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Management of migraine

Migraine is a common problem in patients presenting to their GP. There are a number of pitfalls to be aware of in the assessment, acute treatment and prophylaxis of migraine.

CATHERINE D. STARK
MB BS

RICHARD J. STARK
MB BS, FRACP, MACLM

Dr Catherine Stark is a Neurology Fellow at the Department of Neurology, Austin Health, Melbourne. Associate Professor Richard Stark is a Neurologist and Honorary Clinical Associate Professor at the Neurology Department, Alfred Hospital and Department of Medicine, Monash University, Melbourne, Vic.

Migraine is an extremely common and disabling condition, which is often poorly managed. The incidence of migraine is about 18% in women and 6% in men. A large portion of these patients do not seek medical attention and self-medicate. Patient awareness of specific treatments is insufficient and potentially harmful codeine-based analgesics can be over relied on. This article outlines some of the issues in the management of migraine.

Diagnosis

Migraine is a syndrome of recurrent headaches with specific criteria (see the box on page 17).[1] If the criteria for migraine are met and the presentation is typical, there is no need to perform cerebral imaging or pathology tests. However, it is important to remember that headache can also be the presenting feature of several serious conditions that require further investigation.

There are some red flags that the clinician should be aware of that indicate further investigation is needed.

- new pattern of headache, especially abrupt onset or relentless progression
- the presence of any focal symptoms or signs (except for typical migraine aura)
- the presence of fever, confusion, an altered mental state or neck stiffness/meningism

Also, the possibility of temporal arteritis should be considered if the patient is older than 55 years of age.

Treatment

The management of migraine requires an individualised approach for every patient. The three main factors in migraine management are the avoidance of trigger factors, the management of acute attacks and, if appropriate, prophylaxis.

Trigger factors

The trigger factors for migraine vary greatly from individual to individual. Often the patient will be aware of precipitants from previous experiences. Common triggers include various foods, in particular cheese, chocolate, red wine and oranges. The potential for common daily foods such as bread

IN SUMMARY

- **Migraine is a common condition that is often managed suboptimally.**
- **Acute treatment is best initiated early in the course of a migraine attack, partly because gastric stasis may affect treatment efficacy.**
- **Prophylaxis is effective and underused.**
- **Beware of medication overuse, which can increase headache frequency and decrease the effectiveness of prophylactic agents.**
- **If the diagnosis is unclear or management is ineffective, consider referring the patient to a neurologist.**

International Headache Society 2 criteria for the diagnosis of migraine[1]

Migraine without aura

At least five attacks fulfilling the following three criteria:

- Headache attacks lasting from 4 to 72 hours
- Headache with at least two of the following:
  - unilateral location
  - pulsating quality
  - moderate or severe intensity
  - aggravation by simple exertion
- Headache with presence of at least one of:
  - nausea and/or vomiting
  - photophobia and phonophobia

Plus secondary causes should have been clinically excluded.

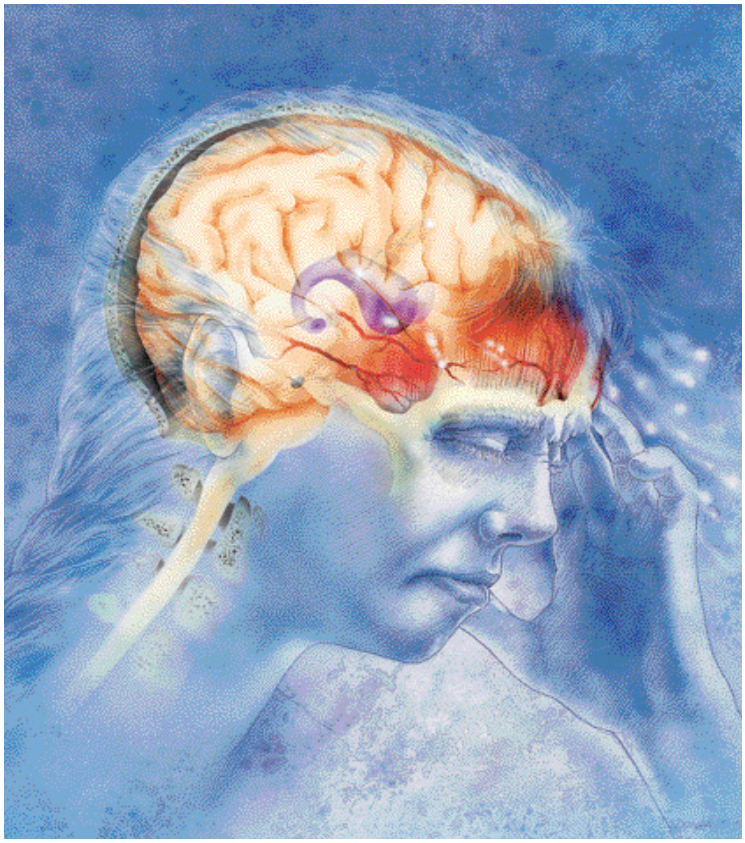
Migraine with typical aura

At least two attacks fulfilling the following three criteria:

- Aura consisting of at least one of the following, but with no motor weakness:
  - fully reversible visual symptoms including positive features (e.g. flickering lights, spots or lines) and/or negative features (e.g. loss of vision)
  - fully reversible sensory symptoms including positive features (e.g. pins and needles) and/or negative features (e.g. numbness)
  - fully reversible dysphasic speech disturbance
- Presence of at least two of the following:
  - homonymous visual symptoms and/or unilateral sensory symptoms
  - at least one aura symptom developing gradually over five minutes or longer and/or other aura symptoms occurring in succession over five minutes or longer
  - each symptom lasting between 5 and 60 minutes
- Headache beginning during the aura or following aura within 60 minutes

Plus symptoms cannot be attributed to another disorder.

Management of migraine



Migraine is a common condition affecting 18% of women and 6% of men. The condition is often poorly managed, and a large portion of patients do not seek medical attention and self-medicate. However, modern treatments mean that most patients with migraine can be treated effectively.

and milk to be trigger factors in some patients is more controversial.

Hormonal factors are important triggers, and frequent links are seen between migraines and a patient's menstrual cycle. Elements of a patient's lifestyle such as stress, irregular sleep patterns or irregular meals can be major factors, and physical trauma to the head or neck (e.g. from heading the ball at soccer or whiplash injuries) can precipitate migraine events.

A headache diary detailing the factors present at and around the time of the headache can be a useful tool to help the patient and clinician identify possible precipitants.

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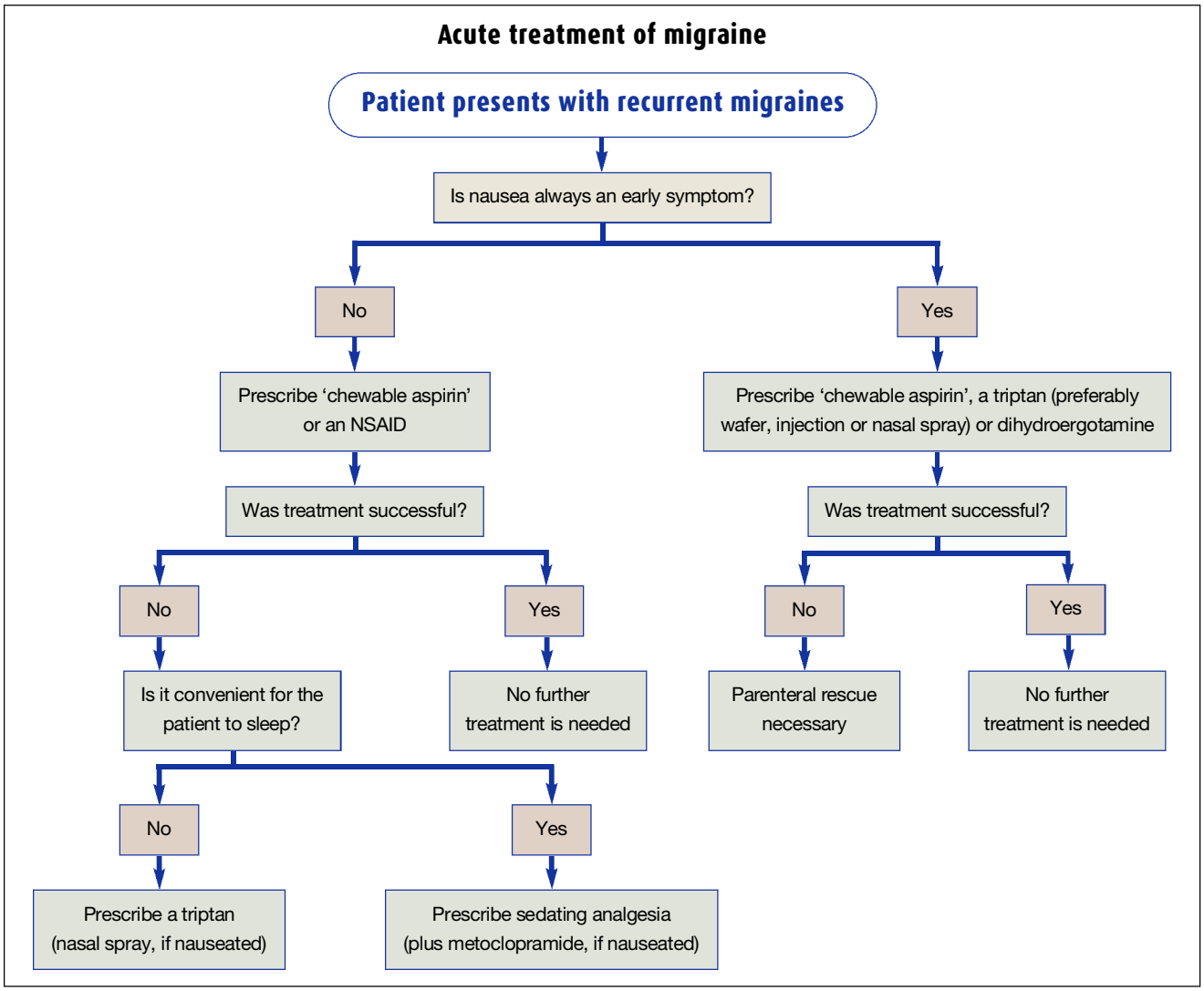

Management of acute attacks

The treatment of an acute attack can either address specific symptoms or be migraine specific (see the flowchart on this page). The types of symptomatic treatments that can be used include analgesics, sedatives, antiemetics and anti-inflammatories. There are a number of factors to be considered in the choice of acute therapy (Table 1). These include:

- the usual severity and frequency of attacks
- the duration and reliability of warning signs
- the presence and timing of any nausea and vomiting.

The patient's social context is also important because it determines whether he or she is able to rest (so that drugs with sedative effects may be appropriate, because sleep is often therapeutic) or needs to keep functioning. By the time a patient receives medical attention, he or she has often tried one or more symptomatic treatments, so it is important to take into account the efficacy and side effects of previously used drugs. Finally, there is a cost differential between some of the medications, which may be important for some patients.

Finding the optimal acute treatment for a patient may be by trial and error, and it is important that the patient is aware of this at the outset. The clinician should have a low threshold for a trial of a triptan. In some patients, triptans are dramatically effective and, even if used infrequently, can give a patient a feeling of control.

Gastric stasis is an intrinsic part of a migraine attack and must be considered in the setting of acute treatment. One strategy to circumvent this problem is to treat the patient with an effective drug early in the attack. Many patients delay taking their medications until the headache is established, by which time the efficacy of enteral medications is much reduced. Another strategy is to utilise medications that bypass the stomach. Intravenous, intramuscular and subcutaneous medications are all available, as well as suppositories. A

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Table 1. Approaches to acute therapy based on migraine headache frequency

Infrequent migraines	Frequent migraines
Strategic aim	
• Rapid and highly effective treatment	• Effective treatment but minimising the risk of medication-overuse headache
Practical options	
• Early use of a drug or a combination of drugs that has previously proved to be most reliably effective	• Two-stage approach • First stage: early use of rapidly absorbed NSAIDs particularly aspirin
• Early use of triptans should be considered	• Second stage: if first-stage treatments fail, use triptans, but limit use to a maximum of one to two days per week
• Use of strong analgesics or opioids may be a reasonable option	• Opioids are to be avoided

Table 2. Factors to consider when choosing a triptan to use

Clinical issue	First-choice triptan	Problems
Early vomiting	Rizatriptan wafers Sumatriptan nasal spray	Recently introduced and thus less familiar to doctors Can be awkward to use; bad taste
Patient concerned about side effects	Naratriptan tablets	Can be slow to work
Patient keen for speedy treatment with maximal efficacy	Zolmitriptan tablets	More frequent side effects than with naratriptan use
Parenteral treatment required	Sumatriptan subcutaneous injection	Expensive

'chewable' aspirin formulation that is absorbed via the oral mucosa and a sumatriptan nasal spray absorbed via the nasal mucosa are available.

The classes of drugs that have been shown to be effective as treatment for acute migraine are NSAIDs (such as aspirin, diclofenac, naproxen), selective serotonin 5-$HT_{1B/1D}$ agonists (such as triptans – ergotamines probably also work in this way) and dopamine antagonists (such as chlorpromazine and prochlorperazine), which appear to have a migraine-lytic effect as well as an antiemetic effect. Pure analgesics should be used as a last resort.

Triptans

There are a number of different triptans on the market in Australia (Table 2); the best agent for an individual will vary.

- Oral sumatriptan was the first triptan available and is thus familiar to many GPs. It works well for many patients but absorption can be variable, so some neurologists would usually choose naratriptan or zolmitriptan ahead of it. Sumatriptan also comes as a nasal spray and subcutaneous injection, which are useful options for patients with early vomiting.
- Oral naratriptan is a gentle agent with a long half-life, making it a good choice for patients who are anxious about possible side effects.
- Oral zolmitriptan works faster and is more potent than other triptans. It is therefore appropriate for patients who have maximal efficacy as their first concern.
- Rizatriptan wafers for sublingual use are now available in Australia. They have the advantages of rapid absorption and are useful for patients with rapidly evolving attacks or early vomiting.

Patients and doctors need to be aware of certain financial issues when considering the use of triptans. A PBS authority prescription will be the cheapest way for healthcare card holders such as pensioners to obtain their medication, but for others the cost of a PBS prescription (for four tablets of any triptan or two sumatriptan nasal sprays) may be greater than the cost of these drugs on private prescription, especially when a larger supply is provided.

Prophylaxis

The current practice recommended by the Australian Therapeutic Guidelines is to

Table 3. Evidence levels for the efficacy of migraine prophylaxis drugs

Drug	Dose	Problems
Level 1 evidence		
Propranolol	40 to 120 mg twice daily	Contraindicated in patients with asthma, Raynaud's syndrome, hypotension and peripheral vascular disease
Topiramate	25 to 100 mg twice daily	May cause dysphasia, paraesthesiae, renal calculi or weight loss
Sodium valproate*	400 to 600 mg twice daily	May cause weight gain and is teratogenic
Amitriptyline*	10 to 75 mg at night	May cause dry mouth or drowsiness
Level 2 evidence		
Pizotifen	0.5 to 2 mg daily	May cause weight gain or drowsiness
Methysergide	1 to 2 mg two to three times daily	May cause retroperitoneal fibrosis, drowsiness or cramps
Clonidine	50 mg twice daily	May cause drowsiness or dry mouth, and has a variable efficacy
Cyproheptadine	4 to 12 mg daily	May cause weight gain, drowsiness or dry mouth
Verapamil*	160 to 320 mg daily	May cause constipation, ankle swelling or cardiac conduction abnormalities
Botulinum toxin A*	Three monthly intramuscular injections	Is expensive and has a variable efficacy
Candesartan*	16 mg daily	May cause hypotension and hyperkalaemia

* Used off label for migraine prophylaxis.

commence a patient on regular preventive treatment if they have more than two or three acute attacks of migraine per month.[2] The decision is made in conjunction with the patient on the basis of the frequency, severity and duration of the attacks and the degree of disability caused. Patients with unusually disabling attacks, such as those that are always prolonged and resistant to acute treatments or that arise out of sleep and are already associated with severe nausea and vomiting, may opt for prophylaxis even when attacks are less frequent than twice a month.

There is a wide array of agents used for migraine prophylaxis.[3] These drugs generally have appeared on the market for migraine after establishing themselves for other indications such as hypertension or epilepsy. Despite this, there is excellent evidence available for the use of many of these agents (Table 3).

There seems to be a strong bias in Australia for the use of propranolol or pizotifen,[4] but these are not always the most appropriate choice. As is often the case in conditions with many effective drugs of similar efficacy, the usual first choice of prophylactic agent tends to vary between practitioners, but the general approach to decision-making should be similar. The initial choice of agent is often based on the side effect profile.

A prophylactic drug should be given for long enough for its effect to be established, which can take up to three months. Drugs that are ineffective after this time should be discontinued and others considered. It is worth remembering that prophylactic agents can work for a while and then become ineffective so the clinician should be prepared to rotate through several options.

Chronic daily headache

A history of episodic migraine in a patient can sometimes transform into a pattern of chronic daily headache. Chronic daily headache is defined as daily or near-daily headache lasting more than four hours a day for more than 15 days a month. It is common, being present in 4% of the population.

Half of all cases and the majority of disabling cases of chronic daily headache are due to transformed migraine. Other causes of chronic daily headache include chronic tension-type headache (usually less severe) and the uncommon conditions new daily persistent headache and hemicrania continua. Any of these headache types can be, but are not always, related to medication overuse.

Medication overuse can be defined as the use of ergotamine, a triptan or codeine for more than 10 days a month, or use of simple analgesics or caffeine for more than 15 days a month.[1] Overuse of codeine is frequent in Australia and is widely recognised as being particularly difficult to manage.

When managing a patient with chronic

daily headache, eradicating medication overuse is the first step. Treatment for the underlying condition (i.e. migraine prophylaxis) is often ineffective when the rebound cycle is established, but can become effective later. For successful withdrawal of medication, it is critical that the patient understands the reasoning behind this withdrawal and is motivated to modify their behaviour. A psychiatric assessment is often useful in these patients. Abrupt withdrawal of the offending agent is best, but this inevitably results in a medication-withdrawal headache. Management options for this short-term problem include regular NSAIDs or prednisolone. If the patient has been using large amounts of analgesia, inpatient management may be required. Intravenous dihydroergotamine or lignocaine are then available options. Inpatient observation alone is used in some centres.

There have been limited data on the efficacy of prophylaxis in transformed or chronic migraine, but recent publications support the use of topiramate or botulinum toxin in this context.[5,6]

When to refer to a neurologist

Many patients with migraine can be managed appropriately by their GP. However, in some circumstances a referral to a neurologist is necessary. If there is an element of diagnostic uncertainty because of atypical features or 'red flags', it is best to obtain a neurological opinion. Another indication for referral would be worsening severity or frequency of symptoms despite appropriate prophylaxis and acute treatment.

Conclusion

Given the incidence of migraine in the community and the substantial levels of disability it can produce, all doctors, and particularly GPs, should have a sound understanding of the condition and at least a moderately sophisticated approach to its management. Modern treatments mean that most patients with migraine can be treated effectively and success in relieving the suffering of these patients is one of the most rewarding experiences in medicine. MT

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