Migraine

Some answers to some challenging questions

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Migraine is a common condition[1] that can be very troublesome for patients and challenging for their doctors. There are several good up-to-date published reviews on migraine that discuss its epidemiology, pathophysiology, diagnosis and treatment.[2,3,4,5,6] The purpose of this article is not to give an overview of migraine as these reviews do, but to address some of the specific questions on the management of migraine that have challenged me in my practice as a GP. I have restricted my discussion to the management of migraine in adults.

To answer these questions I have referred to key review articles and guidelines that have been published in the last seven years. Two of these warrant special mention. The International Headache Society first published diagnostic criteria for headache disorders in 1988. These have become widely regarded as the standard diagnostic criteria to use in research and clinical practice. The long-awaited and revised second edition has just been published.[1] In 1999 the US Headache Consortium produced evidence-based guidelines on the diagnosis and management of migraine, aimed particularly at primary care.[7,10,12,14] These guidelines are probably the most comprehensive migraine guidelines published so far. Both of these documents are referred to in this article.

Table 1. Non-opiate medications for severe migraine (adapted from guidelines from Canada,[8] the British Association for the Study of Headache[9] and the US Headache Consortium[7,10]).

Medication	Dosage	Additional points
Sumatriptan	6mg sc	
Diclofenac	75mg IM	
Chlorpromazine	25–50mg IM or 12.5mg IV by slow push, repeat if needed after 30 min	Chlorpromazine, metoclopramide and prochlorperazine may cause extrapyramidal side effects and sedation.
Metoclopramide	10mg IM or IV	
Prochlorperazine	5–10mg IM or IV	Chlorpromazine may cause postural hypotension. When this is given IV, a normal saline infusion is also recommended to prevent this
Dexamethasone*	12–20mg IV	

**According to the US Headache Consortium Guidelines, there was insufficient evidence at the time of writing to provide evidence-based guidance about the use of dexamethasone in this setting.*

Are there effective alternatives to opiate analgesics for patients that present acutely with severe migraine?

Many of us are reluctant to use opiate analgesics to treat such patients because of concerns about opiate dependency and abuse. Often these patients have significant nausea or vomiting and are unable to take oral medications. Established alternatives to opiate analgesics are summarised in Table 1. Interestingly there is some evidence that metoclopramide, prochlorperazine and chlorpromazine relieve the pain of migraine as well as the associated nausea and vomiting.[11]

Some of these options are difficult to employ in general practice. Sumatriptan injection is not available on a practitioner's supply order. Intravenous chlorpromazine is given as a slow bolus along with normal saline to prevent hypotension, and therefore requires the appropriate environment and supervision to do this safely. Parenteral dihydroergotamine appears to be another useful drug in this situation[7,8,10] but to my knowledge is not available to GPs in New Zealand, although it is used in the hospital setting.

Are there effective non-pharmacological interventions that reduce the frequency and severity of migraines?

The importance of encouraging regular meals, sleep, exercise, work habits and relaxation for patients with troublesome migraines is often empha-

Table 2. Preventive therapies for migraine (from the US Consortium Guidelines[7,14])

Medium/high efficacy, good strength of evidence, and mild/moderate side effects	Lower efficacy than those listed in first column or limited strength of evidence, and mild/moderate side effects	Clinically efficacious based on consensus & clinical experience, but no scientific evidence of efficacy, mild/moderate side effects	Medium/high efficacy, good strength of evidence, but with side effect concerns	Evidence indicating no efficacy
Propranolol Timolol Amitriptyline Sodium valproate Lisuride	Atenolol Metoprolol Nadolol Fluoxetine Gabapentin Verapamil Nimodipine Ketoprofen Mefenamic acid Naproxen Aspirin Feverfew* Magnesium Vitamin B2	Doxepin Imipramine Nortriptyline Paroxetine Sertraline Venlafaxine Bupropion Topiramate Diltiazem Ibuprofen Cyproheptadine	Pizotifen	Acebutolol Oxprenolol Pindolol Clomipramine Mianserin Carbamazepine Clonazepam Lamotrigine Vigabatrin Nifedipine Indomethacin Clonidine Tropisetron

**A Cochrane review evaluating the effectiveness of feverfew for migraine prophylaxis concluded that its efficacy hasn't been established beyond reasonable doubt.[15]*

sised.[2,5] Avoidance of predictable dietary triggers may be helpful for some patients. These recommendations appear to be based on clinical experience.

There is some evidence that relaxation training, biofeedback therapy and cognitive behavioural therapy can be helpful[7,12,13] although access to affordable, skilled therapists is likely to be a barrier for many of our patients. Evidence about the effectiveness of acupuncture, TENS or cervical manipulation is very limited and doesn't allow, as yet, evidence-based recommendations about these.[7,12,13]

When the decision has been made to trial prophylactic medication for migraine, which drug should I recommend and how should I prescribe it?

The US Headache Consortium addressed this question in their guidelines.[7,14] They evaluated 69 medications – the large number likely to reflect the fact that no one medication stands out as being particularly good. For each medication the scientific evidence for its efficacy, tolerability and safety was considered. Where scientific evidence was lacking the views of experts were sought. A summary of the findings (adapted to include only those medications available in New Zealand) is given in Table 2.

As an indication of the most widely used medications, the authors of several reviews recommend choosing from a beta-blocker (propranolol, metoprolol or atenolol), amitriptyline, sodium valproate, pizotifen and methysergide.[2,4,5,6,9] To my knowledge however, methysergide is no longer readily available in New Zealand. Patient co-morbidity, and the side effect profile and safety of each medication guide choice. With respect to safety it is important to bear in mind the potential teratogenicity of these medications, in particular sodium valproate.

All of these medications offer modest benefit only. At best, on average two-thirds of patients given any of these medications can expect a 50% reduction in the frequency and/or severity of their headaches.[4]

It is advisable to start treatment at a low dose and increase the dose until clinical benefits are achieved or side effects are unacceptable. Full clinical benefit may take two to three months to achieve.[7,14] After a period of good headache control, it is reasonable to consider a phased withdrawal of medication.[7,14]

When should I suspect medication-overuse headache and how should I treat it?

Medication-overuse headache (MOH) should be considered in all patients with migraine who experience frequent headaches. This type of headache can develop in any susceptible headache sufferer (migraine or otherwise) who overuses simple analgesics (including NSAIDs), opiates, ergotamine or triptans, and may have features of tension and/or migraine headache.[1,16,17] Typically these headaches don't respond to migraine prophylactic medication.[18] The International Headache Society diagnostic criteria for MOH are summarised in Table 3.

According to these criteria the critical threshold for what constitutes overuse is defined as use on >15 days/month of simple analgesics and >10 days/month of opiates, ergotamine or triptans.[1] Frequent and regular use of headache medication (i.e. on several days a week) appears to be important in developing MOH. Bunching of treatment days with long medication-free periods in between is less likely to cause MOH.[1]

Research on the treatment of MOH is scanty and of poor quality,[19] and treatment recommendations are based on expert opinion. It is essential that overused medications are ultimately discontinued. Patients can do this abruptly or by reducing the dose each week (e.g. by 10%). Some advocate a small dose of regular NSAIDs to help relieve the inevitable withdrawal headaches, and/or introducing a prophylactic medication (e.g. amitriptyline) as the dose of overused medication is reduced.[18] Withdrawal symptoms may last for some time. In one study of patients with MOH who abruptly stopped their medication, the mean duration of withdrawal headache was four days in those overusing triptans, seven days in those overusing ergotamine and 10 days in those overusing analgesics. Eighty-five per cent of those overusing triptans, but only 57% of those overusing ergotamine and 23% of those overusing analgesics were free of headache after 14 days.[20]

Table 3. Diagnostic criteria for medication-overuse headache (adapted from the International Headache Society diagnostic criteria[1])

1. The headache occurs on >15 days/month
2. There is regular overuse of abortive headache medication for >3 months. For simple analgesics this is use on >15 days/month. For opiates, ergotamine and triptans this is use on >10 days/month.
3. Headaches have developed or markedly worsened during the period of medication overuse.
4. Headaches resolve or revert to the previous pattern within two months of discontinuation of the overused medication.

Many of us know that treating patients with MOH can be exceptionally challenging. It therefore makes sense to work hard to prevent patients developing MOH in the first place, with good patient education and skilled migraine management, including careful prescribing.

What treatment can I offer women troubled by migraine associated with menstruation?

While menstruation is a well-known trigger for migraine, there is uncertainty about whether migraine associated with menstruation should be regarded as a separate diagnostic entity.[1] The International Headache Society has included 'pure menstrual migraine' and 'menstrually-related migraine' as tentative subtypes of migraine without aura.[1] Pure menstrual migraine refers to migraines that occur during or close to menstruation, but at no other time, while menstrually-related migraine refers to migraines that occur throughout the cycle but increase in frequency during or close to menstruation.[21]

The mainstay of management is effective acute treatment, when required, using the standard medications (simple analgesics including NSAIDs, ergotamine or sumatriptan, combined when appropriate with metoclopramide or prochlorperazine).[21] However there is some evidence that migraine associated with menstruation can be less responsive to these medications than migraine occurring at other times in the cycle.[21]

If migraines are sufficiently troublesome to warrant prophylactic medication, the approach depends on the headache pattern. If the pattern is consistent with menstrually-related migraine it is appropriate to consider standard migraine prophylactic medication (as discussed earlier in this article). However if the pattern is more consistent with pure menstrual migraine there are several widely recommended options that are summarised in Table 4.[2,6,9,21] These recommendations appear to be based largely on expert opinion, with limited support from a small number of trials.

Table 4. Treatment options for menstrual migraine [2,6,9,21]

Medication	Dosage	Additional points
NSAIDs	e.g. mefenamic acid 500mg tds or naproxen 550mg once or twice daily from first to last days of menstruation.	May be particularly useful for women with dysmennorhea or menorrhagia.
Transdermal oestrogen	100ug patches (50ug if not well tolerated) twice weekly from three days before menstruation for seven days.	Transdermal route recommended over oral route because of more stable levels of oestrogen.
Combined oral contraceptive pill	Hormone pill taken continuously for nine weeks followed by pill-free interval of one week ('tricycling').	Care needed for women with migraine with aura (refer elsewhere in this article). Headaches during pill-free interval may be a problem.
Depo provera		

Can I safely prescribe the combined oral contraceptive pill to women with migraine?

While use of combined oral contraceptives (COCs) may worsen women's migraines,[22] the safety concern relates to the risk of ischaemic stroke.

COCs are a risk factor for ischaemic stroke with a relative risk of

around two for COCs containing less than 50ug of oestrogen.[22] Migraine in general is a risk factor for ischaemic stroke in women under the age of 45 years, with a relative risk of around three.[22] It is uncertain whether migraine without aura is a risk factor – there is more evidence for migraine with aura, which has a relative risk of around six.[22] Furthermore there appears to be a multiplicative effect on the risk for ischaemic stroke when both migraine and COCs use occur together.[22,23] How this translates into absolute risks for women has been estimated and summarised in a very useful table (Table 5).

Table 5. Expected incidence of ischaemic stroke per 100 000 women per year[22]

		Women without migraine		Women with migraine with aura	
Age	Overall*	No COC use	COC use	No COC use	COC use
15–19	0.6	0.4	0.8	2	5
20–24	1.8	1.4	3	8	16
25–29	2.7	1.9	4	11	23
30–34	3.3	2.4	5	14	29
35–39	4.8	3.4	7	20	41
40–44	16.2	11.6	23	70	139

**These figures include patients with diabetes, hypertension, and other risk factors (including smoking). As a result, the stroke incidences shown in the other columns may be less if only women without these additional risk factors are considered.*

Many guidelines (mainly UK guidelines) state that migraine with aura is an absolute contraindication to use of COCs.[24] In contrast, other guidelines take a more flexible approach and recommend carefully balancing the needs of a woman with her particular cardiovascular risk profile.[23] Clearly there is a big difference between prescribing the COC pill to an 18-year-old who experiences infrequent migraine with aura but has no other cardiovascular risk factors, and a 36-year-old with migraine with aura, who smokes, has hypertension and a family history of premature arterial disease.

A summary of the recommendations of the International Headache Society Task Force on Combined Oral Contraceptives and Hormone replacement Therapy is: *'There is no contraindication to the use of COCs in women with migraine in the absence of migraine aura or other (cardiovascular) risk factors. Women should be counselled and regularly assessed for the development of additional risk factors. There is a potentially increased risk of ischaemic stroke in women with migraine who are using COCs and have additional risk factors which cannot easily be controlled, including migraine with aura. One must individually assess and evaluate these risks. Combined oral contraceptive use may be contraindicated. Identify and evaluate risk factors.'*[23]

Use of progestogen-only hormonal contraception does not appear to be associated with an increased risk of stroke.[23]

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