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Review Article

Migraine Headache : An Overview

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Abstract

The history of headache can be traced almost to the beginning of the history of humankind. Among the many causes of it, migraine headache is a debilitating disorder affecting millions of people in the United States and worldwide. The diagnosis of migraine can significantly affect quality of life, health care costs and daily productivity. Hundreds of trials and many guidelines have documented various approaches to migraine management, whether via acute treatment or chronic migraine prophylaxis. Acute or abortive migraine management encompasses specific and nonspecific migraine therapeutics including non-opioid and opioid analgesics, triptans and ergotamines. Prophylactic migraine management data span the pharmacological spectrum from antiepileptic and antihypertensive agents to botulinum toxin type A. Special considerations for migraine management also must be applied in various populations including children, pregnant women and the elderly. Although hundreds of clinical trials are available regarding migraine treatment modalities, this review serves as an introduction to current accepted therapeutics for migraine treatment and an overview of pharmacological prophylaxis in the modern management of migraine.

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Introduction

Headache affects nearly everyone at least occasionally and it is among the most common reasons that patients seek medical attention.[1] Migraine is an important cause of it and an estimated 187,000 attacks are experienced every day, and almost 90,000 people are absent from work or school because of migraine every working day[2] and approximately 13 million visits each year in the United States to physicians' offices, urgent care clinics and emergency departments with headache disorders.[3.] Migraine occurs in 12-15% of the UK population, in women more than men in a ratio of 3:1[4]. WHO ranks migraine in its top 20 disabling conditions. It is estimated that migraine costs the UK almost £2 billion a year in direct and indirect costs[5].

Diagnosis

Migraine (with and without Aura**)** are diagnosed on the basis of diagnostic criteria proposed by International Headache Society in 'The International Classification of Headache Disorders'.[6]

Simplified Diagnostic Criteria for Migraine[6] is repeated attacks of headache lasting 4–72 hrs in patients with a normal physical examination, no other reasonable cause for the headache and:

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At least 2 of the following features:

(1)Unilateral pain

(2) Throbbing pain

(3) Aggravation by movement

(4) Moderate or severe intensity

Plus at least 1 of the following features:

(1) Nausea/vomiting,

(2) Photophobia and phonophobia.

Investigations

Patients with migraine often do not require to perform investigations unless the history and neurological findings are suggestive of structural disease.[7] Occasionally neuroimaging may be required on an individual basis if a patient is disabled by fear of serious pathology and in most cases, CT scan and MRI are equally sensitive.[5]

Management

A stepped approach to migraine management consists of avoidance of any precipitating factors together with symptomatic and prophylactic treatment and assurance as well[3]. During acute attacks, many patients find it helpful to rest in a quiet, darkened room until symptoms subside. To prevent medication overuse, use of simple analgesics should be limited to 15 days or less per month and combination analgesics should be limited to less than 10 days per month[3].

Successful treatment of migraine involves 5 steps[8]:

Step 1

An accurate clinical diagnosis based on the IHS criteria with full neurological examination during the first visit.

Step 2

A disability assessment to quantify the extent of disability on the first visit as well as follow-ups.

Step 3

Step 3 consists of stratified care for the acute treatment of headache[9]. Patients who have mild symptoms and disability can be adequately treated with acetaminophen, nonsteroidal anti-inflammatory drugs (NSAIDs), propoxyphene or a combination of these. Acute treatment is most effective when given within 15 minutes of pain onset and when pain is mild.[10] Patients with moderate disability need migraine-specific oral medications. The 2 categories of such medications are triptans and ergot alkaloids. The specific triptans are sumatriptan, rizatriptan, zolmitriptan, naratriptan, almotriptan, eletriptan, and frovatriptan[11]. Patients with severe headaches need oral, subcutaneous or intravenous formulations of these drugs. Patients with severe nausea and vomiting at the onset of an attack may respond best to intravenous prochlorperazine. These patients may be dehydrated and adequate hydration is necessary.

Approximately 40% of all attacks do not respond to a given triptan or any other substance. If all else fails, an intractable migraine attack (status migrainosus) or an attack lasting longer than 72 hours should be addressed in an urgent care or emergency department. In rare cases, patients may need to be hospitalized for a short period and may need to be treated with intravenous valproate or dihydroergotamine (subcutaneously/ intramuscularly/ intravenously) for a few days[12]

Step 4

Step 4 is to individualize treatment on the basis of the patient's profile. No two patients with migraine are the same. Each patient has a unique psychosocial environment that heavily influences his or her treatment.

Step 5

Step 5 is patient education, which is key to successful long-term management. It includes teaching the patient to avoid trigger-factors that precipitate a migraine attack (eg, lack of sleep, fatigue, stress, certain foods, use of vasodilators) and a lifestyle change at some level.

Emergency treatment at home

This usually falls to general practitioners. If an effective therapy has not been established previously, the options are: intramuscular diclofenac 75mg (not pethidine:) and/or intramuscular chlorpromazine 25-50mg (potent antiemetic and sedative). Early follow-up is recommended.

Treatment of recurrence within the same attack after initial home treatment

Symptomatic medications (steps one and two) may be repeated within their dosage limitations.

In the case of triptans, there is evidence of efficacy of a second dose for recurrence but no evidence that it is the most appropriate treatment. There is informal evidence that repeated dosing with these drugs quickly gives rise to repeated rebound, perhaps over several days. Instead diclofenac may be tried where recurrence is usual and expected. DHE or ergotamine may be useful for this purpose but safety and efficacy have not been formally established; they should not be used within 12 hours after any triptan.

Patients who consistently experience recurrence
There is some evidence that this occurs more in those whose untreated attacks last longer than 24 hours. Naratriptan may be the triptan of choice. Ergotamine has a prolonged duration of action and trials suggest that it is associated with significantly less recurrence.

Long-duration migraine
Migraine lasting longer than 3 days is uncommon. Apparently long-duration attacks may be migraine with a superseding tension-type headache for which naproxen or diclofenac are preferable to specific anti-migraine drugs.

Status migrainosus is extremely rare. Multiple recurrences with repeated doses of a triptan are now a well-recognised complication and correct management is withdrawal of triptan. Diclofenac should be used until symptoms settle. Patients who show susceptibility to this problem should try ergotamin**e** instead, but be very cautious in repeating the dose.

Slowly developing migraine

Some patients develop attacks slowly and are initially uncertain whether a headache is migrainous or not. If treatment is required at this stage, simple analgesics are recommended and may prevent further development. Triptans should not be used, if at all, until it is certain that the headache is migrainous (there is some evidence that delayed use of triptans does not significantly impair their efficacy).

Migraine in pregnancy and lactation
Paracetamol in moderation is safe throughout pregnancy and breastfeeding. Aspirin is safe except near to term. For nausea, prochlorperazine is unlikely to cause harm throughout pregnancy and lactation. Metoclopramide and domperidone are probably safe in second and third trimesters.

Prevention of headache disorders
Migraine prophylaxis is rewarding to some extent and when indicated, prophylactic therapy is used in addition to, not instead of, acute therapy.

Indications[3]
Therapy to prevent migraine is indicated if
(1) the patient has more than 2 migraine attacks per month,
(2) the patient has single attacks that last longer than 24 hours,
(3) the headaches cause major disruptions in the patient's lifestyle,
(4) abortive therapy fails or is overused,
(5) the patient has complicated migraine and
(6) Over-frequent use of acute therapy.

Goals of preventive therapy
The goals of preventive therapy are:
(1) to reduce attack frequency, severity, and/or duration,
(2) to improve responsiveness to acute attacks, and
(3) to reduce disability.

Classes of Migraine Prophylaxis
There are 3 classes of medications that are effective for migraine prevention - antiepileptics, antidepressants, and antihypertensives. Botulinum toxin A may be another effective medication[13,14]

First-line prophylactic drugs
Beta-adrenergic blockers without partial agonism, propranolol, metoprolol, atenolol etc if not contraindicated[15]. Cardioselectivity and hydrophilicity both improve the side-effect profile and are to be preferred. Once-daily dosing is associated with significantly better compliance. On these grounds, bisoprolol 5-10mg od may be the beta-blocker of choice.

Sodium valproate 0.6-2.5g daily [16]

Pizotifen 1.5mg daily is sedative and should be taken at bedtime.

Amitriptyline 10-150mg daily, usually at night, is first-line prophylactic when (a) migraine coexists with tension-type headache (b) there is associated depression; or (c) there is disturbed sleep. It may be used concomitantly with a beta-blocker as second-line.

Desipramine, nortriptyline, protriptyline etc may also be used.

Second-line prophylactic drugs

Methysergide 1-2mg tds

Beta-blocker and amitriptyline together used in prophylaxis but with limited efficacy Calcium channel antagonists are of uncertain value. Verapamil modified release, 120-240mg bd is well tolerated, with headache sometimes a side-effect. Clinical trials evidence of efficacy is limited.

Selective serotonin reuptake inhibitors are second-line to tricyclics. Fluoxetine 20mg alter die to 40mg od is best studied. Clinical trials evidence of efficacy against migraine is inconclusive (against depression, its efficacy in higher doses is established).

Prophylaxis for hormone-related migraine

An effect of hormones on migraine is common, and greater for migraine without aura . Empirical evidence suggests oestrogen withdrawal triggers migraine in some women[17]

Menstrual migraine, defined as attacks of migraine without aura that occur regularly on day 1 of menstruation ± 2 days and at no other time, is rare[18]. Correct diagnosis of menstrual migraine is essential for successful hormonal management. The diagnosis is clinical and confirmed by diary card evidence over three months.

Depending on need for contraception, several options can be tried in whatever order seems appropriate. Prophylaxis should be tried for a minimum of three cycles at maximum dose before it is deemed ineffective.

A) Non-hormonal prophylaxis does not depend on regular menstruation. Mefenamic acid 500mg tds-qds can be given from the onset of menstruation until the last day of bleeding. It is recommended as first-line in migraine occurring with menorrhagia and/or dysmenorrhoea.

B) Hormones for menstrual migraine are supplements: if the women has an intact uterus and is menstruating regularly, no progestogens are necessary. oestradiol 1.5mg in 2.5g gel is applied daily from day -3 for 7 days.

C) Combined oral contraceptives (COCs) and injectable depot progestogens inhibit the ovarian cycle. Migraine in the pill-free interval is most notable with high-progestogen contraceptives[19]

Oral progestogen-only contraception does not inhibit ovulation.

Migraine and hormonal contraception

Headache is a common side-effect of COCs and many women report onset of migraine after starting them. Others report improvement of pre-existing migraine[20]. There is concern that migraine and COCs are both independent risk factors for stroke in young women, in the latter case related to the ethinyloestradiol component. This has led to the development of opinion-based recommendations for the use of COCs in migraineurs-[21] although not all experts agree.

Progestogen-only contraception is acceptable with any type of migraine contraindicating synthetic oestrogens. The progestogen-only pill has a higher failure rate but Depo-Provera and the Mirena intrauterine system both have lower failure rates than COCs. Women can switch immediately from COCs to progestogen-only contraception.

Migraine in pregnancy and lactation: Most women with migraine improve during pregnancy. If not, prophylactics should be restricted but, when necessary, propranolol has best evidence of safety during pregnancy and lactation.[22]

Women should be counselled with regard to the relative risks and benefits.

Migraine and hormone replacement therapy (HRT)[23]

Hormone replacement therapy is not contraindicated After hysterectomy, oestrogen implants are an option.

Duration of use: There is no good guide for what should be the minimum period but once a drug has

been found to help, it should be continued for several months. If the patient remains headache-free, the dose can then be tapered and the drug eventually withdrawn.[7] Uninterrupted use over a year or longer is rarely appropriate. Prophylactic drugs that are apparently not effective should not be discontinued too soon or patients must not be labeled non-responders prematurely. and 3 cycles in the case of specific therapy for hormone-related migraine. Patients should be discouraged from stopping too soon unless they have unacceptable side-effects.[23]

If prophylaxis fails:
If prophylaxis fails, review diagnosis, compliance (often poor) and concordance (often very poor, especially with multiple daily doses). Review other medication, especially for medication overuse. Consider combinations if any. If prophylaxis still fails to have measurable benefit, discontinue it[6].

Referral: When to Refer a patient with migraine are[3]:

- Frequent migraines not responsive to standard therapy.
- Migraines with atypical features.

Conclusion

A stepped approach for acute treatment of migraine is required since it is associated with significant disability and is often under-treated. Medication overuse results in the development of chronic daily headache. The risks of medication-overuse headache should be discussed with all patients when initiating acute treatment for migraine. Stopping medication-overuse may result in improvement in headache frequency and severity. The great frequency of migraine-headache in clinical practice coupled with a very low relative incidence of serious causes makes it difficult to maintain an appropriate level of suspicion. If it is approached with a standard operating procedure that supplements history with fundoscopic examination, brief but comprehensive neurological examination and the use of diaries to record headaches, associated symptoms and medication use and an awareness of the few important serious causes, errors should be avoided. Clinician`s review and analysis of a prospective diary that records headache symptoms over a few weeks can improve management.

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