



Migraine and Hormonal Changes

Prevalence of Migraine in Women

Migraine is a predominantly female disorder that affects 1 in 5 women and 1 in 13 men during their reproductive years. During childhood, boys and girls are equally affected by migraine. At puberty, the incidence of migraine without aura rises in females, with 10% to 20% of women reporting migraine during the same year as their first menstrual period. Throughout the reproductive years, menstruation is one of the most significant risk factors for migraine without aura. Postmenopause is associated with improvement in migraine.

Impact

The World Health Organization recognizes migraine as a leading cause of years of life lived with a disabling condition, ranking 12th for women, compared to 19th for men. Moderate or severe migraine-related disability is approximately twice as frequent among women compared to men, impeding performance in school, at work, and at home and preventing participation in social activities.

Menstrual Migraine

Between 50% and 60% of female migraineurs report an association between migraine and menstruation. The risk of migraine without aura is increased during a 5-day perimenstrual window that starts 2 days before the onset of the menstrual period and continues through the first 3 days of menstruation. Compared to all other days of the menstrual cycle, women are over 70% more likely to have migraine in the two days before the first day of a menstrual period. The risk of migraine is more than double on the first day of menstruation and the following two days.

The International Headache Society recognizes two types of menstrual migraine:

- Menstrually related migraine: migraine without aura that regularly occurs on or between day -2 to +3 of menstruation, with additional attacks of migraine with or without aura at other times of the cycle;
- Pure menstrual migraine, which is migraine without aura that occurs only on or between day -2 to +3, i.e., with no attacks at any other time of the cycle.

Diagnosis

To confirm the diagnosis, migraine attacks during the window between days -2 to +3 must occur in at least two of three menstrual cycles and establish a relationship that is greater than by chance alone. Relying on the history to confirm the diagnosis can be misleading. Use of a 3-month diary to record migraine patterns can reveal the predictable patterns associated with menstrual migraine, aiding diagnosis.

Differences between Menstrual and Nonmenstrual Attacks of Migraine

Menstrual attacks are of longer duration and greater severity, with greater susceptibility to relapse, greater resistance to treatment, and greater disability than migraines occurring at other times of the menstrual cycle.

Pathophysiology

Menstrual migraine is associated with the natural fall in estrogen that occurs just before menstruation. Prostaglandin release associated with heavy, painful periods has also been implicated in menstrual migraine.

Management

Acute treatment, if effective, may be all that is necessary for control. Evidence of efficacy, with acceptable safety and tolerability, exists for sumatriptan 50 mg and 100 mg, mefenamic acid 500 mg, rizatriptan 10 mg, and a combination of

sumatriptan/naproxen 85 mg/500 mg. Prophylactic strategies can reduce the frequency and severity of attacks and make acute treatment more effective. Predictable menstrual attacks offer the opportunity for perimenstrual prophylaxis with transcutaneous estradiol 1.5 mg, frovatriptan 2.5 mg twice daily, or naratriptan 1 mg twice daily. Contraceptive strategies offer the opportunity for treating menstrual migraine in women who also require effective contraception.

Contraception

Healthy women with migraine without aura can use combined hormonal contraceptives up to the age of 50 years. During the monthly hormone-free interval, estrogen withdrawal increases the risk of migraine without aura. These attacks can be prevented by changing to long-cycle or continuous hormones. Contraceptive estrogens should not be used by women who have migraine with aura because of the synergistic increased risk of ischemic stroke. Effective contraception need not be compromised because progestogen-only and nonhormonal methods are not associated with increased risk.

Pregnancy and Breastfeeding

Up to 80% of women with migraine experience fewer attacks during pregnancy compared to before, particularly if migraine was previously associated with menstruation; in around 20%, the attacks completely disappear. Migraine itself does not adversely affect the outcome of pregnancy. However, women with migraine should be monitored during pregnancy, as there is an increased risk of arterial and venous thrombosis, preeclampsia, and gestational hypertension. Breastfeeding is generally associated with sustained improvement in migraine.

Menopause and Hormone Replacement Therapy

Migraine is a common problem during perimenopause, as estrogen levels fluctuate. Women with menopausal symptoms, such as hot flashes and sweats, may benefit from replacement therapy. Nonoral routes are less likely to have a negative effect on migraine than oral formulations of estrogen replacement. Continuous combined hormone replacement therapy, rather than cyclical combined therapy, appears to be better tolerated.

References

- [1] Headache Classification Subcommittee of the International Headache Society (IHS). The International Classification of Headache Disorders, 2nd ed. *Cephalgia* 2004;24(Suppl 1):1–160.
- [2] MacGregor EA. Headache in pregnancy. *Neurol Clin*; in press.
- [3] MacGregor EA. Progress in the pharmacotherapy of menstrual migraine. *Clin Med Insights Therapeutics* 2011;3:245–73.
- [4] MacGregor EA. Migraine headache in perimenopausal and menopausal women. *Curr Pain Headache Rep* 2009;13:399–403.
- [5] MacGregor EA. Migraine and use of combined hormonal contraceptives: a clinical review. *J Fam Plann Reprod Health Care* 2007;33:159–69.