



Complete Summary

GUIDELINE TITLE

Special treatment situations: menstrual migraine and menstrually-related migraine. Standards of care for headache diagnosis and treatment.

BIBLIOGRAPHIC SOURCE(S)

Diamond M. Special treatment situations: menstrual migraine and menstrually-related migraine. In: Standards of care for headache diagnosis and treatment. Chicago (IL): National Headache Foundation; 2004. p. 108-14. [9 references]

GUIDELINE STATUS

This is the current release of the guideline.

** REGULATORY ALERT **

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory information has been released.

- [June 15, 2005, COX-2 Selective \(includes Bextra, Celebrex, and Vioxx\) and Non-Selective Non-Steroidal Anti-Inflammatory Drugs \(NSAIDs\)](#): Labeling revised to include a boxed warning and a Medication Guide, highlighting the potential for increased risk of cardiovascular (CV) events and life-threatening gastrointestinal (GI) bleeding.
- [April 7, 2005, Bextra \(valdecoxib\), Cox-2 inhibitors, Celebrex \(celecoxib\), Non-steroidal anti-inflammatory drugs \(NSAIDs\) \(prescription and OTC, including ibuprofen and naproxen\)](#): Bextra (valdecoxib) withdrawn from the market and labels for other Cox-2 inhibitors and NSAIDs revised to include a boxed warning and a Medication Guide, highlighting the potential for increased risk of cardiovascular (CV) events and life-threatening gastrointestinal (GI) bleeding.

Additional Notices

- [May 2, 2007, Antidepressant drugs](#): Update to the existing black box warning on the prescribing information on all antidepressant medications to include warnings about the increased risks of suicidal thinking and behavior in young adults ages 18 to 24 years old during the first one to two months of treatment.
- [July 19, 2006, Triptans](#): Healthcare professionals and consumers of new safety information regarding taking triptans together with selective serotonin

reuptake inhibitors (SSRIs) and selective serotonin/norepinephrine reuptake inhibitors (SNRIs).

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** REGULATORY ALERT **

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SCOPE

DISEASE/CONDITION(S)

- Menstrual migraine
- Menstrually-related migraine

GUIDELINE CATEGORY

Management
Prevention
Treatment

CLINICAL SPECIALTY

Family Practice
Internal Medicine
Neurology
Obstetrics and Gynecology

INTENDED USERS

Health Care Providers
Physicians

GUIDELINE OBJECTIVE(S)

- To improve the medical treatment of headache
- To provide recommendations for the treatment of menstrual and menstrually-related migraine (MRM)

TARGET POPULATION

Women with menstrual or menstrually-related migraine (MRM) including migraines during pregnancy, postpartum, and menopause

INTERVENTIONS AND PRACTICES CONSIDERED

Acute Treatment

1. Nonsteroidal anti-inflammatory drugs (NSAIDs)
 - Naproxen
 - Diclofenac
 - Ketoprofen
 - Ibuprofen
 - Arthrotec®
2. Dihydroergotamine (DHE)
3. Triptans
 - Sumatriptan
 - Rizatriptan
 - Zolmitriptan
4. Aspirin + acetaminophen + caffeine (AAC)
5. Analgesics
6. Corticosteroids
7. Acetaminophen with or without an antiemetic (i.e., prochlorperazine)
8. Opioids
 - Meperidine
 - Butorphanol
 - Morphine
 - Hydromorphone

Preventive Treatment

1. Increasing preventive therapy dose prior to menstruation (for those women already taking preventive medications)
2. Nonsteroidal anti-inflammatory drug
 - Naproxen sodium
3. Triptan
 - Naratriptan
 - Sumatriptan
 - Frovatriptan
4. Methylergonovine
5. Dihydroergotamine nasal spray or injection
6. Magnesium
7. Supplemental estrogen
 - Estradiol (preferred form) tablet or patch
8. Hormone replacement with estrogens alone or in combination with progestins
9. Hysterectomy/oophorectomy (considered, but not recommended)
10. Beta-blockers
 - Propranolol
 - Atenolol
 - Labetalol
11. Antidepressants
 - Amitriptyline
 - Fluoxetine

Non-Pharmacologic Management

1. Obtaining a sexual and contraceptive history
2. Assessing risk of unplanned pregnancy and informing patient about the potential risk of drugs that are taken
3. Behavioral management/lifestyle improvements
 - Maintain predictable lifestyle in terms of diet, mealtimes, sleep, exercise, and "let down"
 - Avoidance of known triggers
 - Stress management
 - Biofeedback
 - Visualization
4. Rest and ice packs

MAJOR OUTCOMES CONSIDERED

Not stated

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Not stated

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The guidelines presented in this monograph represent the consensus of an advisory panel of practitioners chosen by the National Headache Foundation (NHF) for their expertise. In addition to incorporating the US Headache Consortium's recommendations, their conclusions reflect clinical experience and the most recent medical literature.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Not stated

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not applicable

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Menstrual Migraine and Menstrually-Related Migraine (MRM)

Premenstrual migraine can occur 7 days to 1 day before the onset of menses. True menstrual migraine is usually defined as an attack that occurs in a woman between 1 day before and up to 4 days after the onset of menses, and does not occur in that woman at any other time. True menstrual migraine is relatively uncommon, affecting about 14% of women. Of women with migraine, 60% report that their attacks occur at various times associated with menses. These attacks are termed menstrually-related migraine (MRM). Because the exact relationship between menses and migraine remains unclear, any attack that occurs within 2 days before and up to 2 days after menses is considered MRM. Using a headache diary or calendar to confirm the association with menses may provide further guidance. Dysmenorrhea is often associated with migraine. Premenstrually, attacks may be accompanied by other features of premenstrual dysphoric disorder (PMDD), including mood changes, backache, nausea, and breast tenderness and swelling.

Treatment

MRM has historically been considered more virulent and more difficult to treat than non-MRM. However, according to recent clinical trials of triptan drugs, the response of MRM does not appear to be different from that of non-MRM. Therefore, it may be the predictability of MRM that makes it unique.

In general, MRM can be effectively managed with strategies similar to those used for non-MRM. Behavioral management is an important concept in menstrual as well as nonmenstrual migraine. Women should be instructed that menstruation is one of many factors that put them at risk for migraine. The hormonal changes are just one of many potential trigger factors. Therefore, encourage women with MRM to limit their exposure to other known trigger factors perimenstrually, when they are more headache-prone.

Most patients are treated with acute medications. When attacks are very frequent, severe, or disabling, preventive treatment may be required. Study results on the effectiveness of nonpharmacologic treatment strategies for hormonal-related headaches are mixed. However, behavioral therapy should be considered during pregnancy because of its low associated risks to fetal development.

Acute Treatment

Medications that have been proven effective or that are commonly used for the acute treatment of MRM include nonsteroidal anti-inflammatory drugs (NSAIDs), dihydroergotamine (DHE), the triptans, and the combination of aspirin, acetaminophen, and caffeine (AAC). If severe attacks cannot be controlled with these medications, consider treatment with analgesics, corticosteroids, or a course of intravenous (IV) DHE.

Preventive Treatment

Women with very frequent and severe attacks are candidates for preventive therapy. For patients taking preventive medications who experience migraine attacks that break through the preventive therapy perimenstrually, the dose can be raised prior to menstruation. For patients not taking preventive medication, or for those with true menstrual migraine, short-term prophylaxis taken perimenstrually can be effective. Agents that have been used effectively perimenstrually for short-term prophylaxis include: naproxen sodium (or another NSAID) 550 mg twice a day; a triptan, such as naratriptan 1 mg twice a day/sumatriptan 25 mg twice a day/ or, /frovatriptan 2.5 mg twice on the first day and then 2.5 mg daily; methylergonovine 0.2 mg twice a day; DHE either via nasal spray or injection 1 mg twice a day; and magnesium, equivalent to 500 mg twice a day.

The triptans, ergotamine, and DHE can be used at the time of menses without significant risk of developing dependence. As with the NSAIDs, these drugs will also be more effective as preventive medications if started 24 to 48 hours before the onset of the expected MRM.

Fluoxetine, especially if the headache is associated with other premenstrual dysphoric disorder symptoms, can be an effective headache preventive between ovulation and menses.

Hormonal Therapy

If standard preventive measures are unsuccessful, hormonal therapy may be indicated. This may involve the use of a supplemental estrogen taken perimenstrually either by mouth or in a transdermal patch. Estradiol (0.5 mg tablet twice a day, or 1 mg patch) is the preferred form of estrogen because it does not convert to the other active forms of estrogen.

For women using traditional estrogen/progesterone oral contraceptives for 21 days per month, the supplemental estrogen may be started on the last day of the pill pack. Another approach for women who take an estrogen/progesterone oral contraceptive is to take it daily—that is, without the monthly break—for 3 to 6 months. This has become accepted as a standard practice, and in Europe this approach has been used for up to a year with safety. The reduction in menstrual periods provides a method of preventive treatment.

Special Considerations for Women of Reproductive Age

Because pharmacologic therapies pose a potential risk to fetal development, special consideration is in order for female patients of reproductive age and childbearing potential. Whenever possible, the clinician and the patient should discuss the patient's plans for childbearing prior to the patient's pregnancy. It is also important take a sexual and contraceptive history in order to assess the risk of an unplanned pregnancy. In the event of an unplanned pregnancy, the patient should be informed about the potential risks of the drugs that were taken. If oral contraceptives are discontinued as part of migraine therapy, be sure to discuss the possibility of pregnancy and to consider alternative methods of contraception. If there is a history of miscarriage, especially in a patient with migraine with aura, check for antiphospholipid antibodies. Consider adding 4 mg per day of folate supplementation for all women of childbearing potential, particularly for patients who are taking divalproex sodium.

Migraine during Pregnancy

In most cases, migraine improves or disappears during pregnancy. However, some women may experience their first attack during this period. Lifestyle improvements are among the first steps in migraine management for women who wish to become pregnant. They should strive to maintain a predictable lifestyle in terms of diet, mealtimes, sleep, exercise, and "let down." Avoidance of known triggers should be encouraged. Techniques such as stress management, biofeedback, and/or visualization provide a positive method of addressing migraine prevention. The use of nonpharmacologic techniques along with rest and ice packs may help in the acute management of attacks. First-time mothers should be taught that parenthood begins with pregnancy. Lifestyle modification is the first of many important changes that the mother will make as part of parenting. Provide reassurance and positive suggestions to the mothers for handling this important period in their lives.

Clinicians should be aware of the potential risks associated with all medications and should take the time to properly educate their patients about these risks. The Food and Drug Administration (FDA) lists 5 categories of labeling for drug use in pregnancy:

- Category A: Controlled human studies show no risk to humans
- Category B: No evidence of risk in humans but no controlled human studies
- Category C: Risk to humans not ruled out
- Category D: Positive evidence of risk to humans from human and/or experimental animal studies
- Category X: Contraindicated in pregnancy

The major concern in managing migraine during pregnancy is risk to the fetus. Medication may be required, but it should be limited. The woman's partner should also be consulted to ensure that both parents-to-be agree with the treatment plan. First-line therapy consists of acetaminophen with or without an antiemetic. The efficacy of this therapy should be evaluated, and women should be informed that other treatments are available if these medications are ineffective. NSAIDs may be used except early in pregnancy (prior to implantation) and within 12 weeks of estimated delivery. Maternal bleeding is the major risk of NSAID use early in pregnancy, and there is a possible association of fetal pulmonary hypertension with NSAID use in the last trimester. Several of the NSAIDs are rated category B, including naproxen, diclofenac, ketoprofen, and ibuprofen. All the others are category C except for the branded compound Arthrotec®, which contains misoprostol, a known abortifacient.

Other factors to consider when using medical therapies during pregnancy are related to the mother's health in terms of migraine. Severe pain may affect fetal well-being, since the mother may not be able to take appropriate care of herself. In addition, repeated episodes of nausea and vomiting along with the anorexia commonly associated with migraine may compromise fetal nutrition. However, most medications that would be considered for treating migraine in pregnancy are category C drugs; that is, they have not been determined to be safe, but no specific data suggest that they are unsafe either. For sporadic severe attacks, opioids (e.g., meperidine, butorphanol, morphine, hydromorphone) may be given along with intravenous prochlorperazine.

For women with frequent severe migraine attacks, preventive pharmacologic treatment should be considered. Communication and cooperation with the patient's obstetrician/fetal specialist/neonatologist may provide optimal management. Among the medications commonly used in pregnancy and found to be relatively safe are the beta-blockers (e.g., propranolol, atenolol, labetalol) and the antidepressants (e.g., amitriptyline, fluoxetine), especially if comorbid depression is present. A course of corticosteroids for several days can also abort status migraine.

New onset of headache occurring during pregnancy provides additional diagnostic challenges since neuroradiologic procedures are best avoided during pregnancy. In the last half of pregnancy, it is important to rule out preeclampsia. Vascular organic causes of headache (such as venous sinus thrombosis or other vascular causes) may develop if a patient is pregnant, if there are positive findings on neurologic examination (such as abnormal reflex), or if papilledema is found on

ophthalmologic examination. Appropriate psychosocial examination should be conducted if there is evidence of comorbid depression or anxiety.

Postpartum Migraine

If headache onset occurs in the immediate postpartum period, different factors may need to be explored. The development of recurrent or increased headache in a known primary headache patient may represent effects of the hormonal changes associated with the end of pregnancy. In addition, postpartum depression may be a contributing factor. The lactating female has special concerns, since most drugs enter the breast milk in very small amounts. Expressing and discarding milk after acute treatment is an option. Although no studies exist, it is probably safe to resume breast-feeding after the passage of 5 half-lives of the drug. Consequently, acute treatment drugs with shorter half-lives may be preferable. Recently, the American Academy of Pediatrics approved sumatriptan, rizatriptan, and zolmitriptan as being safe to use during breast-feeding.

Menopausal Migraine

For menopausal migraine patients, hormone replacement with estrogens, alone or in combination with progestins, is often used to treat symptoms as well as to prevent osteoporosis. Treatment of these patients can be difficult, however, as headaches may develop from the treatment itself. Female patients who present with hormone-related headache present specific challenges to clinicians. Although the most common hormone is derived from a natural animal source, the relative ratio of the estrogen compounds may adversely influence migraine in some women. In this situation, the purified estradiol products may be preferred. Hysterectomy/oophorectomy should be avoided, as these procedures generally decrease migraine frequency only slightly, if at all, and have been associated with exacerbation of migraine. In addition, patients with migraine with aura are at higher risk for stroke, although the absolute risk is small. Use of the lowest effective estrogen dose for those taking oral contraceptives or postmenopausal estrogen is recommended in this group. Adequate assessment of cardiac and cerebrovascular risk in women over the age of 50 is important before treating with a triptan or an ergot derivative.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of evidence supporting the recommendations is not specifically stated.

In addition to incorporating the US Headache Consortium's recommendations, the conclusions reflect clinical experience and the most recent medical literature.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate treatment of women with menstrual or menstrually-related (MRM) migraine

POTENTIAL HARMS

- Maternal bleeding is the major risk of nonsteroidal anti-inflammatory drug (NSAID) use early in pregnancy, and there is a possible association of fetal pulmonary hypertension with nonsteroidal anti-inflammatory drug use in the last trimester. Several of the nonsteroidal anti-inflammatory drugs are rated category B, including naproxen, diclofenac, ketoprofen, and ibuprofen. All the others are category C except for the branded compound Arthrotec®, which contains misoprostol, a known abortifacient.
- For menopausal migraine patients, hormone replacement with estrogens, alone or in combination with progestins, is often used to treat symptoms as well as to prevent osteoporosis. Treatment of these patients can be difficult, however, as headaches may develop from the treatment itself.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

Drug therapy is constantly evolving as new research, clinical trials, case reports, and opinions are published. Many of the drugs recommended in these guidelines are not approved by the US Food and Drug Administration (FDA) for treatment of headache, nor are they necessarily the same as those therapies recommended by the manufacturer for labeled indications. Their use in headache, however, may be supported by the scientific literature and by the authors' clinical experiences. While efforts have been made to ensure accuracy, the authors and publisher do not assume responsibility for the consistent updating of available information for these guidelines, nor for any errors or omissions, nor for any consequences thereof. The onus is on the practitioner to evaluate recommendations in light of the clinical condition of the patient and recent medical literature. The authors advise the practitioner to consult other sources, especially the manufacturers' warnings and precautions, before prescribing any drug with which they are unfamiliar. Practitioners are also advised that while these guidelines will address the needs of many patients, there will be circumstances calling for exceptions to these recommendations.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Chart Documentation/Checklists/Forms
Foreign Language Translations
Patient Resources
Slide Presentation
Staff Training/Competency Material

For information about [availability](#), see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness
Staying Healthy

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Diamond M. Special treatment situations: menstrual migraine and menstrually-related migraine. In: Standards of care for headache diagnosis and treatment. Chicago (IL): National Headache Foundation; 2004. p. 108-14. [9 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2004

GUIDELINE DEVELOPER(S)

National Headache Foundation - Private Nonprofit Organization

SOURCE(S) OF FUNDING

National Headache Foundation

GUIDELINE COMMITTEE

Not stated

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Author: Merle Diamond, MD

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: None available

Print copies: Available from the National Headache Foundation, 820 N. Orleans, Suite 218, Chicago, IL 60610; Phone: (888) NHF-5552; Web address: www.headaches.org

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- The complete headache chart. Chicago (IL): National Headache Foundation (NHF); 2 p. Electronic copies available in Portable Document Format (PDF) from the [National Headache Foundation Web site](http://www.headaches.org)
- National Headache Foundation fact sheet. Chicago (IL): National Headache Foundation (NHF); 2004 Oct. 2 p. Electronic copies available in Portable Document Format (PDF) from the [National Headache Foundation Web site](http://www.headaches.org).
- Women's issues in migraine. A continuing education program. Chicago (IL): National Headache Foundation (NHF); 2003. 14. p. Electronic copies available in Portable Document Format (PDF) from the [National Headache Foundation Web site](http://www.headaches.org).
- Women's issues in migraine. Power Point presentation. Chicago (IL): National Headache Foundation (NHF). Electronic copies available from the [National Headache Foundation Web site](http://www.headaches.org).

Print copies: Available from the National Headache Foundation, 820 N. Orleans, Suite 218, Chicago, IL 60610; Phone: (888) NHF-5552; Web address: www.headaches.org

PATIENT RESOURCES

The National Headache Foundation (NHF) has created a variety of educational resources for patients, including informative brochures, a patient diary for migraines, Power Point presentations, and patient guides; many of these resources are available in both Spanish and English. Some of these items are available as print copies for purchase through the [NHF online store](http://www.headaches.org). Electronic

versions of other resources are available through the consumer education section of the [NHF Web site](#).

Print copies: Available from the National Headache Foundation, 820 N. Orleans, Suite 218, Chicago, IL 60610; Phone: (888) NHF-5552; Web address: www.headaches.org.

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC STATUS

This NGC summary was completed by ECRI on April 13, 2005. The information was verified by the guideline developer on April 26, 2005. This summary was updated by ECRI on June 16, 2005, following the U.S. Food and Drug Administration advisory on COX-2 selective and non-selective non-steroidal anti-inflammatory drugs (NSAIDs). This summary was updated by ECRI on August 29, 2006, following the U.S. Food and Drug Administration advisory on Triptans, SSRIs, and SNRIs. This summary was updated by ECRI Institute on November 9, 2007, following the U.S. Food and Drug Administration advisory on Antidepressant drugs.

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