

Migraine headaches, menopause and HRT

Migraine headaches are characterised by a throbbing hemicranial headache accompanied by photophobia, and commonly nausea and vomiting. It is more common in women than in men and often related to hormonal changes. 60% of migraineurs experience a **prodrome** e.g. euphoria, depression, irritability, food cravings, constipation, neck stiffness, or increased yawning. 25% may experience an **aura** most often visual, but it can also be sensory, verbal, or motor disturbances. In migraine with aura, occasionally the headache may be very mild or absent so that the diagnosis of migraine can be obscure.

Reproductive life events affect migraine without aura differently to migraine with aura. The onset of migraine without aura occurs after menarche suggesting that the development of the female menstrual cycle plays a role in its initiation. Migraine with aura is not so influenced by reproductive hormonal changes.

Falling oestrogen, and not falling progesterone, levels are the trigger for the migraine in menstrual migraine. Experimental hormonal manipulation of the late luteal phase has shown that the administration of oestrogen will delay the migraine but not the menses, whereas administration of progestin will delay the period but not the migraine. Pre-existing migraine most often improves during pregnancy where sex hormones levels are sustained and high¹. However, hormonally sensitive migraine often worsens during perimenopause during a time of wide fluctuations of oestrogen². The timing of migraine often evolves, as perimenopause approaches, from one which occurs only at menses to one which occurs twice during the cycle (once at menses when the oestradiol falls and once after ovulation when the oestradiol also falls but to a lesser degree) to one which is completely erratic and unpredictable in timing.

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 last menstrual period. This improvement is attributable to the lack of variation in sex hormone levels. Unfortunately many of the studies of migraine at menopause have included both post menopausal and perimenopausal women. These two states have very different effects on hormonally sensitive migraine. One study did show that almost two thirds of women with migraine experienced an improvement after menopause was established³. Surgical menopause leads to abrupt changes in hormone levels and is likely to lead to an initial exacerbation in migraine. This may signify that there is an oestrogen "threshold" below which migraine is triggered in sensitive women. Although data are scarce, clinical impression is that the frequency of migraine with aura is little changed by the menopause.

The risk of stroke is raised in migraine with aura and further increased with the use of the oral contraceptive pill and with smoking. There are no specific data about the risk of stroke with the use of HRT in migraine, and migraine is not considered a contraindication to the use of HRT.

The indication for HRT in postmenopausal women with migraine is not to improve the migraines but to treat the menopausal symptoms. Depending upon the dosage regimen and the delivery system HRT may improve migraine, worsen migraine or not have any effect on migraine. Acute treatment of a migraine in the perimenopause or menopause should follow the standard practice for migraine management.



As a general rule, cyclical hormone replacement is recommended for women who are within 12 months of their last menopausal period because early institution of continuous hormone replacement may lead to breakthrough bleeding.

However, some women are sensitive to progestin such that the progestin phase of a cyclical regimen or progestin alone may trigger migraine. If this is the case and when added progestin is necessary (in women with an intact uterus), one study has found that continuous combined HRT is less likely to trigger headache than a cyclical regimen especially if there is an "off hormone" phase or a low oestrogen phase. Although data specifically relating to migraine are lacking, the lower progestin levels obtained with the use of the levonorgestrel IUD may be an argument for using that delivery system for HRT in women who are sensitive to progestin.

Modification of HRT regimen, dose and delivery may be appropriate in women with hormonally sensitive migraine. Transdermal oestrogen delivery is less likely to trigger migraine than oral oestrogen delivery⁴. This form of delivery may be superior because it maintains a more stable delivery of oestrogen and avoids fluctuating serum oestradiol levels. Contrary to what one might expect, studies have shown that, in oestrogen-only regimens, transdermal oestrogen using the 100µg patch has a greater preventative benefit for migraineurs over the 50µg patch - again a suggestion that there is an oestrogen threshold which is beneficial for migraine prevention.

Practice points

- Migraine is not a contraindication to using hormone replacement therapy
- Migraine without aura is more sensitive to hormonal flux than migraine with aura
- Falling oestrogen commonly triggers the onset of an hormonally sensitive migraine
- Therefore maintaining stable oestrogen levels is important and transdermal delivery is preferable

Further reading

Useful review

MacGregor, E. A. (2009). "Migraine headache in perimenopausal and menopausal women." *Current Pain & Headache Reports* 13(5): 399-403

Heavy duty reading

Martin VT, Behbehani M. Ovarian hormones and migraine headache: understanding mechanisms and pathogenesis--part I. *Headache* 2006; 46 (1) 3-23.

Martin VT, Behbehani M. Ovarian hormones and migraine headache: understanding mechanisms and pathogenesis--part 2. *Headache* 2006; 46(3):365-86 (3) 365-86.

References

- 1 Sances, G., Granella, F., Nappi, R.E., Fignon, A., Ghiotto, N., Polatti, F. & Nappi, G. (2003) Course of migraine during pregnancy and postpartum: a prospective study. *Cephalalgia* **23**, 197-205.
- 2 Mattsson, P. (2003) Hormonal factors in migraine: a population-based study of women aged 40 to 74 years. *Headache* **43**, 27-35.
- 3 Neri, I., Granella, F., Nappi, R., Manzoni, G.C., Facchinetti, F. & Genazzani, A.R. (1993) Characteristics of headache at menopause: a clinico-epidemiologic study. *Maturitas* **17**, 31-37.
- 4 Nappi, R.E., Cagnacci, A., Granella, F., Piccinini, F., Polatti, F. & Facchinetti, F. (2001) Course of primary headaches during hormone replacement therapy. *Maturitas* **38**, 157-163.