

Pharmacologic Therapy, Nondrug Therapy, and Counseling Are Keys to Effective Migraine Management

Fred D. Sheftell, MD, DABPN

A recent study on the epidemiology of migraine showed migraine to be present in 17.6% of females and 5.7% of males. The survey results suggested that both patients and physicians believe migraine treatment is elusive and that patients are becoming increasingly frustrated and dissatisfied with treatment outcomes. With increased knowledge of headache and a variety of treatment options, family practice physicians can better educate, counsel, and treat patients.

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Increasingly, migraine sufferers are looking for improved management of their disease. By discussing the variety of available nonpharmacologic therapies, such as behavioral approaches (diet modification, biofeedback, and relaxation exercises), and pharmacologic treatment options, physicians and patients can tailor therapy to meet individual needs and maximize clinical benefits.

A survey by The Johns Hopkins University School of Medicine involving 20 468 respondents was conducted from 1989 to 1990 to establish the epidemiologic nature of migraine in the United States and to determine patient attitudes, patient behavior, and treatments used for different headache types.^{1,3} The survey employed modified International Headache Society criteria⁴ to categorize and identify migraine patients.

Results showed migraine to be present in 17.6% of females (about 18 million) and 5.7% of males (about 5.6 million) in the United States, many of whom reported moderate to severe disability associated with migraine.¹ Although avoidance of trigger factors can be effective in migraine management, survey results showed that only 20% or fewer migraine patients were

advised to do so by their physicians. Results further showed that most migraine sufferers are unaware that migraine is a treatable disorder² and that most patients are not satisfied with current migraine treatments. These findings suggest a need for physician and patient education in migraine management and a need for improved treatment regimens, both pharmacologic and nonpharmacologic. In addition to pain relief, patients seek an understanding of their disorder and acceptance by the medical profession and society.

THE PHYSICIAN'S ROLE IN MANAGING HEADACHE

Physicians must play an integral and diversified role in patient treatment to improve headache control. In addition to managing the headache and accompanying symptoms, physicians must take into consideration the many needs of patients with headache. Patients who visit physicians because of headache are looking for understanding, compassion, explanation, and symptom relief; therefore, it is important to form a collaborative relationship.^{5,6}

One study found that 46% of headache sufferers visit physicians primarily to more fully understand their headaches, while 31% visit primarily for pain relief.⁷

From the Department of Psychiatry, New York Medical College, Valhalla, and New England Center for Headache, Stamford, Conn.

Both physicians and patients should know that headache cannot be cured, but it can be successfully controlled with proper diagnosis, counseling, and treatment. Once the physician and patient understand headache patterns and characteristics, a treatment regimen can be implemented that best meets the patient's needs. Patients can learn to avoid trigger factors, use behavioral techniques, and determine which medications are most effective for their specific headache type. The more patients understand headache disorders and treatment strategies, the greater the potential for compliance and headache relief.^{5,6}

The role of the physician begins with an accurate and detailed history

of the patient's headaches.^{8,9} This initial evaluation may require at least 30 minutes, during which patients are questioned about headache triggers, family history of migraine, behavior patterns, previous diagnostic tests, and previous headache treatment and degree of success. Detailed questioning about headache timing, duration, location of pain, and accompanying symptoms, such as nausea, vomiting, photophobia, and phonophobia, is also necessary. Medications used in the past should be recorded, along with doses, schedules of administration, and relief attained. For women, menstrual cycles should be recorded. A headache "calendar" or "diary" may be used to track a patient's progress with time (**Figure 1**).⁶

After the initial evaluation, follow-up visits should be scheduled, each lasting approximately 15 to 20 minutes. During follow-up, physicians should counsel patients. By reviewing the headache diary, physicians may note significant side effects of medication, noncompliance, or other potentially correctable problems. The ultimate goals of the follow-up visits are to ensure that the patient is receiving optimal treatment for the condition and to improve quality of life as much as possible.

A recent study¹⁰ reported that the quality of life of migraine sufferers is comparable to or lower than that of patients with other chronic disorders, such as hypertension, diabetes, and arthritis. Measures of phys-

Headache Calendar

#1 Mild headache
 #2 Moderate headache
 #3 Incapacitating headache

Name _____ Month _____ Year _____

	01	02	03	04	05	06	07	08	09	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31		
Morning																																	
Afternoon																																	
Evening																																	
Sleeptime																																	
Medication	_____																																

Relief 0-1-2-3 (0)-None (1)-Slight relief (2)-Moderate relief (3)-Complete relief

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Triggers:

--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--

Periods:

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Figure 1. An example of a headache "calendar" used to record headache severity, duration, and timing as well as trigger factors and medication use.

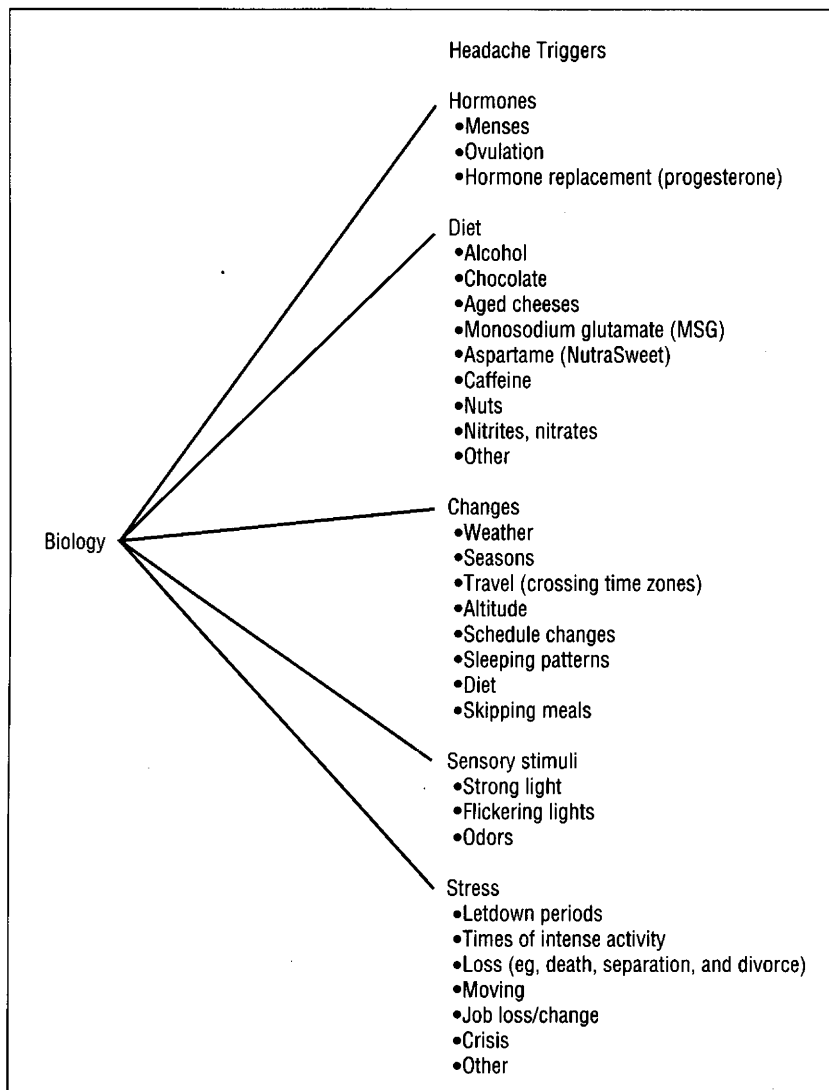


Figure 2. Common headache triggers in patients with underlying biologic predisposition to headache include hormones, dietary factors, changes (eg, schedule and weather changes), sensory stimuli, and stress.

ical function, social function, mental health, energy, and fatigue were obtained in migraine sufferers and compared with previously published data on patients with the other chronic conditions. It was found that migraineurs' social function, pain, and mental health scores were even lower than those of patients with other chronic conditions, indicating a lower quality of life.¹⁰

NONPHARMACOLOGIC MANAGEMENT OF MIGRAINE

A variety of nonpharmacologic options are available to migraine sufferers. Avoidance of trigger factors, diet mod-

ification, behavioral medicine, biofeedback, and relaxation exercises may be effective in managing migraine, either alone or in combination with pharmacologic therapy.¹¹⁻¹⁸

Trigger Factors: What to Avoid

In patients with a biologic predisposition to headache, certain factors can exacerbate or trigger migraine (**Figure 2**). However, it should be noted that these triggers alone do not cause migraine; rather, they aggravate the existing condition. For example, in women who are predisposed to migraine, hormonal fluctuations are a common trigger.

"Menstrual migraine" affects some women before or during menstruation. Oral contraceptives and estrogen therapy have also been known to trigger migraine in some women¹⁹; however, the role hormones play in causing migraine is unknown.

Diet is another important factor in migraine. Alcohol, chocolate, aged cheeses, monosodium glutamate (found in many Chinese foods), aspartame (NutraSweet), caffeine, nuts, nitrites, and nitrates (found in hot dogs and other prepared meats) are all potential triggers.^{13-15,20} Physicians and patients can work together to create a diet that eliminates these triggers.

Changes in environment or lifestyle may also aggravate migraine. These include weather variations, such as seasonal changes, and travel that entails crossing time zones or changing altitudes. Other deviations from normal patterns of behavior, such as an altered schedule, letdown periods, and changes in sleeping habit or diet, may also trigger migraine.²¹

Advising patients to avoid changes that have triggered their migraine in the past may help to reduce or eliminate some migraine attacks. At times, life-style changes, such as smoking cessation or elimination diets (eg, diets to avoid caffeine intake), may improve headache treatment. However, other therapeutic intervention may be necessary to manage migraine optimally.

Behavioral Medicine

Behavioral medicine, in which the patient plays an active role in the treatment process, has been used in migraine management.^{5,6,21,22} For maximum benefit, the patient needs to understand and accept the treatment rationale and be sufficiently motivated to apply it to daily activities. An important preliminary step is to counsel the patient about factors that cause headache and how to avoid them. Patients who are willing to take responsibility for their treatment have a better prognosis than those who sim-

ply await treatment by physicians.⁶ Again, patients must understand that successful management is in reach with proper guidance and a tailored treatment regimen.

Biofeedback

The use of biofeedback for headache treatment began in the 1960s.²³ Because dilated blood vessels in the extracerebral circulation are thought to be involved in migraine, channeling blood flow away from the head could be effective in preventing a migraine attack.²⁴ Thus, with sufficient monitoring, patients could use biofeedback to raise skin temperature in their extremities (an indirect expression of vasomotor activity). A popular method of biofeedback relies on an electromyogram of the frontal or temporal muscles.²⁵ One study reported that patients using this procedure had a significant reduction in muscle activity and headache and were able to reduce intake of analgesics and tranquilizers.²⁶ Some of these patients were able to maintain this beneficial effect for up to 18 months. Other studies using electromyography feedback have confirmed its efficacy in reducing the frequency and severity of headache.^{27,28}

Further research has shown that a number of cognitive and behavioral changes occur in patients undergoing biofeedback therapy, and these changes promote enhanced coping skills and the ability to regulate tension levels.²²

Relaxation and Meditation Techniques

Another option in the nonpharmacologic treatment of migraine is relaxation training. Stress and anxiety are recognized as common precipitants of headache, and techniques that relax contracted skeletal muscles have been shown to abort or lessen the severity of migraine attacks.²⁹ Some studies^{25,29} have shown a marked reduction in headache frequency and severity, as well as a reduction in medication use as a result of relaxation

and meditation techniques; however, pharmacologic support is still necessary in most patients.⁵ Simple means of relaxation include massage, manual stretching of the neck and shoulder muscles, hot baths, and local application of heat.⁵ Relaxation training requires patients to engage in a period of muscle tensing and relaxing exercises, promoting a generalized state of relaxation. Other forms of relaxation include meditation, yoga, acupuncture, acupressure, and autogenic exercises.²²

THE ROLE OF PHARMACOLOGY IN HEADACHE MANAGEMENT

A recent study³⁰ evaluated the efficacy of nondrug vs pharmacologic treatment of headache. The largest to date, this study compared biofeedback, prophylactic drug therapy (propranolol and amitriptyline), and abortive/analgesic treatment (ergotamine and analgesics). The study involved 544 patients with either migraine or mixed (migraine plus tension-type) headache. Results suggested that the most effective migraine treatment may be a combination of nondrug and drug therapy. Seventy-four percent of patients receiving combined therapy experienced improvement in headache. No more than 62% of patients receiving any one of the currently available treatments experienced improvement in headache.

Pharmacologic options for man-

aging migraine include acute and preventive therapies (**Table**).

Preventive Pharmacologic Treatment Options

Prophylactic treatment of migraine should be considered when patients average two or more severe attacks per month and when headaches interfere with daily activities.³¹ Before beginning any regimen, it is imperative to establish doses that will not result in overuse of ergotamine or analgesics.⁶ Generally, prophylactic therapy should begin at low dosages, with gradual increases during a 2- to 3-month period, if necessary. Patients with similar headache types do not always respond to the same preventive medication or to the same dosage. The best approach may be to try various drug combinations, taking into consideration any side effects or contraindications, until an effective agent is found. No preventive medication for migraine should be taken indefinitely. Once migraine is sufficiently managed, patients should gradually discontinue preventive therapy.³²

Nonselective β -adrenergic receptor blockers, such as propranolol hydrochloride (80 mg once or three times daily), timolol maleate (10 to 30 mg/d), and nadolol (up to 80 mg/d), have been shown to be effective in decreasing attack frequency.^{33,34} The selective β -blockers metoprolol (25 to 100 mg/d) and atenolol (25 to 100 mg/d) may reduce severity and duration of attacks and as-

Acute Treatment	Preventive Treatment
Ergotamine tartrate	β -Blockers
Dihydroergotamine mesylate	Tricyclic antidepressants
Analgesics	Calcium antagonists
Naproxen sodium	Methysergide maleate
Metoclopramide hydrochloride	Clonidine hydrochloride
Promethazine hydrochloride	Cyproheptadine hydrochloride
Prochlorperazine maleate	Divalproex sodium
Chlorpromazine hydrochloride	Monoamine oxidase inhibitors
Isometheptene mucate	Nonsteroidal anti-inflammatory drugs
Sumatriptan succinate	Aspirin

sociated symptoms.^{35,36} It is recommended that a baseline electrocardiogram be obtained before prescribing a β -blocker.

Tricyclic antidepressants, such as amitriptyline hydrochloride (25 mg once or three times daily) and nortriptyline hydrochloride (25 mg once or three times daily), work with analgesiclike action. Although effective in migraine prophylaxis, they may cause side effects, including weight gain, lethargy, dry mouth, and constipation.³⁷ Other, less widely used tricyclic antidepressants include imipramine hydrochloride (25 to 150 mg/d) and doxepin hydrochloride (25 to 150 mg/d).

Calcium antagonists—verapamil (80 to 120 mg three times daily), diltiazem hydrochloride (90 to 360 mg/d), nifedipine (10 to 20 mg three times daily), and nimodipine (60 mg every 4 hours)—are often used in migraine prophylaxis. These agents block the entry of extracellular calcium into vascular smooth muscle and are considered moderately effective.³⁷

Methysergide maleate (4 to 8 mg/d), a serotonin (5-hydroxytryptamine [HT]₂) antagonist, can be used in migraine prophylaxis, but it is associated with side effects such as nausea, vomiting, abdominal discomfort, drowsiness, dizziness,³⁷ and, rarely, retroperitoneal fibrosis.

Other drugs used in migraine prophylaxis include clonidine hydrochloride, cyproheptadine hydrochloride, divalproex sodium (an anticonvulsant), monoamine oxidase inhibitors, nonsteroidal anti-inflammatory drugs, and aspirin in low doses.^{6,37}

Acute Pharmacologic Treatment of Migraine: An Overview

Even with successful preventive management, acute pharmacologic therapy is often necessary for “break-through attacks.” Oral ergotamine tartate (up to 4 mg per attack) is among the agents currently available for the acute treatment of mi-

graine. Ergotamine acts via vasoconstriction and by blocking neurogenically mediated inflammation.³⁸ Dihydroergotamine mesylate (up to 3 mL per attack), a parenteral form of ergotamine, has also shown efficacy in aborting migraine.^{39,40} Side effects associated with ergotamine include nausea, vomiting, and habituation when prescribed or taken improperly.⁴¹ Although rare, symptoms of ergotism may develop from overdosage of ergotamine.

Aspirin (325 to 650 mg three or four times daily) and acetaminophen (325 to 650 mg three or four times daily) are also widely used in acute migraine treatment. Considered moderately effective, these analgesics may also produce rebound phenomena.²¹

Because of the risk of rebound headache syndrome, which occurs as a result of ergotamine or analgesic overuse, physicians should stress the importance of compliance when prescribing these drugs. What begins as a gradual increase in medication may become chronic overuse, leading to symptoms of rebound headache between doses. (These rebound headaches are interpreted by the patient to be a return of the original headache.) A medication-headache cycle then begins, leading to the rebound headache syndrome.

It is possible that analgesic or ergotamine overuse may, in part, cause a gradual transformation of intermittent migraine attacks into chronic daily headache (referred to as “transformed migraine”). Research^{5,42,43} suggests that these two conditions may be physiologically related, representing a clinical continuum rather than two separate entities. These studies have shown that patients often suffer symptoms characteristic of both headache types; pain may be suggestive of both muscular and vascular origins. Furthermore, that patients with chronic daily headache often respond well to therapy usually prescribed for migraine, and vice versa, also supports the clinical continuum model.

Rebound headache must be fully managed before any other therapeutic regimen is started. Treatment of rebound headache involves complete abstinence from analgesics or ergotamine for several weeks followed by an appropriate migraine treatment regimen.⁴⁴ Headache calendars are useful in identifying these patterns of overuse.

Nonsteroidal anti-inflammatory drugs, such as naproxen sodium (up to 500 mg twice daily), are used in acute migraine treatment. Metoclopramide hydrochloride (10 mg), an antidopaminergic agent with anti-nauseant properties, has also been used; however, because it does not produce analgesic effects, addition of a pain-relieving agent may be necessary. Other pharmacologic agents for treatment of acute migraine include antiemetics, such as promethazine hydrochloride (25 mg), prochlorperazine (5 to 10 mg), and chlorpromazine hydrochloride (10 to 25 mg), which should be given as a single dose before administration of ergots or analgesics. Also helpful may be isometheptene mucate (65 mg)/dichloralphenazone (100 mg)/acetaminophen (325 mg), two tablets of which should be given at once, followed by one tablet every hour until pain is relieved (up to five tablets every 12 hours).

Research in migraine therapy currently focuses on serotonin (5-HT). Serotonin receptors, commonly categorized as 5-HT₁, 5-HT₂, 5-HT₃, and 5-HT₄,⁴⁵ are currently being investigated for their role in migraine. It has been found that levels of serotonin are reduced during migraine. Drugs aimed at increasing serotonin levels, although successful in abolishing migraine, have been clinically unacceptable in the past because of widespread side effects.⁴⁶ However, research focusing on certain serotonin receptors has shed new light on acute treatment of migraine.

Sumatriptan succinate, a highly selective 5-HT₁ receptor agonist, represents a significant advance in acute migraine management and has recently been approved for this indi-

cation. In clinical trials, sumatriptan (6 mg injected subcutaneously) significantly reduced headache pain in 70% of migraine sufferers and reduced clinical disability in 76% of sufferers with minimal side effects.³¹ Pain relief began within 10 minutes of administration. Sumatriptan has been shown to be effective in ameliorating the entire migraine symptom complex, which includes pain, nausea, vomiting, photophobia, and phonophobia.^{31,47,48} As a result, patients' normal functioning is rapidly restored. The drug is not habit forming, and it can be used effectively at any time during an attack.^{47,48} Of additional importance to patients, sumatriptan is available in the form of a subcutaneous self-injection system that uses single-dose, prefilled syringes; this facilitates accurate dosing at any time or place. Because of the potential for coronary vasospasm, this drug is not recommended for patients with ischemic heart disease, Prinzmetal's angina, or uncontrolled hypertension.

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Reprint requests to New England Center for Headache, 778 Long Ridge Rd, Stamford, CT 06902 (Dr Sheftell).

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