REVIEW

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Women and headache: A treatment approach based on life stages

ABSTRACT

Effective headache management in women requires an understanding of the unique epidemiologic and pathophysiologic factors affecting women. We present preventive, abortive, and nonpharmacologic approaches to headache treatment that vary with the chronologic and hormonal stages of a woman's life, with special attention to headache during pregnancy and later in life.

KEY POINTS

Menarche, menstruation, pregnancy, and menopause are the four important stages in a woman's life that require individualized treatment strategies.

Pharmacologic therapy should be avoided during pregnancy, especially during the first trimester.

The impact of oral contraceptives on migraine is unpredictable.

Headaches may increase during the perimenopausal period when sex hormones fluctuate.

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HEADACHE is one of the most important medical issues in women's health,[1–4] as it is more common in women than in men, it is influenced by hormonal levels that change throughout a woman's life, and it has great clinical, quality-of-life, and economic impact.

Primary care physicians have the unique opportunity to treat women throughout the chronologic and hormonal stages of their lives. By understanding the life-stage needs and the disorders that may coexist with headache, physicians can provide comprehensive pharmacologic and nonpharmacologic interventions.

In this review, we discuss the general principles of headache management, followed by more detailed discussion of headaches during the various stages of a woman's life.

MORE COMMON IN WOMEN

Headache is much more common in American women than in men. For example, 18% of women have migraines, vs 6% of men. The greatest gender disparity occurs between age 30 and 45 years.[5,6] More women than men also have tension-type headaches.[7]

More women seem to be diagnosed with headache and receive treatment for it now than in the past. For example, the percentage of people meeting the criteria for migraine who were actually diagnosed by a physician as having migraine increased from 38% in 1989[8] to 48% in 1999.[6] While the overall prevalence of migraine has remained the same,[6] heightened awareness and the increasing need to perform daily activities without headache-associated disability may be responsible for this increase in diagnosis.

TABLE 1

Clinical features of migraine and tension-type headaches

FEATURE	MIGRAINE	TENSION-TYPE HEADACHE
Gender ratio (F:M)	3:1	1:1
Age of onset	Teens–20s	Any
Family history of headache	Usually	Not usually
Location of pain	Unilateral	Bilateral temporal, frontal, or global
Intensity	Moderate to severe	Mild to moderate
Quality of pain	Throbbing	Pressure, ache
Duration	4–72 hours	Hours-days
Aura	10%–20% of patients	No
Nausea and/or vomiting	Usually	No
Photophobia, phonophobia	Usually	Not usually
Aggravated by movement	Usually	No

Possible physiologic reasons why women have a higher prevalence of headache include neural differences in the brain,[9] differences in sex hormones,[9] alterations in prostaglandin, prolactin, and opioid levels,[10,11] and pharmacokinetic and pharmacodynamic differences.[12] Possible psychosocial factors include different coping strategies and learned behaviors.

TYPES OF HEADACHE

The International Headache Society classifies tension-type and migraine headaches as primary headaches (TABLE 1).[13]

Episodic tension-type headaches occur in 42% of women and 36% of men.[7] They may last hours to days and occur on fewer than 15 days per month. The pain is located in the bitemporal or frontal area, is mild to moderate in intensity, and is usually described as a pressure or dull ache.

Chronic tension-type headaches have a similar clinical presentation, but occur on more than 15 days per month.

Migraine is characterized by unilateral throbbing pain that is moderate to severe in intensity and is aggravated by activity. Attacks may last 4 to 72 hours and are often accompanied by nausea, photophobia, and phonophobia. Eighty-five percent of migraines are without aura; 15% are with aura.

Migrainous headaches meet some but not all of the International Headache Society criteria for migraine.

In practice, however, classification is not so simple. Migraineurs experience a spectrum of headache types in addition to migraine that may include episodic tension-type and migrainous headache.[14] Episodic migraine may transform into daily headaches as a result of analgesic overuse and rebound headache.

18% of women have migraines, vs 6% of men

PATHOPHYSIOLOGY IS UNCLEAR

The pathophysiology of migraine and tension-type headaches is unclear. Some believe the different types of headaches are distinct entities,[13] while others believe they represent a continuum of symptoms arising from a common substrate.[14–17]

Migraine mechanisms. Migraine is linked to hyperexcitable cortical neurons in the brain, the trigeminal nerve, and the cranial blood vessels it supplies. Neuropeptides and plasma proteins perpetuate the migraine syndrome when they escape from dilated blood vessels and produce inflammation.[18]

Recent studies show that migraine pain is

TABLE 2

Common triggers of migraine and tension-type headache

	MIGRAINE	TENSION-TYPE HEADACHE
Stress	Yes	Yes
Stress "letdown"	Yes	No
Too little sleep	Yes	Yes
Oversleeping	Yes	No
Weather changes	Yes	Yes
Hormonal changes	Yes	No
Odors	Yes	No
Missing a meal	Yes	Yes
Foods	Yes	No

accompanied by increased skin sensitivity,[19–21] suggesting that migraine involves not only irritation of the meningeal perivascular fibers but also a transient increase in the sensitization of central pain neurons. Burstein et al[22] found that 79% of patients with migraine also had cutaneous allodynia (pain resulting from a non-noxious stimulus to normal skin) and muscle tenderness.

Recent research[23] points to activation of the brain stem, which causes hyperoxia of the red nucleus and substantia nigra and produces nociceptor and autonomic dysfunction.

Chronic tension-type headache mechanisms possibly include low serotonin levels with receptor up-regulation,[24] central hyperexcitability of pain systems,[25] *N*-methyl-D-aspartate receptor dysfunction,[26] low beta-endorphin and opioid states,[27] and analgesic overuse.[28]

Headache management requires both drug and nondrug therapy

HEADACHE MANAGEMENT IS MULTIFACETED

Comprehensive headache management involves both nonpharmacologic and pharmacologic therapy to prevent and abort headaches.

Nonpharmacologic therapy

Lifestyle modifications are essential for headache prevention and commonly include:

- Establishing good sleep habits and stress management techniques
- Maintaining a healthy diet
- Exercising regularly
- Minimizing caffeine consumption
- Eliminating nicotine
- Identifying and avoiding known triggers (TABLE 2). (However, there is little evidence to link dietary factors with migraine, and strict avoidance of some foods may lead to inadequate nutrition, especially in adolescents.[29])

There are three categories of behavioral and physical interventions used to prevent headache: relaxation training (muscle relaxation, visual imaging), biofeedback therapy (hand warming and electromyographic feedback), and cognitive behavioral training (psychotherapeutic stress management).

While developing evidence-based practice guidelines for headache, experts reviewed multiple studies of behavioral and physical treatments[30] and calculated that:

- Various relaxation treatments reduced headaches by 32%[31–34]
- Biofeedback reduced headaches by 37%[30,35–38]
- Cognitive-behavioral therapy reduced headaches by 49%.[30,32,34]

In general, behavioral and physical interventions can modestly reduce the frequency of migraines and are particularly valuable for pregnant or lactating women who are motivated to avoid pharmacologic therapy.

Drugs as preventive therapy

Long-term preventive therapy with drugs is recommended for patients with frequent migraines, migraines with prolonged aura, and migraines inadequately controlled by abortive therapy.[39]

At best, however, drugs can reduce the frequency of headaches by only about 50%.[40] Patients need to be aware of the limitations and possible side effects of prophylactic medications to avoid unrealistic expectations.

The choice of preventive drugs (TABLE 3) can be individualized on the basis of symptoms and comorbid conditions (eg, hypertension, depression, seizure disorder). No clinical trials have shown selective serotonin reuptake

TABLE 3

Commonly prescribed preventive migraine medications

MEDICATION	DAILY DOSAGE (MG)	SIDE EFFECTS
Propranolol	40–160	Fatigue, bradycardia, hypotension
Verapamil	240–480	Constipation, dizziness, peripheral edema, hypotension
Amitriptyline	10–150	Fatigue, dry mouth, weight gain, blurred vision
Divalproex sodium	250–1,500	Gastrointestinal upset, sedation, weight gain, tremor, hair loss, polycystic ovarian syndrome, acute pancreatitis, 1%–2% risk of neural tube defects if used during pregnancy
Naproxen sodium	550–1,100	Gastrointestinal upset
Methysergide	6	Nausea, diarrhea, cramps, drowsiness, hallucinations
Cyproheptadine	8–16	Weight gain

inhibitors (SSRIs) to prevent migraines, although they have been used anecdotally.[41]

General principles include:

- Start low, go slow.
- Don't expect an immediate response. These drugs can take up to 1 month to affect the pattern of migraines, and their benefits may continue to increase over 3 months.
- Don't continue forever. The duration of therapy depends on the improvement in headache and other comorbid symptoms. If possible, try to taper and stop the medication every 3 to 6 months.
- Discuss plans for pregnancy so medications can be tapered and stopped before conception.

Abortive therapy

Traditionally, abortive drugs were given in a stepped-care approach. Treatment began with inexpensive first-line agents, and more aggressive treatments were then prescribed sequentially if the first-line agents failed to provide relief.[42,43]

This trial-and-error approach had shortcomings. It assumed that all patients have similar needs. It was also frustrating and redundant, since most patients try over-the-counter medications and find them wanting before they consult a physician.

Therefore, a stratified, patient-centered approach is quickly emerging.[42–44] This approach matches the intensity of treatment to the severity of headache and takes the patient's preferences into account.

HEADACHES AND LIFE STAGES

Because headaches recur throughout life for many women, their management must take into account the patient's stage of life and associated hormonal function.

Try to taper and stop preventive drugs after 3-6 months

Childhood migraine

Migraine occurs in approximately 5% of children younger than 15 years.[45] Before puberty, its prevalence is equal in boys and girls. Its peak incidence is between ages 5 and 11 years in boys and between ages 12 and 17 years in girls.[46]

Children rarely can express their discomfort as "headache" before age 5. Younger children with headache may have episodes of irritability and vomiting without concurrent illness. Migraines in children are often bilateral, last as short as 1 hour,[47] and may be relieved by sleep.

Parents play a key role in their children's management, helping them identify and avoid potential triggers and maintain regular eating and sleeping habits. School officials need to cooperate so that children have access to their medications at school; doing so might prevent

school avoidance behavior and facilitate rapid return to normal function.

Migraine medications for children

Medications commonly used to prevent migraines in children include cyproheptadine, amitriptyline, and propranolol, but they have not been systematically studied in controlled clinical trials.

Acute abortive medications for children often include nonsteroidal anti-inflammatory drugs (NSAIDs) and acetaminophen. Ibuprofen may be somewhat more effective than acetaminophen,[48] and either drug can be given in doses slightly larger than usual at the earliest sign of headache.

Antiemetic medications in oral or suppository formulations have the added benefit of inducing sleep.

A recent study[49] reported that sumatriptan nasal spray was well tolerated in children younger than 10 years and had an efficacy rate of 86% (as measured 2 hours after the dose), but no triptan is approved for patients younger than 18 years.

No triptan is currently approved for children

Migraine in adolescents

Beginning at puberty, the prevalence of migraine increases more rapidly in girls than in boys.[46] This increase has been linked to estrogen and progesterone,[50,51] as menarche is brought on by changes in the hypothalamic-pituitary axis and sex hormone control.[52]

Adolescents develop an adult pattern of migraine characterized by unilateral pain, increasing headache duration, and worsening disability.

Abortive and preventive therapies for adolescents are similar to those recommended for adults. Although parents still play an important role, adolescents should start assuming responsibility for their own headache care.

Recent studies found sumatriptan nasal spray to be effective and well tolerated for adolescent migraine, with a response rate of 63% as measured 2 hours after the dose.[53,54] Rizatriptan is also undergoing clinical trials in adolescents.[55]

Cyproheptadine, often used as a preventive therapy in children, may cause unwanted weight gain and sedation in adolescents, an important consideration in light of eating disorders and body-image issues in adolescent girls.[56]

Chronic tension-type headache in adolescents

Chronic tension-type headache is associated with stress and is rare before adolescence. However, Billie[45] reported that 54% of children experienced infrequent nonmigraine headaches by age 15 years.

The treatment strategy should allow adolescents to stay in school and maintain normal daily activities while coping with headache. The goal is to reduce the frequency of headaches. Importantly, since pain-response behavior is learned early, timely intervention is necessary to foster positive coping mechanisms.

Young women with chronic tension-type headache benefit from a supportive approach with counseling, stress management, and medication. Biofeedback can provide valuable self-management skills to reduce medication use.

Preventive drug therapy may include tricyclic and SSRI antidepressants, started at low doses and then titrated for efficacy and side effects.

Acute abortive therapies should be closely monitored to avoid analgesic overuse. NSAIDs are the abortive medications of choice, with a note of caution regarding gastrointestinal upset and overuse. Opioid analgesics should be avoided as first-line agents.

ADULTHOOD

Adulthood is a time of expanding roles for women. The demands of education, career, marriage, and family are greatest during this period and coincide with the highest prevalence of migraine in the 35-to-45-year-old age group.

Headaches impair quality of life[57] and interfere with home life and work. Women with migraine require an average of 5.6 days of bed rest per year, compared with 3.8 days for men.[58] The economic burden of headache continues to grow and includes health care costs, lost work productivity, and reduced effectiveness.

TABLE 4

Recommended dosage of triptans for treatment of acute migraine

MEDICATION	DOSE	REPEAT DOSE	MAXIMUM DAILY DOSAGE
Almotriptan (Axert)			
Tablets (12.5 mg)	12.5 mg	After 2 hours	25 mg
Sumatriptan (Imitrex)			
Tablets (25, 50, 100 mg)	50–100 mg	After 2 hours	200 mg
Nasal spray (5, 20 mg)	5–20 mg	After 2 hours	40 mg
Subcutaneous injection (6 mg)	6 mg	After 1 hour	12 mg
Zolmitriptan (Zomig)			
Tablets (2.5, 5 mg)	2.5–5 mg	After 2 hours	10 mg
(orally disintegrating tablets, 2.5, 5 mg)			
Rizatriptan* (Maxalt)			
Tablets (10 mg)	10 mg	After 2 hours	30 mg
MLT (orally disintegrating tablets, 10 mg)	10 mg	After 2 hours	30 mg
Naratriptan (Amerge)			
Tablets (1, 2.5 mg)	2.5 mg	After 4 hours	5 mg

*Reduce single dose to 5 mg and total dose in 24 hours to 15 mg if patient is receiving propranolol

Migraine medications for adult women

Triptans. 5-HT-1 agonists, or triptans, revolutionized migraine abortive therapy (TABLE 4). They are indicated for migraine with or without aura and are contraindicated in basilar and hemiplegic migraine.

Triptans act on serotonin receptors on intracranial blood vessels and the trigeminal nerve. Activation of these receptors causes vasoconstriction and inhibits neurogenic inflammation.

The triptans are effective at any point in the headache, but they should be taken as early as possible to maximize benefit.[59] Migraines may recur within 24 hours of initial treatment but usually respond to a second dose of medication.

A few patients may respond to one triptan but not another; lack of efficacy with one triptan does not preclude a trial with another.

Common side effects, collectively called 'triptan sensations,' include:

- Paresthesias
- Dizziness
- Flushing
- Asthenia
- Feeling of heaviness or pressure in the throat and chest.

Ergots. Other abortive medications are most effective when taken at the mild stage of a migraine attack (TABLE 5). Ergot-containing medications are used to treat migraine because they constrict blood vessels, but they may cause rebound headache if taken more than 2 days a week. Dihydroergotamine may be given by intravenous, intramuscular, or subcutaneous injection or intranasal spray.

Analgesic combinations containing butalbital and caffeine may provide relief for some patients. However, they are not approved by the US Food and Drug Administration for treatment of migraine and have a high potential for causing rebound headache. The psychoactive properties of these medications make them likely to be abused and misused by some patients, and many experts prefer migraine-specific drugs such as the triptans for first-line therapy.

Metoclopramide 10 mg can be added to treatment regimens to control nausea.

Triptan side effects:
- **Paresthesias**
- **Dizziness**
- **Flushing**
- **Asthenia**
- **Heaviness or pressure in the throat and chest**

TABLE 5

Recommended dosage of other acute migraine medications

MEDICATION	DOSING	SIDE EFFECTS
Isometheptene mucate 65 mg Dichloralphenazone 100 mg Acetaminophen 325 mg	2 capsules, may repeat 1–2 capsules after 1 hour as needed Maximum: 5 capsules/24 hours	Drowsiness, dizziness
Ergotamine tartrate (1–2 mg) Caffeine 100 mg	1–2 tablets, may repeat every 30–60 minutes as needed Maximum: 5 doses/24 hours	Nausea, jitteriness
Dihydroergotamine mesylate 4 mg/mL	One spray in each nostril, repeat in 15 minutes	Rhinitis, nausea
Ibuprofen	600–800 mg, may repeat after 1 hour as needed	Gastrointestinal upset
Naproxen sodium	550 or 660 mg (3 Aleve) may repeat after 1 hour as needed	Gastrointestinal upset

Tension-type headache in adult women

Episodic tension-type headaches may be relieved by eliminating the precipitating event. Most respond quickly to acetaminophen or NSAIDs, but overuse of these drugs should be avoided.

Keeping a headache diary helps patients with chronic tension-type headache and superimposed migraine to identify headache triggers and assess the effectiveness of treatment. Patients with rebound headache due to analgesic overuse must stop the offending drug and begin preventive therapy to reduce the need to take analgesics frequently.

For most women, menstruation is only one trigger for migraine

Is migraine linked to premenstrual dysmorphic disorder?

There is debate about whether premenstrual dysmorphic disorder (PMDD) is linked to migraine.[60,61] Many believe that PMDD symptoms are related to changes in progesterone that occur during the late luteal phase of the menstrual cycle. These symptoms may represent an autonomous cyclic disorder that is cued by the menstrual cycle.

Alternatively, PMDD symptoms may be triggered by hormonal events that occur before the late luteal phase, a theory consistent with reports that suppression of ovulation with gonadotropin-releasing hormone usually decreases PMDD symptoms.[62–65]

When headache and PMDD occur in the same patient, an SSRI antidepressant may successfully manage both disorders.[66–68]

Menstrually associated migraine

Menstrually associated migraine is defined as migraine without aura that occurs during the perimenstrual period.[69]

For most women, menstruation is only one trigger for migraine. Although 60% of female migraineurs report worsening of their headache related to menses, only 7% to 14% have migraine that occurs *only* during menses.[50,69] Moreover, prospective diary studies demonstrate that a patient's report of a link between menstruation and migraine is not always verifiable, and highlight the need to determine the true relationship between headache and the menstrual cycle before embarking on specific treatment.

The pathophysiology of menstrually associated migraine may be related to declining estrogen levels during the late luteal phase of the menstrual cycle.[70] Other possible mechanisms include changes in progesterone, prostaglandins, opioid, or melatonin levels.[10,51,52]

In the general population, there is no scientific evidence that menstrually associated migraine lasts longer, is more difficult to treat, is more refractory to treatment, or is more

severe than migraine that occurs at other times of the month.

Abortive therapy for menstrually associated migraine. Subcutaneous and oral sumatriptan,[71,72] rizatriptan,[73] zolmitriptan,[74] and aspirin-acetaminophen-caffeine combinations[75] appear to be as effective in treating this type of headache as they are in treating migraine that occurs at other times of the month. Naratriptan, with its longer half-life and low recurrence rate, may be ideal for this type of headache as an abortive therapy.

Preventive therapy for menstrually associated migraine. If menstrually associated headache is refractory to optimal abortive therapy, preventive therapy may be appropriate. If the patient's cycles are regular, short-term preventive medication limited to the perimenstrual period may be helpful.

NSAIDs can be used on a scheduled basis.[76,77]

Supplemental estrogen (transdermal 0.1 mg) can be started 2 to 3 days before the onset of menses and continued throughout the menses and other periods of headache vulnerability.[69]

Short-term prophylaxis with sumatriptan or naratriptan has demonstrated efficacy in menstrually associated migraine.[78,79]

Daily oral magnesium therapy has been recommended if standard treatment or short-term prophylaxis cannot be used.[52] This therapy is supported by evidence that supplemental magnesium is helpful in eliminating migraine attacks and treating other menstrually associated migraine symptoms.[80]

In refractory cases, suppression of menses with oral contraceptives or medroxyprogesterone acetate may provide relief.[81]

Gonadotropin-releasing hormone agonist therapy or oophorectomy may eliminate estrogen fluctuations, but they necessitate long-term hormone replacement,[62–65] and ooph-orectomy or hysterectomy are not usually recommended for treatment of menstrually associated migraine.[74]

Tamoxifen, an antiestrogen drug and forerunner of the new class of selective estrogen receptor modulators, has also been evaluated for short-term prophylaxis.[82,83] However, the beneficial effect of these newer drugs is yet to be evaluated. These treatments should be considered only for patients whose migraine does not respond to adequate trials of more traditional therapies, in which the risks and benefits are better established.

Migraine and oral contraceptives

There are two concerns about the use of oral contraceptives in women with migraine: whether these drugs increase the frequency and severity of migraines, and whether they increase the risk of stroke.

The impact of oral contraceptives on migraine is not predictable.[52,84,85] For some women, oral contraceptives worsen their migraines, while others have marked improvement.[52]

Migraine may be worse during the entire month with oral contraceptives, or only in the pill-free or placebo week. In the latter case, the active drug can be given continuously. New low-dose pills that minimize the duration of the pill-free period may be helpful by minimizing hormonal fluctuations.

The risk of stroke in women with migraine who take oral contraceptives is controversial, dating back to the use of early high-dose estrogen pills and their relatively high risk of thrombotic events and stroke. With the current low-dose estrogen combination and progesterone-only pills,[86–88] these risks are lower. In general, the risk of stroke in women with migraine is approximately 2 to 3 times higher than in those without migraine[89]; however, the baseline risk is still very low and any increase due to oral contraceptives is minimal.

The risk of stroke in migraineurs who take oral contraceptives is controversial

On the other hand, oral contraceptives increase the risk of ischemic stroke associated with migraine to a greater extent for patients who smoke or have high blood pressure; no differences are observed between migraine with aura and migraine without aura.[90,91] Therefore, caution should be used when prescribing oral contraceptives to women with migraine who have these risk factors, and lifestyle modifications should be encouraged.

Oral contraceptives are not contraindicated in migraineurs, but the physician and patient together should make a decision based on the individual woman's risks and possible benefits.

Discuss migraine options before pregnancy

Since 50% of pregnancies in the United States are unplanned, the possibility of pregnancy in any migraineur of reproductive age should be included in all treatment discussions.

Ideally, patients should discuss their treatment options with their physicians and should try to get their migraines under optimal control without medication *before* they become pregnant. When patients are trying to conceive, headache management should be similar to management during pregnancy. Therefore, nonpharmacologic therapies should play a primary role in both prevention and treatment.

One should use only medications with low risks to the fetus. Most acute care medications can be used in the follicular stage of the menstrual cycle. However, caution should be used after ovulation to avoid the risk of teratogenicity.

Headaches during pregnancy

During pregnancy, migraine improves in 60% to 70% of women, but it can also occur for the first time (in 1.3% to 16.5%), worsen (in 4% to 8%), or remain unchanged.[92]

Avoid or minimize drug use during pregnancy, especially the first trimester

In the first trimester, when hormone fluctuations are greatest, women may continue to experience migraine. Moreover, although some retrospective studies reported improvement in migraine during the second and third trimesters,[93] a prospective study demonstrated an increase in headache during the third trimester, especially in multiparous patients.[94]

Tension-type headache is one of the most common neurologic complaints during pregnancy. However, new-onset or atypical headaches during pregnancy must be carefully evaluated, as possible causes include rapid growth of certain brain tumors and increased intracranial pressure associated with hypertension. The risk of subarachnoid hemorrhage is also increased in the peripartum period.

A history and physical examination followed by appropriate imaging studies or lumbar punctures are essential in cases of new-onset headache during pregnancy. Necessary diagnostic procedures should not be avoided during pregnancy, although risks to the fetus must be taken into account.

Headache treatment during pregnancy

Headaches themselves do not pose a threat to the developing fetus, and neither should headache treatment.

Pharmacologic therapy should be avoided or minimized during pregnancy, especially during the first trimester. Emphasis should be placed on identifying and avoiding potential triggers. Symptomatic treatment with ice or heat, massage, relaxation techniques, exercise, and sleep are preferred.

Biofeedback may be effective, and women may be motivated to practice nonpharmacologic therapy during pregnancy.[95,96] One study demonstrated significant headache relief in 80% of patients who used physical therapy, relaxation training, and biofeedback during their pregnancies.[97]

Not all medications have been studied thoroughly in human pregnancies; however, on the basis of accumulated experience and knowledge, some medications are believed to be relatively safe.[98] **Acetaminophen** and **codeine** can be used cautiously. Simple analgesics are preferred to reduce fetal exposure.

Ergotamines are absolutely contraindicated in pregnancy due to the potential for reduced uteroplacental perfusion.

Triptans are listed in pregnancy category C (ie, inadequate data exist about their effects on human pregnancies), and they should used only if their benefit outweighs the risks. Registries have been established to collect and review voluntary reports of pregnancy following triptan use. To date, there is no evidence of an increased risk of birth defects in patients taking triptans compared with the general population, but the sample size is still small. However, reports from the registries are encouraging in regard to the risk from inadvertent single exposures in early pregnancy.[99–101]

No major differences in the rates of live births, spontaneous abortions, therapeutic abortions, or major birth defects were seen following use of sumatriptan in the first trimester in one disease-matched control study.[101] Another recent study indicated that use of sumatriptan in early pregnancy did not result in a large increase in teratogenic risk.[102] However, a Danish study of sumatriptan exposure during pregnancy found an increased risk

of preterm labor and low birth weight.[100] This may reflect the impact of the disease rather than the treatment.

Intravenous hydration and **parenteral narcotics** and **antiemetics** should be considered if the patient or fetus is at risk due to protracted vomiting, anorexia, or dehydration as a result of headache.[103]

Preventive migraine therapy is usually withheld during the first trimester, but **propranolol** and **amitriptyline** are possible choices in the second and third trimester if the headaches are severe or debilitating.[104]

Postpartum return of headaches

While pregnancy may provide a respite from migraine, headaches usually return postpartum. Again, fluctuations of estrogen levels play a precipitating role. Lactation provides a protective effect in approximately half of migraineurs who breast-feed.

Tension-type headaches may also occur postpartum and may be compounded by new life stressors, sleep disruption, and mood fluctuations.

Triptans and breast-feeding. Drug treatment options must be carefully considered in women who are breast-feeding, owing to potential effects on the infant or on lactation.[105] Wojnar-Horton et al[106] measured the concentration of sumatriptan in breast milk following use of subcutaneous sumatriptan and calculated the level of exposure to the infant to be approximately 0.49% of the maternal dose on a weight-adjusted basis. Maternal plasma levels were below the level of detection (1 ng/mL) after 6 hours in all samples.[106]

Because many of the triptans have short half-lives, we allow patients to treat individual headaches, then pump and discard breast milk for a period of time equal to three to four half-lives of the drug. If headache treatment is not allowed during lactation, some migraineurs may stop breast-feeding. We believe that the benefits of continued breast-feeding outweigh the risks of treatment when administered as described. We also prefer to use migraine-specific agents rather than nonspecific or sedative drugs, which can make the mother and infant drowsy.

HEADACHES IN MENOPAUSE

Overall, the prevalence of migraine decreases as women age. In one clinical study,[107] migraines improved during menopause in 62% of women, but they worsened in 18%, and remained unchanged in 20%. Women who experienced surgical menopause were more likely to have worsening of their migraines than were women who experienced natural menopause.

The prevalence of tension-type headache also generally decreases with age,[7] but one study[107] reported worsening of tension-type headaches in 42% of postmenopausal women, improvement in 30%, and no change in the remaining patients.

Hormone replacement therapy

Headaches may increase in the perimenopausal period when sex hormones fluctuate. Sleep patterns and mood may be labile, which may affect migraine frequency.

Hormone replacement therapy has an unpredictable effect on migraine.[108] The decision whether to use hormone replacement therapy should be based on factors other than headache. If headaches worsen significantly with hormone replacement therapy, a lower dose of hormone or the use of synthetic estrogens or estradiols may produce fewer headaches.[52] Continuous oral or transdermal therapy may be preferred to cyclic estrogen.

Migraine treatment in older women

Migraine treatment in older women should be adjusted for coexisting illnesses. Since older people are at increased risk of cardiovascular disease, vasoconstrictors should be used with caution. The preventive and abortive treatment of migraine is otherwise similar to that used in younger adults.

New-onset headache in older patients should be evaluated carefully. Intracranial causes such as primary or metastatic tumor, subdural hematoma, and stroke must be ruled out. Giant cell arteritis is another cause of headache in patients older than 50 years and can be associated with irreversible vision loss if left untreated.

Migraineurs may continue to have typical

New-onset headache in older patients should be evaluated carefully

aura but may no longer suffer the headache phase of migraine. On the other hand, patients with new-onset aura without headache should be evaluated for transient ischemic attack or stroke.

Chronic tension-type headache in older women

Chronic tension-type headache in older adults may be accompanied by depression, anxiety, and insomnia. Preventive medication to reduce headache frequency is the mainstay of treatment.

Tricyclic antidepressants or SSRIs may be useful. However, older women may be more sensitive to the sedative and hypotensive effects of tricyclic antidepressants. In addition, since tricyclics also affect heart rhythm, they may not be the best option for this population.

NSAIDs must be used cautiously as acute medication until headache frequency is reduced, as the elderly are at increased risk of gastrointestinal bleeding. Cyclo-oxygenase 2 inhibitors may be a useful option.

Opioids may be warranted if treatment with triptans is limited by comorbid disease; however, alteration in alertness remains a concern.

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