MENSTRUAL MIGRAINE:
Breaking the Cycle

Learning Objectives

After completing this activity, participants should be better able to:

- Explain current neural and vascular concepts of migraine pathophysiology
- Incorporate into clinical practice an understanding of the relationship between hormonal fluctuation and the etiology of menstrual migraine
- Utilize emerging protocols to identify and assess patients with menstrual migraine and methods to predict headache onset
- Differentiate among standard and emerging treatment options for menstrual migraine prevention, acute treatment, and ongoing management

Menstrual Migraine: A Pervasive Problem

Migraine headache is a common condition. A prevalence rate of approximately 12% annually has been consistent over the last 20 years. In a study of patients presenting with episodic headache, migraine was the most common diagnosis: 76% were diagnosed with migraine and 18% were considered to have probable migraine.[1] Genetics play a role in migraine expression, with positive family histories found in 75% to 80% of migraine patients.[2]

The annual incidence of migraine among women is approximately 18%—triple the incidence among men (Figure 1).[3-5] Migraine is the headache that drives patients to seek medical help, and most of these patients are women.

For many of these women, the time of menstruation increases the risk of a migraine event. It is estimated that 60% of female migraineurs have menstrual migraines—46% with migraines that occur at menses as well as at other times (classified as "menstrually related migraine") and 14% with "pure menstrual migraine" that occurs only at menstruation.[6]

The high incidence of menstrual migraine results in a significant socioeconomic burden, which is associated with all migraine. Recent estimates of the annual costs for these often disabling headaches total $13 to $17 billion, including the costs of care and lost productivity.[7] In a 3-month study period, 35.1% of patients with migraine had at least 1 day of

Migraine related to menstruation requires a unique treatment approach.

What is the proper ICD-9 coding for menstrual migraine?
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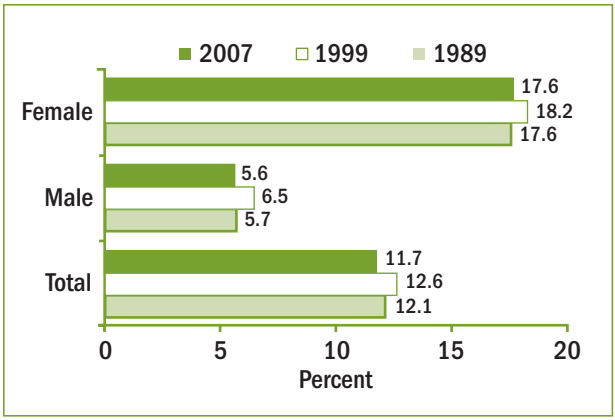


Figure 1. Migraine prevalence in 3 population-based studies. Stewart WF, et al[3]; Lipton RB, et al.[4,5]

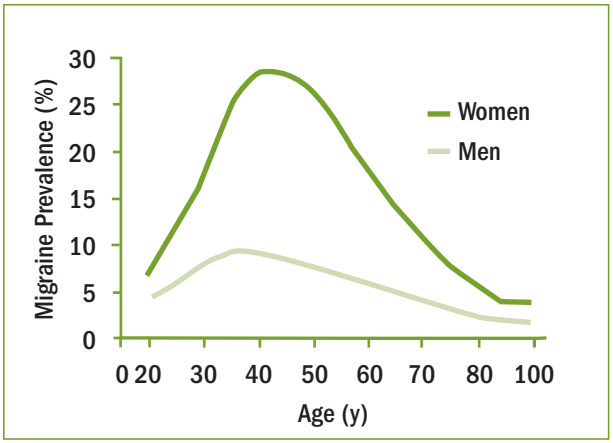


Figure 2. Migraine prevalence by age and sex: disproportionate impact on women during peak years of productivity (age 30 to 50 years). Lipton RB, et al.[4] Copyright © 2001 *Headache*. Reproduced with permission of Blackwell Publishing Ltd.

activity restriction related to headache.[5] Half of patients with migraine report a 50% decline in school or work productivity.[4] Women are disproportionately affected by migraine in their reproductive years (aged 30 to 50) (Figure 2); thus, lost productivity is a significant issue related to menstrual migraine.[4]

Pathophysiology

At one time, migraine was considered a vascular headache caused by a vasodilatory event. Today, migraine is better characterized as the result of a cascade of neurovascular triggers. Acute migraine does not result from a primary vascular event in the brain. Rather, neural events trigger a dilation of blood vessels that cause pain and set off additional nerve activation.[2,8]

The fundamental neural mechanism of migraine is dysfunction of the calcium-ion channel in the nuclei of the brain stem—a channel that normally modulates sensory input and cranial vessel function.[8] Dysfunction in the ion channel may be genetically determined. Specific and differing genetic mutations may be responsible for headache pain and aura in migraine, which may explain why not all migraine sufferers experience aura.[8]

Studies from nonhuman primates show that stimulation of vascular afferent fibers activates neurons in the superficial layers of the trigeminal nucleus caudalis region of the trigeminocervical complex. Peripheral trigeminal activation causes release of calcitonin gene-related peptide (CGRP), a vasodilator.[8]

During the initial phases of a migraine attack, the first-order trigeminal nerve (cranial

nerve 5) becomes activated, causing throbbing pain. This peripheral nerve activation leads to sensitization of the second-order neurons in the brain stem, specifically in the trigeminal nucleus caudalis where cranial nerve 5 makes its connection. Dysfunction in this area of the brain stem sends afferent, nociceptive (ie, stimuli-processing) input through an arc, which ultimately leads to the trigeminal ganglion. The cascade of neurochemical events that follows includes release of proinflammatory neuropeptides (eg, substance P) and inflammation and dilation of the meningeal and dural blood vessels (Figure 3). The ophthalmic division of the trigeminal nerve may generate pain by promoting vasodilation of large cranial and proximal intracranial vessels; at the same time, branches of C2 nerve roots may generate pain in structures of the dura mater. The involvement of the ophthalmic division of the trigeminal nerve, along with dura mater innervated by C2, may explain why migraine pain often occurs over the frontal and temporal regions. Pain in migraine that occurs toward the back of the head (parietal and occipital regions) is most likely referred pain.[8]

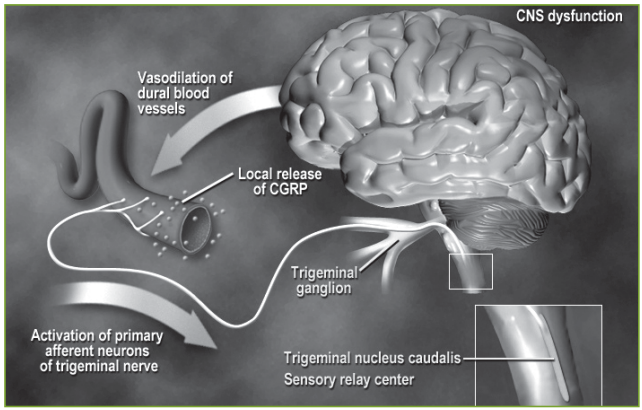


Figure 3. Vasodilation and neurogenic inflammation occur during a migraine attack. There are 3 key events in the migraine process: 1) Activation of the trigeminal nerve (cranial nerve 5) with its 3 divisions: ophthalmic (V1), maxillary (V2), and mandibular (V3); 2) Activation of the brain stem where cranial nerve 5 makes its connection to the brain stem: the trigeminal nucleus caudalis; 3) Inflammation and vasodilatation of the meningeal and dural blood vessels. CNS = central nervous system.

In patients predisposed to this dysfunctional pain signaling, many factors may precipitate an acute migraine event, including diet, physical stimuli, and psychological change. For women of childbearing age, one of the most important factors is the drop in estrogen levels that occurs at menstruation.[2]

During the normal menstrual cycle, levels of estrogen fall during the late luteal phase and are at their low point a few days before and after the onset of menses. Estrogen decline is the primary trigger of menstrual migraine. A study of 38 women with menstrual migraine found that the cyclic decline in estrogen levels was inversely proportional to the prevalence of migraines (Figure 4).[9]

It has been hypothesized that as estrogen levels decline, there is a concurrent drop in levels of brain serotonin (5-hydroxytryptamine [5-HT]) or endorphin levels, leaving the patient more vulnerable and sensitive to pain.[10,11] Other mechanisms, unrelated to estrogen, may also contribute to menstrual migraine, including elevated prostaglandins (possibly due to endometrial prostaglandin production), decreased responsiveness to endogenous opioid activity

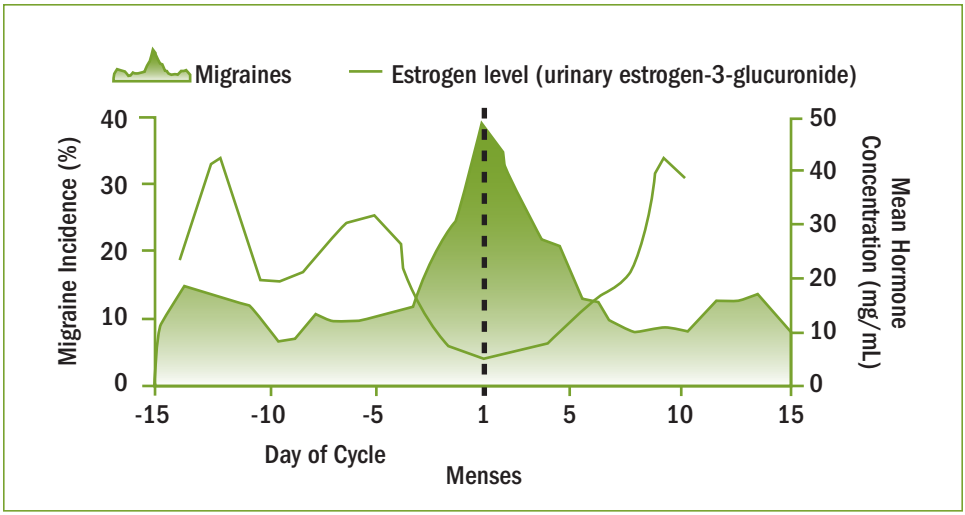


Figure 4. The relationship of estrogen level to migraine prevalence during the menstrual cycle. Study examined estrogen and progesterone metabolites with occurrence of migraine in 38 women who had a diagnosis of menstrual migraine. All participants had regular menses and were not taking oral contraception. Adapted from MacGregor EA, et al.[9]

(decreased opioid tonus), and a decline in circulating ionized magnesium levels.[10,11] The exact mechanisms of menstrual migraine, however, are not fully understood.

Patient Assessment and Migraine Prediction

The diagnosis of menstrual migraine first requires clear differentiation of migraine with or without aura. The International Classification of Headache Disorders II (ICHD-II) was developed by the International Headache Society (IHS) to provide structured criteria for clinical trials and to help clinicians make a differential diagnosis. Migraine without aura is an episodic attack of headache lasting 4 to 72 hours typically with[12]:

At least 2 of the following:

- Unilateral location
- Pulsating quality
- Moderate to severe intensity
- Aggravation by routine physical activity

At least 1 of the following:

- Nausea or vomiting
- Photophobia and/or phonophobia

Migraine with aura includes an aura phase before the headache in addition to all criteria for migraine without aura.[12] Aura symptoms may consist of[12]:

- Reversible positive (flickering lights) or negative (loss of vision) visual symptoms

- Reversible sensory symptoms (eg, tingling, feeling of numbness)
- Reversible speech disturbance (eg, slurred speech)
- At least 1 of these symptoms occurs over at least 5 minutes and lasts no more than 60 minutes. Typically aura lasts for 15 to 20 minutes followed by the headache.

Note: There is *no* motor weakness in migraine with aura; the presence of motor weakness as part of aura suggests hemiplegic migraine.

A simple yet highly sensitive (81%) and specific (75%) assessment tool called the ID Migraine™ Screening Test was developed and validated by Lipton and colleagues.[13] There are 3 questions in this test that address the symptoms most highly correlated with migraine diagnosis. These questions, which are easily incorporated into the clinical interview, a waiting room questionnaire, or an office information management system, ask[13]:

- Has a headache limited your activities for a day or more in the last 3 months?
- Are you nauseated or sick to your stomach when you have a headache?
- Does light bother you when you have a headache?

Affirmative answers to more than 1 of these questions indicate a likely diagnosis of migraine with a positive predictive value of 93% in the primary care setting.[4]

In diagnosing migraine, clinicians need to rule out a headache secondary to another medical condition. One clue to secondary headache is a patient who complains of a particular headache rather than recurrent headaches.[14] A useful mnemonic to aid the differential diagnosis is SNOOP[14]:

- **S**ystemic involvement (eg, fever, malaise) or disease (eg, cancer, AIDS)
- **N**eurologic signs or symptoms of another condition
- **O**nset sudden (eg, thunderclap headache that wakes a patient suddenly)
- **O**nset after 40 years of age (elderly: think temporal arteritis)
- **P**attern of change: progressive headache, greater frequency over time, or change in headache characteristics (eg, "worst headache of patient's life")

The Migraine Disability Assessment (MIDAS) Questionnaire assesses headache-related disability in work and education, household tasks, and family and leisure activities.[15] The MIDAS score is the sum of the number of days lost from those activities and can be used to stratify therapy, starting with nonspecific migraine treatments for lower scores and targeted migraine medications for high scores that indicate significant disability. The test is available to download and reproduce at the National Headache Foundation Web site: http://www.headaches.org.pdf.MIDAS.pdf.

Diagnosing Menstrual Migraine

Once migraine is diagnosed, menstrual migraine can be identified. In the patient with menstrual migraine, headaches are predictably timed to the menstrual cycle, but patients frequently have headaches at other times as well.[16] Reports from specialty clinics suggest that menstrual migraine may be more persistent, painful, and resistant to treatment than migraine

occurring at other times, but this finding has not been confirmed in population-based research.[6] Although menstrual migraine is not a separate diagnostic category, ICHD-2 has established criteria for use in clinical trials of menstrual migraine: migraine without aura occurring between 2 days prior and 3 days after the onset of menses (days −2 through +3) and in 2 of 3 (66%) menstrual cycles.[12] Women may experience migraine with aura perimenstrually. However, menstrual migraine, by definition, is migraine without aura.

In clinical practice, it is important to assess the relationship between headache onset and menstruation. Although timing can be suspected based on patient history, it should be corroborated with a headache diary or calendar; data from these sources are crucial for accurate diagnosis and subsequent treatment planning.[16] Diaries and calendars provide a wealth of information on headache triggers, severity, and duration; quality of life; and efficacy of prescribed therapy and self-care. Patients can use a regular calendar or date book. Clinicians and patients can also download diaries from the American Headache Society (AHS) (www.americanheadachesociety.org) and the National Headache Foundation (NHF) (www.headaches.org).[17,18] Ongoing use of headache diaries and calendars can help monitor therapy. For maximum benefit, it is important that clinicians provide patients with regular education and support, reinforce compliance, and ask the patient to bring the diary to every follow-up visit. As of October 1, 2008, menstrual migraine has been assigned its own ICD-9 codes.[19] To use the coding, the migraine must be without aura and occur in −2 to +3 days of the menstrual cycle in 2 of 3 months (66% of the time). Codes are 346.40 for menstrual migraine that is not intractable (not lasting longer than 72 hours) and 346.41 when migraine is intractable.[19]

Treatment of Menstrual Migraine

Goals of Therapy

The primary goal of acute therapy for menstrual migraine is to abort the current attack, freeing the patient of pain, nausea, vomiting, and photo- or phonophobia if present.[19] Patients want relief as quickly as possible, so therapy must aim for prompt resolution.[19] To achieve acute relief, clinicians may choose from either pharmacotherapy that is nonspecific to migraine or migraine-specific pharmacotherapy. Factors that ensure optimal outcomes include use of an appropriate medication at an adequate dose and treatment at the early and mild stages of an episode.[16]

Nonspecific pharmacotherapy includes nonsteroidal anti-inflammatory drugs (NSAIDs) and compounds of aspirin, acetaminophen, and caffeine; butalbital compounds; opioids; and antiemetic dopamine-2 antagonists. The 2 migraine-specific classes are triptans and ergot derivatives. Intravenous or intramuscular antiemetic drugs (eg, metoclopramide) may be used as adjunctive therapy for nausea and vomiting, and may help increase absorption of the primary treatment. Table 1 lists both nonspecific and specific agents for acute treatment of migraine.[8,21]

Selecting acute treatment involves consideration of the frequency and severity of attacks, degree of associated symptoms like nausea, and patient preference.[8] For some patients with

Table 1. Drugs for Acute Treatment of Migraine

Category/Examples	Efficacy	Tolerability
Migraine-specific drugs		
Triptans (sumatriptan SC, IM, S; oral frovatriptan; rizatriptan; zolmitriptan; almotriptan; eletriptan; naratriptan)	Generally +++ (naratriptan ++)	• CAEs: flushing, lightheadedness, asthenia, chest pain, neck tightness, rebound (overuse) headache • Contraindicated in patients with CAD or CAD risk factors
Ergot alkaloids and derivatives (DHE IV, SC, IM, NS; ergotamine ± caffeine PO)	Wide ranging (eg, ergotamine +; DHE SC/IM +++/++)	• CAEs: nausea, vomiting, vasospasm of the fingers and toes, rebound (overuse) headache with ergotamine (not DHE) • Contraindicated in patients with vasospastic disorders, CAD, pregnancy
Nonspecific drugs		
NSAIDs (eg, aspirin, ibuprofen, naproxen PO)	+ to ++	• CAEs: GI adverse events, rebound (overuse) headache • Contraindicated for use with other NSAIDs, with antithrombotic therapy, or in bleeding disorders
Aspirin, acetaminophen, and caffeine compound PO	+++	• CAEs: GI adverse effects, caffeinism, rebound (overuse) headache • Contraindicated for use with other NSAIDs, with antithrombotic therapy, or in bleeding disorders
Butalbital compounds (eg, butalbital, aspirin, caffeine, and codeine PO)	++	• CAEs: GI problems, agitation, drug overuse; rebound (overuse) headache • Contraindicated in patients with a history of drug addiction/dependence and liver disease; NSAID contraindications
Opioids (butorphanol NS; various opioids alone or with acetaminophen PO; IM/IV opioids)	++ to +++	• CAEs: sedation, abuse liability, rebound (overuse) headache • Contraindicated in patients with a history of drug addiction/dependence

+ = level of efficacy; CAD = coronary artery disease; CAE = common adverse event; DHE = dihydroergotamine; GI = gastrointestinal; IM = intramuscular; IV = intravenous; NS = nasal spray; PO = by mouth; S = suppository; SC = subcutaneous. Loder E [16]; Silberstein SD.[21]

migraine, an NSAID taken as soon as headache symptoms emerge is sufficient to relieve an attack.[8] Thus, for patients with little headache-related disability, it is rational to initiate therapy with a simple, low-cost NSAID analgesic and to switch to other therapy only if the analgesic proves ineffective.[8] There is no evidence that butalbital-containing compounds are more effective than other analgesics, so it may not be worthwhile to take the additional risk associated with the butalbital component.[16] Opioids generally are avoided because they pose risks of sedation and abuse that are not justified by increased efficacy.[8]

Many migraine patients require migraine-specific therapy—triptans or ergot derivatives. Although most of the ergotamine and dihydroergotamine (DHE) ergot derivatives are inexpensive and have a long history of use, many disadvantages have put them in disfavor. These include complex pharmacology, erratic pharmacokinetics, and little evidence supporting effective doses. Moreover, their generalized vasoconstrictor effects are potent and sustained and have been associated with adverse vascular events. This class of drugs also is associated with a high risk of overuse syndrome and rebound headache.[8] As a result, the ergot derivatives have been largely supplanted by the newer triptan class of drugs.[16] Additionally, ergots and ergot derivatives are category X for pregnancy and should be avoided in women of childbearing age if there is any chance of pregnancy.

Triptans as a class offer clinicians and migraineurs numerous advantages: highly selective pharmacology, consistent pharmacokinetics, evidence-based prescribing instructions, established efficacy based on numerous well-controlled trials, moderate side effects, and a well-established safety record.[8] Triptans mimic serotonin, with agonist activity at

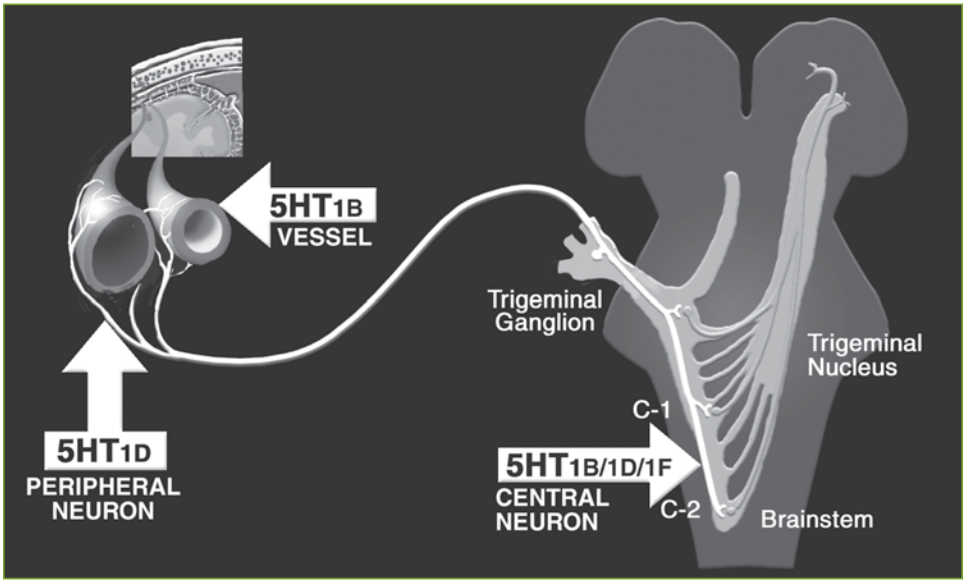


Figure 5. Trigeminal nerve and blood vessels are targets for acute migraine treatment. Adapted from Goadsby PJ, et al.[8]

the 5HT 1B/ID receptors in the brain stem and trigeminal nerve (Figure 5); this action diminishes neurogenic inflammation of brain vasculature, reduces pain signaling at the trigeminal nucleus caudalis, and produces cerebral vasoconstriction to relieve migraine.[20] In a large meta-analysis of 53 controlled clinical trials involving more than 24,000 patients, approximately 40% to 70% of treated patients reported improvement in headache at 2 hours postdose, with about 15% to 40% of patients headache-free at the 2-hour point.[8,22] Like other medications for acute treatment, triptans should be used as early as possible, while migraine pain is still mild, for the most potent effect.[23]

Numerous triptans are available in a variety of dosing forms (Table 2). Selecting among triptans was the subject of the TRIPSTAR study, which found that efficacy attributes were the most important characteristics of a triptan in clinical practice; newer oral triptans (almotriptan, eletriptan, rizatriptan) showed more of the desired efficacy attributes than the older drug, sumatriptan.[24] TRIPSTAR found that in the clinical setting, early, sustained pain-free status was the most valued of all efficacy attributes.[24] In this regard, the longer half-life of triptans (notably frovatriptan) may provide extended duration of action (Table 2).

Although triptans generally are well tolerated, they may produce flushing, lightheadedness, asthenia, chest pain, and neck tightness (Table 1). Triptans may moderately constrict the lumen of the coronary arteries, and in rare instances have been associated with myocardial infarction. They are contraindicated in patients with coronary artery disease.[8,16,21]

Table 2. Triptans for Acute Migraine Treatment

Name	Optimum/Maximum Dose[a]	Forms	Half-Life (h)
Sumatriptan	50 or 100 mg/200 mg	Tablet, NS, SC, S	1.5-2.5
Sumatriptan/ naproxen fixed dose	85-mg sumatriptan/ 500-mg naproxen	Tablet	2/19
Rizatriptan	10 mg/30 mg	Tablet, ODT	2-3
Zolmitriptan	2.5 or 5 mg/10 mg	Tablet, ODT, NS	3
Almotriptan	12.5 mg/25 mg	Tablet	3-4
Eletriptan	40 mg/80 mg	Tablet	4
Naratriptan	2.5 mg/5 mg	Tablet	6
Frovatriptan	2.5 mg/7.5 mg	Tablet	26

[a]Optimum dose = highest effective dose with fewest side effects. ODT = orally dissolving tablet.
Smith TR.[20] Physicians' Desk Reference. 61st ed. Montvale, NJ: Thomson PDR; 2007; Physicians' Desk Reference. 63rd ed. Montvale, NJ: Thomson PDR.

All agents used for migraine can cause rebound headache, also called medication overuse headache[21] (Table 1). Clinicians can minimize this phenomenon by limiting the number of days a patient uses acute therapy.[21] It is recommended that use of acute symptomatic migraine therapy, regardless of agent, be limited to no more than 2 days a week.[20]

Special Considerations in Acute Care of Menstrual Migraine

Migraine related to menstruation requires a unique treatment approach. Women with migraine related to menses have a tendency to delay initiation of treatment, which can make the headaches difficult to control. Reasons for delay include waiting to see if it's "really a migraine" or hoping that the headache won't "turn into a migraine."[23] Thus, these patients need encouragement to start medication as soon as headache symptoms emerge. They also may benefit from a "phase-based" strategy for acute treatment in which the choice of treatment is more aggressive depending on the headache phase at which a drug is initiated. For example, an NSAID or oral triptan may be an optimal choice for migraine at the mild phase, but a headache that has advanced to a very severe or intractable level may require intravenous DHE or subcutaneous sumatriptan.[23] Clinicians should educate the patient to be aware of the time of menses, have appropriate medications on hand, and use medication at the earliest sign of headache.[23]

Several studies have assessed 5 oral triptans in patients with menstrual migraine: eletriptan 40 mg, rizatriptan 10 mg, sumatriptan 100 mg, zolmitriptan 2.5 mg, and frovatriptan 2.5 mg.[23,25-30] These trials found that the efficacy of triptans in menstrual migraine was comparable to that in nonmenstrual migraine.

Prevention of Menstrual Migraine

General Principles

The prevention of migraine integrates nonpharmacologic therapy with a regularly scheduled pharmacologic regimen.[8] According to guidelines from the American Academy of Neurology, preventive drug therapy should be considered if a patient: (1) has more than 2 to 3 migraine attacks per month; (2) has attacks lasting more than 48 hours; (3) has difficulty in maintaining daily function; or (4) is troubled by rebound headache from overuse of acute medication.[3] The goals of prevention are to reduce the frequency and severity of headache by half in 8 to 12 weeks and improve responsiveness to acute therapy, quality of life, and function.[31]

Nonpharmacologic management should be offered to all patients, including those who are not candidates for preventive drug therapy. Nonpharmacologic measures include education; avoidance of trigger foods (eg, red wine or aged cheese); and maintenance of a regular daily routine of sleep, meals, and activity.[8] The patient with migraine is prone to an attack when the "peaks and troughs" of life become too extreme.[8] Other evidence-based nonpharmacologic approaches include magnesium and vitamin supplementation, relaxation training with or without thermal feedback, electromyographic biofeedback, and cognitive behavioral therapy. Other techniques, such as acupuncture or transcutaneous electrical nerve stimulation do not

have sufficient supportive data to be recommended, but may be useful for some patients.[32,33] Numerous drugs for migraine prevention are available. These include[8]:

- **Antihypertensives.** Beta blockers are well accepted for migraine prevention; propranolol, and timolol are US Food and Drug Administration (FDA)-approved for this indication. Calcium channel blockers are widely used, but only flunarizine appears clearly beneficial for migraine.
- **Anticonvulsants.** This class of drugs is established preventive therapy for migraine; valproic acid and topiramate are FDA-approved for this use.
- **Antidepressants.** Tricyclic antidepressants (eg, amitriptyline) are well established for migraine prevention, but not FDA-approved; selective serotonin reuptake inhibitors (SSRIs) and selective norepinephrine serotonin reuptake inhibitors (SNRIs), although used frequently, are not FDA-approved for migraine prevention.

NSAIDs and ergot derivatives may be used for preventive therapy, and may offer a modest preventive effect in some patients.

Special Considerations in Prevention of Menstrual Migraine

For the patient with menstrual migraine, an emerging therapy is short-term, 5- to 7-day "mini-prophylaxis" taken the days before and after the onset of menses.[16] Several drug types may be used for this mini-prophylaxis, although no agents are FDA-approved for this purpose.

NSAIDs. Pre- and perimenstrual use of NSAIDs is a simple and inexpensive method of migraine prophylaxis. Naproxen (550 mg twice daily) is the best studied NSAID regimen for this use; flurbiprofen (100 mg 3 times daily) also is used frequently. However, all NSAIDs are likely to provide preventive benefit.[16]

Triptans. Frovatriptan, naratriptan, and zolmitriptan have been evaluated in double-blind, placebo-controlled trials for short-term prevention of menstrual migraine.[34-38] These trials showed that triptan prophylaxis started just before the expected onset of menses achieved significant reductions in menstrual migraine frequency.[35-38] Naratriptan is the most extensively studied and has the strongest evidence base for preventive use.[16] In the trial comparing frovatriptan to placebo, prophylaxis with the active drug decreased the incidence of moderate and severe headache during the perimenstrual period.[35] No triptan medication has been approved by the FDA for preventive migraine treatment.

Short-term hormonal therapies. Short-term estradiol administration, using an estradiol patch, appears effective in reducing menstrual migraine. The most effective dose of the patch for this treatment is 100 µg (.1 mg). However, the risks of estrogen therapy have to be weighed against the benefits. Other add-back estrogen regimens include the use of a topical gel or oral estrogen.[16]

Ergot derivatives. These agents have been recommended for use prior to the onset of menstruation. For example, ergotamine tartrate is suggested 1 hour before sleep for 5 days prior to menses; DHE formulations also may be effective. Adverse events associated with this class of drugs limit acute and prophylactic use.[16]

For some patients, continuous prophylaxis with oral contraceptives (OCs) effectively

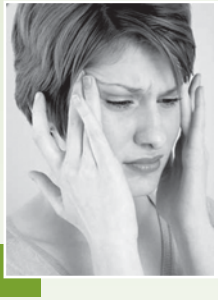
prevents menstrual migraine; use of this approach is based on prevention of estrogen withdrawal, thereby suppressing the main trigger of menstrual migraine.[16,39] In a study by Sulak et al,[39] headache incidence with continuous versus cyclical (21/7 days) administration of an OC product was compared. There was less headache, less pelvic pain, and improved mood in those patients taking continuous OC.[38] The risks of OCs have to be weighed against the benefit in any woman. However, for the majority of female migraineurs, low-dose OC use is safe.

Ensuring an Integrative Approach

The patient with menstrual migraine requires therapy specifically tailored to her unique syndrome. The process begins with careful assessment and documentation of migraine that coincides with menstruation. Detailed evaluation, including the use of a headache diary or calendar, validates the diagnosis and serves as a tool for patient education and ongoing monitoring. All patients with menstrual migraine should be afforded nonpharmacologic means of preventing migraines along with effective pharmacotherapy for acute attacks. These women should be encouraged to take medication sooner rather than later—as early as possible after onset of migraine pain or other premonitory symptoms. For those patients who still report frequent, long-lasting, or disabling migraine, or who are bothered by rebound headaches, migraine prophylaxis should be prescribed. An emerging approach to prevention of menstrual migraine is short-term mini-prophylaxis using an NSAID, triptan, or other agent taken immediately pre- and perimenstrually. This model of integrative, responsive care ensures the best possible long-term outcomes for women who suffer from menstrual migraine.

CASE STUDY

A 40-Year-Old Woman With Recurrent Headache Refractory to Over-the-Counter Analgesics



Presentation

A 40-year-old woman visits her primary care clinician to ask for stronger medication for a recurrent "tension headache." The patient reports that the over-the-counter NSAID she takes for the headache is losing effect. The headaches are so severe sometimes that she is unable to go to work or has to leave for the day. She says that the pain has been getting progressively worse over the past 18 months and she is concerned about missing more days at the office.

Initial Examination and History

- Physical examination and laboratory normal
- Headache:
  - Frequency: 3 to 4 times/month
  - Duration: up to 72 hours
  - Quality: severe, pulsating, unilateral, no aura
  - Timing: often occurs at menses
  - Associated symptoms: nausea, vomiting
  - Activities of daily living: missing work; bedridden during headaches

Clinical Decision Point

What should be the next step for this patient?

- Conduct additional assessments
- Make a diagnosis now

Comment

This is a healthy patient with a symptom profile indicative of menstrually related migraine; secondary headache can be ruled out on the basis of SNOOP criteria. To make a differential diagnosis, the clinician (1) conducts an ID Migraine™ Screening Test at the office visit, and (2) asks the patient to complete a headache diary and bring it to the 2-month follow-up visit.

The patient gives positive answers to 3 of 3 questions on the ID Migraine™ Screening Test (nausea, photophobia, activity limitation ≥1 day), indicating migraine headache. The clinician prescribes initial therapy with:

- Rizatriptan to be taken orally as soon as migraine headache pain begins
- Over-the-counter naproxen as needed for mild headache
- Magnesium 400 mg/d

Follow-up Visit

- Physical examination and laboratory normal
- 2-month headache calendar shows:
  - Occurrence of headache at 2 of 2 menses, days −1 and +2, respectively
  - Headache frequency: 2 in month 1; 3 in month 2
  - Pain severity greatest at menses
- Treatment and compliance:
  - Triptan is providing quick relief, but it sometimes wears off too soon. The patient also acknowledges that she sometimes takes triptan too late. The patient is missing work less, but still has 2 to 3 headaches a month

Clinical Decision Point

How should the patient be managed?

- Change acute treatment
- Offer migraine-preventive therapy

Comment

The clinician switches the patient's acute treatment to frovatriptan; this agent has a long half-life, which may resolve the reported end-of-dose failure. The patient receives recommendations for short-term prophylaxis with over-the-counter naproxen, starting 2 days before and ending 3 days after menses begins. The patient is also referred for cognitive behavioral therapy and is reminded to eat, sleep, and exercise on a regular schedule. Finally, she is asked to continue with the headache diary for 4 more months. At subsequent telephone follow-up, the patient reports that she is rarely missing work and feels as though she is "getting her life back."

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PCEFORUM **It's your turn. Post your comments to this clinical question:**

How do you manage a patient with migraine who has tried multiple triptans without success, is not interested in beta-blockers or topiramate, and wants something stronger?

Post your answer to this question and more on the PCE Forum **www.practicingclinicians.com/forumhomestudy**

QUESTIONS From Symposium Participants

Q: In the assessment of suspected menstrual migraine, should clinicians consider a computed tomography (CT) scan or magnetic resonance imaging (MRI)?

A: The use of imaging studies rarely is warranted when a patient is being followed regularly and history and symptom patterns clearly point to migraine. However, an MRI may be advisable if there is a progressive worsening of headache because that may indicate a comorbid process of secondary headache. MRI generally provides more information in these patients than CT scan.

Q: Does the preventive treatment of migraine help to alter a patient's pain threshold?

A: Changing the pain threshold is a complex aspect of headache management. The hypothesis is that patients whose nervous systems are assaulted by repeated, unrelieved migraine pain develop a lower pain threshold, making them more vulnerable to events that trigger subsequent migraine; therefore, if migraine prevention can interrupt this process, it might reduce a patient's vulnerability to headaches over time. But regardless of pain threshold, repeated migraine takes a psychological/medical toll that prevention can ameliorate. People live in fear that migraine is going to come back, and this fear limits their quality of life. When a migraine occurs, even if they get relief from medication, they behave for the rest of the day as if migraine could return at any moment. They miss work, cancel plans, and fail to meet their responsibilities. Prevention may help these patients embrace a fuller life.

Q: Is swelling of the throat a meaningful side effect of triptans?

A: "Throat swelling" with triptans is a misnomer. What patients typically feel is a tightness in the muscles of the jaw, neck, or chest. This can produce some difficulty in swallowing. It helps to reassure patients the adverse event is short-lived and not very intense. In a way, the tightness signals that the medicine is working. However, if this adverse reaction is very troubling, the clinician can try a different triptan. If that fails, clinician and patient can discuss the pros and cons of trying a different class of medication. A caveat is that any patient who experiences true throat swelling, as in anaphylaxis, must be evaluated carefully to determine the trigger for the reaction.

Read more Q&A from the live symposia at www.practicingclinicians.com/H2_2009/mmqa.pdf