Management of migraine in Australian general practice

Richard J Stark, Lisa Valenti and Graeme C Miller

ABSTRACT

Objectives: To determine the proportion of patients who have a diagnosis of migraine in a sample of Australian general practice patients, and to review the prophylactic and acute drug treatments used by these patients.

Design, setting and participants: A cohort of general practitioners collected data from about 30 consecutive patients each as part of the BEACH (Bettering the Evaluation and Care of Health) program; this is a continuous national study of general practice activity in Australia. The migraine substudy was conducted in June–July 2005 and December 2005–January 2006.

Main outcome measures: Proportion of patients with a current diagnosis of migraine; frequency of migraine attacks; current and previous drug treatments; and appropriateness of treatment assessed using published guidelines.

Results: 191 GPs reported that 649 of 5663 patients (11.5%) had been diagnosed with migraine. Prevalence was 14.9% in females and 6.1% in males. Migraine frequency in these patients was one or fewer attacks per month in 77.1% (476/617), two per month in 10.5% (65/617), and three or more per month in 12.3% (76/617) (missing data excluded). Only 8.3% (54/648) of migraine patients were currently taking prophylactic medication. Patients reporting three or more migraines or two migraines per month were significantly more likely to be taking prophylactic medication (19.7% and 25.0%, respectively) than those with less frequent migraine attacks (3.8%) ($P < 0.0001$). Prophylactic medication had been used previously by 15.0% (96/640). The most common prophylactic agents used currently or previously were pizotifen and propranolol; other appropriate agents were rarely used, and inappropriate use of acute medications accounted for 9% of "prophylactic treatments". Four in five migraine patients were currently using acute medication as required for migraine, and 60.6% of these medications conformed with recommendations of the National Prescribing Service. However, non-recommended drugs were also used, including opioids (38% of acute medications).

Conclusions: Migraine is recognised frequently in Australian general practice. Use of acute medication often follows published guidelines. Prophylactic medication appears to be underutilised, especially in patients with frequent migraine. GPs appear to select from a limited range of therapeutic options for migraine prophylaxis, despite the availability of several other well documented efficacious agents, and some use inappropriate drugs for migraine prevention.

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It is recognised worldwide that migraine is common, underdiagnosed and often inadequately treated. The prevalence of migraine is about 6% in men and 18% in women, as assessed in community surveys.[1-3]

Modern studies define migraine by criteria published by the International Headache Society.[4] A recent community-based study in the United States revealed that, in patients with migraine as defined by these criteria, 52% had not been diagnosed by a doctor, and 57% took only over-the-counter medications.[5] Even those patients who had not been medically diagnosed were substantially disabled by migraine, with 24% missing at least a day of work, and 45% having at least a day of reduced productivity in the previous 3 months.

There have been recent advances in both the acute treatment and prophylaxis of migraine.[6-8] The introduction of triptans has improved the chances of obtaining swift and substantial relief from migraine attacks for many patients. There has also been recent emphasis on the difficulty in managing frequent migraine attacks. Chronic daily headache (at least 15 headache days per month) occurs in 4% of the population, and in half of these it arises from migraine ("chronic migraine" or "transformed migraine").[9] In some of these cases, the transformation from episodic to chronic migraine results from overuse of acute headache medication, especially narcotic- or codeine-based analgesics, but also ergotamines, triptans and even simple analgesics. There is thus a great need to optimise the use of available effective prophylactic agents.

Our aims in this study were to determine:

- the proportion of Australian general practice patients diagnosed with migraine;
- the usual acute treatments these patients used; and
- the approaches to prophylactic medication, including which drugs were currently used and which had been previously trialled.

METHODS

The BEACH (Bettering the Evaluation and Care of Health) program is a continuous national study of general practice activity in Australia; sampling and methods have been described in detail elsewhere.[10] In summary, each year a random sample of practising general practitioners, drawn from Australian Government GP service claims through Medicare, are invited to participate. About 1000 GPs participate annually, by completing a questionnaire about themselves and their practice, and recording patient morbidity and management details for each of 100 consecutive patient encounters on structured paper forms.

Throughout the year, a series of sub-studies are conducted in conjunction with the ongoing data collection from the GP patient encounters. In each 5-week collection period, about 100 GPs each record information for about 30 patients for each topic. These substudies, known as SAND (Supplementary Analysis of Nominated Data), investigate aspects of patient health not necessarily managed at the encounter (full methodology reported elsewhere).[11] Responses are recorded by the GP about the patient, in discussion with the patient. Using a qualified medical practitioner to record morbidity in conjunction with patient self-report may provide a more accurate classification of patients' health problems than self-report alone.[12,13] Two SAND subsamples — June–July 2005 and December 2005–January 2006 — were used to investigate the prevalence of migraine among patients attending general practice, frequency of migraine attacks, current and previous prophylaxis and current acute medications.

1 Classification of drugs for migraine prophylaxis*

Treatment level	Efficacy	Evidence	Side effects
Level 1	Medium–high	Good	Mild–moderate
Level 2	Lower efficacy than Level 1†	Limited†	Mild–moderate
Level 3	Clinical consensus	None	Mild–moderate
Level 4	Medium–high	Good	Concern
Level 5	None over placebo	Various	Various

* Based on American Academy of Neurology guidelines.[15]
† The criterion for Level 2 drugs is either lower efficacy than Level 1 drugs or limited evidence. ◆

The number of questions that could be asked was limited by the space available on the recording form. Each GP was asked to record whether or not, in his or her opinion after speaking with the patient, each of 30 consecutive patients suffered from migraine attacks. If the response was "no", the questions ended. Where a "yes" response was recorded, the GP was asked to report the usual migraine frequency per month (four tick-box options: < 1, 1, 2 and ≥ 3). Prophylactic medications and current medications for acute treatment were described in free text, and the reason for discontinuation of previous prophylaxis was requested with a series of tick boxes (lack of efficacy, cost, withdrawal after successful treatment, and side effects).

Classification of medications

All medications used for migraine were classified according to the Anatomical Therapeutic Chemical classification.[14]

Prophylactic drugs were grouped according to the American Academy of Neurology guidelines[15] into five treatment levels based on evidence, efficacy, and side effects (Box 1). Treatment Level 1 is the "gold standard" for prophylactic medication, with Level 2 also acceptable based on current scientific knowledge and evidence. Doctors were permitted to record multiple prophylactic medications per patient, but we counted only the highest ranked (ie, lowest numbered) medication for each patient.

Medications for acute treatment were grouped using National Prescribing Service (NPS) recommendations,[16] which divide medications into two treatment groups — one group for mild to moderate migraine, and a second group for severe or unresponsive migraine. Up to two acute medications used at the time of a migraine attack were specified by the GP.

Statistical methods

A cluster sample design was used. The GP was the primary sampling unit, and the unit of analysis was patients at the GP–patient encounter. Robust 95% confidence intervals were determined, accounting for the cluster sample study design, using procedures in SAS software (version 8.2, SAS Institute, Cary, NC, USA). Rates and percentages were judged significantly different by non-overlapping 95% confidence intervals. The Cochrane–Armitage test was used to assess trends.

2 Prevalence of migraine among 5663 patients attending general practice

	No. with migraine	Prevalence of migraine (robust 95% CI)
All patients	649	11.5% (10.0%–12.9%)
Sex-specific rate*		
Male ($n = 2185$)	133	6.1% (4.7%–7.4%)
Female ($n = 3457$)	514	14.9% (13.0%–16.7%)
Age-specific rate*		
0–14 years ($n = 812$)	10	1.2% (0.5%–2.0%)
15–24 years ($n = 551$)	59	10.7% (7.5%–14.0%)
25–44 years ($n = 1448$)	255	17.6% (14.9%–20.3%)
45–64 years ($n = 1517$)	234	15.4% (13.1%–17.8%)
65+ years ($n = 1319$)	89	6.8% (5.0%–8.5%)

* Missing data were removed from calculations (sex was missing for 21 patients, and age for 16 patients). ◆

Ethics approval

The BEACH survey and this substudy were approved by the ethics committees of the University of Sydney and the Australian Institute of Health and Welfare.

RESULTS

Responses were received for 5663 patients from 191 GPs. The GPs reported that 649 patients (11.5%) had been diagnosed (on that day or previously) with migraine (Box 2). Prevalence was significantly higher among female (14.9%) than among male (6.1%) patients ($P < 0.0001$). Migraine prevalence was least among children aged under 15 years (1.2%) and was highest among patients aged 25–44 years (17.6%), followed by those aged 45–64 years (15.4%) (Box 2).

Data on migraine frequency were available for 617 of the 649 patients with diagnosed migraine. More than three-quarters (77.1%) of these 617 patients reported usual migraine frequency as one or fewer attacks per month. An average of two attacks per month was reported by 10.5%, and three or more per month by 12.3% (Box 3).

Prophylactic medication

Fifty-four (8.3%) of the patients with migraine reported they were currently taking prophylactic medication. Most (49) were taking one medication, four were taking two, and one was taking three medications. The proportion taking current prophylaxis increased with migraine frequency ($P < 0.0001$); patients reporting three or more migraines and those reporting two migraines per month were significantly more likely to be taking prophylactic medication (19.7% and 25.0%, respectively) than those with less frequent migraine attacks (3.8%) (Box 3).

Prophylactic medication had been used previously by 96 (15.0%) of the 640 migraine patients who responded to this question. As migraine frequency increased, the likelihood of previous use of prophylactic medication increased ($P < 0.0001$) (Box 3). Multiple responses to "reasons for discontinuing previous prophylaxis" were allowed; the most common reasons were lack of efficacy (46%), side effects (28%), and successful treatment (19%). Of the 96 patients who previously took prophylactic medication, 16 (17%) had switched to another prophylaxis. Therefore, most (83%) were not taking second-line prophylaxis (results not shown).

3 Frequency of migraine, current and previous use of prophylactic medication, and current use of acute migraine medication among 649 patients diagnosed with migraine

	Frequency of migraine		Current prophylaxis		Previous prophylaxis		Current acute medication	
	No.	% of respondents (robust 95% CI)*	No.	% (robust 95% CI)*	No.	% (robust 95% CI)*	No.	% (robust 95% CI)*
Respondents	617	100%	648	100%	640	100%	605	100%
Total (% of respondents)	617	100%	54	8.3% (6.0%–10.6%)	96	15.0% (11.8%–18.2%)	480	79.3% (75.2%–83.5%)
Frequency (% of frequency group)								
⩽ 1 per month	476	77.1% (73.2%–81.1%)	18	3.8% (1.9%–5.6%)	51	10.8% (7.7%–14.0%)	335	76.3% (71.3%–81.3%)
2 per month	65	10.5% (7.7%–13.3%)	16	25.0% (13.5%–36.5%)	13	20.3% (8.7%–32.0%)	57	90.5% (83.4%–97.6%)
⩾ 3 per month	76	12.3% (9.5%–15.1%)	15	19.7% (10.5%–29.0%)	27	37.0% (25.0%–49.0%)	64	87.7% (79.6%–95.8%)
Missing data	32	—	5	—	5	—	24	—
P (trend test)	—	—	—	< 0.0001	—	< 0.0001	—	0.005

* Missing data were removed from calculations. ◆

Few patients were currently using multiple prophylactic medications (six of 54 patients, the remainder taking a single agent). Two-thirds (67%) of patients were currently taking treatment Level 1 or Level 2 prophylactic medication. Fourteen (26%) of these 54 patients were taking Level 1 prophylaxis (predominantly propranolol, 12/14), and 22 (41%) were using Level 2 prophylaxis (predominantly pizotifen, 17/22). The remaining third of patients used Level 3–5 or inappropriate medications for prophylaxis, such as hormones, acute or herbal medications (Box 4 and Box 5).

The pattern was similar for the prophylactic medications used previously. Of the 84 patients for whom the previous medication was specified, 22 (26%) had used Level 1 medications (77%, propranolol) and 55% had used Level 2 medications (94%, pizotifen). For both current and previous prophylaxis, Level 1 or 2 medications other than propranolol and pizotifen were rarely used (Box 4 and Box 5).

Acute medications

In contrast to the infrequent use of prophylaxis, four in five migraine patients (79.3%) were currently using acute medication as required for migraine. Likelihood of its use was related to migraine frequency ($P < 0.01$): 76.3% of those who experienced one migraine or fewer per month, 90.5% of those who experienced two per month, and 87.7% of those who experienced three or more per month used acute medication (Box 3).

GPs listed 495 acute medications used at the time of a migraine attack. About three in five (60.6%; 95% CI, 55.5%–65.7%) of these medications were those recommended by the NPS as options for acute drug treatment of migraine. These included simple analgesics or non-steroidal anti-inflammatory drugs (NSAIDs), with or without an anti-emetic, for mild to moderate migraine,

4 Current and previous use of migraine prophylactic medications*

	Current use ($n = 54$)		Previous use ($n = 84$)	
Treatment category	No.	% of patients (95% CI)	No.	% of patients (95% CI)
Level 1	14	26% (14%–38%)	22	26% (15%–38%)
Level 2	22	41% (26%–55%)	46	55% (44%–66%)
Level 3	3	6% (0–12%)	5	6% (0.7%–11%)
Level 4	3	6% (0–12%)	3	4% (0–8%)
Level 5	3	6% (0–12%)	2	2% (0–6%)
Acute (inappropriate use)	5	9% (1%–17%)	6	7% (2%–13%)
Hormones	3	6% (0–12%)	0	—
Herbal (ginger)	1	2% (0–6%)	0	—
Total medications	60	100%	88	

* Missing data were removed from calculations: the medication was not specified for 12 patients who had previously used prophylaxis. Multiple medications could be reported per patient, but only the medication with the highest ranking (ie, lowest numbered) treatment level was counted for each patient. ◆

5 Number of patients using prophylactic medications currently (previously)

Level 1: propranolol, 12 (17); amitriptyline, 2 (2); valproate, 1 (3); timolol, 0 (0); topiramate, 0 (0).

Level 2: pizotifen, 17 (43); metoprolol, 2 (1); atenolol, 2 (0); gabapentin, 1 (0); magnesium aspartate, 1 (0); feverfew, 1 (0); naproxen, 0 (2); candesartan, 0 (0); verapamil, 0 (0).

Level 3: cyproheptadine, 2 (2); dothiepin, 1 (0); nortriptyline, 0 (1); other antidepressant, 0 (2).

Level 4: methysergide, 3 (3).

Level 5: carbamazepine, 1 (0); phenytoin, 1 (0); enalapril, 1 (0); ramipril, 1 (0); clonidine, 0 (1); indomethacin, 0 (1); celecoxib, 0 (1).

Acute treatment (inappropriate): ergotamine, 2 (4); codeine-based compound analgesics, 2 (1); oxycodone, 1 (0); sumatriptan, 1 (2); zolmitriptan, 1 (0); paracetamol, 0 (2).

Hormones: 3 (0).

Herbal: ginger, 1 (0).

Total medications: 60 (88). ◆

6 Critique of the current management of migraine by Australian general practitioners

What do Australian GPs do well in managing migraine?

- The underdiagnosis of migraine appears to be less in Australian general practice than has been recorded elsewhere in the world.
- Australian GPs appear, in general, to follow recommended guidelines in the use of acute medications. However, combined analgesics containing codeine are still overused.

How can we improve practice for patients with migraine?

- Consider use of prophylactic agents when headache frequency is greater than two per month.
- Consider using a broader range of preventive agents. If side effects or contraindications limit the use of an agent (eg, asthma for propranolol; or obesity or weight gain for pizotifen), or if the agent first chosen proves ineffective, consider the many other agents that may be suitable.
- Be alert to the risk of medication-overuse headache, and try to limit frequent use of ergotamines, triptans and particularly opioids. ◆

and triptans or ergotamine, with or without an anti-emetic, for severe or resistant migraine (results not shown).

Non-recommended drugs prescribed included opioids (188 of the 495 medications or 38%), with combination analgesics containing codeine predominating (157 medications, 32%). Morphine or pethidine were used in 14 patients.

DISCUSSION

Prevalence of migraine: In this study, GPs reported that 14.9% of female patients and 6.1% of male patients experienced migraine. Community-based studies from around the world indicate that the prevalence of migraine is about 18% in women and 6% in men.[1-3] One might conclude that migraine is not substantially underdiagnosed in Australia. However, at least a proportion of migraineurs require prescription medication for their condition, increasing the likelihood of presenting to a GP, and the figures might thus be skewed to recording a higher-than-true prevalence of migraine. Conversely, patients with undiagnosed migraine would not be recorded by our methodology. Based on experience from other countries, we would expect that many cases of migraine would be misclassified as other forms of headache, both by patients[17] and by their treating doctors.[18]

Frequency of migraine: 12.3% of patients reported three or more migraines per month, while 77.1% reported one or fewer per month. These findings contrast with previous data. Stewart et al reported a median frequency of 1.5 per month.[19] Community-based studies of chronic daily headache (defined as 15 or more headache days per month) indicate a prevalence of 4%, with about half of these cases being migrainous.[9] On this basis, the reporting of frequent migraine in our study may be below that expected and may reflect misclassification of frequent migrainous headaches as tension-type headaches, as has been documented in other populations.[18]

Use of acute medication: Most patients reported using simple analgesics available over the counter. This is in keeping with published guidelines. For acute drug treatment of migraine, the NPS recommends analgesia or NSAIDs, with an anti-emetic if necessary, for mild to moderate migraine.[16] For severe migraine, or where there is no response to analgesia, the recommendation is a triptan or ergotamine. While guidelines emphasise the need for caution with opioids, especially combined analgesics,[20] these accounted for 38% of acute treatments. This suggests the need for further education not only of GPs, but also of the general public, as many combined analgesics are available over the counter.

Use of prophylactic medication: Australian Therapeutic Guidelines recommend regular preventive treatment if the patient continues to experience more than two or three acute attacks of migraine per month.[20] Other experts highlight that some patients with prolonged or disabling attacks might warrant prophylaxis with a lower attack frequency.[7] About 20% of the patients in our study who had three or more migraines per month were currently receiving prophylaxis; of those not taking prophylaxis, 33% had previously tried it but stopped, while 67% had never received such treatment. This finding suggests a reluctance to use such treatments and raises the question of why this should be. We can only speculate on this. GPs may underestimate the impact that frequent migraine has on patients. GPs or patients may be satisfied with the control provided by acute medications. They may be suspicious of side effects in available medications, or doubt their efficacy. In this study, when preventive agents were discontinued, it was because of lack of efficacy in 46% of patients and side effects in 28%.

Choice of prophylactic medication: The American Academy of Neurology has published an influential practice parameter and evidence-based review of migraine treatment.[15] The classification of preventive treatments outlined in Box 4 is based on this. Pizotifen is not available in the US and is not listed in that review; however, based on review of evidence (predominantly small and, by modern standards, poorly designed trials from the 1960s and 1970s[21]), it would fall into treatment Level 2. In the current study, pizotifen and propranolol were the predominant choices with regard to current prophylactic therapy (31% and 22% of patients, respectively) and previous prophylactic therapy (51% and 20% of patients, respectively). Other medications from treatment Levels 1 and 2 were rarely used. The failure of GPs to prescribe drugs other than pizotifen or propranolol may suggest a lack of familiarity with alternatives that are well supported by published data and guidelines, or lack of confidence in using these drugs. However, GP prescribing of valproate and topiramate for migraine may be inhibited by other factors: the NPS states, "While the anti-epileptics valproate and topiramate have demonstrated efficacy, valproate is not approved for migraine prophylaxis and topiramate is not available through the PBS [Pharmaceutical Benefits Scheme] for its migraine prevention indication".[16] Lack of a PBS subsidy results in greater out-of pocket expense for the patient. GPs are more likely to prescribe new drugs when they have been strongly promoted by the pharmaceutical industry;[22] lack of Therapeutic Goods Administration and/or PBS listing of Level 1 drugs for migraine, and, in many cases, expiry of patent may inhibit pharmaceutical promotion of these drugs.

Of particular concern was the use of acute agents (analgesics, triptans and ergotamines) as prophylaxis, with 9% of patients reporting using such an approach. The risk of medication-overuse headache is high in these circumstances,[23] and the American Academy of Neurology practice parameter notes that many experts limit the use of ergotamines, triptans and opioids to two headache days per week for this reason.[15] Regular daily use of these agents is clearly inappropriate.

A critique of the current management of migraine by Australian GPs is provided in Box 6.

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COMPETING INTERESTS

Richard Stark has acted as a consultant to Janssen-Cilag, Allergan and Pfizer. He has received speaker fees from Janssen-Cilag.

AUTHOR DETAILS

Richard J Stark, FRACP, MACLM, Neurologist[1] and Honorary Clinical Associate Professor[2]
Lisa Valenti, BEc, Senior Research Analyst[3]
Graeme C Miller, PhD, FRACGP, Associate Professor and Medical Director[3]

1 Neurology Department, Alfred Hospital, Melbourne, VIC.
2 Department of Medicine, Monash University, Melbourne, VIC.
3 Family Medicine Research Centre, School of Public Health, University of Sydney, Sydney, NSW.

Correspondence:
richard.stark@med.monash.edu.au

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