Migraine: Diagnosis and Prophylactic Management

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Abstract

Migraine is the most common type of vascular headache characterized by recurrent attacks of headache, which typically lasts for 4 to 72 hours. Recurrent attacks of migraine affect the patients' quality of life, social activities and family life. Migraine is recognized as a major cause of disability worldwide. Migraine was cited as the 19th leading cause of years lived with disability (YLD) among both males and females of all ages combined and the 12th leading cause of years lived with disability among females of all ages. The management of migraine may include non-pharmacological and/ or pharmacological treatment. The pharmacological treatment of migraine can be acute (abortive) or preventive, and patients with frequent severe headaches often require both approaches. Preventive migraine treatment also includes non-pharmacological therapy. Preventive treatment is used to reduce the frequency, duration or severity of attacks. Additional benefits include improvement of responsiveness to acute attack treatment, improvement of function and reduction in disability. It might preclude the progression of episodic migraine to chronic migraine and result in reductions in the cost of healthcare.

Keywords: Migraine, Non-pharmacological treatment, Prophylactic management, Pharmacological treatment

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Introduction

The term 'migraine' is derived from the Greek word 'hemicrania' which was coined by Galen in Approximately 200 AD thus clearly, migraine was well known in the ancient world.[1,2] Migraine is a neurological syndrome characterized by headaches (unilateral, throbbing in nature, and moderate to severe in intensity), altered perception and nausea.

The pain may start on one side and become generalized, and usually alternates sides from one attack to the next. The pain usually lasts between 4 and 72 hours in adults and 2 and 48 hours in children. The frequency of attacks is extremely variable, from a few in a lifetime to several times a week, and an average migraneur experiences from one to three headaches a month. Nausea occurs in almost 90 percent of patients, while vomiting occurs in about one third of patients.

Many patients experience sensory symptoms such as; photophobia, phonophobia, and seek a dark and quiet room.[2] Other symptoms like Blurred vision, nasal stuffiness, diarrhea, polyuria, pallor or sweating may also be seen. Some of the signs that may be seen in a patient of migraine are; localized edema of the scalp or face, scalp tenderness, prominence of a vein or artery in the temple, or stiffness and tenderness of the neck.

Impairment of concentration and mood are common. Lightheadedness, rather than true vertigo and a feeling of faintness may occur.[3]

Definition: The International Headache Society (IHS) defines migraine as a recurring disorder characterized by intermittent attacks of headache combined with nausea, photophobia and/or phonophobia lasting from 4-72 hours.[4,5]

Triggers of Migraine: In many patients, migraine attacks seem to be triggered by external factors.[2,6]

Possible triggers include:

1. **Environmental:** Walking in the sun, bright light, strong winds, odour or changes in altitude can all trigger migraine.
2. **Sensitivity to chemicals and preservatives in foods**: Certain articles such as aged cheese, alcoholic beverages, caffeine, ice-cream, chocolate and food additives such as Nitrates and monosodium glutamate may be responsible for triggering migraine attacks.
3. **Emotional Stress**: This is the most common triggers of migraine headache. During stressful events, certain chemicals in the brain are released, these chemicals can provoke vascular changes that can cause migraine.
4. **Drugs**: Nitroglycerin, histamine, reserpine, hydralazine, ranitidine, estrogen etc.

5. **Other factors**: Menstrual periods, excessive fatigue, skipping meals, changes in normal sleep pattern, loud noise, flickering lights, smoky or stuffy atmospheres etc.

Diagnosis & Classification of Migraine: The Headache Classification Committee of the International Headache Society (IHS-2004) published the classification and diagnostic criteria for headache disorders. The terms "common migraine" and "classical migraine" have been replaced by" migraine without aura" and "migraine with aura" respectively as they were widely confused and did not convey any information.[7] In 15% of patients migraine attacks are usually preceded or accompanied by transient focal neurotic symptoms, which are usually visual; such patients have migraine with aura.[8]

In migraine without aura (previously known as common migraine) attacks are usually associated with nausea, vomiting, or sensitivity to light, sound, or movement and when treated, the attacks typically last 4 to 72 h. A combination of features is required for the diagnosis, but not all features are present in every attack or in every patient.[7]

Migraine without Aura

A. At least 5 attacks fulfilling criteria B-D
B. Headache attacks lasting 4-74 hours (untreated or unsuccessfully treated)
C. Headache has at least two of the following characteristics:
   a. Unilateral location
   b. Pulsating quality
   c. Moderate or severe pain intensity
   d. Aggravation by or causing avoidance of routine physical activity (e.g. walking or climbing stairs)
D. During headache at least one of the following:
   a. Nausea and/or vomiting
   b. Photophobia and phonophobia

Migraine with Aura

A. At least 2 attacks fulfilling B
B. Migraine aura fulfills criteria for typical aura, hemiplegic aura, or basilar-type aura
C. Not attributed to another disorder.

Typical aura

1. Fully reversible visual, sensory, or speech symptoms (or any combination) but no motor weakness
2. Homonymous or bilateral visual symptoms including positive features. (e.g. Flicking of lights, spots, lines) or negative features (e.g. Loss of vision), or unilateral sensory symptoms including positive features (e.g. Visual loss, pins and needles) or negative features (e.g. Numbness), or any combination.
3. At least one of
   a. Symptom develops gradually over a minimum of 5 min or different symptoms occur in succession or both.
   b. Each symptom lasts for at least 5 min and for no longer than 60 min.
4. Headache that meets criteria for migraine without aura begins during the aura or follows aura within 60 min.

Indications for migraine prevention include:[1-5]

1. Two or more attacks per month that produce disability lasting 3 or more days per month.
2. Contraindication to, or failure of, acute treatments.
3. The use of abortive medication more than twice per week.
4. The presence of uncommon migraine conditions, including hemiplegic migraine, migrain with prolonged aura, or migrainous infarction.

Goals of migraine prophylaxis:[2,9]

1. Reducing migraine frequency, severity, duration, and disability
2. Reducing reliance on ineffective acute headache medication
3. Improving responsiveness to the treatment of acute attacks
4. Improving the patient's quality of life and ability to function
5. Preventing disease progression

Management of Migraine

The management of migraine may include non-pharmacological and/or pharmacological treatment. The pharmacological treatment of migraine can be acute (abortive) or preventive, and patients with frequent severe headaches often require both approaches. Preventive migraine treatment also includes non-pharmacological therapy.[10]

Non-Pharmacologic Measures in Migraine Prophylaxis: The standard non-pharmacologic approach is the avoidance of triggers factors. The triggering factors may differ among patient but their avoidance may lower headache frequency by 50%.

Some of the measures that can be employed are:[2,11,12]

1. Avoidance of stress, noise, odour, bright and flickering lights, exertion.
2. Behavioral changes—avoid sleep deprivation, excessive sleep.
3. Medications — avoid oral contraceptives, hormone replacement therapy, histamine - 2 blockers.
4. Proper diet — avoid fasting, skipping meals & food that are known to cause migraine.
5. Relaxation therapy—breathing exercises and muscle relaxation.

6. Cognitive-behavioral therapy—identification and avoidance of behaviors or responses to Migraines that may exacerbate a migraine attack.
7. Homeopathy (no better than placebo in most studies).
8. Acupuncture.
9. Reflexology.
10. Massage.
11. Temperature changes (hot or cold packs).[13]

There is little evidence of the effectiveness of these therapies but since most of these do not cause any adverse effect and benefits have been seen in some patients when used alone or in combination with pharmacological therapy, the non-pharmacological therapies should be promoted for prophylaxis of migraine.[14]

General principles of pharmacological management:[9]

1. Start treatment with a low dose and escalate over a period of time
2. Many preventive medications require 3-6 weeks for therapeutic response or even longer.
3. Establish a comprehensive migraine management plan including maintaining a migraine diary, Regular follow up, Information on adverse events etc.
4. A preventive drug should be chosen based on its proven efficacy, the patient's preferences and Headache profile, the drug's side effects, and the presence of any coexisting disease.[9]

The major classes of agents available for prophylactic treatment include beta blockers, calcium channel blockers, NSAID's, serotonin receptor antagonists, antidepressants, anticonvulsants

Pharmacological Measures in Migraine Prophylaxis

Drugs with proven role in migraine prophylaxis:

First line agents

1. Beta blockers: The site of action of beta-blockers is central and it acts by inhibiting central^2 receptors, thereby inhibiting neuronal hyperexcitability, interaction with 5-HT receptors and cross-modulation of serotonin system. Some of the commonly used beta blockers are propranolol, metoprolol, timolol, atenolol and nadolol. Only propranolol 80-240mg/day and timolol 20-30mg/day have been approved for migraine prevention by the FDA in the United States.

Adverse effects reported most commonly with beta-blockers were fatigue, depression, nausea, dizziness, and insomnia.

These medications are contraindicated in certain disorders such as asthma, chronic lung disease, diabetes, hypoglycemia, bradycardia, hypotension, Raynaud's disease, peripheral vascular disease and severe depression.[15]

2. Antidepressants: Antidepressants in migraine are likely to be considered only if concomitant depression (or other psychiatric disease) exists. Amitriptyline has been more frequently studied than the other antidepressants and is the only one with consistent support for efficacy in migraine prevention.

Amitriptyline is effective in the prophylaxis of migraine at a dose of 10-75 mg per day. It is more efficacious than propranolol for patients with mixed migraine and tension-type headache. Selective serotonin reuptake inhibitors (SSRIs) have not shown significant benefits in migraine prophylaxis. Drowsiness, weight gain, and anticholinergic symptoms are frequently reported with the tricyclic antidepressants.[16] Serotonin norepinephrine reuptake inhibitors like venlafaxine, duloxetine, mirtazapine may have a role in prevention of migraine.

3. Antiepileptic's: Some antiepileptic drugs (AEDs) are effective in the prevention of migraine. A rationale for this use is the hypothesis that migraine and epilepsy share several pathogenic mechanisms. At present, controlled clinical studies indicate that divalproex sodium (500-1500mg/day), Valproic acid (800-1500mg/day), Topiramate (50-200mg/day) and Gabapentin (900-2400mg/day) might be useful in migraine prevention. Adverse events include weight gain, hair loss, tremor, and teratogenic potential, such as neural tube defects. These agents may be especially useful in patients with prolonged or atypical migraine aura.[17,18]

Second line agents

1. Calcium channel blockers: Mechanism of action of CCB is uncertain. However, they may have the ability to block 5HT release, interfere with neurovascular inflammation, or interfere with the initiation and propagation of spreading depression that is critical. Flunarizine, 10mg/d, has proven efficacy in the prevention of migraine and is most commonly used. The most common side effects reported with calcium channel antagonists are constipation and fluid retention in the ankles, depression, weight gain and secondary Parkinson's syndrome. Calcium channel antagonists are contraindicated in congestive heart failure, heart block, bradycardia, sick sinus syndrome and other cardiac problems. It should be used with caution in elderly patients. Unlike beta blockers it can safely be used in asthmatic and diabetic patients.[19]

2. Non-steroid anti-inflammatory drugs: Non-steroidal anti-inflammatory drugs (NSAIDs) can be used daily or intermittently. Naproxen sodium (500-1100mg/day) is the most commonly used NSAID for

migraine prophylaxis and menstrual migraine. Other NSAIDs that may be substituted for naproxen are mefenamic acid, flurbiprofen sodium, fenoprofen calcium, ketoprofen, and aspirin. Adverse effects include dyspepsia, erosive gastritis, peptic ulceration. Used with caution in elderly, renal & liver abnormalities, hypersensitivity to aspirin and other NSAID's.[20]

Third line agents

Two medications that have proved effective in prophylaxis but are reserved for severe or refractory cases are methysergide and phenelzine sulfate. Methysergide (2-6 mg/day) is the fourth agent indicated and approved for migraine prophylaxis by the FDA. Its continuous use for a period more than 6 months can lead to fatal retro-pleural, retroperitoneal, or cardiac fibrosis.[21]

Drugs with Unproven Role in Migraine Prophylaxis: The efficacy of fluoxetine hydrochloride has not been well established in prophylaxis, but some experts already consider it a viable alternative to tricyclic antidepressants.[20,21,23,34] Other selective serotonin-reuptake inhibitors may prove to be useful, but the evidence for their efficacy is so far weak or nonexistent.[20] Some evidence exists that riboflavin (vitamin B2) in high doses (400mg daily) has some effect in migraine prophylaxis. Because of its low cost and low side-effect profile, it may prove to be a useful alternative.[25] Similarly, magnesium at doses of 400 to 600 mg daily may also be of benefit, but there is less evidence for its efficacy than that for riboflavin. Some other drugs that have been found effective in migraine prophylaxis are:[2]

Vitamin B12, fish oil, coenzyme Q10, SAMe (S-adenosyl-Lmethionine), melatonin and certain herbs such as Feverfew (Tanacetum parthenium), butterbur extract (Petasites hybridus).

Management of Migraine in Special Situations

Pregnancy: Women of childbearing age should be counseled regarding the teratogenicity of the drugs before pregnancy. Drugs like propranolol, topiramate, amitriptyline and gabapentin may be used and are highly efficacious. Drug like fluoxetine may be used, though there is doubt regarding its efficacy. Valproic acid, high dose riboflavin, lisinopril and candesartan should not be used in pregnancy.

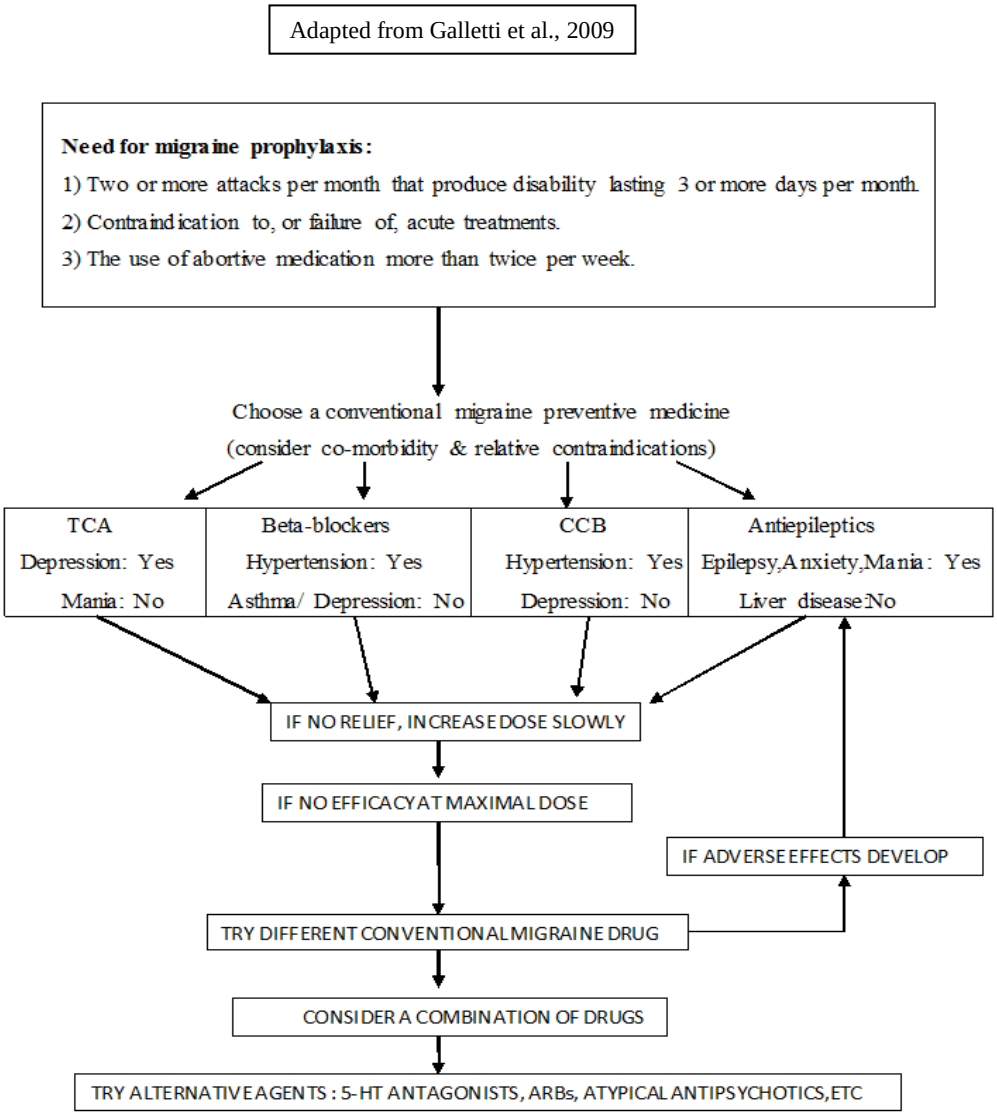
Children: In a Cochrane systematic Review Propranolol was found to be effective.[22] However, benefit of other agents could not be validated because of small study sample size.

Author's Conclusion

Migraine is the most common cause of primary headache and still it is underdiagnosed and under treated. About one-third of the patients require prophylactic treatment. The management of migraine consists of pharmacological, non-pharmacological approaches & prevention of migraine attacks by avoiding trigger factors. The drugs with proven role in migraine prophylaxis are beta-blockers (Propranolol), Flunarizine, Divalproex sodium, Topiramate & Amitriptyline. The choice of drug should be individually based for every patient of migraine considering the clinical characteristics of the attack, its severity, and associated co-morbidity if any, the impact of migraine in developed as well as developing countries is immense, especially in societal and economical fronts. It is important for every physician to keep the records of their headache cases so that a proper data bank can be established for estimation of disease burden in our country.

It is also to be remembered that public awareness for this common disorder needs due emphasis through education, media and advertisement, so that the disease is diagnosed early and appropriate therapy instituted.

Algorithm for Prophylactic Management of Migraine:



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References

1. Critchley M .Migraine: From Cappadocia to Queen Square. Background to Migraine In: Smith R, ed. London: Heinemann. Volume 1;1967.
2. Goyal M, Bansal M. Understanding migraine: an overview. IJCP.2010;21(3):137-141.
3. Headache Classification Subcommittee of the International Headache Society. The international classification of headache disorders. 2nded. (Cephalalgia, 24 - S 1). Oxford: Blackwell Publishing;2004.
4. Mathew N T. Migraine. In: Evans R W, Mathew N T. Handbook of Headache. Second Edition. Lippincott Williams & Wilkins. 2005:28-55.
5. Limmroth V and Michel M C .The prevention of migraine: a critical review with special emphasis on beta-adrenoceptor blockers. J Clin Pharmacol 2001;52:237-243.
6. International Headache Society, International classification of headache disorders. Cephalalgia 2004; 24(Sup.1):1–160.
7. Rasmussen, B.K., Olesen, J. Migraine with aura and migraine without aura: an epidemiological study. Cephalalgia 1992;12:221–228.
8. Olesen, J., Lipton, R.B, Migraine classification and diagnosis. International Headache Society criteria. . Neurology 1994;44: S6–S10.
9. Silberstein SD, Winner PK, Chmiel JJ. Migraine preventive medication reduces resource utilization. *Headache.*2003;43:171-8.
10. Silberstein, S.D. et al. Migraine preventive medication reduces resource utilization. Headache 2003;43:171-178.
11. Pfaffenrath V, Wessely P, Meyer C, et al. Magnesium in the prophylaxis of migraine-a double-blind placebo-controlled study. Cephalalgia 1996;16:436-440.
12. Ernst E. Homeopathic prophylaxis of headaches and migraine? A systematic review. J Pain Symptom Manage 1999;18:353-357.
13. Knott L. Taking control of migraine and headache. Practitioner.1999;243:33-38.

14. Evans RM. Managing migraine today (II): pharmacologic and nonpharmacologic treatment [JAMA Migraine Information Center Website]. October 1998. Available at: http://www.ama-assn.org/special/migraine/treatmnt/managmig/managmig.htm. Accessed August 6, 2014.
15. Weber RB, Reinmuth OM.The treatment of migraine with propranolol. Neurology 1971;21:404–405.
16. Couch JR, Hassanein RS. Migraine and depression: effect of amitriptyline prophylaxis. Trans Am Neurol Assoc 1976;101:234-7.
17. Jensen R, Brinck T, Olesen J. Sodium valproate has a prophylactic effect in migraine without aura: a triple-blind, placebo-controlled crossover study. Neurology1994;44:647-51.
18. Edwards KR, Glantz MJ, Shea P, et al, Topiramate for migraine prophylaxis: a double blind, randomized, placebo-controlled study. Headache 2000;40: 407.
19. Reveiz-Herault L, Cardona AF, Ospina EG, Carrillo P. Effectiveness of flunarizine in the prophylaxis of migraine: a meta-analytical review of the literature. Rev Neurol,2003;36:907–912.
20. Ramadan NM, Silberstein SD, Freitag FG, Gilbert TT, Frishberg BM, for the US Headache Consortium. Evidence-based guidelines for migraine headache in the primary care setting: pharmacological management for prevention of migraine [Am Acad Neurol Web site].
21. Noble SL, Moore KL. Drug treatment of migraine: part II. Preventive Therapy. Am Fam Physician 1997;56:2279-2286.
22. Victor S, Ryan SW. Drugs for preventing migraine headaches in children. Cochrane Database Syst Rev.2003;(4):CD002761.
23. Evans RM. Managing migraine today (II): pharmacologic and nonpharmacologic treatment [JAMA Migraine Information Center Website]. October 1998. Available at: http://www.ama-assn.org/special/migraine/treatmnt/managmig/managmig.htm. Accessed August 6, 2014.
24. Schwetschenau KH. Prophylactic treatment of migraine: possibilities for pharmacist interventions. Pharmacy Times 2000 Apr; pp 72-78.
25. Schoenen J, Jacquy J, Lenaerts M. Effectiveness of high-dose riboflavin in migraine prophylaxis: a randomized controlled trial. Neurology 1998;50:466-470.