

# Identifying and Treating Chronic Migraine

Gordon Robinson, MD, FRCPC

## Case Study

- Female patient, 48 years old
- 25-year history of frequent migraine headaches
- Typically only has 5-10 headache-free days per month, although headache severity varies from day to day
- Most headaches last 8-10 hours
- Treats most attacks with triptan medication ± over-the-counter analgesics
- Frequently misses work because of her headaches

Chronic migraine is a distinct neurological condition with specific diagnostic criteria. The International Headache Society defines chronic migraine as, "headache occurring on 15 or more days per month for more than 3 months, which has the features of migraine headache on at least 8 days per month."<sup>1</sup>

Identifying this condition among patients who present complaining of headache involves taking a careful history to ensure diagnostic criteria are satisfied, as well as considering other potential diagnoses. Statistics have shown that chronic migraine is substantially underdiagnosed and, even among those who do receive a diagnosis, undertreated.<sup>2</sup>

This short review summarizes the epidemiology, burden, diagnosis, screening, treatment and referral for chronic migraine.

### EPIDEMIOLOGY OF CHRONIC MIGRAINE

There are currently no reliable Canadian epidemiologic data on chronic migraine. However, the authors of a systematic international literature search reported that the most commonly reported prevalence rates for chronic migraine were in the 1.4% to 2.2% range.<sup>3</sup> Applying these figures to a Canadian adult population estimate of approximately 28.6 million,<sup>4</sup> the estimated number of Canadians living with chronic migraine is in the range of 400,000-600,000 individuals. The prevalence

has been reported to be considerably higher in women than in men, with reported rates ranging from 2.5- to 6.5-fold higher in women.<sup>3</sup>

### BURDEN OF CHRONIC MIGRAINE

In general, migraine is associated with substantial burden on patients.<sup>5,6</sup> The condition is associated with debilitating pain, nausea, vomiting, photophobia and phonophobia. Given that patients who fit the criteria for chronicity experience the features of migraine at least eight days per month (and often far more frequent than that), it is not surprising that this condition has a negative impact on normal life activities, including the ability to work, perform other routine daily activities, and participate in social and family relationships.

For chronic migraine in particular, the burden on individual patients is significantly greater than for episodic migraine in terms of disability, health-related quality of life, anxiety, depression and use of health-care resources.<sup>6-8</sup>

### DIAGNOSIS, CLASSIFICATION AND DIFFERENTIATION

Research has shown that chronic migraine is underdiagnosed. In an American survey of headache sufferers, 520 of the 16,573 respondents had chronic migraine. However, only 20.2% of these patients had received such a diagnosis from a health-care professional.<sup>6</sup>

The diagnosis of chronic migraine can be broken down into three basic steps: 1) excluding secondary headache; 2) identifying the primary syndrome based on attack frequency and duration; and 3) diagnosing the specific headache disorder. Going through these components requires taking a careful patient history.



**Gordon Robinson, MD, FRCPC**

Clinical Professor  
Director of Undergraduate Education  
Division of Neurology  
University of British Columbia  
Medical Manager, Neurology  
Vancouver General Hospital  
Vancouver, British Columbia

# Identifying and Treating Chronic Migraine

**Excluding secondary headache.** There are many potential causes of secondary headache, including trauma/injury, cranial or cervical vascular disorders, non-vascular intracranial disorders, substance use or substance withdrawal, infection, disorders of homeostasis and psychiatric disorders. The presence of red flags can signal the possibility that the headache is secondary to another condition. These are summarized by a helpful mnemonic, SNOOP, which is detailed in Table 1.<sup>9</sup> If any of these red flags are encountered, the patient should be worked up for secondary headache.

Comorbidities are common among patients with migraine and may complicate the diagnostic process. Being aware of any comorbidities and discussing with the patient the timing of headache with respect to symptoms of their comorbidity(ies) may help distinguish whether the headache is a separate entity or secondary to the other condition. The proportion of patients with major depression who also experience chronic migraine, for example, is approximately 14%.<sup>10</sup> Given that the lifetime prevalence of major depression is approximately 10% in Canada,<sup>11</sup> this is a comorbidity to be aware of among patients presenting with headaches. Looked at the other way, among patients with chronic migraine, more than half will experience comorbid depression,<sup>12</sup> and this can have an impact on treatment selection for both disorders.

**Identifying the primary syndrome.** This involves two components; frequency and duration. Episodic headache is present on fewer than 15 days per month, while chronic headache involves 15 or more days per month. Importantly, when counting headache days, every headache needs to be counted, not just those that are severe. This may require probing during the history taking, as patients may not think to report milder, less debilitating headaches. One might consider asking, "How many days are you completely free of headache?" The use of a headache diary is highly recommended.

With respect to duration, the most important threshold is whether the headaches are more or less than four hours in duration.

**Diagnosing the specific headache disorder.** If secondary headache has been ruled out and the frequency and duration have been recorded, one can then explore the features of the headache in order to determine the correct diagnosis. The diagnostic features of migraine are shown in Table 2.<sup>1</sup>

The major differentiating features of chronic migraine compared to chronic tension-type headache are that migraine is typically unilateral and pulsating, while tension-type headache is bilateral and non-pulsating. In addition, migraine is often aggravated by physical activity, while tension-type headache is typically not aggravated in this way. Furthermore, migraine attacks are of a moderate to incapacitating severity.<sup>1</sup>

**Classification and nomenclature.** The terms discussed above are those that are the currently accepted standards in the classification of headache. Several previously used terms should no longer be used. This may be important in the selection of

Table 1 Red Flags for Secondary Headache: SNOOP<sup>9</sup>

- Systemic symptoms/signs (fever, myalgias, weight loss) or systemic disease (malignancy, HIV/AIDS)
- Neurologic symptoms or signs
- Onset sudden
- Onset after age 40
- Pattern change (progressive headache with loss of headache-free periods, change in type of headache)

treatment, as certain treatments are only indicated and/or recommended for specific diagnoses.

For example, if a patient experiences both tension-type and migraine headaches and the frequency is 15 or more episodes per month, the diagnosis is chronic migraine.<sup>1</sup> Previously this was known as "mixed headache."<sup>1</sup>

The term "transformed migraine," which was used to describe a patient who previously fit the criteria for episodic migraine and went on to meet the criteria for chronic migraine, is no longer used.<sup>1</sup>

**Screening for chronic migraine.** While a well-conducted history is usually sufficient to make a diagnosis of chronic migraine, there are tools that can be informative and help

 Only 20.2% of patients with chronic migraine received this diagnosis from a healthcare professional.

save time for busy clinicians. The Identify Chronic Migraine (ID-CM) tool was specifically developed to help identify chronic migraine among patients with severe headache.<sup>13</sup>

The ID-CM is a 12-question survey that can be completed by patients in the waiting room or prior to the visit. It should take no longer than five minutes to complete. This tool has an 80.6% sensitivity for chronic migraine, a specificity of 88.6%, negative predictive value of 75.0%, and a positive predictive value of 91.5%.<sup>13</sup>

## TREATMENT OPTIONS AND CONSIDERATIONS

One of the key elements of treatment for chronic migraine—as is the case with all chronic conditions—is patient education. Providing counselling about the condition and its treatment can help the patient make informed decisions, foster a positive clinician-patient relationship, and increase the likelihood of adherence.

Time and resource constraints may limit the amount of time the clinician can interact with each patient, so it is most helpful to have educational materials on hand and be able to refer patients to trusted internet resources. Among the latter options are:

- Headache Network Canada (<http://headachenetwork.ca>)
- MyChronicMigraine (<http://www.mychronicmigraine.ca>)

**Table 2** Diagnostic Criteria for Migraine Headache—ICHD-3<sup>1</sup>

**I: Migraine without aura**

- A. At least five attacks fulfilling criteria B-D (below)
- B. Headache attacks lasting 4-72 hours (untreated or unsuccessfully treated)
- C. Headache has at least two of the following four characteristics:
  - 1. Unilateral location
  - 2. Pulsating quality
  - 3. Moderate or severe pain intensity
  - 4. Aggravation by or causing avoidance of routine physical activity (e.g., walking or climbing stairs)
- D. During headache at least one of the following:
  - 1. Nausea and/or vomiting
  - 2. Photophobia and phonophobia
- E. Not better accounted for by another ICHD-3 diagnosis

**II: Migraine with aura**

- A. At least two attacks fulfilling criteria B and C (below)
- B. One or more of the following fully reversible aura symptoms:
  - 1. Visual
  - 2. Sensory
  - 3. Speech and/or language
  - 4. Motor
  - 5. Brainstem
  - 6. Retinal
- C. At least two of the following four characteristics:
  - 1. At least one aura symptom spreads gradually over  $\geq 5$  minutes, and/or two or more symptoms occur in succession
  - 2. Each individual aura symptom lasts 5-60 minutes
  - 3. At least one aura symptom is unilateral
  - 4. The aura is accompanied, or followed within 60 minutes, by headache
- D. Not better accounted for by another ICHD-3 diagnosis, and transient ischemic attack has been excluded

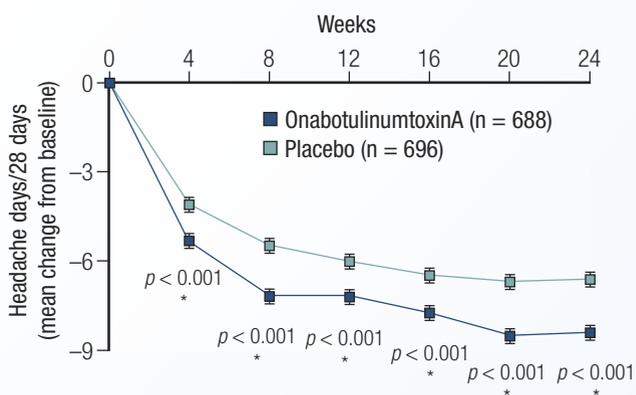
ICHD-3: International Classification of Headache Disorders, 3rd edition

The treatment of chronic migraine is multifactorial, and can include lifestyle/behaviour changes (e.g., healthy eating, regular exercise, smoking cessation), psychotherapeutic approaches (e.g., cognitive behavioural therapy, meditation/mindfulness) and pharmacotherapy.<sup>14-16</sup> Research has shown that chronic migraine is undertreated. In a patient survey, only 31.6% of respondents with chronic migraine indicated that they were using migraine-specific acute treatments.<sup>6</sup> Fewer than half (48.1%) were satisfied with their acute therapy. The proportion of chronic migraine sufferers who were using preventive medications was also low, at 33.3%.<sup>6</sup>

**OnabotulinumtoxinA.** With respect to pharmacotherapy, there is only one treatment approved by Health Canada for chronic migraine. OnabotulinumtoxinA injections are indicated for the prophylaxis of headaches in adults with chronic migraine ( $\geq 15$  days per month with headache lasting 4 hours a day or longer).<sup>17</sup> The key data to support this indication come from two randomized, controlled clinical trials, PREEMPT 1 and PREEMPT 2, published in 2010.<sup>18,19</sup> These trials had identical designs: 24-week randomized, double-blind phase, followed by a 32-week open-label phase. In the double-blind phase, patients were randomized to receive either onabotulinumtoxinA (155-195 U) or placebo injections every 12 weeks, with the primary endpoints (mean change in frequency of headache days) evaluated at 24 weeks.

In a pooled analysis of both studies (total n = 1,384),<sup>20</sup> the frequency of headache days was significantly reduced by 8.4 days for onabotulinumtoxinA compared to 6.6 days for placebo ( $p < 0.001$ ). The difference was significant at all time points evaluated (Figure 1). Most adverse events (AEs) in the trials were mild to moderate in severity; the proportions of

**Figure 1** Mean Change in Frequency of Headache Days (per 28 days), OnabotulinumtoxinA vs. Placebo (PREEMPT Pooled Analysis)<sup>20</sup>



patients discontinuing due to AEs were 3.8% for onabotulinumtoxinA and 1.2% for placebo.

**Topiramate.** Although not approved for chronic migraine in Canada, oral topiramate has also demonstrated a significant reduction in mean number of headache days when administered as prophylaxis among patients with chronic migraine.<sup>21</sup> In a randomized clinical trial involving 328 patients with chronic migraine, topiramate was associated with a mean reduction of 5.6 headache days from baseline, which was significantly greater than the mean 4.1-day reduction in the placebo group. Discontinuations due to AEs were reported in 10.9% of topiramate-treated subjects

# Identifying and Treating Chronic Migraine

and 6.1% of those in the placebo group.

**Implications of medication overuse.** In addition to issues of prophylaxis, patients experiencing migraines may also treat their headaches symptomatically (e.g., with triptan medications and/or analgesics).<sup>22</sup> Overuse of medications (defined as  $\geq 10$  triptans or  $\geq 15$  over-the-counter treatments per month for  $> 3$  months) can cause medication overuse headache.<sup>1</sup> Importantly, this diagnosis can be made in conjunction with chronic migraine.<sup>1</sup> Many patients with overuse headache improve after discontinuation of the overused medication, and their responsiveness to preventive treatment is also enhanced.<sup>1</sup>

## REFERRAL FOR CHRONIC MIGRAINE

Differentiation and diagnosis of specific headache type is certainly possible in primary care. However, for those cases where diagnostic uncertainty persists, referral to a headache specialist is in the patient's best interest. Patients not respond-

ing to medication or who are overusing medications should also be considered for referral.

## CONCLUSIONS

Chronic migraine is a common condition that is underdiagnosed and often undertreated. To aid in diagnosis, clinicians should familiarize themselves with the current diagnostic criteria and nomenclature, and consider incorporating the ID-CM as a tool for their patients with severe and chronic headaches.

Effective treatments exist both for treatment of migraine (e.g., triptans) and for prophylaxis (e.g., onabotulinumtoxinA). Patient education is also a critical part of the treatment plan.

For those patients in whom there is uncertainty regarding either diagnosis or treatment, referral to a headache specialist is recommended.

## Case Study Conclusion

- History shows that the patient meets the criteria for chronic migraine and medication overuse headache
- The patient receives education directed towards her specific headache diagnose
- Lifestyle modifications, including regular exercise and sleep hygiene, are suggested
- Acute medications are restricted to no more than twice a week
- Prophylaxis with onabotulinumtoxinA is started using the PREEMPT protocol
- After 6 months of management, the patient's migraine headaches are reduced to an average of once a week, responsive to the triptan drug

Development of this article was sponsored through an educational grant from Allergan. The author had complete editorial independence in the development of this article and is responsible for its accuracy. The sponsor exerted no influence in the selection of the content or material published.

### References:

1. Headache Classification Committee of the International Headache Society (IHS). The International Classification of Headache Disorders, 3rd edition (beta version). *Cephalalgia* 2013; 33(9):629-808.
2. Lipton RB, Diamond S, Reed M, et al. Migraine diagnosis and treatment: results from the American Migraine Study II. *Headache* 2001; 41(7):638-45.
3. Natoli JL, Manack A, Dean B, et al. Global prevalence of chronic migraine: a systematic review. *Cephalalgia* 2010; 30(5):599-609.
4. Statistics Canada. Table 051-0001 – Estimates of population, by age group and sex for July 1, Canada, provinces and territories, annual (persons unless otherwise noted), CANSIM (database). (Accessed: 2015-06-26).
5. Manack AN, Buse DC, Lipton RB. Chronic migraine: epidemiology and disease burden. *Curr Pain Headache Rep* 2011; 15(1):70-8.
6. Bigal ME, Serrano D, Reed M, et al. Chronic migraine in the population: burden, diagnosis, and satisfaction with treatment. *Neurology* 2008; 71(8):559-66.
7. Blumenfeld AM, Varon SF, Wilcox TK, et al. Disability, HRQoL and resource use among chronic and episodic migraineurs: results from the International Burden of Migraine Study (IBMS). *Cephalalgia* 2011; 31(3):301-15.
8. Stokes M, Becker WJ, Lipton RB, et al. Cost of health care among patients with chronic and episodic migraine in Canada and the USA: results from the International Burden of Migraine Study (IBMS). *Headache* 2011; 51(7):1058-77.
9. Dodick DW. Clinical cues and clinical rules: primary vs secondary headache. *Adv Stud Med* 2003; 3(6C):S550-S555.
10. Hung CI, Liu CY, Juang YY, et al. The impact of migraine on patients with major depressive disorder. *Headache* 2006; 46(3):469-77.
11. Patten SB, Williams JV, Lavorato DH, et al. Descriptive epidemiology of major depressive disorder in Canada in 2012. *Can J Psychiatry* 2015; 60(1):23-30.
12. Juang KD, Wang SJ, Fuh JL, et al. Comorbidity of depressive and anxiety disorders in chronic daily headache and its subtypes. *Headache* 2000; 40(10):818-23.
13. Lipton RB, Serrano D, Buse DC, et al. Improving the detection of chronic migraine: development and validation of Identify Chronic Migraine (ID-CM). *Cephalalgia* 2015; May 22 [Epub ahead of print].
14. Dodick DW. Clinical practice. Chronic daily headache. *N Engl J Med* 2006; 354(2):158-65.
15. Silberstein SD, Lipton RB, Saper JR. Chronic daily headache including transformed migraine, chronic tension-type headache, and medication overuse headache. In: Silberstein SD, Lipton RB, Dodick DW (eds): *Wolff's Headache and Other Head Pain*, 8th ed. New York: Oxford University Press; 2008: 315-77.
16. Gallagher RM, Cutrer FM. Migraine: diagnosis, management, and new treatment options. *Am J Manag Care* 2002; 8(3 Suppl):S58-73.
17. Allergan Inc. BOTOX® product monograph. Date of approval: July 07, 2014.
18. Aurora SK, Dodick DW, Turkel CC, et al. OnabotulinumtoxinA for treatment of chronic migraine: results from the double-blind, randomized, placebo-controlled phase of the PREEMPT 1 trial. *Cephalalgia* 2010; 30(7):793-803.
19. Diener HC, Dodick DW, Aurora SK, et al. OnabotulinumtoxinA for treatment of chronic migraine: results from the double-blind, randomized, placebo-controlled phase of the PREEMPT 2 trial. *Cephalalgia* 2010; 30(7):804-14.
20. Dodick DW, Turkel CC, DeGryse RE, et al. OnabotulinumtoxinA for treatment of chronic migraine: pooled results from the double-blind, randomized, placebo-controlled phases of the PREEMPT clinical program. *Headache* 2010; 50(6):921-36.
21. Silberstein SD, Lipton RB, Dodick DW, et al. Efficacy and safety of topiramate for the treatment of chronic migraine: a randomized, double-blind, placebo-controlled trial. *Headache* 2007; 47(2):170-80.
22. Worthington I, Pringsheim T, Gawel MJ, et al. Canadian Headache Society Guideline: acute drug therapy for migraine headache. *Can J Neuro Sci* 2013; 40(5 Suppl 3):S1-S80.