

Menstrual-Associated Migraine (2000)

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Although the tendency to get frequent, severe headaches is probably inherited, environmental factors play an important role in determining how that tendency is expressed. Among the environmental trigger factors which seem to influence headaches, menstruation has received a great deal of attention. Of women with migraine, almost half notice some connection between menstrual periods and migraine (menstrual-associated migraine), but only 14% have migraine exclusively with their periods (so-called "true menstrual migraine").

There is good reason to believe that hormonal factors play a role in migraine.

The hormonal milestones of menarche, pregnancy and menopause are often associated with changes in headache frequency and severity, and the use of exogenous estrogens, whether oral contraceptives or estrogen replacement therapy can also influence migraine. Early work done by Somerville suggests that falling estrogen levels are primarily responsible for increasing susceptibility to migraine; however, this work involved a small number of patients and has never been replicated. Falling estrogen levels alone are probably not the only factor involved in menstrual-associated migraine. The density and sensitivity of opioid receptors in the central nervous system also changes throughout the menstrual cycle.

Although hormonal factors may seem to be a very prominent trigger for headaches in many patients, it is rare that they are the only trigger, and some caution should be exercised in making a diagnosis of menstrual-associated migraine. Treatment aimed at menstrual-associated migraine can be very successful, but that success depends on an accurate diagnosis; it is not uncommon, for example, for women to pay more attention to headaches around their menses and underreport shorter, milder headaches at other times. Treatment intended for use only once a month may end up being used by these women to treat other headaches, with possible medication overuse and side effects resulting.

At a minimum, women should be asked to keep a record of all headaches and their menstrual cycle for at least three months. This will help establish not only the connection between headaches and menses, but also the regularity of the menstrual cycle, the length and severity of headaches and their timing in relation to menses. Some women tend to get headaches one to two days before the actual menstrual flow begins, and knowledge of this is essential in planning appropriate treatment.

Nonpharmacologic approaches to the treatment of menstrual migraine can be helpful in many cases. Regular aerobic exercise is always useful and more scrupulous avoidance of known headache triggers may be necessary around the time of the period and less important the rest of the month. For example, a woman may find it helpful to be especially careful about getting enough sleep, eating regular meals and avoiding alcohol intake if she knows she is expecting her period and is more vulnerable to headaches.

Special treatment for menstrual migraine is not always necessary: although triggered by menstruation these headaches are still migraine, and often respond to traditional migraine treatment which the woman may be using to treat headaches at other times during the month. If that is not the case, the use of special strategies aimed at the period-associated headache can be considered.

Nonsteroidal anti-inflammatory agents play an important role in the treatment of migraine associated with menses because of their effects on prostaglandins, which may be responsible not only for menstrual cramping but also for augmenting the headache response. If the period is regular and the headache occurs in predictable relation to it, it is worth trying a scheduled dose of an anti-inflammatory medication beginning 24 hours prior to expected onset of the headache (which may differ from onset of the period) and continue that for the expected duration of the headache; for example, flurbiprofen 100 mg tid for 3-5 days. This form of treatment is often referred to as "mini-prophylaxis". Sumatriptan 25 mg tid was also used in this way in one small, open-label trial.

Other triptans are being studied for this kind of prophylactic use, but trial results are not available at this time. Their efficacy in single doses for menstrual migraine has also been the subject of great interest. Naratriptan, with its long

half-life and lower recurrence rate, has been anecdotally reported to be helpful for menstrual migraine, but published, controlled studies are lacking. Zolmitriptan has been shown to be equally effective in migraine occurring in relation to the menstrual period as in migraine occurring at other times. At the current time, it seems likely that all triptans will ultimately prove to be effective in treatment of acute menstrual migraine, with some being more effective than others for prophylaxis, based on half-lives or dosing regimen.

The doses of prophylactic agents being used throughout the month can be increased perimenstrually to cope with an expected menstrual-associated headache, and some practitioners even advocate the use of typical migraine preventives only in the peri-menstrual period. Again, well-done, controlled studies are lacking and practice in this area is largely based on expert consensus and personal experience. There is no evidence that hysterectomy and oophorectomy are useful in treating menstrual migraine; women who undergo this procedure face the risk of major surgery and then face decisions about hormone replacement therapy, which can also aggravate headache in some cases.

Hormonal manipulation can be considered for women whose headaches do not respond to previously mentioned therapies. Adding back estrogen during the period, either orally or with the estrogen patch, has been reported to help some women. Side effects can include irregular menses, however, which ultimately makes further treatment impossible. Continuous low-dose oral contraceptives (OCs) abolish the hormonal fluctuations which trigger migraine in susceptible women and can also be considered in refractory menstrual associated migraine. Continuous low-dose OCs are often employed for endometriosis or other conditions where, as in migraine, cycling estrogen levels can be problematic. Other hormonally active treatments, including tamoxifen, bromocriptine and GnRH therapy with add-back estrogen are anecdotally reputed to have been helpful in refractory cases. Their use without specialty consultation and exhaustion of other treatment alternatives should probably be avoided.

A final note on the subject of menstrual-associated migraine is important: in our zeal to help patients identify and treat headache triggers, we must be careful not to overemphasize the role of menstruation as a headache trigger. Review of data from recent trials of headache medications, in which information has been collected about headache length, severity and relationship to menstruation, has not shown any difference in headache severity or response to treatment for those headaches associated with menstruation compared to those headaches not associated with menstruation. This information is at odds with the clinical impression that headaches associated with menstruation are longer, more severe and more difficult to treat than other headaches. What accounts for this discrepancy between perception and reality?

Menstruation is a normal event but one which is conspicuous and which carries a great deal of cultural and emotional significance. Events, including headache, which occur in relation to the period are more likely to be remembered and may be attributed to the period even if that association is by chance alone. When one considers that the average menstrual period lasts four to five days and occurs once every twenty-eight days, it becomes clear that a significant number of headaches which occur in relation to the menstrual cycle do so by chance alone. In addition, headaches which occur with other symptoms of menstruation such as abdominal cramping may be perceived as more troublesome not because they are more severe but because in association with other symptoms they are more difficult to tolerate.

Overemphasis on menstruation as a trigger, or on "special" treatment for headaches associated with menstruation may inadvertently increase, rather than decrease, the distress of patients by making them feel they are at the mercy of their hormones and that headaches with menstruation are inevitable. Recognizing hormonal fluctuations as one trigger among many and emphasizing the active role which women can play in helping to manage and prevent such headaches is a more useful approach to the problem of migraine occurring in association with the menstrual period.