

## Menstrual Migraine

Dr Anne MacGregor

Migraine affects three times more women than men, typically during their most productive years. This can lead to significant disruption to a person's life, which for many years has gone unrecognised. Recent research by the World Health Organization has established migraine as a leading cause of years of life lived with a disabling condition - 12th for women - compared to 19th for men.<sup>1</sup>

### What is menstrual migraine?

Studies show that migraine is most likely to occur in the two days leading up to a period and the first three days of a period.<sup>2</sup> Most women have attacks at other times of the month as well but a few have 'pure' menstrual migraine, only with their periods.

### What is different about 'menstrual' attacks?

Menstrual attacks are typically more severe, last longer, and are more likely to recur the next day than non-menstrual attacks. This means that many women who find that their migraine treatment works well most of the time may still have a problem with managing their menstrual attacks.

### Who gets 'menstrual' migraine?

Around 50 per cent of women notice a link between migraine and their periods. This may not be apparent until a woman reaches her late 30s or 40s, despite having had migraine since her teens or 20s. Women with other period problems often do not recognize that the accompanying headaches are actually migraine. This under-recognition of migraine by patients

is compounded by a similar under-recognition of migraine by doctors.<sup>3</sup>

### What causes 'menstrual' migraine?

Studies have shown that migraine can be triggered by a drop in oestrogen levels, such as naturally occurs around menstruation.<sup>4</sup> Oestrogen 'withdrawal' also triggers migraine in other situations such as the pill-free interval of combined oral contraceptives.<sup>5</sup> However, oestrogen is not the only hormone responsible for 'menstrual' migraine. Other studies have shown that women who notice migraine during the first few days of their period may be susceptible to the hormone prostaglandin. This hormone is at its highest level in the body during a period, particularly in women who have heavy or painful periods, and can be associated with headache.<sup>6</sup> Research is ongoing as it's quite likely that there are other causes for 'menstrual' migraine as the menstrual cycle is extremely complex. It involves a number of brain chemicals, known as neurotransmitters, that alter the effect of hormones such as oestrogen. It also involves other neurotransmitters known to be involved in migraine such as serotonin.

### How do I know I've got 'menstrual' migraine?

Keep diary cards for at least three menstrual cycles. This will help to confirm the relationship between migraine and your periods. You can just keep a note of migraine attacks and the first day of your period in your personal diary or you can download monthly diaries from [www.colmc.org.uk](http://www.colmc.org.uk)

## the City of London Migraine Clinic

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You might worry that you should have some investigations such as a test of your hormones or a brain scan. These tests are usually only necessary if your doctor thinks the problem is something other than migraine. This is because there is nothing different about your hormones than other women who don't have migraine – the difference is just that you are more sensitive to normal hormone fluctuations, which can then trigger migraine.

## Will it get better?

Migraine typically worsens as you get closer to the menopause, partly because periods come more often and partly because the normal hormone cycle becomes disrupted. The good news is that once periods stop and the hormones settle down, migraine improves.

## What can I do to help myself?

Most women with migraine can manage menstrual attacks in the same way as non-menstrual migraine. Keeping diaries can help you anticipate when your period is due. Look especially at the non-hormonal migraine triggers as avoiding these pre-menstrually may be sufficient to prevent what appears to be an hormonally linked attack. For example, take care not to get over tired and, if necessary cut out alcohol. Eat small, frequent snacks to keep blood sugar levels up as missing meals or going too long without food can trigger attacks. Treat an attack with your usual medication and don't delay – treatment is more effective the earlier it is taken. If the migraine attack returns later the same day or the next day, repeat the treatment. This can sometimes go on for four or five days around period time.

## What can my doctor do to help me?

If diary cards confirm that your attacks always occur two or three days around the first day of

your period, your doctor might consider ways to prevent migraine. They are less effective in women with additional attacks at other times of the cycle resulting from non-hormonal triggers. Depending on the regularity of your menstrual cycle, whether or not you have painful or heavy periods, menopausal symptoms, or if you also need contraception, several different options can be tried. Although none of the drugs and hormones recommended below are licensed specifically for management of menstrual migraine, doctors can prescribe them for this condition if they feel that this would be of benefit to you.

## Non-Steroidal Anti-Inflammatory Drugs

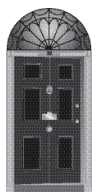
**Mefenamic acid** is an effective migraine preventative and has been reported to be particularly helpful in reducing migraine associated with heavy and/or painful periods, although no clinical trials have been undertaken specifically for menstrual migraine. A dose of 500 mg, three to four times daily, may be started either 2 to 3 days before the expected start of your period, but is often effective even when started on the first day: this is useful if periods are irregular. Treatment is usually only necessary for the first two to three days of your period.

**Naproxen** has also been found to be effective on doses of around 500 mg once or twice daily around the time of menstruation.<sup>7,8</sup>

## Oestrogen supplements

Unless a woman also needs contraception, supplementing oestrogen for several days around the time of your period (perimenstrual treatment) can prevent the natural oestrogen drop that can trigger migraine.<sup>9-11</sup>

Perimenstrual oestrogen supplements can only be used when your periods are regular and predictable.



**Oestrogen patches** in a dose of **100 micrograms** can be used from around 5 days before you expect your period to start and up to the 5th day of menstruation. The dose should be tapered off for the last few days of treatment by cutting the patch in half.<sup>12</sup> If this regimen is effective but side-effects are a problem (bloating, breast tenderness, leg cramps, nausea) a 50 microgram dose should be tried for the next cycle.

Alternatively, **estradiol gel 1.5 mg** can be applied daily from around 5 days before expected menstruation up to the 5th day of menstruation, again tapering off the dose of oestrogen for the last few days of treatment.<sup>12</sup> There is evidence that some women who benefit from oestrogen supplements experience delayed attacks when the supplements are stopped.<sup>11,13</sup> In these women, treatment can be extended until day 7 of the cycle, when a woman's own oestrogen starts to rise. Long-term use of oestrogens for hormone replacement therapy by women after the menopause has been associated with increased risk of breast cancer.<sup>14</sup> In contrast, there is no evidence that supplemental oestrogens used by premenopausal women who are still having natural periods carries the same risks.<sup>15</sup> However, supplemental oestrogens are not recommended for women who are at high risk for breast cancer.

## Triptans

Recent studies with perimenstrual triptans have proved promising. Although not currently recommended, it is likely that this treatment may become licensed for the prevention of 'menstrual' migraine.

## Continuous hormonal strategies

If you need contraception, or your periods are irregular, there are a number of contraceptive strategies that can also help treat 'menstrual' migraine, as follows:

**Combined hormonal contraceptives (CHC)** contain oestrogen and progestogen. The most common one is the 'pill' although weekly patches are also available. These 'switch off' the natural menstrual cycle and maintain fairly stable oestrogen levels for the 21 days of active hormone. However, migraine often occurs in the seven day hormone-free interval, as oestrogen levels drop. It is increasingly acceptable to reduce the number of hormone-free intervals, and hence migraine attacks, by taking three or four consecutive packs before taking a seven day break.<sup>16</sup> Taking CHCs continuously without a break may be even better for some women, if breakthrough bleeding is not a problem.<sup>17</sup> Although this can be an effective strategy for women who have migraine without aura, contraceptive oestrogens should not be used by women who have migraine with aura due to the potential increased risk of ischaemic stroke.<sup>18</sup> For such women, progestogen-only methods are recommended. **Progestogen-only pill (Cerazette®)** works in a similar way to combined hormonal contraceptives but does not contain oestrogen. Because the pill is taken every day, without a break, many women do not have periods, although irregular bleeding can be an occasional problem. Unlike Cerazette, other brands of progestogen-only pills do not switch off the cycle and are unlikely to help menstrual migraine.

**Injectable depot progestogens** also work in a similar way to combined hormonal contraceptives and are given every 12 weeks. Although most women having depot progestogens find that their periods stop completely, it can take a few months before this happens. Until then, migraine can occur with bleeding.<sup>19</sup> It is therefore important to persevere until bleeding settles down, which may not be until the 3rd or 4th injection

**Levonorgestrel (Mirena®) Intra-uterine System (IUS)** is licensed for contraception but is also

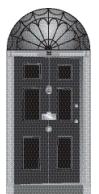
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highly effective at reducing menstrual bleeding and associated pain. It may be effective in migraine that is related to heavy or painful periods that has responded to non-steroidal anti-inflammatory drugs (NSAIDs) such as mefenamic acid or naproxen. It is not effective for women who are sensitive to oestrogen withdrawal as a migraine trigger, as the normal hormone cycle continues.

## Should I have a hysterectomy?

**Hysterectomy** has no place solely in the management of migraine. Studies show that migraine is more likely to deteriorate after-surgery.<sup>20</sup> However, if other medical problems require a hysterectomy, which can induce the menopause, the effects on migraine are probably lessened by subsequent oestrogen replacement therapy.

**Gonadotrophin-releasing hormones** create a medical 'menopause' and have been used to assess the likely outcome of a hysterectomy, although symptoms of oestrogen deficiency such as hot flushes, limit their use.<sup>21,22</sup> The hormones are also associated with bone thinning (osteoporosis) and should not usually be used for longer than six months without regular monitoring and scans to test bone density. 'Add-back' continuous combined

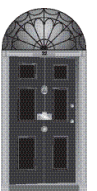
oestrogen and progestogen can be given to counter these difficulties. Given these limitations, in addition to their high cost, this type of treatment is generally only used in specialist departments.

## Hormone Replacement Therapy

The menopause marks a time of increased migraine. HRT can help, not only by stabilising oestrogen fluctuations associated with migraine, but also by relieving night sweats that can disturb sleep. Unlike oestrogen supplements, which are just used around the time of the period, HRT is taken throughout the cycle. It should only be started when periods become irregular and/or other menopausal symptoms such as hot flushes are present. If taken for only a couple of years to control symptoms, there is no evidence of increased risk of breast cancer.<sup>23,24</sup>

**Every effort has been taken to ensure that this article is accurate and complete but this cannot be guaranteed. Rapid advances in medicine may cause information contained here to become outdated, invalid or subject to debate.**

**The City of London Migraine Clinic is not responsible for the results of your decisions resulting from the use of this information.**



## References

1. World Health Organization. *Mental Health: New Understanding, New Hope*. Geneva: WHO, 2001.
2. MacGregor EA, Hackshaw A. Prevalence of migraine on each day of the natural menstrual cycle. *Neurology* 2004;**63**(2):351-3.
3. Lipton R, Stewart W, Celentano D, Reed M. Undiagnosed migraine headaches: a comparison of symptom-based and reported physician diagnosis. *Arch Intern Med* 1992;**152**:1273-1278.
4. Somerville BW. The role of estradiol withdrawal in the etiology of menstrual migraine. *Neurology* 1972;**22**(4):355-65.
5. Macgregor EA, Hackshaw A. Prevention of migraine in the pill-free interval of combined oral contraceptives: a double-blind, placebo-controlled pilot study using natural oestrogen supplements. *J Fam Plann Reprod Health Care* 2002;**28**(1):27-31.
6. Chan W. Prostaglandins and nonsteroidal antiinflammatory drugs in dysmenorrhoea. *Ann Rev Pharmacol Toxicol* 1983;**23**:131-49.
7. Szekely B, Meeryman S, Post G. Prophylactic effects of naproxen sodium on perimenstrual headache: a double-blind, placebo-controlled study. *Cephalalgia* 1989;**9**:452-3.
8. Nattero G, Allais G, De Lorenzo C, et al. Biological and clinical effects of naproxen sodium in patients with menstrual migraine. *Cephalalgia* 1991;**11**(suppl 11):201-2.
9. de Lignières B, Vincens M, Mauvais-Jarvis P, Mas JL, Touboul P, Bousser MG. Prevention of menstrual migraine by percutaneous estradiol. *BMJ* 1986;**293**(6561):1540.
10. Dennerstein L, Morse C, Burrows G, Oats J, Brown J, Smith M. Menstrual migraine: a double-blind trial of percutaneous estradiol. *Gynecol Endocrinol* 1988;**2**:113-120.
11. MacGregor EA, Frith A, Ellis J, Aspinnall L. Estrogen 'withdrawal': a trigger for migraine? A double-blind placebo-controlled study of estrogen supplements in the late luteal phase in women with menstrually-related migraine. *Cephalalgia* 2003;**23**:684.
12. MacGregor EA. *Migraine in Women*. 3rd ed. London: Martin Dunitz, 2003.
13. Somerville BW. Estrogen-withdrawal migraine. I. Duration of exposure required and attempted prophylaxis by premenstrual estrogen administration. *Neurology* 1975;**25**(3):239-44.
14. Beral V, Hermon D, Kay C, Hannaford P, Darby S, Reeves G. Mortality associated with oral contraceptive use: a 25-year follow up of 46,000 women from the Royal College of General Practitioners' oral contraception study. *BMJ* 1999;**318**:96-100.
15. Collaborative Group on Hormonal Factors in Breast Cancer. Breast cancer and hormonal contraceptives: collaborative reanalysis of individual data on 53,297 women with breast cancer and 100,239 women without breast cancer from 54 epidemiological studies. *Lancet* 1996;**347**:1713-27.
16. Nelson AL. Extended-cycle oral contraception: a new option for routine use. *Treat Endocrinol* 2005;**4**(3):139-45.
17. Thomas S, Ellertson C. Nuisance or natural and healthy: should monthly menstruation be optional for women? *Lancet* 2000;**355**:922-4.
18. World Health Organization. *Improving access to quality care in family planning. Medical eligibility criteria for initiating and continuing use of contraceptive methods*. Third ed. Geneva: WHO, 2004.
19. Somerville B, Carey M. The use of continuous progestogen contraception in the treatment of migraine. *Med J Aust* 1970;**1**:1043-5.
20. Neri I, Granella F, Nappi R, Manzoni G, Facchinetti F, Genazzani A. Characteristics of headache at menopause: a clinico-epidemiologic study. *Maturitas* 1993;**17**:31-7.
21. Holdaway IM, Parr CE, France J. Treatment of a patient with severe menstrual migraine using the depot LHRH analogue Zoladex. *Aust NZ J Obstet Gynaecol* 1991;**31**(2):164-165.
22. Murray SC, Muse KN. Effective treatment of severe menstrual migraine headaches with gonadotropin-releasing hormone agonist and 'add-back' therapy. *Fertil Steril* 1997;**67**(2):390-3.
23. Chlebowski R, Hendrix S, Lander R, et al for the Women's Health Initiative Randomised Trial. Influence of estrogen plus progestin on breast cancer and mammography in healthy postmenopausal women. *JAMA* 2003;**289**:3243-53.
24. Million Women Study Collaborators. Breast cancer and hormone-replacement therapy in the Million Women Study. *Lancet* 2003;**362**:419-27.

