

HORMONAL HEADACHES IN THE PERIMENOPAUSE

Migraine is one of the most prevalent causes of years lost to disability in females, and research has highlighted how the perimenopause can be particularly challenging. This article looks at the issue of migraine during this period

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Migraine is a common, debilitating condition, rated by the World Health Organisation as one of the top 20 causes of years lost to disability worldwide.¹ The prevalence in women is known to be higher than in men, making migraine the ninth most prevalent cause of years lost to disability in females. Women have long reported a suspected link between their migraines and hormonal cycles, and perimenopause has traditionally been a difficult time for women suffering from migraine. Recent studies have confirmed that headache and migraine frequency can increase around the time of the menopause.² This article looks at the current guidance and offers suggestions for the management of perimenopausal women with migraines.

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The International Menopause Society defines menopause as the permanent cessation of menstruation resulting from the loss of ovarian follicular activity.³ Natural menopause occurs with the last menstrual period, but is known with certainty only in retrospect 12 months after the last menstrual period. The average age of menopause is 51, but there is a huge age range. Around 1% of women have premature ovarian insufficiency, entering menopause before the age of 40. Women are typically symptomatic for four years, but 10% of women have symptoms for 12 years or more.⁴

The perimenopause is a time of hormonal fluctuation,⁵ and this has been linked to hormonal migraines and worsening of existing headaches. The sensitivity of some migraines to hormonal flux explains the exacerbation in migraine in the perimenopausal years. Once menopause is well established, migraine is likely to improve, although this is unlikely to occur immediately after the cessation of menstruation and may take several years.

Menstrual migraines are often linked to the natural fall in oestrogen levels pre-menstrually, and this trend often continues through the perimenopause. High-oestrogen states are also associated with the

development of migraine aura in women who have not previously had migraine or who had attacks only of migraine without aura. This occurs in susceptible women starting combined oral contraceptives, hormone replacement therapy (HRT), and during pregnancy, but is also seen in some women during perimenopause when oestrogen levels can fluctuate wildly. Transient increases in oestrogen levels occur with surges in FSH. Resolution of aura typically occurs following a return to lower-oestrogen states.

The type of menopause has a substantial effect on migraine. Natural menopause is associated with a lower prevalence of migraine compared to surgical menopause. In a postmenopausal outpatient survey, Neri et al found that 62% of women with a history of migraine reported improvement after spontaneous menopause, and 33% improved after induced (surgical) menopause. Migraine worsened in 9% of women after spontaneous menopause and in 67% of women after surgical menopause.⁶ A retrospective study of 164 postmenopausal women with migraine without aura attending specialist headache centres in Italy compared surgical and natural menopause. Surgical menopause was associated with worsening of migraine, natural menopause was associated with eventual improvement.⁷ Data from Taiwan further supports the clinical impression that migraine prevalence increases before menopause and declines after spontaneous menopause. However, in this study this trend occurred only in women with increased vulnerability to hormonal change, such as those with premenstrual syndrome. The presence of low estrogen and high follicle-stimulating hormone levels predicted lower migraine prevalence, whereas a history of hysterectomy was related to higher prevalence.⁸

Management

The NICE guidance on menopause states that it is possible to diagnose the following without laboratory tests in otherwise healthy women aged over 45 years with menopausal symptoms:

- perimenopause based on vasomotor symptoms and irregular periods
- menopause in women who have not had a period for at least 12 months and are not using hormonal contraception

■ menopause based on symptoms in women without a uterus.⁹

A detailed symptom diary is invaluable in assessing headaches in the perimenopausal woman. This should document headaches and migraines, periods, and medication taken, including any hormonal treatments. A sample diary is available at <http://www.nationalmigrainecentre.org.uk/wp-content/uploads/2014/09/NMC-monthly-diary.pdf>. It is also important to identify other perimenopausal symptoms including vasomotor symptoms such as night sweats, hot flushes, and insomnia; memory loss/forgetfulness and mood swings; musculoskeletal symptoms, for example, joint and muscle pain; urogenital symptoms, for example, vaginal dryness; and sexual difficulties, for example, low sexual desire.

Migraine is not a risk factor for stroke in women older than 45 and is not a contraindication for HRT

Treatment options

As with all migraine patients, offer lifestyle advice and guidance on trigger avoidance. Migraine triggers often work in combination and so minimising exposure to other triggers such as low blood sugar, dehydration and lack of sleep, may reduce the number of migraines. Sleep patterns are often disrupted in the perimenopause and this can become an additional trigger for many women.

Effective acute treatment is also important. The British Association for the Study of Headache (BASH) recommends aspirin 600-900mg dissolved in a sweet, fizzy drink, taken with a prokinetic antiemetic such as metoclopramide 10mg, in order to reverse gastric stasis and improve absorption of analgesia.¹⁰ BASH advocate a stepwise approach to acute treatments, as detailed in Table 1. If symptoms are not relieved by oral or rectal analgesia, then step three is to take a triptan.¹⁰ Frovatriptan is particularly useful in perimenopausal women who are still having menstrual migraines. It has a longer half-life than other triptans and so can be helpful for women experiencing prolonged attacks. For a summary of acute treatments, please see “Hormonal Headaches in pre-menopausal women” published in Women’s Health in May/June 2015.¹¹

Prophylaxis

There is no absolute guidance for when to start prophylactic medication, so the physician should be led by the patient’s symptoms and how disruptive they are to her usual routine.

TABLE 1: ACUTE TREATMENT LADDER, AS RECOMMENDED BY BASH

Acute treatment	analgesic	Anti-emetic	
Step I	Over-the-counter analgesic +/- anti-emetic	Aspirin 600-900mg Or Ibuprofen 400-600mg	Metoclopramide 10mg
Step II	Rectal analgesic +/- anti-emetic	Diclofenac suppository 100mg	Metoclopramide 10mg
Step III	Specific anti-migraine drug	Triptan Eg: sumatriptan 50-100mg	

TABLE 2: SUGGESTIONS FOR PREVENTION OF MIGRAINES

Prophylaxis	Starting dose
Trigger avoidance and lifestyle measures	
Propranolol	40mg twice daily
Topiramate	25mg daily
Amitriptyline	10mg nocte
Riboflavin	400mg daily

Standard migraine prophylactic medication can be useful in the perimenopause, (Table 2). NICE recommends topiramate or propranolol in the first instance.¹² Amitriptyline is also useful, particularly in women with poor sleep patterns.¹³ The dose of these drugs should be titrated slowly to minimise side effects. Riboflavin (vitamin B2) can also be helpful, would need to be taken for many weeks before any benefit is seen. These drugs all raise the threshold for triggering a migraine and so reduce the frequency of attacks.

As hormonal fluctuations are implicated in worsening of migraines around the perimenopause, using hormonal treatments can alleviate many of the symptoms.

No studies have assessed the relationship between migraine, HRT and stroke. Migraine is not a risk factor for stroke in women older than 45 and is not a contraindication for HRT. Furthermore, women can be reassured that expert opinion concludes that there is no compelling evidence that transdermal HRT increases or decreases the risk of ischaemic stroke in women with migraine, with or without aura.¹³

To minimise side effects, HRT should be used in the lowest effective dose in order to control vasomotor symptoms. Women with a uterus require combined HRT, whereas unopposed oestrogens can be used in women who have had a hysterectomy. After hysterectomy, oestrogen implants are an option. The risks and benefits of HRT should be discussed with the patient as per the NICE guidance.⁹

The Mirena intrauterine system (IUS) can be used for contraception to control heavy/painful periods, and to act as the progestogen component of HRT. One advantage is that it acts directly on the womb, with low levels of hormone absorbed systemically. This means that side effects are generally very few. Another advantage is that if a perimenopausal woman has an IUS, it is easy to adjust the dose of oestrogen to suit her needs. The aim is to use the lowest effective dose of oestrogen to control vasomotor symptoms and reduce the frequency of migraines, whilst minimising potential side effects. Many women find that their periods become very light, or stop completely while they are using an IUS. If migraine was linked to troublesome periods, this in itself can make migraine less likely to occur, even without the addition of oestrogen.

Unscheduled vaginal bleeding is a common side effect of HRT within the first three months of treatment in women with a uterus, and should be reported at the three-month review appointment, or promptly if it occurs after the first three months. Menstrual migraines may accompany this bleeding, but should settle as hormonal levels stabilise with continued treatment.

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In practice, a number of women on HRT do find that their migraine becomes worse. Often this can be resolved by changing the dose or delivery method of the HRT. One small study has shown that the transdermal route for oestrogen administration is less likely than the oral route to make migraine worse.¹⁵ This is supported by expert opinion.

Headache associated with cyclical progestogens may be controlled by changing the type of progestogen, using transdermal progestogens or IUS, or changing to progesterone (delivered via vaginal gel pessary or suppository).

Vaginal oestrogen is often prescribed to help control local symptoms of pain and dryness in perimenopausal women who have no problems with hot flushes or sweats, or who still get vaginal symptoms despite using HRT. When a woman first starts to use vaginal oestrogens, a rise in oestrogen has been measured in the blood stream.¹⁶ Higher levels persist for a couple of weeks and then drop back down. This rise and fall can be sufficient to trigger migraine in susceptible women. With continued use of vaginal oestrogens, usually only necessary just once or twice a week, oestrogen levels settle and are less likely to trigger migraine.

Stopping treatment

The BASH recommendation is that the effective dose of any medication used for migraine prevention should be continued for around six months. The dose should then be slowly reduced, which may be over two-three months. If migraine returns after a drop in dose, then the dose should be increased back up to dose that effectively controlled attacks for a further few weeks before trying a dose reduction again. This helps to define the lowest effective dose to control migraine, and guides how long a patient actually needs to stay on treatment.

NICE states that “gradually reducing HRT may limit recurrence of menopausal symptoms in the short term. Gradually reducing or immediately stopping HRT makes no difference to symptoms in the longer term.”⁹

Other treatments

There are women for whom HRT may not be suitable, for example, women who have previously had breast cancer or are at high risk of breast cancer. If these women require treatment for menopausal symptoms and associated migraines, they should be referred to a menopause clinic for specialist advice.⁹ NICE does not advise the routine use of selective serotonin reuptake inhibitors (SSRIs), serotonin and norepinephrine reuptake inhibitors (SNRIs) or clonidine as first-line treatment for vasomotor symptoms alone. However, when treating vasomotor symptoms and migraine, there may be a place for the SNRI venlafaxine, which has some migraine preventative properties as well as some efficacy for vasomotor symptoms.^{17,18} As with all migraine prophylactic medication, this should be started at low dose and slowly titrated.

Follow up

Patients should be encouraged to try each regime for three cycles to assess efficacy, while keeping detailed symptom diaries. Even if a preventative regime is effective, the underlying migraine pattern is highly likely to change during this time of hormonal fluctuation, so continuing migraine prophylaxis should be reviewed six months after the start of prophylactic treatment.

KEY POINTS

- 1 Migraine tends to become more frequent and severe around the perimenopause
- 2 Falls in oestrogen trigger oestrogen withdrawal migraines (without aura)
- 3 High oestrogen states are associated with migraine aura
- 4 Surgical menopause is associated with worsening of migraines
- 5 Transdermal HRT offers stable levels of hormones, which can improve perimenopausal migraine symptoms; with no increased risk of stroke or venous thromboembolism.

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