenously. Migraine disability assessment score is a well validated, easy to use tool. It is helpful for patients to understand that migraine is an inherited tendency to headache; and migraine can be controlled and modified by lifestyle adjustments and medications but it cannot be eradicated.

Nonpharmacological Management

Nonpharmacological approaches are also effective in managing migraine. Avoidance of specific headache triggers is important in prevention of migraine attacks. A healthy lifestyle which includes regular exercise, regular sleep pattern, avoidance of excess caffeine and alcohol, and avoidance of acute stress is helpful. Stress response can be decreased by yoga, transcendental meditation, hypnosis and conditioning techniques, such as biofeedback. This approach is an adjunct to pharmacological treatment.

Management of Acute Attack of Migraine

Oral agents can be used to manage mild migraine attacks. Nearly 50 to 70% is the average efficacy rate. Parenteral therapy may be required in severe migraine attacks. Classes of drugs effective in the treatment of migraine are: Anti-inflammatory agents, 5-HT_{1B/1D} receptor agonists and dopamine receptor antagonists. There is no standard approach for treatment of all migraine patients and, therefore therapy needs to be individualized.

Nonsteroidal Anti-inflammatory Drugs

Both the severity and duration of a migraine attack can be reduced significantly by NSAIDs, such as ibuprofen,

naproxen, tolfenamic acid, etc. A general consensus is that NSAIDs are most effective when taken early in the migraine attack. Dyspepsia and gastrointestinal irritation are important side effects of NSAIDs.

5-hydroxytryptamine Receptor Agonists:

Oral: Nonselective receptor agonists are ergotamine and dihydroergotamine, while selective 5-HT_{1B/1D} receptor agonists are triptans. A variety of triptans,¹³ 5-HT_{1B/1D} receptors agonists—naratriptan, rizatriptan, eletriptan, sumatriptan, zolmitriptan, almotriptan, and frovatriptan are now available for treatment of migraine. Monotherapy with a selective oral 5-HT_{1B/1D} agonist does not result in rapid, consistent, and complete relief of migraine in all patients. Triptans are not effective in migraine with aura unless given after the aura is completed and headache initiated. 5-HT_{1B/1D} agonists should not be used in individuals with a history of cardiovascular and cerebrovascular disease. Ergotamine preparations offer a nonselective means of stimulating 5-HT₁ receptors. Dose of ergotamine, which do not cause nausea, should be used as the nausea-provoking dose which is very high and may intensify headache. Except for a sublingual formulation of ergotamine, oral formulations of ergotamine also contain 100 mg caffeine. The average oral ergotamine dose for a migraine attack is 2 mg. In general, ergotamine appears to have a much higher incidence of nausea than triptans, but less headache recurrence.

Nasal: The fastest acting nonparenteral antimigraine therapies that can be self-administered include nasal formulations of dihydroergotamine, zolmitriptan and sumatriptan. The nasal sprays result in substantial blood levels within 30 to 60 minutes.

Parenteral: Parenteral administration of drugs, such as dihydroergotamine and sumatriptan is approved by the food and drug administration for the rapid relief of a migraine attack.

Prophylactic Therapy (Preventing Future Headaches)

The treatment of recurrent headaches begins with the interview, not with the prescription. Patient satisfaction with the initial consultation predicts success better than any other specific intervention.¹⁴ One study showed that patients referred to a neurology clinic were more interested to have an explanation of the causes of their headache than to receive treatment.¹⁵ Physicians also should focus on the lifestyles of the patients: A correlation of headaches with "daily hassles" has been documented.¹⁶ Regular exercise and stress reduction (through biofeedback, meditation, and so on) help the patient become an active participant in the management

of his or her headaches. Physicians should understand that withdrawal of medication is required in treatment of daily rebound headache. For prophylaxis, tricyclic antidepressants are a good first choice for young people with difficulty falling asleep; verapamil is often a first choice for prophylaxis in the elderly.

Most common primary headache is tension type headache (TTH) and it is common in all ages. The pain is generally not as severe as in migraine.⁷ The pain is characteristically pressing or tightening in quality, typically bilateral and mild to moderate in intensity. Nausea absent and the headache is not intensified by physical activity. Pericranial tenderness, sensitivity to light or sensitivity to noise may be associated with headache. Episodic tension-type headache occurs in episodes of variable duration and frequency. Chronic tension-type headache (CTTH) occurs on more than 15 days per month for more than three months.^{2,7}

Tension-type Headache Treatment

Pain can be managed generally with simple analgesics, such as acetaminophen, aspirin, or NSAIDs. Often related to stress; responds to behavioral approaches including relaxation. Amitriptyline may be helpful for CTTH (>15 days per month) prophylaxis. Many experts believe that TTH and migraine form a continuum and cannot be readily distinguished.¹⁷ For example, features that accompany migraine, such as unilateral headache, throbbing-pain, nausea, or photo- and phonophobia, are occasionally seen in TTH, while neck muscle tenderness may be seen in migraine patients.¹⁸ Many patients do have both migraine and TTH.

Pathophysiology of Migraine and TTH

The current understanding of migraine origin has evolved from vascular models¹⁹ to a trigeminovascular model,^{20,21} toward a central neuronal model of migraine as a disturbance of the serotonergic system of the mid-brain.²² The concept of a "migraine generator" refers to activation of dorsal raphe nucleus of midbrain.²³ Midbrain has receptors for serotonin (5-hydroxytryptamine, or 5-HT).²⁴ Specific medications and all drugs, which prevent migraine attack or treat it, influence serotonin pathway.²⁵ Vascular changes are secondary phenomenon in migraine and not causative.

Headaches are also commonly believed to have a psychological basis, but related studies have had varying results. People with high level of anxiety or depression are affected by migraine as shown in many studies.²⁶ In one study, however, the Minnesota Multiphasic Personality Inventory patterns of patients with migraine headaches were normal; those of patients with tension

type headache or combined migraine-TTH were moderately abnormal (indicating "neuroticism"); and those of patients with posttraumatic headache (daily headache following trauma) were abnormal.²⁷ Trigeminal autonomic cephalalgias (TACs) are rare and are characterized by attacks of severe unilateral pain in a trigeminal distribution. Prominent ipsilateral cranial autonomic features are associated with TAC. Cluster headache (CH) is the most common TAC. Paroxysmal hemicrania (PH) is not recognized much.^{2,28} It includes Short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing and short-lasting unilateral neuralgiform headache attacks with cranial autonomic symptoms, which are very rare.

Cluster Headache Treatment

A rare form of primary headache²⁹ which is characterized by episodes of recurrent, deep, unilateral, retro-orbital searing pain. Unilateral lacrimation and nasal and conjunctival congestion may be present. Rare complaints are visual, nausea, or vomiting. Patients with CH are uneasy and move about during attacks unlike migraine. A core feature is periodicity. Typically, daily bouts of one to two attacks of relatively short-duration unilateral pain for 8 to 10 weeks a year; usually followed by a pain-free interval that averages a little less than a year. Alcohol may provoke attacks. Prophylaxis with verapamil (40–80 mg twice daily to start), lithium (400–800 mg per day), or prednisone (60 mg per day for 7 days followed by a taper over 21 days). For acute attack, High-flow oxygen (10–12 L/min for 15–20 min) or sumatriptan (6 mg SC or 20 mg nasal spray) is effective.³⁰ Deep-brain stimulation of the posterior hypothalamic gray matter is successful for refractory cases as is the less-invasive approach of occipital nerve stimulation. Hemicrania continua is a continuous, strictly unilateral headache that waxes and wanes. Brief stabbing pain may be superimposed on the continuous headache and may be accompanied by ipsilateral autonomic features. While it is rare, it is an important diagnosis to consider as there is an absolute response to indomethacin.^{2,28} Patients with a new suspected hemicrania continua should be referred for specialist assessment.

Chronic Daily Headache, Drug Rebound Headache

Drug rebound headache is referred to as an unrecognized epidemic.³¹ A low-grade daily headache, which may become severe at times and have migrainous features is CDH. Mathew³² described the transformation of episodic migraine into a daily headache. Drug rebound headache

is more common when using ergotamines, narcotics, and products that combine caffeine with aspirin or acetaminophen.^{33,34} Even patients who take as little as 1000 mg per day of aspirin or acetaminophen may develop drug rebound headache.³⁵ Many clinicians believe that the frequency of use is most important, and they limit the use of all symptomatic medication to two days a week. Withdrawing the causative medication is proper treatment of drug rebound headache. The addition of prophylaxis without withdrawal of the offending medication is a futile gesture. In pharmacologic treatment, attempt is made to do one or more of the following:

- Raise the pain threshold,
- Interrupt the mechanism producing pain,
- Reduce the emotional tension and anxiety associated with the pain.

New Daily Persistent Headache

Headache, i.e., daily and unremitting from onset is classified as new daily persistent headache.² It is essential to consider secondary headache and allow 3 months to elapse before a diagnosis of primary new daily persistent headache can be made. New daily persistent headache can have any phenotype. Secondary headaches to consider are subarachnoid *hemorrhage* (SAH), meningitis, raised intracranial pressure, low cerebrospinal fluid pressure, giant cell arteritis, and post-traumatic headache.³⁶

Indomethacin Responsive Headaches

Physicians should base their selection of symptomatic medication on the past experience of the patient; the severity of the headache; associated symptoms; and side-effect profiles. Aspirin and NSAIDs, such as ibuprofen³⁷ or naproxen³⁸ are effective for the most milder headaches, although they often require high doses.³⁹ Dosage, timing, mode of administration, tolerance, influence of pathological states, cumulative action and individual idiosyncrasy of the patient are factors of great importance. A diverse set of disorders that respond often exquisitely to indomethacin (25 mg 2 to 3 times daily), includes:

Paroxysmal hemicrania: Frequent unilateral, severe, short-lasting episodes of headache that are often retro-orbital and associated with autonomic phenomena, such as lacrimation and nasal congestion.

Hemicrania continua: Moderate and continuous unilateral pain associated with fluctuations of severe pain that may be associated with autonomic features.⁴⁰

Primary stabbing headache: Stabbing pain confined to the head or rarely the face lasting from 1 to many seconds or minutes.

Primary cough headache: Transient severe head pain with coughing, bending, lifting, sneezing, or stooping and lasts for several minutes. Usually benign, but posterior fossa mass lesion in some patients; therefore, consider Brain MRI.

Primary exertional headache: Features similar to cough headache and migraine, but precipitated by any form of exercise. Is it a “worrisome” headache? Both patients and physicians fear the possibility of headache as a symptom of brain tumor or hemorrhage. The “classic” brain tumor headache, which is worse in the morning, worse with Valsalva maneuvers, and associated with nausea and vomiting, is uncommon. Rather, the brain tumor headache lacks diagnostic features, is often mild and intermittent, and resembles a TTH.⁴¹ In series of patients studied with modern neuroimaging, only 30⁴² to 50%⁴¹ of brain tumor patients complained of headache. A review of the neuroimaging of 897 patients with migraines noted only four with abnormal scans (three tumors and one arteriovenous malformation).⁴³ Of these four, one tumor was incidental (the migraines continued after surgery) and two patients had seizure disorders. These findings led the American Academy of Neurology to recommend that imaging is not warranted in patients with stable migraine who have no history of seizures and no neurologic signs or symptoms. Recommendations for imaging TTHs were not made because of insufficient evidence. Unlike the dilemma of chronic headaches, the sudden onset of what a patient refers to as the “worst headache ever” is well recognized as a symptom of SAH. However, only two-thirds of patients with a SAH present with a headache.⁴⁴ Neck pain and nausea are the other common symptoms. The accuracy of computed tomography (CT) in finding such a hemorrhage falls to 58% by day 5 and is 92% on the 1st day.⁴⁵ Some patients with a sudden, severe headache called a “thunderclap headache” and normal CT and lumbar punctures have been found through angiography to have an aneurysm.⁴⁶

CONCLUSION

Every presentation of headache requires care to exclude organic disease, and every presentation provides the opportunity to relieve suffering.

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