ESSENTIALS OF HEADACHE AND MIGRAINE

Introduction

Headaches are among the most common disorders of health worldwide. They are frequently difficult to treat and are often associated with significant disability and impairment of quality of life.¹ During a lifetime, just over three-quarters of the population will experience tension-type headache (TTH) and one in six will suffer from migraine. Headache may be exacerbated by normal physiological changes (e.g. hormonal cycles), medical and psychological comorbidities, as well as inappropriate use or overuse of over-the-counter (OTC) and prescription medications. All of these factors complicate both diagnosis and management and, if management is inadequate, acute episodic pain may progress to a chronic pain state that might be very difficult to treat. Consequently, the ideal approach to headache is a multidisciplinary one, where appropriate use of pharmacotherapy and combinations of medications with complementary mechanisms of action can significantly improve the long-term outcome.

KEY MESSAGES

- Headache is best managed by the general practitioner, who is informed about the patient’s personal and social circumstances
- Primary care practitioners need to be alert to ‘red flag’ signs indicating the need for immediate referral
- Common pathological mechanisms link headache and psychiatric morbidity
- The most effective acute treatment for migraine is a triptan, such as zolmitriptan, rizatriptan or naratriptan. Response to these agents varies between individuals
- Prophylactic therapy must follow tested clinical principles – useful guidance is provided by the Scottish Intercollegiate Guidelines Network (SIGN)
- Memantine use has recently been shown in a double-blind placebo-controlled study to reduce monthly migraine attack frequency by 62%
- Careful clinical assessment, consideration of comorbidities and a multidisciplinary approach can reduce morbidity caused by headache and migraine.

Chronic migraine

The International Headache Society defines chronic migraine as headaches on ≥15 days/month for ≥3 months, of which ≥8 days fulfil the criteria for migraine without aura, which were successfully treated with acute care medications, such as ergots or triptans.² Chronic migraine evolves from episodic migraine, with an incidence of 2.5% in episodic migraine sufferers, such that the prevalence is approximately 2-4% of the population. It often leads to overuse of acute medication, leading to exacerbation in the form of medication overuse headache (MOH).
Medication overuse headache

MOH is the third most common headache type with a prevalence of 1-2%. It is characterised by headache on 15 or more days every month and is caused by chronic excessive use of medication to treat headache. It is therefore avoidable. All medications used for the acute symptomatic treatment of headache (OTC and prescription) can cause MOH. Although the pathogenesis of MOH probably varies depending on the different causative agents, frequency of use is important, with low daily doses being more likely to cause MOH than larger weekly doses. The headache is persistent and often worse on awakening in the morning, leading to a vicious cycle of headache and analgesic use, the latter sometimes used pre-emptively with the intention of preventing the progressively worsening, oppressive and persistent pain.1

Quality of life

People suffering from headache have significantly impaired quality of life. Around one in three people with migraine will experience four or more serious attacks per month and two-thirds will have up to four. Considering that migraine episodes may last up to 72 hours, just one episode per month can impair normal activities for up to three days.

Repeated headache attacks are often accompanied by constant fear of the next episode and disruption of family life, social life, relationships and employment.1 Fewer than 10% of migraineurs are free from impairment during the headache. The majority require bedrest.

Multidisciplinary approach to treatment

The majority of patients with headache are best managed by the general practitioner, who is likely to be the one most informed about the patient’s personal and social circumstances. However, early referral is recommended where a specific diagnosis indicates it or where there are warning signs that suggest more specialised investigation and management are required (Table 1).

Migraine or other headaches during pregnancy or in the postnatal period, as well as menstrual migraines, which may respond to hormonal manipulation (e.g. the oral contraceptive pill), may require referral to a gynaecologist.

Headache and the psychiatrist

Chronic pain is strongly associated with psychiatric comorbidities, particularly anxiety, depression and insomnia.4 However, there is a bidirectional relationship between chronic pain and these symptoms. Patients with somatisation, health-seeking behaviours and poor sleep are at high risk of developing chronic widespread pain, including musculoskeletal pain and headaches. The risk increases in tandem with severity of anxiety, depression or sleep problems, and those with multiple predisposing factors are at the highest risk.5

There is strong epidemiological and clinical evidence to suggest common pathological mechanisms linking headache and psychiatric morbidity. Depression and/or anxiety are comorbid in as many as 80% of migraine sufferers. The monoamines (serotonin, noradrenaline and dopamine), which have a central role in these psychiatric morbidities, also play important roles in migraine and in
migraine chronification. Comorbid psychiatric conditions affect both prognosis and treatment of headache and increase the risk of suicide in those suffering from severe or persistent headache. Traumatic experiences during childhood may affect brain development, causing disturbances in the monoamine systems, whereas post-traumatic stress disorder (PTSD) is associated with changes in both the monoamine systems and hypothalamic-pituitary-adrenal (HPA) axis and therefore with pain syndromes that may be difficult to treat.

Pharmacotherapy for migraine
Pharmacotherapy for migraine may take the form of acute treatment of individual headaches or prophylactic therapy.

Acute therapy for migraine
1. The most effective acute treatment for migraine is a triptan (sumatriptan, zolmitriptan, rizatriptan, naratriptan) administered early in the headache. The effect of individual triptans is idiosyncratic and patients who do not respond to one may have a good response to another.\(^3\)
2. A nonsteroidal anti-inflammatory drug (NSAID), such as ibuprofen, is inexpensive and may be effective alone or in combination with a triptan.\(^3\)
3. For migraines that persist despite initial treatment, administration of oxygen or olanzapine may be beneficial.
4. Opioids should be avoided and are generally only suitable for chronic pain in carefully selected patients under specialist care.
Prophylactic therapy for migraine

The goal of prophylactic therapy is to reduce attack frequency, severity and duration, improve responsiveness of acute attacks to treatment and reduce migraine-associated disability. Prophylactic therapy may be considered for patients in whom migraine attacks have a significant impact on health and daily activities, despite appropriate use of acute medications, trigger management and lifestyle modification, or where there is a high frequency of migraine attacks with risk for medication overuse (>3 moderate or severe headache days a month when acute medications are not reliably effective, or >8 headache days a month even when acute medications are optimally effective). Therapy may be considered effective when headache frequency is reduced by 50% or more.

General principles for prophylactic therapy are as follows:³

- Most preventive drugs should be titrated slowly to an effective or maximum dose in order to minimise side effects
- Preventive medication should be given a trial of at least 6-8 weeks following dose titration
- Choice of medication should be guided by side effect profile and the presence of comorbidities.
- Adherence to treatment is likely to be better with medications that are taken once daily
- After 6-12 months of effective prophylaxis, gradual tapering and withdrawal should be considered
- If headache frequency increases with drug withdrawal, the dose can be increased again or, in the case of discontinuation, the drug may be restarted.

Potential options for prophylactic therapy are listed in Table 1. Medications with high-quality evidence that supports a strong recommendation for efficacy include topiramate, propranolol and amitriptyline.

<table>
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<tr>
<th>Drug</th>
<th>Potential adverse effects</th>
<th>Comments</th>
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<tbody>
<tr>
<td>Amitriptyline</td>
<td>Sedation, dry mouth, constipation, dizziness, confusion, weight gain, urinary retention, orthostatic hypotension, reflex tachycardia, palpitations</td>
<td>Good initial choice for migraine prophylaxis; Useful for patients with depression/anxiety, insomnia or associated TTH; Start with low dose (10mg) and increase slowly (10mg weekly or every two weeks)</td>
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<tr>
<td>Beta-blockers (e.g. propranolol, metoprolol)</td>
<td>Drowsiness, fatigue, lethargy, nightmares, depression, hallucinations, memory disturbance, decreased exercise tolerance, orthostatic hypotension, bradycardia, erectile dysfunction, stroke (patients with aura)</td>
<td>Few side effects; Usual dose is 16mg</td>
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<tr>
<td>Candesartan</td>
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<td>Few side effects; Usual dose is 20mg</td>
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<tr>
<td>Duloxetine</td>
<td>Nausea/vomiting, constipation, anorexia, dry mouth, dizziness</td>
<td>Useful in patients with depression</td>
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<tr>
<td>Flunarizine</td>
<td>Weight gain, hypotension, dizziness, somnolence</td>
<td>Avoid in depressed patients</td>
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<tr>
<td>Lisinopril</td>
<td>Cough, dizziness</td>
<td>Usual target dose is 20mg</td>
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<tr>
<td>Topiramate</td>
<td>Paraesthesias, fatigue, drowsiness, nausea, weight loss, taste perversion, cognitive impairment, language disorder, visual field loss, acute myopia with glaucoma (rare)</td>
<td>Useful in overweight patients; Use with caution in depressed patients; Start with low dose and increase slowly; Usual target dose is 100mg</td>
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<tr>
<td>Valproic acid</td>
<td>Nausea, vomiting, gastrointestinal disorders, abnormal liver function tests, weight gain, tremor, hair loss, hyperandrogenism and ovarian cysts</td>
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<tr>
<td>Venlafaxine</td>
<td>Nausea, vomiting, drowsiness, tachycardia</td>
<td>Use with caution in depressed patients; Start with low dose and increase slowly; Usual target dose is 100mg</td>
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Refraotory headache

Patients with headache that is refractory to monotherapy may benefit from combination therapy, which may also permit lower doses of the combined individual medications.

The following combinations may be useful in patients with refractory migraine:

- Beta-blocker and topiramate
- Beta-blocker and valproate
- Beta-blocker and amitriptyline
- Amitriptyline and topiramate

Patients requiring prophylactic polypharmacy should be considered for specialist referral.

Memantine

Increased glutamate transmission may be important in the pathogenesis of chronic pain. In patients with chronic migraine, glutamate levels in the cerebrospinal fluid are increased, suggesting that glutamate is important in progression from episodic to chronic migraine. Memantine is an N-methyl-D-aspartate (NMDA) receptor antagonist approved for the treatment of dementia associated with Alzheimer’s disease. It has also been shown in a number of clinical studies to be effective in migraine prophylaxis and improves cognitive performance in these patients.\(^{10-12}\)

In a recent placebo-controlled study in patients with chronic migraine, memantine was associated with an average 62% reduction in monthly attack frequency (vs 17% in the placebo group) and significantly greater reduction in the number of migraine days and headache severity. Memantine was associated with a greater reduction in number of days absent from work and significant improvements in disability score. It was well tolerated; side effects were uncommon and generally mild.\(^{12}\)

Botulinum toxin

Observations that migraine might be improved in patients receiving injections of onabotulinum toxin A (OBTA) for wrinkles prompted studies of the potential for this treatment approach in patients with migraine. In comparison with placebo, although OBTA injection was not shown to significantly reduce frequency of migraine episodes, it was associated with a significant reduction in headache days and clinically relevant improvements in functioning and health-related quality of life.\(^{10}\)

Conclusions

Headaches and migraine are extremely common and among the primary reasons for visits to general practitioners, specialists and emergency departments. Although serious pathology is rare, headache is responsible for substantial disability, impaired quality of life, and considerable costs in terms of expenditure on healthcare and to the economy. Careful clinical assessment, consideration of comorbidities and a multidisciplinary approach to investigation and management can help reduce morbidity and prevent unnecessary suffering and waste of resources. It is

<table>
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<th>Table 2. The American Headache Society ‘Choosing Wisely’ recommendations(^{13})</th>
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<td>1. Don’t perform neuroimaging studies in patients with stable headaches that meet criteria for migraine</td>
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<td>2. Don’t perform CT imaging for headache when MRI is available, except in emergency settings</td>
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<td>3. Don’t recommend surgical deactivation of migraine trigger points outside of a clinical trial</td>
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<td>4. Don’t prescribe opioid- or butalbital-containing medications as first-line treatment for recurrent headache disorders</td>
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<td>5. Don’t recommend prolonged or frequent use of OTC pain medications for headache.</td>
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important to remember that inappropriate management not only increases costs, but may lead to MOH and chronic pain syndromes that are extremely difficult to treat. In this regard, it is worthwhile taking note of the five ‘Choosing Wisely’ proposals recommended by the American Headache Society (Table 2).

References


This article is based on presentations by Dr Johan Smuts and Dr Dion Opperman at the Cipla Psychiatry Forum on 18 March 2017 at the Arabella Hotel, Kleinmond, Western Cape.

The article was written for deNovo Medica by Dr David Webb.