Migraine Management During Menstruation and Menopause

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ABSTRACT

Purpose of Review: Migraine is most prevalent in women during their reproductive years. An understanding of the effects of menstruation and menopause on migraine can enable neurologists to provide targeted and appropriate medical and hormonal strategies, enabling their patients to achieve better control of migraine and reduced disability. This article reviews the effects of hormonal events on migraine and summarizes the evidence-based options available for management.

Recent Findings: Estrogen ''withdrawal'' during the late luteal phase of the natural menstrual cycle and the hormone-free interval of combined hormonal contraceptives has long been implicated in the pathophysiology of menstrual migraine. However, more recent research suggests that other independent mechanisms may be relevant. Prostaglandin inhibitors used for management of dysmenorrhea are effective for associated menstrual migraine, suggesting a common pathophysiology. The interplay between serotonin and estrogen also deserves further research.

Summary: Menstrual and perimenopausal migraine can be managed effectively using a variety of strategies, the choice of which depends on the efficacy of acute treatment, predictability and regularity of menstruation, use of contraception, and presence of menstrual disorders or perimenopausal vasomotor symptoms.

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INTRODUCTION

Up until puberty, migraine affects both sexes equally. Following puberty, migraine is more prevalent in women, in whom migraine attacks are also more frequent, longer lasting, more severe, and more likely to relapse.[1]

The most likely reason for the increased prevalence of migraine in women compared to men following puberty is the effect of female sex hormones. Puberty, which begins in girls around 10 to 11 years of age, is initiated by increasing levels of sex steroids resulting from a complex hypothalamic-pituitary-ovarian feedback system. The first menstrual period typically starts around 12 to 13 years of age, followed by marked fluctuations in hormone levels for another 2 to 3 years until puberty is complete and menstruation becomes regular. At the other end of the reproductive spectrum, menopause is marked by the last menstrual period around 51 years of age. Menopause is preceded by several years of fluctuating hormones typically associated with irregular periods with the addition of vasomotor symptoms. Following menopause, lower levels of hormones continue to fluctuate for another 4 to 5 years.

Both adolescence and perimenopause (the years immediately preceding and following menopause) are associated with increased risk of migraine, evidenced by a bimodal prevalence distribution.[2] The incidence of migraine with aura peaks

during early puberty, whereas the incidence of migraine without aura peaks during late puberty (**Figure 3-1**[3]). By 30 years of age, migraine is 3 times more prevalent in women than in men.[4]

EFFECTS OF MENSTRUATION ON MIGRAINE

Menstruation is a significant risk factor for migraine *without* aura but not migraine *with* aura. In population- and clinic-based studies, between 20% and 60% of women with migraine report an association with menstruation.[5–7]

The incidence of migraine without aura is greatest during 5 days of the menstrual cycle, beginning 2 days before menstruation and continuing through the first 3 days of bleeding.[8–10] In both women with natural cycles and women using combined hormonal contraceptives, at least a twofold increased risk of migraine exists on the first 3 days of bleeding compared to all other days of the cycle.[9,11]

Most women with menstrual exacerbation of migraine have additional attacks of migraine with or without aura at other times of the cycle (menstrually related migraine). Fewer than 10% of women report migraine exclusively with menstruation and at no other time of the month ("pure" menstrual migraine) (**Table 3-1**).[12] The term *menstrual migraine* is often used to encompass both conditions. A few women report exacerbation of migraine following ovulation, but no evidence supports this association.[13]

In women with menstrually related migraine, menstrual attacks are more severe and disabling, last longer, and are less responsive to symptomatic medication compared to attacks at other times of the cycle (**Figure 3-2**).[14–16]

EFFECTS OF MENOPAUSE ON MIGRAINE

Although perimenopause is a time of increased risk of migraine, postmenopause sometimes brings respite for migraine without aura. Improvement is associated with increasing time since menopause.[17,18] Surgical menopause, with or without oophorectomy, is typically associated with initial worsening of migraine compared to natural menopause.[19] Migraine with aura appears to be unaffected by menopause.[18]

DIAGNOSING MENSTRUAL MIGRAINE

Diagnosis of menstrual migraine is based on the history, examination, and diary analysis, with investigations only indicated to exclude secondary headache. Diaries recording migraine and menstruation, kept over a minimum of three complete menstrual cycles, can confirm attacks of migraine without aura starting on days –2 to +3 of menstruation in at least two of three consecutive menstrual cycles (**Table 3-1**).[12] Relying solely on the patient history is unreliable, with both underestimation and overestimation of menstrual migraine.[13] It is important to ensure that attacks with menstruation are a true association rather than chance association, so menstrual migraine should not be diagnosed in women with frequent migraine. Several proposals for

KEY POINTS

- The most likely reason for the increased prevalence of migraine in women compared to men following puberty is the effect of female sex hormones.
- The menstrual period is a significant risk factor for migraine *without* aura but not migraine *with* aura.
- The incidence of migraine without aura is greatest during 5 days of the menstrual cycle, beginning 2 days before menstruation and continuing through the first 3 days of bleeding.
- Menstrual migraine attacks are more severe and disabling, last longer, and are less responsive to symptomatic medication compared to attacks at other times of the cycle.

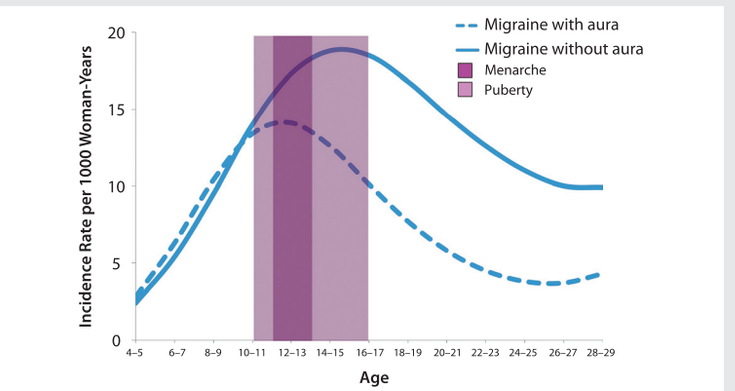


FIGURE 3-1 Incidence of migraine in puberty and adolescence.

Adapted with permission from Stewart WF, et al, Am J Epidemiol.[3] © 1991 Oxford University Press. *aje.oxfordjournals.org/content/134/10/1111.short*.

KEY POINT

- As well as confirming the association between migraine and menstruation, simple diaries can assess menstrual regularity and duration and likely menopause status.

TABLE 3-1 *ICHD* Diagnostic Criteria for Menstrual Migraine[a]

▶ **Pure Menstrual Migraine Without Aura**

A. Attacks in a menstruating woman[b] fulfilling criteria for migraine without aura and criterion B below.

B. Documented and prospectively recorded evidence over at least three consecutive cycles has confirmed that attacks occur exclusively on day 1 ± 2 (ie, days –2 to +3)[c] of menstruation in at least two out of three menstrual cycles and at no other times of the cycle.

▶ **Menstrually Related Migraine Without Aura**

A. Attacks in a menstruating woman[b] fulfilling criteria for migraine without aura and criterion B below.

B. Documented and prospectively recorded evidence over at least three consecutive cycles has confirmed that attacks occur on day 1 ± 2 (ie, days –2 to +3)[c] of menstruation in at least two out of three menstrual cycles, and additionally at other times of the cycle.

ICHD = International Classification of Headache Disorders.

[a] Reprinted with permission from Headache Classification Committee of the International Headache Society (IHS), Cephalalgia.[12] © 2013 International Headache Society. *www.ihs-classification.org/_downloads/mixed/International-Headache-Classification-III-ICHD-III-2013-Beta.pdf*.

[b] For the purposes of *International Classification of Headache Disorders, Third Edition, beta version* (*ICHD-3 beta*), menstruation is considered to be endometrial bleeding resulting from either the normal menstrual cycle or from the withdrawal of exogenous progestogens, as in the use of combined oral contraceptives or cyclical hormone replacement therapy.

[c] The first day of menstruation is day 1 and the preceding day is day –1; there is no day 0.

statistical confirmation of the association have been published.[13,20,21]

As well as confirming the association between migraine and menstruation, simple diaries can assess menstrual regularity and duration and likely menopause status. Premenopausal women typically have regular menstrual cycles ranging from 21 to 35 days with a mean of 28 days, with menstruation ranging from

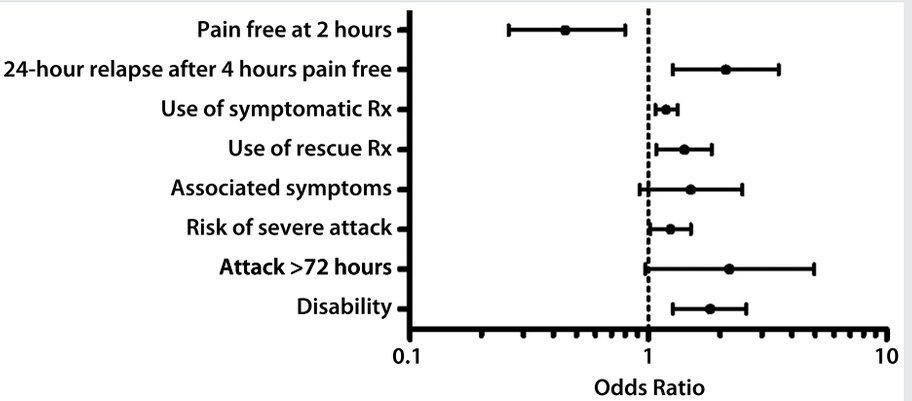
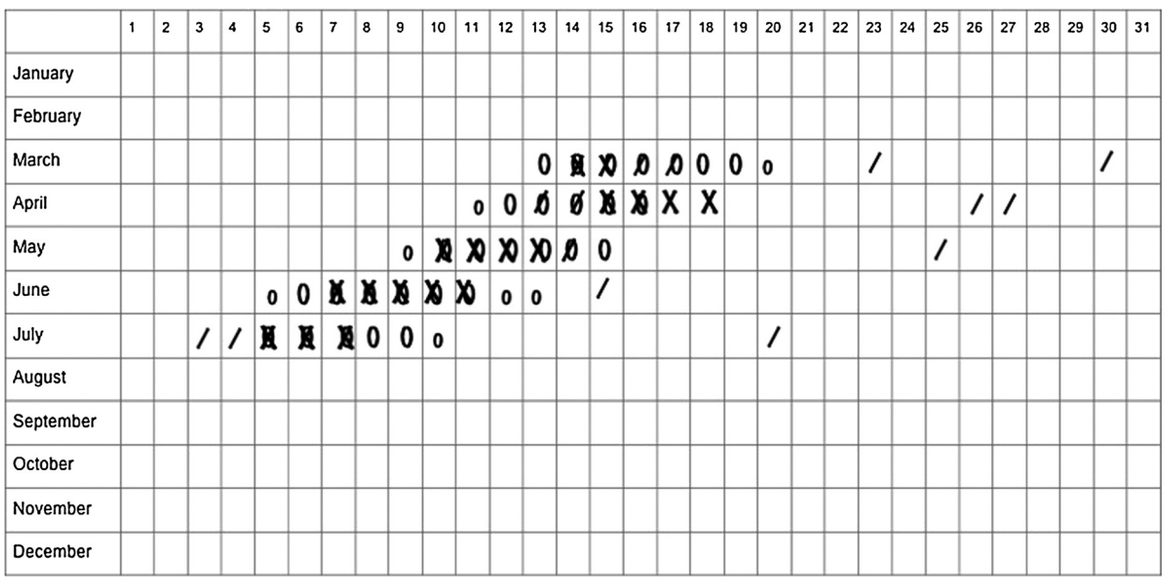


FIGURE 3-2 Risk of migraine features in menstrual versus nonmenstrual attacks in women with menstrually related migraine.

Rx = prescription.

Data from Pinkerman B, Holroyd K, Cephalalgia.[15] *cep.sagepub.com/content/30/10/1187.short*.

Symptomatic drug: Simple analgesic and triptan
Daily prophylactic drugs: none
Hormones: none
Other regular medication: none



	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31
January																															
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FIGURE 3-3 Example of a menstrual migraine diary from a 34-year-old premenopausal woman. 0 = period; o = spotting; X = migraine; / = headache.

2 to 8 days, typically lasting 4 to 6 days (**Figure 3-3**). During perimenopause, cycles become irregular and unpredictable (**Figure 3-4**).

PATHOPHYSIOLOGY

Much research has focused on the association between changes in menstrual cycle hormones and risk of migraine. The timing of menstrual attacks of migraine is consistent with the natural fall in estrogen during the late luteal phase of the menstrual cycle (**Figure 3-5**). This estrogen "withdrawal" trigger is independent of ovulation, as it can trigger migraine during the hormone-free interval of combined hormonal contraceptives. It is also independent of menstruation and the presence or absence of progestin, as migraine can be triggered following an estrogen challenge in women who have had hysterectomies.[22]

It is unlikely that estrogen withdrawal is the sole trigger for menstrual migraine. The observation that menstrual migraine can be associated with dysmenorrhea, both of which respond to nonsteroidal anti-inflammatory drugs (NSAIDs), implicates prostaglandins in the pathophysiology.[23] During the luteal phase of the menstrual cycle, uterine prostaglandin levels increase threefold, with a further increase during the first 48 hours of menstruation, mirroring the timing of increased migraine risk.

MANAGEMENT OF MENSTRUAL MIGRAINE

The choice of strategy for management of menstrual migraine depends on the efficacy of acute treatment, predictability and regularity of menstruation, use of or need for contraception, and presence of

Symptomatic drugs: triptan
Daily prophylactic drugs: none
Hormones: none
Other regular medication: none

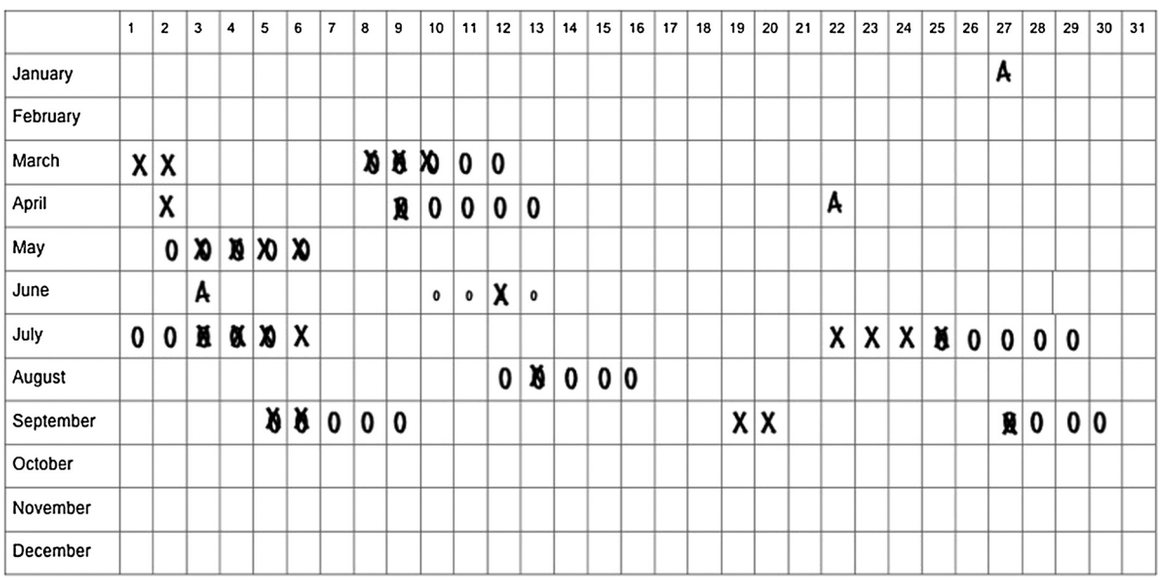

FIGURE 3-4 Example of a menstrual migraine diary from a 49-year-old perimenopausal woman.
0 = period; o = spotting; X = migraine without aura; A = migraine with aura.

KEY POINTS

- The choice of strategy for management of menstrual migraine depends on the efficacy of acute treatment, predictability and regularity of menstruation, use of or need for contraception, and presence of menstrual disorders or perimenopausal vasomotor symptoms.
- Women with regular cycles and menstrual exacerbation of migraine may benefit from short-term perimenstrual prophylaxis, targeted to the time of increased risk.

menstrual disorders or perimenopausal vasomotor symptoms (**Figure 3-6**[24]).

Acute Treatment

All treatments licensed for migraine can be used for acute treatment of menstrual migraine. A number of drugs have shown efficacy in randomized controlled trials (**Table 3-2**). These are largely post hoc analyses of acute treatment comparing menstrual and nonmenstrual attacks in women who have not received a diagnosis of menstrual migraine. Hence, the true efficacy in women with menstrual migraine is unclear. Because of the long duration of menstrual attacks, repeated relapse can be a problem, as illustrated in **Case 3-1A**.

Prophylaxis

Women with frequent migraine throughout their cycle, with or without menstrual exacerbation, are most likely to benefit from standard prophylactic strategies. If prophylaxis reduces the frequency and severity of nonmenstrual attacks but not menstrual attacks, then perimenstrual prophylaxis is indicated.

Perimenstrual prophylaxis. Women with regular cycles and menstrual exacerbation of migraine may benefit from short-term perimenstrual prophylaxis, targeted to the time of increased risk (**Table 3-3**). For perimenstrual prophylaxis, the method of administration is different from the label, so the drug must be prescribed off-label.

Nonsteroidal anti-inflammatory drugs. NSAIDs may be particularly effective for women with dysmenorrhea and menstrual migraine in whom prostaglandin release may be a significant trigger. Level B evidence (one class I or two class II trials) exists for naproxen 550 mg 2 times a day taken for 7 to 14 days starting during the week before expected onset of

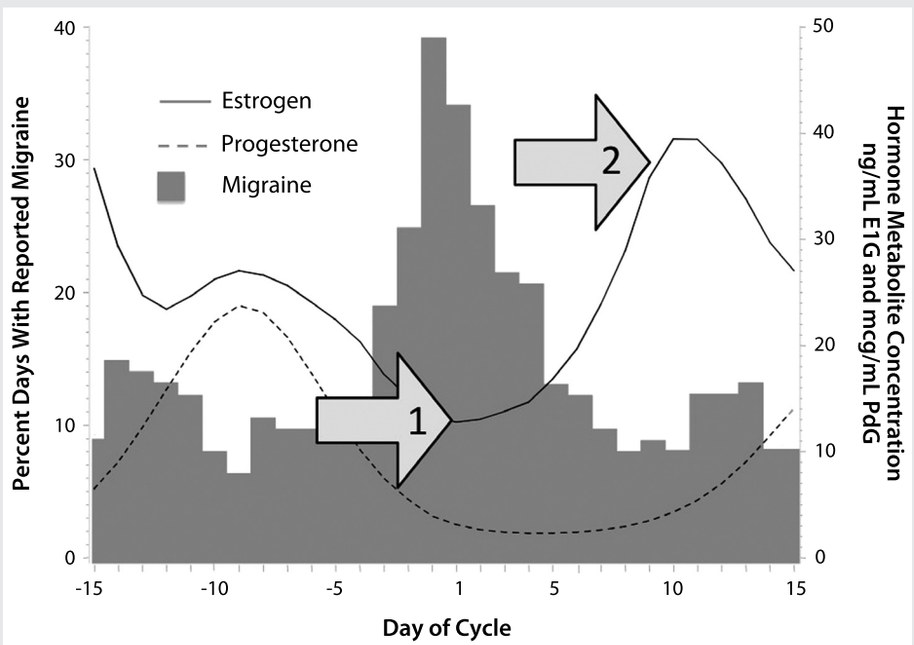

FIGURE 3-5 Inverse relationship between migraine incidence and estrogen levels.

1: Falling estrogen associated with high migraine incidence
2: Rising estrogen associated with low migraine incidence

E1G = estrone-3-glucuronide; PdG = pregnanediol-3-glucuronide.

Adapted with permission from MacGregor EA, et al, Neurology.[10] © 2006 American Academy of Neurology. *www.neurology.org/content/67/12/2154.short*.

KEY POINT

■ Women at risk of gastrointestinal bleeding should avoid nonsteroidal anti-inflammatory drugs, and gastroduodenal protection should be considered whenever nonsteroidal anti-inflammatory drugs are prescribed.

menstruation. (Refer to **Appendix C** for the American Academy of Neurology [AAN] classification of evidence for the rating of a therapeutic study and **Appendix D** for the classification of recommendations.) Although a potential risk exists for the development of medication-overuse headache, NSAIDs appear to protect against chronification of migraine.[26] Women at risk of gastrointestinal bleeding should avoid NSAIDs, and gastroduodenal protection should be considered whenever NSAIDs are prescribed. Some women develop hypertension as a consequence of fluid retention and edema, which resolves following cessation of treatment.

Triptans. Level A evidence (two or more class I trials) exists for the efficacy of frovatriptan for the short-term prevention of menstrual migraine.[27] (Refer to **Appendix A** for a summary of the AAN's evidence-based guideline for clinicians.) Treatment is taken for 6 days, starting 2 days before the expected onset of menstrual migraine. A loading dose of 5 mg 2 times a day is taken on the first day, followed by 2.5 mg 2 times a day on days 2 to 6. The risk of posttreatment migraine is not increased.[28]

Level B evidence exists for naratriptan and zolmitriptan.[27] Naratriptan 1 mg 2 times a day is taken for 6 days, starting 3 days before the expected onset of menstrual migraine. An increased risk of migraine exists immediately following treatment. Zolmitriptan 2.5 mg 2 times a day or 3 times a day is taken for 7 days, starting 2 days before the expected onset of menstruation. The risk of posttreatment

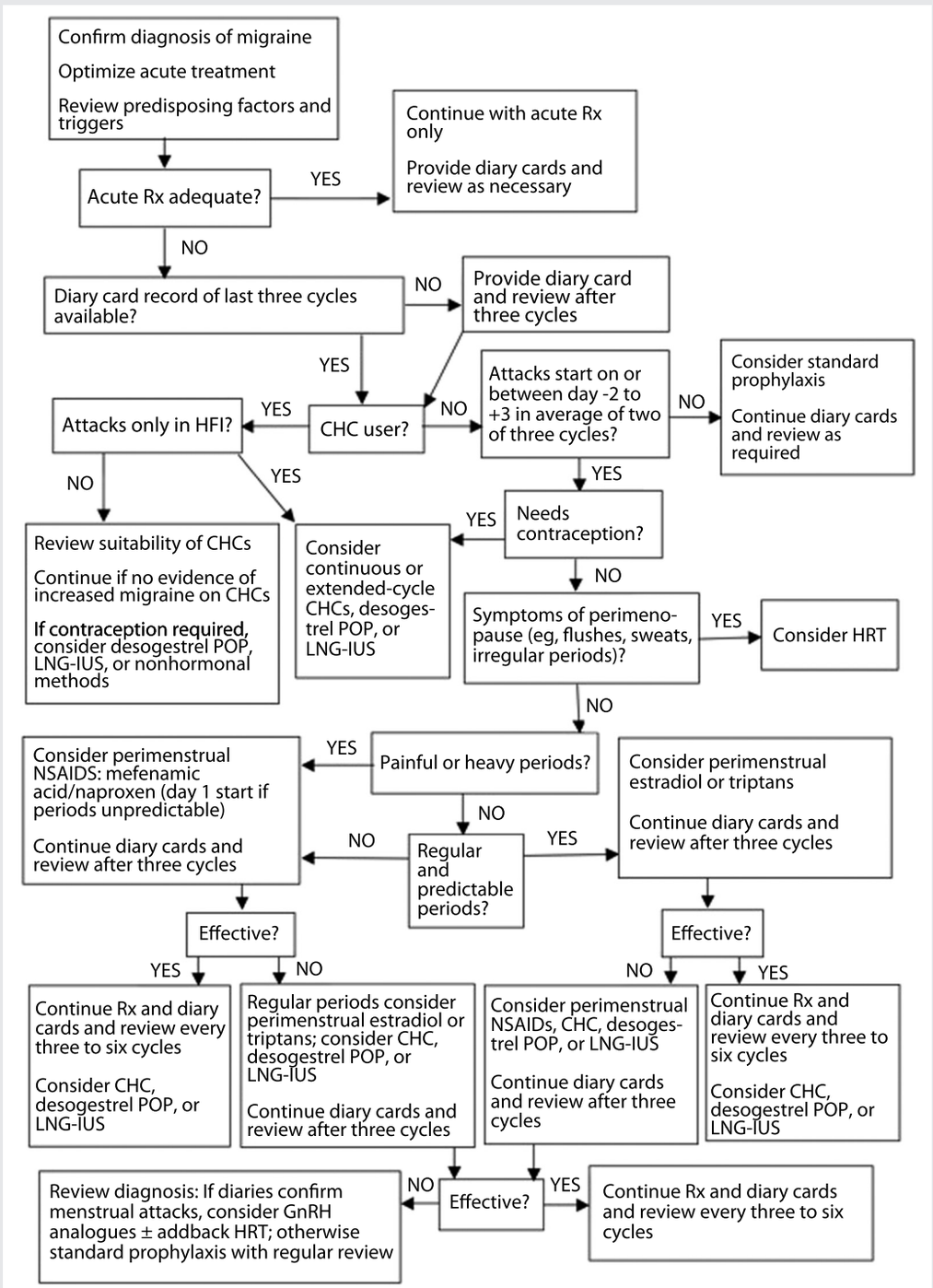

FIGURE 3-6 Algorithm for management of menstrual migraine.

CHC = combined hormonal contraceptive; GnRH = gonadotrophin-releasing hormone; HFI = hormone-free interval; HRT = hormone replacement therapy; LNG-IUS = levonorgestrel-releasing intrauterine system; NSAID = nonsteroidal anti-inflammatory drug; POP = progestin-only pill; Rx = prescription.

Adapted with permission from MacGregor EA, J Fam Plann Reprod Health Care.[24] © 2007 Faculty of Sexual & Reproductive Healthcare of the Royal College of Obstetricians & Gynaecologists. *jfprhc.bmj.com/content/33/1.toc*.

TABLE 3-2 Acute Treatment of Menstrual Attacks of Migraine

Drug	Route	Dose	Maximum Daily Dose
Acetaminophen 250 mg, aspirin 250 mg, caffeine 65 mg	Oral	2 caplets	8 caplets
Mefenamic acid	Oral	250–500 mg	1500 mg
Triptans			
Almotriptan	Oral	6.25–12.5 mg	25 mg
Eletriptan	Oral	20–40 mg	80 mg
Frovatriptan	Oral	2.5 mg	7.5 mg
Naratriptan	Oral	1–2.5 mg	5 mg
Rizatriptan	Oral	5–10 mg[a]	30 mg
Sumatriptan	Oral	25–100 mg	200 mg
	Subcutaneous	6 mg	12 mg
	Intranasal	5–20 mg	40 mg
Sumatriptan 85 mg, naproxen 500 mg	Oral	1 tablet	2 tablets
Zolmitriptan	Oral	2.5 mg	10 mg
	Intranasal	5 mg	10 mg

[a] In patients taking propranolol, initial dose of rizatriptan is 5 mg and maximum daily dose is 15 mg.

KEY POINT

■ Perimenstrual prophylaxis with triptans is well tolerated with adverse events similar to those reported in acute treatment trials.

migraine following zolmitriptan has not been assessed.

Perimenstrual prophylaxis with triptans is well tolerated with adverse events similar to those reported in acute treatment trials.

Estrogen supplements. Level C evidence (one class II trial) exists for estradiol gel 1.5 mg daily used for 7 days starting between 2 and 5 days before expected onset of menstruation.[27] This maintains luteal phase estradiol levels, preventing the natural late luteal phase drop in estrogen that can trigger estrogen withdrawal migraine. It is important that women using this strategy are menstruating regularly and natural progesterone following ovulation provides endometrial protection. Treatment is well tolerated but can be followed by an increase in migraine.[29] Clinical experience suggests that this is less likely to occur if treatment is continued to day +7 of the cycle, although this can result in menstrual irregularity.

Continuous hormonal options. The aims of continuous hormonal treatments are to suppress ovarian activity and maintain a stable hormonal milieu.

Contraceptives. For women with menstrual migraine who also need contraception, several contraceptive strategies may also benefit migraine, as illustrated in **Case 3-1B**. In the absence of migraine aura, combined hormonal contraceptives have additional noncontraceptive benefits, including reduced risk of endometrial and ovarian cancer.[30] Estrogen withdrawal during the hormone-free interval can trigger migraine but can be

Case 3-1A

A 34-year-old woman presented for treatment of migraine that occurred around the start of her menstrual period, although she usually had two additional attacks each month. Nonmenstrual attacks lasted the better part of a day, but menstrual attacks continued for several days.

She said she woke with nasal congestion, which developed into a unilateral headache. The headache was stabbing and thumping in character and associated with nausea and sensitivity to light and sound. She was disabled by the menstrual headaches, as she was unable to continue her usual daily activities without treatment. She took acetaminophen 1 g, which usually helped nonmenstrual attacks but had little effect on menstrual attacks, even when she repeated the dose.

She had not lost time from work, as her part-time status enabled her to plan work around her monthly cycle. However, the monthly headaches were a source of friction between the patient and her husband as he often had to leave work early to pick the children up from school. When she did not have a headache, she felt well, with no other medical concerns.

Her menstrual periods were regular, every 27 to 29 days, lasting 5 days. The first couple of days, her flow was sometimes heavy with dysmenorrhea. Migraine usually started on the second or third day of menstruation.

Comment. Most women who present with menstrual or menstrually related migraine have a history of migraine unrelated to menstruation for many years previous. Diary cards are essential, not just to confirm the diagnosis, but also to assess response to treatment and document changes in pattern (**Figure 3-3**). This patient was not using effective symptomatic treatment for migraine and should be prescribed a nonsteroidal anti-inflammatory drug either with or without an oral triptan. For patients who experience repeated relapse, frovatriptan is an appropriate option based on its longer half-life and longer duration of action.[25]

This patient should be encouraged to treat attacks as early as possible, which results in a higher, earlier, and sustained pain-free response; prevents progression to moderate/severe headache; and reduces pain burden and functional disability.

If attacks are not effectively controlled with symptomatic treatment alone, prophylaxis is indicated.

TABLE 3-3 Short-Term Prophylaxis of Menstrual Migraine

Drug	Treatment Regimen
Nonsteroidal anti-inflammatory drugs	
Naproxen	550 mg orally 2 times/d taken for 7–14 days starting during the week before onset of menstruation
Triptans	
Frovatriptan	5 mg orally 2 times/d on day –2 of menstruation; 2.5 mg orally 2 times/d on days –1 to +4 (total of 6 days)
Naratriptan	1 mg orally 2 times/d starting 3 days before expected migraine taken for 6 days (total of 6 days)
Zolmitriptan	2.5 mg orally 2 to 3 times/d on days –2 to +5 of menstruation (total of 7 days)
Estradiol	1.5 mg (1.5 g gel) transdermally daily starting between days –5 and –2 of menstruation for 7 days (total of 7 days)

prevented with estrogen supplements during this time, such as 10 mcg oral ethinyl estradiol, 0.9 mg oral conjugated equine estrogens, 100 mcg estradiol patches, or 2 g estradiol gel.[31] Women using estrogen supplements during the hormone-free interval of combined hormonal contraceptives have endometrial protection from the combined hormonal contraceptive progestogen. However, a simpler strategy is to reduce the number of withdrawal bleeds to four per year with extended-cycle 84/7 regimens or to none by continuous combined hormonal contraceptive use.[31] These strategies are well tolerated; unscheduled bleeding with continuous combined hormonal contraceptives is common in the early cycles of treatment but usually resolves with time. Advising women to ''break with the bleed'' (ie, stop combined hormonal contraceptives for 3 days if troublesome bleeding lasts for more than 3 days) can increase the likelihood of continuing with this strategy. By 10 to 12 months of continuous use, 80% to 100% of women are amenorrheic.[32]

Combined hormonal contraceptives are associated with a twofold increased risk of stroke. Hence, women using them for contraception are screened for the presence of cardiovascular risk factors before prescription.[33] Although migraine without aura is not a significant risk for ischemic stroke, migraine with aura is associated with a twofold increased risk. On this basis, combined hormonal contraceptives can safely be used by women with migraine without aura, unless they have significant cardiovascular risk factors that would in themselves contraindicate use. In contrast, neurologists identifying women with migraine with aura who are using combined hormonal contraceptives should work with the prescribers to ensure that combined hormonal contraceptives are being prescribed in accordance with current guidance. While the absolute risk of stroke in women with migraine with aura who use combined hormonal contraceptives is very low, the impact of a stroke is so devastating that clinicians should consider the use of progestin-only,

KEY POINT

- Estrogen withdrawal during the hormone-free interval of combined hormonal contraceptives can be prevented by continuous use of the combined hormonal contraceptive.

Case 3-1B

The patient returned for follow-up and reported that taking a triptan/nonsteroidal anti-inflammatory drug (NSAID) combination early had enabled her to control her menstrual migraine and also gave her some relief from dysmenorrhea. She asked if anything further could be done to prevent rather than treat these symptoms. The doctor advised that she could take naproxen 550 mg 2 times a day starting a couple of days before the expected onset of menstruation until day +7 as perimenstrual prophylaxis of menstrual migraine, which would also treat her dysmenorrhea. If she developed migraine, she could continue to treat the symptoms with a triptan. The doctor also noted that the patient used a copper intrauterine device for contraception. The doctor suggested that she discuss alternative contraceptive methods with her obstetrician-gynecologist.

Comment. It is important to consider the effect that contraceptive methods may have on menstrual migraine mechanisms. Copper intrauterine devices are associated with dysmenorrhea, menorrhagia, and increased prostaglandin release. These effects can respond to perimenstrual NSAIDs, which inhibit prostaglandin release. However, switching to the levonorgestrel intrauterine device or continuous combined hormonal contraception might be more appropriate.

intrauterine, or barrier contraceptives in this setting.

Few data exist on progestogen-only methods and migraine, although some evidence exists that methods that achieve amenorrhea can benefit migraine.[31] Of interest to the pathophysiology of migraine is the suggested benefit reported by women using the levonorgestrel intrauterine system, which achieves amenorrhea by a local endometrial effect in the absence of ovarian suppression.[34]

Gonadotrophin-releasing hormone analogues. Gonadotrophin-releasing hormone analogues have been reported as effective for treatment of resistant menstrual migraine. They cause a reversible "medical" menopause at the hypothalamic-pituitary level, resulting in cessation of ovarian activity. Add-back hormone replacement therapy is usually necessary to treat vasomotor side effects and prevent loss of bone density.[35]

Surgical options. Since hysterectomy with or without oophorectomy increases risk of migraine, surgery is not generally an option for management of menstrual migraine. However, if a hysterectomy is indicated for gynecologic reasons, the effect on migraine can be reduced by immediate use of continuous transdermal estrogen replacement therapy.[36]

Case 3-2

A 49-year-old woman presented for evaluation of migraine with aura that occurred every 2 to 3 months. These attacks were stereotypical, with fortification spectra lasting 20 to 30 minutes followed by a unilateral severe headache associated with photophobia and nausea. The headaches lasted for a day, and she had to leave work and go to bed. The attack generally resolved with sleep, although she still felt tired and drained the following day. Her doctor had prescribed a triptan, which she took as soon as the aura started. She had not found this any more effective than her previous treatment with ibuprofen.

On further questioning, she reported she also had disabling ''sinus'' headaches with her periods, which she used to be able to manage, as her periods were predictable and she could plan around them. However, her periods had become more frequent and irregular, so she could no longer predict when they were likely to occur. These headaches lasted 1 to 4 days. She used a decongestant, which was sometimes effective if taken early. Even then, it only took the edge off the pain. She was unable to go to work when the pain was severe. When asked about nasal discharge, she said she did not have a purulent discharge accompanying the headaches and was afebrile. She had no ''sinus'' symptoms between attacks.

Her periods usually lasted 5 days and were not otherwise troublesome. She reported that she had night sweats and hot flashes during the week before her period.

Comment. Migraine without aura is often not recognized as migraine, particularly by people who also have migraine with aura and consider the aura to be more typical of migraine. Neither is it uncommon for migraine without aura to be misdiagnosed as sinus headache. In a study of 2991 patients with a history of self-described or physician-diagnosed ''sinus'' headache, 2396 (80%) fulfilled International Headache Society criteria for migraine with or without aura.[37] The diagnosis may be confused by additional symptoms that may occur during migraine but are typically associated with sinusitis, such as sinus pressure, sinus pain, and nasal congestion. This confirms the importance of taking a careful history.

The first step in managing this patient was to confirm the diagnosis of menstrual migraine and encourage her to use the triptan for these attacks. For management of migraine with aura, she was advised to delay taking the triptan until the onset of headache. Given the frequency of her migraines, standard migraine prophylaxis should be considered. Perimenstrual prophylaxis is not indicated because of menstrual irregularity. Although the patient had vasomotor symptoms, these only occurred premenstrually. If they become troublesome, she might consider hormone replacement therapy. In contrast to combined hormonal contraceptives, physiologic doses of natural estrogen used for hormone replacement are not contraindicated in the presence of migraine aura.

PERIMENOPAUSE

Perimenopause marks a time of increased risk of migraine and the additional complication of irregular periods, which prohibits perimenstrual prophylaxis, as illustrated in **Case 3-2**. Troublesome vasomotor symptoms may also warrant specific treatment, most usually with hormone replacement therapy. Oral estrogen can exacerbate migraine so nonoral routes are preferred, administered continuously to ensure stable hormone levels.[36] Endometrial protection with progestin is necessary for women who have not had a hysterectomy, and continuous delivery is better tolerated than cyclical administration.[38] However, continuous progestin is only licensed for use postmenopause, with the exception of the levonorgestrel intrauterine system. This has the advantage of also being licensed for contraception and delivers progestin directly to the endometrium with low systemic absorption.

For women in whom estrogen is contraindicated, paroxetine 7.5 mg at bedtime is the only nonhormonal therapy approved by the US Food and Drug Administration (FDA) for the treatment of vasomotor symptoms. Level A evidence from some randomized controlled trials supports the efficacy of gabapentin for control of vasomotor symptoms, although there is only Level U evidence for migraine prophylaxis (inadequate or conflicting data to support or refute medication use).[11,34]

CONCLUSION

Menstrual exacerbation of migraine is common, particularly during perimenopause. If symptomatic treatment alone is not sufficient to manage the condition, perimenstrual prophylaxis can be offered. Contraceptive strategies may be appropriate for women also needing contraception. Women with troublesome vasomotor symptoms and migraine may benefit from hormone replacement therapy.

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KEY POINTS

- Perimenopause marks a time of increased risk of migraine and the additional complication of irregular periods, which prohibits perimenstrual prophylaxis.
- Women with migraine tolerate nonoral delivery of estrogen better than oral, and it should be administered continuously to ensure stable hormone levels.

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