

Migraine in Women

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The evidence is considerable linking female sex hormones, estrogen and progesterone, to migraine. The female preponderance of migraine would appear largely related to hormonal milestones throughout a female migraineur's life: menarche, oral contraceptive use, pregnancy, the post-partum state and breastfeeding, perimenopause, menopause and the use of hormone replacement therapy. At any stage during the reproductive cycle of a woman these milestones or therapy related to a milestone may alter both prevalence and severity of headache. Migraine is actually more common in boys than in girls with the gender difference in migraine only appearing as young women reach the age of menarche. Migraine is more common in adult women (18%) than in men (6%) and migraine prevalence peaks for both genders in the 25-55 age range. Women have opportunities for their migraine to be influenced during puberty as menstrual cycles begin, throughout their reproductive years, and again at perimenopause and post-menopause. Estradiol levels peak in the late twenties and early thirties and decline thereafter. At each hormonal milestone, opportunities for therapeutic management abound.

MENSTRUAL MIGRAINE

Among women with migraine, 11% have onset of migraine at menarche. Women who begin having migraine attacks at the time of menarche are more likely to experience menstrual migraine. Interestingly, only 14% of women have migraine only in association with their menstrual periods. Approximately 60% of female migraineurs have migraine with menses and at other times during the menstrual cycle. It is commonly reported that the risk of migraine is elevated during the first three days of menstruation, but not with ovulation, however this data is limited by being retrospective and involving small numbers of patients. No formal international headache society classification exists for menstrual migraine, but useful criteria define a migraine occurring without aura and almost exclusively (>90% of time) from one day before menses to four days after start of menstruation. Various definitions are used in different studies and in the triptan studies for mini-prophylaxis, the definition was two days before the onset of menses to three days after the start of menstruation. Dramatic differences in the prevalence of menstrual migraine are observed depending on the definition of menstrual migraine used, and range from 4% to 73%. The underlying pathogenesis for menstrual migraine is felt to be critical to the drop in estrogen occurring during the luteal phase of the menstrual cycle. Indeed, the drop in estradiol on the day prior to menstrual flow correlates with migraine onset in many menstrual migraineurs. Changes in multiple neurotransmitter systems occur with decreases in estrogen. These may include:

- prostaglandin release
- changes in opioid tones

- increased sensitivity of dopamine receptors
- increased serotonergic transmission
- reactivity of cerebrovasculature to serotonin
- lack of normal increase in melatonin at night.

The latter may account for fragmented sleep, which alone may worsen menstrual migraine.

MANAGEMENT

Cornerstones of management in menstrual migraine include clearly identifying the relationship between the menstrual cycle and migraine. A thorough history and patient diary are the two most useful initial approaches. Patient diaries may be kept on block monthly calendars with patients encouraged to circle the days of their menstrual cycle and ovulatory days if they are able to determine these. In addition, patients are asked to mark headache days as well, and months can be compared serially at the time of office visits. Many women have the mistaken notion that headache is merely a part of the premenstrual syndrome which they may have been taught merely to accept. It is important to educate patients that migraine is a biologic disorder and that migraine occurring during the time of either ovulation or menstruation can be treated. It may also be important during this time to help patients to recognize and avoid triggers, which can be considered “stackable”. For example, the patient who may have food or beverage triggers should avoid those specific foods or beverages around the time of vulnerability at menses. Being careful about sleep hygiene may also be helpful during this time of hormonal vulnerability. Patients should be given acute treatment for their menstrual migraine and, if abortive therapy is inadequate to control the headache, prophylactic therapy may be initiated. An adequate trial usually should include treatment through two menstrual cycles at a dose felt to be efficacious and patients may benefit from two to three menstrual cycles on similar management with adequate rescue provided.

Obstacles to diagnosis of menstrual migraine often include the lack of patient awareness of the link between their menstrual cycles and headache. Patients may be fearful in describing prodromal symptoms such as depression, food cravings, yawning, and irritability because they may think these will be viewed as psychiatric or as simply part of the premenstrual syndrome. Many women fail to report symptoms because of the belief that no effective treatment is available, often because they have been given ineffective therapies or have used self-therapies to no avail. Another important issue is recognizing the degree of disability associated with menstrual headache. Many women will simply stop their activities around the time of their menstrual period and specific questions, including the use of disability surveys, may be useful in determining how aggressive therapy needs to be. And lastly, symptoms can be masked by habitual use of NSAIDs for other menstrually related symptoms. Important questions to ask to elicit the diagnosis of menstrual migraine include:

- Do you have any premonition before a severe headache attack?
-Food cravings? Mood Changes? Excessive yawning?
- Do you have any changes in your vision?
- With your headaches, do you have any sensitivity to light or noise?
- Do you have nausea or vomiting?

- Are you able to work or socialize when you have these symptoms?
- Is your pain usually on one side of your head?

Often, many women will not have recognized their headache as being migraine, nor will their previous physicians, if they have migraine without aura, which is more commonly associated with menstruation, and if they do not have nausea and/or vomiting. Reassurance about common triggers seen with menstrual migraine can also be helpful. Over-emphasizing triggers, however, tends to trivialize migraine as a chronic disease and place the burden on the migraineur. Patients should be instructed to look for any offending foods or beverages, particularly alcohol, but otherwise they should not be placed on elimination diets unless they can clearly associate a food trigger, such as MSG, with the precipitation of headache.

ACUTE TREATMENT

Acute treatment can involve multiple choices. Migraine specific therapy, including the triptans, can be extremely effective for most female migraineurs. Other drugs may include ergotamine tartrate, dihydroergotamine, NSAIDs, antiemetics, COX-2 inhibitors, combination analgesics, hormonal therapy, steroids, and opioids or related analgesics. The goal for acute therapy should be relief of pain within 1-2 hours, control of nausea and vomiting, improvement in functional disability, and the elimination of headache recurrence. Abortive therapy should be prescribed to reduce pain and restore function so patients can avoid missing work, school, and other activities. The triptans offer impressive efficacy in all menstrual endpoints, including pain relief, pain free status, control of nausea and vomiting, and relief of functional disability. For example, several studies have shown sumatriptan, both subcutaneous and oral, to be as effective in the treatment of menstrual migraine as it is for non-menstrual migraine. In one study, headache relief four hours after receiving oral sumatriptan 100mg was 67% compared with 33% for placebo. Rates of relief are even higher with subcutaneous sumatriptan and include 80% headache relief at one hour when used for acute treatment of menstrual migraine. Efficacy of rizatriptan 10mg in patients with menstrual versus those with non-menstrual migraine were compared and responder rates at two hours were similar and in some cases higher in the patients who had menstrual associated migraine. Approximately 70% of women achieve receive pain relief after two hours compared with 44% of placebo and 42% of the rizatriptan patients were pain free after two hours. Zolmitriptan has shown similar efficacy and has been shown to be more effective when patients choose to treat at mild versus moderate to severe menstrual migraine. With zolmitriptan, there was a 72% two hour headache response.

Cyclic or mini-prophylaxis with an NSAID or triptan beginning two or three days before menses and lasting for up to one week may be useful for patients who have very predictable menstrual headache. Efficacy in reducing menstrual migraine attacks has been shown for patients using 1mg of naratriptan BID two days before menstruation through three days of menstruation. Similar results have been seen in small studies using sumatriptan. In the frovatriptan mini-prophylaxis study for menstrual migraine, both the 2.5mg dosed daily and dosed BID showed efficacy in reducing menstrual migraine. A dose response curve was seen with higher efficacy in the 2.5mg BID treated patients, and therapy again was begun two days before menstruation and continued into the first three days of menstruation. Mini-prophylaxis has also been studied with naproxen sodium and

33% of patients receiving naproxen dosed TID were free of menstrual headache versus none with placebo in one small study. Naproxen was further associated with a reduction in headache intensity, duration, and number of headache days. Ergotamine tartrate for migraine prophylaxis dosed 1mg BID for 3-5 days has also shown efficacy.

Percutaneous estradiol gel has also been studied for prophylaxis of menstrual migraine and in two double-blind placebo-controlled trials has been shown to result in a reduction in migraine frequency, duration, and severity. Percutaneous estradiol is the treatment of choice in women taking estra-progesterones, since the expected date of the attack is usually known, and it is given during the seven placebo days. If percutaneous estradiol gel is employed, it is started forty-eight hours before the anticipated migraine attack and used daily for the next seven days at a dose of 1.5mg of estradiol, which brings the mean estradiol plasma level to 80pg/ml.

Transdermal estrogen for prophylaxis of menstrual migraine has had inconsistent efficacy reported. No benefit was shown in one small placebo-controlled trial, however a reduction in migraine frequency and use of rescue medicines in an open-label trial of high dose treatment was established. Transcutaneous estradiol patches have also been studied in menstrual migraine prevention. Three doses are available: TTS-25 which delivers 25mcg of estradiol per twenty-four hours, TTS-50, which delivers 50mcg of estradiol per twenty-four hours, and TTS-100, which delivers 100mcg of estradiol per twenty-four hours. The estradiol serum levels reached with these patches are 23pg/ml, 39pg/ml, and 74pg/ml, respectively. TTS-50 was not found superior to placebo for the prevention of menstrual migraine in two double-blind trials, which may be due to inadequate serum levels. TTS-100 was found superior to TTS-25 in one open trial. Transdermal estrogen can be applied 1-2 days before the anticipated drop in estrogen and continued on the basis of patch duration either every three days or every seven days, depending on formulation. Transdermal forms would be preferred in women who have hyperlipidemia.

Specific consideration for anti-convulsant therapy regarding prophylaxis of menstrual migraine relates to changes in the efficacy of birth control pills if also being used for contraception. Gabapentin, topiramate (at dosages used for headache), and levetiracetam do not interfere with birth control pill efficacy. Another important consideration in women of childbearing age is the use of divalproex, which has been associated with neural tube defects and the development of polycystic appearing ovaries. For all women receiving anti-convulsant therapy, 1mg of folic acid is suggested.

Non-pharmacologic therapies may include cognitive or behavioral therapy and biofeedback, although no data exists to suggest that these alone may be useful. It is classically considered that menstrual migraine attacks last longer, are more severe, and are more resistant to therapy than other attacks. This view continues to be debated by headache experts, but regardless of one's view, women who are seen in tertiary headache settings for menstrual migraine do tend to have more resistant attacks, thus accurate diagnosis and hormonal influences on migraine should be firmly established. Cyclic prophylactic therapy may be offered, in addition to acute therapy.

When patients have a high frequency of migraine outside menses, continuous prophylaxis may also be considered. Other options for reducing or preventing menstrual migraine may also include increasing dosages of prophylactic medications around the time of menstrual vulnerability. As with any migraineur, the presence of co-morbid or

coexisting disorders must be considered in selective prophylactic therapy and patients may benefit from choices, which control both conditions. Both catamenial epilepsy and menstrual migraine may occur in the same patient and thus boosting the anti-epileptic therapy used as prophylaxis both for seizures and migraine may be of particular benefit. The addition of low-dose benzodiazapine therapy at bedtime during the premenstrual and menstrual time may benefit a patient with co-existing epilepsy, sleep fragmentation, and menstrual migraine. Patients who have considerable mood lability during their premenstrual and menstrual states may benefit from an escalation in an SSRI or tricyclic, unless bipolar. Conventional prophylactic agents for menstrual migraine may include beta-blockers, calcium channel blockers, anti-convulsants, tricyclic anti-depressants, and magnesium (dosed at 400mg BID with dosage reduction in patients with any renal risk). On a practical note, it may be more useful to dose magnesium continually rather than simply premenstrually, and chelated magnesium is preferred.

Oral contraceptive therapy may also be employed for prophylaxis of menstrual migraine. Lack of consensus on use of oral contraceptives plagues this choice. No randomized-controlled clinical trials exist to show benefit for prophylaxis of menstrual migraine in this setting. Oral contraceptives, however, do have many non-contraceptive benefits including less menorrhagia, dysmenorrhea, less premenstrual tension, less irregular menstruation, and can improve migraine frequency, induce migraine, or produce no change in existing headache patterns. Oral contraceptives can induce the first migraine attack, most often reported in women with a family history of migraine, but existing migraine may exacerbate and headaches may occur on placebo days of oral contraceptives. In general, it may be useful to explain to patients that migraine improves in one-third of patients placed on oral contraceptives, worsens in one-third, and remains unchanged in one-third. Careful diary information will clearly establish into which pattern an individual migraineur falls and will allow for effective use of oral contraceptives in menstrual migraine prophylaxis. Other options may include shortening placebo days or, more recently, the continuous use of oral contraceptives. The strategy employed in this setting is typically to use three consecutive packs of active pill followed by a pill-free interval. During the pill-free interval patients can be placed on mini-prophylaxis often with both an anti-inflammatory drug, either an NSAID or COX-2 inhibitor, along with a triptan. Irregular bleeding can be a complication of this therapy and often patients will, by diary information, show a consistent pattern of bleeding onset at a shorter interval than the typical nine weeks and that can then be used as the marker for continuous pill up to that week.

The second or third generation low-dose formulation combined oral contraceptives are known to be safe and highly effective for contraception. They do provide a risk factor for ischemic stroke, however, with the risk being dependent on the estrogen dose and age of the woman. In the absence of risk factors, however, the ischemic stroke risk is not felt to be increased, but there does seem to be synergism with migraine and combined oral contraceptives for ischemic stroke. The most important combination being migraine with aura, smoking, and combined oral contraceptive use. The European community tends to be much more restrictive in using oral contraceptives in patients who have migraine with aura, but the consensus from the International Headache Society task force on combined oral contraceptives and hormone replacement therapy suggested that one must individually assess and evaluate risk for ischemic stroke

in women with migraine. It may be most critical to identify and evaluate other risk factors for stroke, diagnose the migraine type, with particular attention to aura. Women with migraine who smoke should stop smoking before beginning oral contraceptives and other risk factors such as hypertension, hyperlipidemia, or diabetes should be aggressively treated. Women who have had past histories of thrombosis, ischemic heart disease, stroke, valvular disease, or breast cancer should not be considered candidates for any combined oral contraceptive use in migraine prevention. Hypercoagulable laboratory studies may be useful if there is any question about an individual patient's risk for stroke.

OVULATION

The link between migraine attacks and ovulation has never been confirmed epidemiologically, but merely anecdotally, in headache clinics. The presumed mechanism is that some women go through a hypoestrogenic post-ovulatory phase long enough to trigger an attack. For others, the peak of estrogen at ovulation is of such short duration that it cannot precipitate an ovulatory attack.

PREGNANCY

Improvement or disappearance of migraine during pregnancy has been noted in 55-90% of migraineurs. Migraine, however, may remain unchanged during pregnancy in 5-30% of migraineurs. Some researchers have found the improvement in migraine was limited to migraine without aura and was observed primarily in the second and third trimesters of pregnancy. Other researchers note that more severely affected migraineurs have no change during pregnancy. In general, the beneficial effect of pregnancy on migraine is observed more frequently in women who have menstrual migraine and/or women whose migraine began at menarche. Because migraine generally improves during pregnancy, non-pharmacologic management can be emphasized. Biofeedback, massage, avoidance of triggers, regular exercise, careful sleep, and adequate rest may all tend to minimize attack frequency and severity. Local application of ice or heat and adequate hydration may also be useful. In women who continue to have severe attacks, prophylactic therapy may be indicated, although there are no adequate well-controlled studies in pregnant women. Beta-blockers, specifically branded Inderal, may be used, and it is recommended that it be tapered four weeks prior to delivery. Branded Elavil and Pamelor have also been used in this setting. For acute therapy, NSAIDs may be used after implantation and before thirty-two weeks. Codeine containing agents have Class-B status, as do caffeine and opiates, and in combination with antiemetics, such as promethazine and ondansetron may be useful. Rescue therapy with steroids and IV hydration may be necessary in extreme circumstances.

The use of triptans during pregnancy has not been established, although it has recently been proposed that sumatriptan receive Class-B scheduling for pregnancy use. The sumatriptan pregnancy registry does not show any evidence for adverse outcomes higher than would be expected in controls. During breastfeeding, paracetamol and NSAIDs are felt compatible with breastfeeding, although caution is required with aspirin. Sumatriptan has been used safely in this setting with patients instructed to pump and discard for six hours after use before resuming feeding.

For women during their childbearing years, clinicians have a particular

opportunity to manage their migraine well around the time of conception. Suggestions are that patients be changed to prophylaxis acceptable for continuation during pregnancy, folic acid 1mg a day should be added, magnesium 400mg BID may be of benefit, along with riboflavin 400mg a day. While there is limited data to show efficacy, in this setting these may be of some use while being safely employed. Non-pharmacologic therapies may begin to be emphasized and during pre-ovulatory days, the usual abortive regimen can be continued. During the time when a patient is uncertain as to whether pregnancy has been achieved, or is merely post-ovulation, analgesics, opioids, antiemetics, and corticosteroids can predominate as acute migraine therapy choices.

PERIMENOPAUSE/MENOPAUSE

Vulnerability to migraine during perimenopause and menopause may be seen in women who have had mild menstrual migraine, unrecognized as such until the dramatic fluctuations in estrogen begin to occur during perimenopause. Women who have a history of menstrual migraine may be more vulnerable to exacerbations of migraine during these years of hormonal instability, as may women who have a history of hormonally influenced headache secondary to oral contraceptive use, pregnancy, or in the post-partum state. Women who have undergone surgical menopause may be particularly vulnerable, as two-thirds of these women have an exacerbation in their migraine. The prevalence of migraine is known to decrease with age in both sexes, though the female preponderance persists even after menopause. The classic view has been that migraine tends to worsen during perimenopause or early menopause and thereafter improve. In some studies, however, no change, or worsening has been observed in as many as 50% of patients. Neri reported an improvement after spontaneous menopause in two-thirds of women. In contrast, a worsening occurred in two-thirds of women with migraine after surgical menopause which should never be proposed as a treatment for migraine. Perimenopause is characterized by fluctuating estrogen levels, ultimately with falling estrogen levels and the loss of the orderly pattern of estrogen and progesterone secretion. Menstrual cycle irregularities may lag behind the exacerbation in migraine during perimenopause. An isolated estrogen level may not be as useful as a follicle stimulating hormone level, which may show that a patient is entering perimenopause. As menopause is approached, decreases in ovarian production of both inhibin and estrogen are noted, and a decrease in the inhibition of follicle stimulating hormone (FSH) from the pituitary is seen. These result in the “steady” rises in FSH levels during perimenopause, and the persistent elevation of FSH after menopause. During waning ovarian function, menopausal symptoms begin for many women. These may include emotional fluctuations, unpredictable menstrual cycling, sleep fragmentation, aging skin, reduced muscle tone, fear of loss of attractiveness, and fear of hormone replacement therapy, particularly in light of the recently released study on Premarin and Provera. There does not appear to be a difference between women with migraine or without migraine in age of onset of their menopause. Hormone replacement therapy is not contraindicated in women with migraine. Indeed, migraine no longer appears as a risk factor for stroke after age forty-five. For many women who remain on oral contraceptive therapy during perimenopause the onset of menopause may not be clear. The average age of a woman entering menopause in the United States is 51.5 years with menopause occurring two years earlier in smokers. Estrogen deficiency during menopause can be characterized by

multiple signs and symptoms including hot flushes, night sweats, joint and muscle pain, skin dryness, vaginal dryness, dyspareunia, fatigue, irritability, depression, anxiety, memory loss, and decreased libido to name a few. These symptoms usually dramatically respond to hormone replacement therapy, while the influence of hormone replacement therapy can be variable on the course of migraine. Migraine can improve, worsen, or be unchanged on hormone replacement therapy. Estrogen has multiple effects on vascular wall function and vasoreactivity via an increase in vasodilators(e.g., NO) and a decrease in vasoconstrictors(e.g., endothelin). Further, estrogen can increase HDL-cholesterol and reduce LDL-cholesterol and has been felt to reduce progression of atherosclerotic disease. The effect of hormone replacement therapy on the risk of ischemic stroke is still debated. In the most recent study in which Premarin and Provera were studied in combination, an increased risk of ischemic stroke was noted. Earlier studies had not found a significant association between HRT and risk of ischemic stroke. In the most recent article on post-menopausal hormone replacement therapy in JAMA (August 21, 2002-Volume 288, Number 7), the benefits of HRT, including prevention of osteoporotic fractures and colorectal cancer must be considered based on patient risk factors, and indeed, in the JAMA meta-analysis of nine observational studies, overall stroke mortality among ever HRT users was marginally reduced. The WHI indicated an increased risk for nonfatal stroke and no increase for fatal stroke among HRT users and the HERS data reported no increase in strokes. Since there is insufficient data to support an increased risk of ischemic stroke in women with any type of migraine over age 45, the usual indications and contraindications for HRT should be applied. Given findings showing thermal pain perception to be lower in women on hormone replacement therapy versus women not on hormone replacement therapy and men, careful observation following the initiation of hormone replacement therapy should be noted in terms of headache frequency and severity.

No clinical studies have been performed evaluating the phyto-estrogens or herbal therapies for migraine. Isoflavin (soy), soy isolate, dong quai, vitamin E, bioflavonoids, black cohosh, garden sage, and mother wort are all used for symptoms of menopause but none have been studied for their influence on migraine.

Hormonal replacement therapy (HRT) with estrogens alone or in combination with progestins(in patients with an intact uterus) can be useful in preventing menopausal symptoms and osteoporosis. Various types of estrogens are used: pure estrones, estradiols, and synthetic ethinyl-estradiol. Estrogens are available orally and parenterally in the form of injections, percutaneous gels, transdermal patches, and vaginal creams. Adjunct hormones include progestins and sometimes androgens. Unopposed estrogens and combined regimens in the past were given sequentially for twenty-five days per month but may exacerbate migraine in women who have had a previous history of menstrual migraine. Oral estrogens are associated with wide daily fluctuations which can trigger migraine. Transdermal or percutaneous preparations are associated with more stable estrogen levels. Estradiol implants may be suitable for hysterectomized women, but they are not otherwise indicated due to their long effect on the endometrium. Preferred synthetic estrogens may include oral Estrace 0.5mg BID and transdermal 50mcg per day with Climara™ weekly, Estraderm™, Vivelle™ q 3days. Micronized progesterone at 100mg a day is preferred over medroxyprogesterone given recent study results. Again, headache diaries in the perimenopausal and menopausal migraineur are

critical to establish headache frequency, duration, intensity, and associated disability and to elicit the potential links between menopausal symptoms and migraine. Non-hormonal triggers should be evaluated and the efficacy of acute therapy particularly scrutinized. The old cyclic hormone replacement therapy of estrogen given days 1-25 and progesterone on days 15-25 is rapidly falling out of favor. Continuous hormone replacement therapy of estrogen +/- progesterone, based on an intact uterus, is becoming more standard. Continuous estrogen receptor modulators may be given but their effect on migraine has not been carefully studied. In women who clearly have an exacerbation once hormone replacement therapy is initiated, the choices may be to reduce the dose of estrogen, to change the form of estrogen, or to convert from interrupted to continuous administration. In women who clearly worsen on hormone replacement therapy or who have contraindications including a history of thromboembolism, cancer, or hypercoagulable states, hormone replacement therapy must be stopped. For many of these women if their migraine continues following and during the initial years of menopause, anti-convulsant therapy may be employed. If anti-convulsant therapy is employed as their migraine prophylaxis, the role of AEDs and bone disease must be considered. The bone disease seen in association with anti-convulsant drugs is considered to be a form of osteomalacia. High turnover osteoporosis is often present in this setting and can be associated with hypocalcemia, hypophosphatemia, and muscle weakness. Reduced serum and urine calcium levels, reduced serum 25-hydroxy vitamin D levels, and elevated serum PTH and alkaline phosphatase can be noted. Body weight changes may also be important in menopausal migraineurs and cognitive effects from AED therapy may pose particular challenges. In patients on non-enzyme inducing anti-convulsants, bone changes are not felt to occur, but if older convulsants are employed, serial bone densitometry testing should be performed. For all women in perimenopause and menopause, unless another contraindication exists, the current recommendations are for 1500-2000mg of calcium and vitamin D 400units a day, adequate sunshine, and weight bearing exercise.

CONCLUSION

In conclusion, “the ‘femaleness’ of the migraine condition is inescapable,” as was noted by Welch, Darnley, and Simkins, almost twenty years ago in their review of the role of estrogen in migraine. Estrogen does seem to play a major role in migraine but it is often an unpredictable role. In clinical practice, it may be useful to tell female migraineurs that hormones can and do anything “they” choose to - to migraine. In some women, rising or sustained estrogen levels improve migraine. In others, the same changes worsen migraine. Differences between migraine without aura and migraine with aura may be significant; it may be that these responses to estrogen hold some potential etiologic and therapeutic promise in better understanding underlying mechanisms of hormonally influenced migraine.

For the clinician, approaches to management of hormonally influenced migraine include a clear identification of the relationship between migraine and hormonal change. A thorough history and careful diary are critical in identifying this relationship and in predicting response or following response to hormonal therapies. The evolution of migraine in an individual migraineur may be strongly influenced by hormonal changes.

Some, though limited, clinical evidence exists to suggest that oral contraceptive use, in young women, with episodic migraine may transform their migraine into chronic daily migraine. Thus, particular attention to changes in migraine pattern following either endogenous or exogenous hormonal changes is crucial. Reassurance and education that migraine is a biologic disease, merely influenced by hormonal changes, is important for migraineurs who may have been led to believe that migraine is essentially a psychiatric condition. Pharmacologic measures to abort acute attacks of migraine should be employed and preventive therapies should be added for appropriate patients. Women with migraine should begin to view their migraine as a part of a chronic disease which can wax and wane as they move throughout their hormonal milestones. Preventive therapy may be appropriate for certain intervals and changes in abortive therapy may also be required. Trigger avoidance can be emphasized but should not be over-emphasized, as certainly, the endogenous hormonal influences are outside patient control. Overall wellness should always be emphasized: exercise, balanced diet, smoking cessation, and sleep hygiene are always important features for a woman's health, but migraine should be understood by patients as a biologic disease.

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