



INFORMATION FOR HEALTH CARE PROFESSIONALS



Menstrual Migraine: New Approaches to Diagnosis and Treatment

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Two-thirds of premenopausal female migraine sufferers self-report that migraine attacks consistently occur during peri-menstrual time periods. These headaches have been referred to as “menstrual migraine”. Interestingly, only attacks of migraine without aura occur more frequently during peri-menstrual time periods. Attacks of menstrual migraine have been found to be more severe, disabling and refractory to abortive medications than those that are non-menstrually related.¹

Definition of Menstrual Migraine

Menstrual migraine, as defined by the International Headache Society, has two subtypes. Attacks of *menstrually related migraine without aura* must have an onset during the peri-menstrual time period (2 days before to 3 days after the onset of menstruation) and this pattern must be confirmed in 2/3 of menstrual cycles, but other attacks may occur at other times of the menstrual cycle. Attacks of *pure menstrual migraine without aura* are similar to the above criteria except that migraine headaches are strictly limited to the peri-menstrual time period and do not occur at other times of the month. The prevalence of menstrually related migraine without aura ranges from 35-51% of females with migraine while that of pure menstrual migraine without aura varies from 7-19%.

Pathophysiology

The most plausible trigger for menstrual migraine is the decline in serum estradiol levels that occur shortly before and during the peri-menstrual time period. Other factors may also contribute to its pathophysiology such as: 1) release of prostaglandins from a shedding endometrium that sensitizes peripheral nociceptors, 2) declines in serum magnesium levels and 3) decreases in inhibitory neurotransmitter systems (i.e., serotonergic, GABAergic, etc.) that modulate neuronal firing rates within second order neurons of the trigeminal system.²

Treatments

Acute and preventative therapies may be utilized for the treatment of menstrual migraine. Acute therapies are used to abort the migraine attack once it has begun while preventative therapies are employed to prevent the development of menstrual migraine altogether. Preventative therapies can be subdivided into short- and long-term prophylactic therapies.³ Short-term prophylactic therapies are only given during the peri-menstrual time period. They are initiated 1-2 days before the start of the anticipated menstrual migraine attack and continued for 4-7 days. Continuous prophylactic therapies are given every day of the month and can be used to prevent both menstrually-related and menstrually non-related attacks.

Abortive Therapies

Abortive therapies can be classified as migraine specific and migraine non-specific. Migraine specific therapies (triptans and ergots) are only effective for migraine and cluster headaches while migraine

non-specific therapies (NSAIDS, acetaminophen, narcotics, isometheptane- and butalbital-containing medications) are effective for both migraine and tension-type headaches. Clinical studies have demonstrated that the triptans (eg. almotriptan, eletriptan, frovatripan, naratriptan, rizatriptan, sumatriptan, zolmitriptan) as well as an aspirin/acetaminophen/caffeine combination (Excedrin™) are effective for the abortive treatment of menstrual migraine. Efficacy rates of these therapies for the treatment of menstrual migraine are similar to those observed for non-menstrually related attacks.

Short-term Prophylactic Therapies

Short term prophylactic therapies include NSAIDS, triptans and estrogen transdermal patches/gel. Naproxen sodium at a dosage of 550 mgs BID given 6 days before to 7 days after menses has demonstrated effectiveness in the prevention of menstrual migraine. Three triptans (frovatriptan [2.5 QD or BID], naratriptan [1 mg BID] and zolmitriptan (2.5 mgs BID and 2.5 mgs TID]) when administered for 4-5 days during the peri-menstrual time period are also effective preventative agents. Estradiol patches and gels can also be employed, but the correct dosage of these medications must be used! One hundred microgram transdermal estradiol patches were found to be more effective than 25 and 50 mcg patches in one study.

Continuous Prophylactic Therapies

Continuous prophylactic therapies include hormonal and non-hormonal therapies. Hormonal therapies include long duration oral contraceptives (OC) and gonadotropin releasing hormone agonists (GnRHa). Long duration OC contain three months of active pills containing both ethinyl estrogen and progestin followed by a placebo week as compared to three weeks of active pills followed by a placebo week with more conventional OC. Such pills prevent menstrual migraine because they minimize declines in ethinyl estradiol experienced during the placebo week of OC. GnRHa can be used to induce a medical oophorectomy in rare instances, but estrogen must be added-back to prevent migraine headache in these patients. However, these medications have many side effects (i.e., menopausal symptoms) and should be reserved for the most refractory patients. Non-hormonal therapies such as beta-blockers, calcium channel blocker, tricyclic antidepressants and anticonvulsants can also be used particularly in patients with irregular and unpredictable menses. Some clinicians recommend increasing the dosages of these standard preventatives just during the peri-menstrual time period in an attempt to prevent menstrual migraine although data are lacking for such a practice.

Approach to Treatment of Menstrual Migraine

All patients with menstrual migraine should be given an abortive medication regardless of whether preventative therapies are employed. The choice of a given preventative therapy depends upon a number of clinical factors. If patients are already receiving OC then the easiest intervention would be to use extended duration OC (i.e., omit the placebo week from the first three packs of OC and administer the placebo week with the fourth pack). A short term prophylactic therapy, such as triptans or an NSAID, may be used for patients with regular menstrual periods. A continuous standard preventative is considered for patients with irregular menses. Therefore, an individualized approach to menstrual migraine is necessary to provide optimal treatment to these severe and refractory migraine attacks.

References

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