Chronic Headaches In Family Practice

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Abstract: ***Background:*** **More than 11 million people in the United States have moderate or severe migraine resulting in much suffering and millions of lost work days annually. Staying abreast of current advances in headache management is important for family physicians, who care for most headache patients.**

Methods: **MEDLINE files were searched from 1982 to the present using the key words "headache," "migraine," "serotonin," and "cerebral circulation." Also searched were the journals *Headache* and *Cephalalgia* and the published proceedings of meetings of the American Association for the Study of Headache, the International Headache Society, and the Migraine Trust.**

Results and Conclusions: **A new headache classification based on clinical symptoms has been published by the International Headache Society, which clarifies headache diagnoses. Though headaches with serious underlying disease occur only rarely in family practice, physicians must be familiar with the clinical signs indicating the presence of such problems, and any change in or unusual presentation of headache warrants investigation.**

Headache research has expanded in the past decade, much of which has been directed at raising the standards of treatment. Pharmacologic treatment falls into two categories: acute or abortive treatment and preventive treatment. Analgesic overmedication by headache patients is commonplace and leads to withdrawal symptoms and the development of chronic daily headaches, for which effective treatments are now available at both ambulatory and inpatient levels. At the more basic research level, serotonin receptor studies have provided an impetus for revealing underlying headache mechanisms. A new serotonin agonist, sumatriptan, has proved effective in treating acute migraine and will no doubt be followed by further serotonergic drugs.

Patient education, relaxation therapy, and other nonpharmacological approaches, as well as good overall standards of care, are essential ingredients in headache management. Family physicians are well-equipped to offer these approaches to their patients with headache. (J Am Board Fam Pract 1992; 5:589-99.)

The first clinical account of an acute attack of migraine is attributed to a first-century physician Arateus of Cappadocia in Asia Minor.[1] He described the symptoms with remarkable accuracy, and although the condition has been very familiar to physicians since then, its cause remains unknown, and a cure is still to be found. It was not until the late nineteenth century that Liveing[2] published the first serious work on the subject. Since then, many different theories have been suggested for the cause of migraine, and many different treatments have been presented, only to be discarded in due course.[3] The vascular theory based on Wolff's studies[4] has been most important and for years has guided thinking on the underlying mechanisms of migraine, but now even this respected theory is being challenged.[5]

Methods

Materials for this review were obtained from MEDLINE files from 1982 to the present (key words "headache," "migraine," "serotonin," and "cerebral circulation") as well as from the journals *Headache* and *Cephalalgia* and the published proceedings of national and international meetings of the American Association for the Study of Headache, the International Headache Society, and the Migraine Trust.

Epidemiology

The exact number of individuals in the United States who suffer from migraine is unknown, although a figure as high as 45 million has been suggested.[6] Because of lack of agreement on precise diagnostic criteria and the variation in quality

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of the studies undertaken, published data on migraine in Europe and the United States have been unclear.[7] In the United States it has been estimated that more than 4 percent of all office visits are because of headache.[8] In a recent multicenter headache study, 60 percent of women and 70 percent of men, in a group of 23,611 migraine sufferers selected by a nationwide household survey, reported that they had never had migraine diagnosed, although the survey revealed they clearly had migraine symptoms.[9] More than 80 percent of these individuals reported attacks sufficiently disabling to interfere with work. It has been estimated that for every 100 persons 5.5 days of restricted activity are due to headache.[8] Work loss caused by headache in the United States amounts to 150 million workdays per year.[10] Most headache patients who consult a physician see a family physician, and in a patient survey, most patients who did so reported some dissatisfaction with the treatment received or with the physician's attitude toward them.[11] The most recent migraine prevalence study based on a nationwide household sample, using the new headache classification, showed that 8.7 million women and 2.6 million men in the United States suffer from moderate to severe migraine. Of these, 3.4 million women and 1.1 million men experience one or more severe migraine attacks each month. An unexpected finding in this study was that women aged between 30 and 49 years from lower income groups are at highest risk for acute migraine attacks and that these patients are more likely to seek treatment in emergency departments than in physicians' offices.[12] These data confirm the widespread nature of migraine, which has the proportions of a major public health problem in the United States. Clearly this problem could be addressed more effectively by all physicians who deal with headache patients.

Classification

All headache studies have been plagued by problems in headache definition. A 1962 National Institute of Health ad hoc committee attempted to clarify matters by drawing up a headache classification.[13] This committee defined "classic" and "common" migraine, "tension headache," "mixed headache" and "cluster" headache, which remained the standard for many years. Though it certainly reduced the confusion, definitions remained broad and descriptive and still contained qualifying terms such as "sometimes with," "usually associated," and "often." A good deal of discretion was still being left to the physician in deciding about headache diagnosis. A typical comment of the 1960s was made by Wilkinson[14]: "It is difficult to arrange a clinical trial on headache that has not so many variables as to make the results useless."

The International Headache Society, consulting many workers in the field, published in 1988 a very explicit classification of 129 different headaches and head and neck pains they had defined.[15] Many previously used vague clinical descriptions were abandoned. Categories were subdivided into a multitiered hierarchical system based on the degree of diagnostic exactness needed. Headaches were grouped into 13 different categories with migraine heading the list (Table 1). Migraine was subdivided into 14 different types (Table 2). Category 2 covered tension-type headache, which was divided into 5 types. An important change for practitioners was dropping the terms classic migraine and common migraine for the terms migraine with aura and migraine without aura. Although the new classification was aimed primarily at research, it provides clear clinical descriptions for all headaches, which makes it a valuable reference for all practitioners who see headache patients.

Migraine without Aura — Common Migraine (80 Percent of Migraine)

This commonest form of migraine is characterized by recurrent attacks of moderate to severe headache lasting 4 to 72 hours untreated or un-

Table 1. International Headache Society Headache Classification.

Migraine
Tension-type headache
Cluster headache and chronic paroxysmal hemicrania
Miscellaneous headache with no structural lesion
Headache and head trauma
Headache and vascular disorders
Headache and nonvascular intracranial disorders
Headache and substances or their withdrawal
Headache and noncephalic infection
Headache and metabolic disorders
Headache or facial pain and disorders of cranial neck or cranial structures
Cranial neuralgias
Headache not classifiable

Table 2. Migraine Classification.

Migraine without aura
Migraine with aura
Migraine with atypical aura
Migraine with prolonged aura
Familial hemiplegic migraine
Basilar migraine
Migraine aura without headache
Migraine with acute-onset aura
Ophthalmoplegic migraine
Retinal migraine
Childhood periodic syndromes that could be precursors to or associated with migraine
Benign paroxysmal vertigo of childhood
Alternating hemiplegia of childhood
Complications of migraine
Status migrainosus
Migrainous infarction
Migrainous disorder not fulfilling above criteria

successfully treated. At least two of the following features are present: unilateral location of headache at onset that may spread to involve the whole head, throbbing pain, interference with normal activities, and headache worsening on exercise. Associated symptoms are nausea (almost constant) and vomiting when headache is severe. Photophobia and phonophobia are usually present and osmophobia often occurs. The patient may complain of feeling cold and look pale. There are no neurological findings.

Migraine with Aura — Classic Migraine (20 Percent of Migraine)

Both types of migraines share the same symptoms except that this condition includes preheadache neurological symptoms consisting of an aura. This type of migraine usually remains unilateral, but both types of migraine can occur on different occasions in the same individual.

Migraine Aura

A typical aura appears as a fortification spectrum, i.e., a star-shaped figure near the point of fixation spreading right or left, assuming a laterally convex shape with an angulated scintillating edge, and leaving a varying degree of loss of visual field or scotoma in its wake. There can also be unilateral upper or lower limb weakness, aphasia, or other speech difficulty. Paresthesia, occurring as pins and needles, spreads slowly, followed by numbness. The pattern of the aura usually begins with the visual symptoms, followed by paresthesia, and then by speech and motor weaknesses. For a given patient, the same progressive pattern occurs preceding the headache phase. A history of similar attacks with the characteristic progression helps to differentiate an aura from a transient ischemic attack or embolic stroke.

Migraine aura rarely lasts longer than 60 minutes, but prolonged auras do occur in the condition known as "complicated or hemiplegic migraine." Prolonged auras can occur in first-degree relatives, giving rise to "familial hemiplegic migraine." Persistent auras are always an indication for neuroimaging to exclude an ischemic lesion.

Both types of migraine can be preceded by vague premonitory symptoms during the 48 hours before the onset of headache. There may be mood change[16] or a vague feeling of malaise accompanied by fluid retention. Such symptoms suggest involvement of the central nervous system in precipitating the attack.

Migraine Aura and the Neurogenic Theory

Study of migraine aura has led to the development of a neurogenic theory to explain the underlying basis of migraine and to account for aspects of the migraine syndrome not completely explained by Wolff's vascular theory. Welch,[17] using magnetic encephalography, which records very small magnetic effects in the cerebral cortex, demonstrated small localized areas of cortical neuronal perturbation in migraineurs that accentuate during acute migraine attacks. This response suggests a neuronal instability existing in the cortex of migraineurs (possibly of genetic origin) that becomes aggravated by stress, circulating hormones, dietary factors, or incoming sensory stimuli, which, in turn, cause hypothalamic stimulation and the production of premonitory symptoms. Stimuli are then transmitted to the periphery, where pain-stimulating substances (e.g., serotonin, bradykinin) are released. These substances stimulate the trigeminal nerve and cerebral vessels.[18] The neural migraine pathway continues by the noxious stimuli passing to the trigeminal spinal nucleus and is then relayed to the thalamus and on to the cortex for the completion of a migraine loop and the maintenance of the migraine attack. En route there is radiation to upper cervical segments with the production of referred neck pain. In the midbrain, there is radiation to the vomiting center and other centers to produce the typical array of

symptoms that are part of the migraine attack (Figure 1).

The aura of migraine is produced by cerebral ischemia.[19] The phenomenon of spreading cortical depression of Leao, which is a gradually expanding ring-like suppression of cortical activity, could account for the expanding form of visual aura and progression of the neurological defects. These phenomena are a major focus of current headache research.[20]

Neurologic and vascular factors both play a part in the underlying mechanism of migraine. It remains unclear where the primary cause lies, and a "unification" or neurovascular theory can best accommodate all the known data at present.

Basilar Migraine — Bickerstaff Migraine, Syncopal Migraine

Migraine can involve the basilar artery and during an attack cause brain stem ischemia. This ischemia produces a wide range of disturbing symptoms, such as vertigo, tinnitus, ataxia, bilateral paresthesia, dysarthria, diplopia, and syncope. The condition has been described in young women using birth control pills, and because of the multiple varied symptoms, it has been confused with acute anxiety attacks and hyperventilation.

Ophthalmoplegic and Retinal Migraine

Occasionally in family practice ophthalmoplegic migraine occurs with ptosis, unequal pupils, and diplopia and is caused by ischemic involvement of the blood supply to ocular nerves. Retinal migraine is a rare form of migraine in which retinal ischemia produces a monocular scotoma or complete uniocular transient blindness.

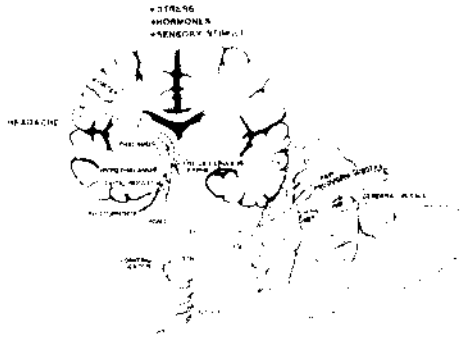

Figure 1. Migraine neural pathway (the migraine loop).

Migraine in Children

Migraine can appear in children as early as age 4 years. It can be without headache in precursor form as migraine equivalents producing periodic vomiting, bouts of nausea, or biliousness. The history is often difficult to obtain and largely depends on the mother's observations. Recurrent bouts of pallor, lethargy, mood change, and loss of appetite, with or without headache, which is usually frontal, should rouse suspicions. Such children are frequently referred to child psychologists because their symptoms are attributed to behavior problems. Family history of migraine, absence of physical findings, and any underlying disease and response to migraine therapy help to confirm diagnosis.

Tension-type Headache — Muscle Contraction Headache

This common headache lasts minutes to days. It is often self-treated by the patient with simple analgesics. The pain is described as a hat-band pressure or tight feeling of mild or moderate intensity, bilateral or global in distribution, and not worsened on movement. *Absence of nausea distinguishes it from migraine.* Temporal and neck areas can be tender on palpation, findings that are also often present in migraine.

Chronic Tension-type Headache

Tension-type headache can continue for long periods with only short intervals of relief. The condition can be difficult to distinguish from a continuous form of migraine, although absence of nausea helps in diagnosis.

There is a growing belief among headache experts, who treat large numbers of cases, that a headache spectrum exists[21] extending from acute migraine with aura at one extreme to tension-type headache at the other, with areas of considerable overlap between, suggesting a common basis for migraine and tension-type headache.

Chronic Daily Headache

This condition is recognized as an increasing problem in family practice involving patients who have a history of migraine and who now claim their headache is unrelenting and present on a daily basis. The daily headache is usually global, can involve the neck and shoulders, and can have many of the features of chronic tension headache.

There are days when the headache is more severe, accompanied by nausea. The picture in chronic daily headache is of continuous headache with migrainous exacerbations. This condition is to be distinguished from status migrainosus, or prolonged migraine attack lasting longer than 72 hours.

Drug Overuse and Chronic Daily Headache

Chronic daily headache should be suspected when patients take analgesics daily for long periods. One hundred or more analgesics a month signals overuse. Use of combination analgesics containing barbiturates, sedatives, or ergotamine preparations more often than three times a week for long periods are indications of drug overuse. Effectiveness of preventive medication is nullified, and when attempts are made to stop the medication, withdrawal symptoms (nausea, vomiting, and headache closely mimicking migraine) prompt restarting the medication.[22] It has been shown that nonnarcotic over-the-counter analgesics, if overused, can also produce this condition.[23]

To prevent drug overuse from developing, all headache medications should be prescribed within limits carefully explained to the patient. Prescribing records should be carefully maintained, and telephone requests for medication should be discouraged and approved by a physician only after a check has been made to assure that the medication request falls within the agreed limits.

Cluster Headache — Horton Headache, Histamine Cephalgia

This very severe headache is strictly unilateral, is localized in the orbital and temporal regions, and is more common in middle-aged men. It is associated with conjunctival injection, lacrimation, nasal congestion, rhinorrhea, forehead and facial sweating, meiosis, ptosis, and eyelid edema. Periods of intensely sharp pain can last from 5 to 180 minutes, occurring as several bouts at a time as often as eight times daily or as seldom as once every other day. Attacks can only occur at nighttime and continue for weeks or months followed by periods of relief lasting 6 to 18 months. During attacks, unlike migraine, patients are restless, pacing the floor unable to remain still. The cause is unknown; attacks are often triggered by stress or alcohol.

Chronic Paroxysmal Hemicrania

These periodic unilateral headaches are less severe than cluster headaches. They may be mistaken for temporal arteritis (see below). They occur in women and are diagnosed by their immediate response to indomethacin.

Other Chronic Headaches

Migraine, tension-type headache, and cluster headache are referred to as primary headaches. Other chronic headaches secondary to underlying disease are known as secondary headaches.

Temporomandibular Joint Dysfunction

This condition is probably overdiagnosed as a primary cause of headache. It is usually caused by bite abnormalities. There can be localized tenderness over one or both temporomandibular joints. Palpation of the joint by pressing on the anterior wall of the external meatus produces exquisite pain. There can be jaw noise on movement, which is often limited, jerky, and painful, and jaw locking can occur. Pain worsens later in the day after chewing and talking. The condition is often seen as part of a stress syndrome associated with teeth grinding (bruxism) or tongue, cheek, or lip biting, and when accompanied by tension headache, the joint pain greatly adds to the head pain. A well-fitting bite plate used at night often helps to improve matters.

Temporal Arteritis — Giant Cell Arteritis

This condition can produce chronic unilateral headache described as burning. The temporal artery is prominent and is tender on palpation. Characteristically there is an elevated sedimentation rate and other manifestations of connective tissue disease of which it is a part. Fibromyalgia can be present. Arterial biopsy, which should involve an adequate length of vessel, showing typical giant cells is the only certain diagnosis. Headache clears with control of the underlying disease process.

Benign Intracranial Hypertension — Pseudotumor Cerebri

The cause of this condition, in which there is increased secretion of cerebral spinal fluid (CSF) is unknown. There is chronic, generalized headache of increasing intensity. Neurologic and funduscopic examination can be normal. A com-

puted tomographic (CT) scan reveals slit-like ventricles resulting from increased cerebrospinal fluid pressure. Papilledema and 6th nerve palsy are late-stage developments. The condition is often seen in overweight adolescent girls and is associated with pregnancy, steroid use, vitamin A, and tetracycline use. Repeated lumbar puncture, initially at daily intervals, to lower pressure to less than 180 mmHg is sometimes necessary to relieve the headache. In most cases, the condition subsides after some months. Lumbar-peritoneal shunting could be required if vision is seriously threatened.

Postlumbar Puncture Headache — CSF Fistula
Transient lowering of CSF pressure following lumbar puncture can produce severe headache that will last for several days. The headache is relieved when the patient lies flat. If the condition worsens or persists, a blood patch might be needed, which consists of injecting 5 mL of the patient's own blood into the lumbar subarachnoid space. The blood is carried by the CSF to the leak, which is then plugged by clot.

Chronic Posttraumatic Headache
Headache is common after head injury. Extensive skull damage is not necessary. Most posttraumatic headaches subside within weeks but can linger for long periods. Such chronic headache states are usually accompanied by other physical and emotional problems. Legal matters related to the injury can add to the problems. Failure to recognize this condition early and to secure appropriate supportive treatment, such as physiotherapy and psychotherapy, can lead to intractable headache and prolonged disability.

Headache and Cerebrovascular Disease

The fear that severe headache will lead to acute cerebrovascular problems is ever present in the patient's mind. There is some evidence that cerebral vascular disease is more frequently found in migraineurs than in the non-headache population. Because migraine involves such a large population, inevitably acute cerebrovascular problems will occasionally arise in these patients, so the possibility should never be ruled out.

Headache can precede or follow stroke. Subarachnoid hemorrhage produces severe global headache accompanied by stiff neck and a raised temperature. Diagnosis is confirmed by CT scan or magnetic resonance imaging (MRI) and CSF examinations. Comatose patients often develop headache as they regain consciousness.

Berry or saccular aneurysm may not cause headache unless leakage or rupture occurs, which will suddenly produce severe increasing headache. An expanding aneurysm in the Circle of Willis can cause double vision and other ocular abnormalities. Such an aneurysm may not be revealed by CAT scan because of location, and an MRI or angiogram might be needed.

Arteriovenous malformation occurs in migraineurs. The abnormal vascular mass is identifiable by CAT scan. When it occurs in the visual cortex area, vivid auras with severe migraine are produced. Removal of such a mass by laser or radiosurgery removes the threat of catastrophic bleeding, but will not necessarily improve the migraine.

When to Suspect Dangerous Headaches

When a new patient has severe headache or when there is a change in headache pattern in a familiar patient, the possibility of a dangerous underlying cause arises. The following headache symptoms should cause the physician to look for an underlying condition:

1. New-onset headache in an older patient
2. Increasing intensity of migraine headache after 24 hours of onset
3. Severe headache in migraine patient reported as "not my usual headache" or "my worst headache ever"
4. Severe headache without a history of migraine with sudden-onset aura that is nonprogressive and persists
5. Severe migraine with neurological abnormalities other than typical aura
6. During severe headache, patient not lying on side in fetal position, typical of acute migraine; instead, patient lying on back with neck stiffness and positive Kernig and Brudzinski signs
7. Periodicity of migraine attacks change from usual pattern; bunching of severe attacks followed by long intervals of freedom can be migraine associated with a cerebral vascular abnormality

Disease or injury to the cervical spine can cause neck pain to radiate into the occipital region of the head and produce headache. Many other conditions, such as osteomyelitis of the skull, Paget disease, multiple myeloma, and diseases of the ear, nose, sinuses, and teeth, as well as glaucoma, refractive errors, and squint, all can cause headache, but these conditions are rarely confused with migraine. Sinus headache is overdiagnosed. Sinusitis of allergic nature causes nasal stuffiness and a sensation of vague fullness in the nasal, frontal, and periorbital areas. Only when an acute or chronic sinus infection causes a localized abscess-like condition in a sinus cavity is much local pain felt. Cranial neuralgias, particularly involving the trigeminal nerve (tic doloreux) can be confused with cluster headache. Persistent headache can be caused by bony encroachment of the 2nd and 3rd cervical nerve roots. Glossopharyngeal neuralgia and one-sided pain in the tongue and side of the neck, as well as carotodynia, can complicate migraine and clear up when the migraine is controlled.

Pharmacological Treatment of Headache

Drug treatment of headache falls into two categories: (1) acute or abortive treatment for the acute attack and (2) preventive treatment (Table 3). Both of these treatment categories can be used concurrently.

Acute or Abortive Medications

Analgesics

Acetaminophen, aspirin, and combination of these with or without caffeine are widely used and often obtained as over-the-counter medications for self-treatment. Overuse can lead to rebound or withdrawal effects and result in chronic daily headache.[23]

Table 3. Medications Used to Treat or Abort an Acute Headache or to Prevent Headache.

Acute or Abortive Medications	Preventive Medications
Analgesics	β-Blockers
Ergot preparations	Calcium channel blockers
Nonsteroidal anti-inflammatory drugs	Antidepressants
	Serotonin antagonists
Antiemetics	Anticonvulsants
Narcotic-analgesic combinataions	Lithium
Anxiolytics and major tranquilizers	
Steroids	

Ergot Preparations

Ergotamine tartrate 1 mg and caffeine 100 mg (Cafergot) are commonly used to abort migraine. Suppository and sublingual forms are available. Use should be restricted to 4 mg of ergotamine per attack or 12 mg/wk. Caution is required because of toxic effects (peripheral vasoconstriction, ergotism). Because nausea can be caused by migraine or ergotamine, pretreatment with an antiemetic (promethazine 25 mg or metoclopramide 10 mg) is helpful. Dihydroergotamine (D.H.E. 45) 1 mg given intramuscularly, preceded by an antiemetic, is useful in aborting attacks.

Nonsteroidal Anti-inflammatory Drugs (NSAIDs)

At an adequate dosage these preparations are useful for acute attacks. Because of side effects, several different forms might need to be tried. Gastrointestinal upset, tinnitus, dizziness, and fluid retention can occur. Because these medications can reactivate ulcers, patients with a history of ulcer disease require monitoring for occult blood loss. Long-term use requires monitoring also for nephrotoxicity. Addiction or rebound headache has not been reported with NSAIDs in acute or chronic treatment of headache. These drugs can be used prophylactically if headaches are predictable, as in menstrually related migraine.

Antiemetics

To some patients, nausea and vomiting can be more distressing than the headache. Antiemetics given orally, by suppository, or by intramuscular injection (promethazine 25 mg, prochlorperazine 12.5 mg, metoclopramide 10 mg) provide rapid relief. Intravenous injection of prochlorperazine (12.5 to 25 mg) can abort all symptoms in some patients.

Narcotic-Analgesic Combinations

Combining two analgesics, acetaminophen and aspirin, can enhance the analgesic effect and reduce side effects. Caffeine can also be added to increase analgesic action. Codeine has a major additive analgesic action when used with these combinations.

Anxiolytics and Major Tranquilizers

Barbiturates and benzodiazepines have stress-reducing effects and contribute to lessening the headache. Their role is minimal, but they can be of value in combination with analgesics. There is little place for the major tranquilizers when treating migraine, but these drugs are required when major emotional disturbance complicates the headache.

Combination drugs, when used for isolated attacks, are of value in treatment of acute migraine. When used in anticipatory fashion for mild headaches or to prevent acute migraine, overuse can develop into habituation, and chronic daily headache will result. All pain medications, alone and in combination, with the apparent exception of NSAIDs, have the potential for creating this problem.

Steroids

Prednisone given for several days in a tapering dosage, starting at a first-day dose of 60 mg, can be of great value in controlling cluster headaches. Ergotamine and oxygen inhalation by face mask (7 L/min for 20 minutes and repeated after 5 minutes, if necessary) in combination with preventive medications (see calcium channel blockers, anticonvulsants, and tranquilizers) are useful in controlling this condition.

Treatment of Drug-Induced Daily Headache

Mathew, et al.[22] recommend cessation of all offending analgesic drugs used in this condition and treatment with valproic acid (Depakote 1000 mg daily) and nonsteroidal analgesics. They report success with this treatment on an outpatient basis. Because controlling analgesic use on an outpatient basis is difficult, it might be necessary to admit the patient to the hospital, as advocated by Raskin.[24] He has shown that intravenous dihydroergotamine (D.H.E. 45, 0.5 to 1.0 mg) combined with intravenous pretreatment with metoclopramide, given at 8-hour intervals for 4 to 7 days, is effective in treating chronic daily headache. Patients are pretreated for 2 weeks with valproic acid to minimize withdrawal effects. During hospitalization, patients require counseling to avoid recurrence of drug overuse in the future. More prolonged behavior modification programs on specialized in-patient units, as advocated by Saper,[25] could be required if chronic daily headache recurs.

Preventive Treatment and Medications

Long-term treatment with preventive drugs should be considered when abortive therapy alone has not produced adequate results. Prolonged severe attacks, or at least two or three incapacitating attacks per month, are indications for long-term treatment. Side effects from abortive therapy or when patients are psychologically unable to cope with the migraine attacks are further indications.

The following medications are used in the preventive treatment of migraine: β-blockers, calcium channel blockers, antidepressants, serotonin antagonists, anticonvulsants, and lithium.

Treatment should start with small doses and progress should be monitored for side effects. Medication should be maintained at the lowest dose that produces the desired effect. There is usually a partial initial response recognized as a decrease in severity and frequency of headaches. Maximum response may require 2 to 3 months of continuous treatment. If there is little or no response or if there are unacceptable side effects, an alternative preventive medication should be introduced. A headache diary and a chart maintained by the patient during this period are necessary to monitor progress (see Nonpharmacologic Therapy). Overuse of abortive medication can reduce the effect of preventive medication.

Preventive medication may be maintained indefinitely. If there is a sustained good response, the medication may be tapered very gradually after 9 to 12 months. Should headaches recur, the medication is reintroduced. Special care should be taken with β-blockers; their use should not be stopped suddenly, because to do so can cause tachycardia arrhythmia. Nonpharmacologic measures are an important addition to preventive management and are the treatment of choice during pregnancy, when drug therapy is best avoided.

β-Blockers

Nadolol (Corgard) 10 to 240 mg/d and propranolol (Inderal LA) 40 to 320 mg/d are most commonly prescribed. Side effects are fatigue, depression, weight gain, and reduction in exercise tolerance. Asthma, congestive heart failure, heart block, and diabetes are contraindications.

Calcium Channel Blockers

Verapamil (Calan SR) 120 to 480 mg/d, nifedipine (Procardia) 30 to 180 mg/d, diltiazem (Car-

dizem) 120 to 360 mg/d are used. Side effects are constipation, diarrhea, skin rash, and hair loss. Congestive heart failure, heart block, sick sinus syndrome, and atrial flutter or fibrillation are contraindications.

Antidepressants

Amitriptyline (Elavil, Endep) 10 to 250 mg/d, nortriptyline (Pamelor, Aventyl) 10 to 100 mg/d, and fluoxetine (Prozac) 20 to 80 mg/d are occasionally of value, particularly when there are clear emotional problems accompanying the headaches. Side effects are drowsiness, dry mouth, weight gain, and constipation. Glaucoma and a history of urinary retention are contraindications.

Serotonin Antagonists

Methysergide (Sansert) 2 to 8 mg/d is a well-established preventive medication for chronic headaches. Side effects are nausea, weight gain, muscle cramps, and peripheral arterial insufficiency. Contraindications are peripheral vascular disease, coronary artery disease, and thrombophlebitis. A severe but rare complication of prolonged methysergide use is retroperitoneal, pulmonary, or endocardial fibrosis. A 3- to 4-week drug-free period is recommended every 3 months, and with long-term use CAT scan monitoring is indicated to detect presymptomatic fibrosis.

Anticonvulsants

Valproic acid (Depakote) 500 to 3000 mg/d at a therapeutic level of 50 to 100 μg/mL is valuable when treating chronic headache. Side effects are nausea, drowsiness, hair loss, platelet dysfunction, and hepatotoxicity. Concomitant use of phenobarbital can cause severe CNS depression. Phenytoin (Dilantin) 200 to 400 mg/d is used for prevention. Hypersensitivity can occur and is a contraindication for its use. Side effects are dizziness, drowsiness, rash, and insomnia. The therapeutic level is between 10 and 20 μg/mL. Carbamazepine (Tegretol) 400 to 1200 mg/d can be helpful. This drug is indicated for control of trigeminal neuralgia (tic doloreux), as well as for prevention of chronic headache. Side effects are nausea, dizziness, rash, leg cramps, fever, and agranulocytosis. A history of liver or renal disease is a contraindication. The therapeutic level is 4 to 12 μg/mL.

Tranquilizers

Lithium (Lithobid) 900 to 1200 mg/d is of value when other preventive medications for cluster headache have been unsuccessful. Side effects are tremor, dyspepsia, and diarrhea. Contraindications are conditions that lead to sodium loss, usually caused by disease or diuretics, when lithium levels can rapidly reach toxic levels. Therapeutic level is 0.5 to 1.4 mEq/L.

Nonpharmacologic Therapy

Although present-day medications have greatly improved headache treatment, and the future for further improvement looks bright, nonpharmacologic therapy is also necessary. By keeping a daily diary and a headache chart, the patient can personally monitor the progress of treatment. Singling out trigger factors in diet, psychosocial factors, related stress, and irregular work and sleep patterns helps to protect the patient from attacks. Recognizing that such factors as weather change, travel, lighting, noise, cigarette smoke, or certain aromas can trigger attacks provides patients with insight into the nature of migraine and an incentive to make appropriate behavioral and other changes to reduce their vulnerability to headache. They learn the important lesson that they must become personally involved in migraine management if their problem is to be adequately controlled.

Progress in treatment occurs more rapidly when patients accept shared responsibility for treating their headaches. They should be encouraged to read about migraine. Feelings of guilt about headache are reduced when they realize that there is a pharmacologic basis to migraine and that they share a problem common to millions. Books on relaxation and audiotapes provide patients with simple exercises that help them to cope with stress. Most migraineurs initially deny that stress is a factor in their headache problem. Depression, secondary to chronic headache, can be a factor, especially in those patients who firmly insist that "no treatment has ever worked" and only "pain medicine" works. Depression as such is a less frequent cause of headache.[26] Referral to a psychiatrist should not be delayed if a patient has made previous suicidal attempts or has suicidal thoughts because of the headache.

Future Developments in Headache Treatment

Headache treatment is changing because of rapid developments in headache research, and no single substance has appeared in the headache research literature more frequently in recent years than serotonin (5-HT, or 5 hydroxytryptamine).[27] Keele[28] first showed that 5-HT can cause pain in man. Sicuteri and colleagues[29] related 5-HT to migraine by showing that its breakdown product (5 hydroxyindole acetic acid) was excreted in the urine during an attack.

When given intravenously 5-HT can alleviate attacks,[30] but because of its toxicity, 5-HT itself has never been developed as a therapeutic agent. Research has shown 5-HT capable of acting on many different tissues in the body, an indication that it has many receptors. It has now been shown that there are at least four different receptors, 5-HT_1, 5-HT_2, 5-HT_3, and 5-HT_4. The 5-HT_1 receptor, particularly its subtype 5-HT_{1D}, appears to be intimately involved in migraine. Stimulation of this receptor by the recently discovered drug sumatriptan has resulted in a major therapeutic advance in the headache field.[31]

Sumatriptan (Imitrex, Glaxo)

Drug trials in the United States and Europe show that 6 mg of sumatriptan given subcutaneously relieves acute migraine with or without aura.[32] Headache, nausea, and photophobia begin to be relieved in 10 to 15 minutes, and maximum response occurs in about 1 hour. The response rate is about 70 percent and side effects are minimal. The oral form has been shown at a 100-mg dose to produce comparable relief.[33] This medication, unlike previous migraine drugs, has been custom-designed to act on a single serotonin receptor thought to play a specific role in the migraine mechanism.[31] This development in the field of headache is important and probably signals the development of further improved therapies for migraine in the future.

Conclusion

The good overall standards of care that are basic to family medicine are essential for effective headache treatment. An empathetic approach by the physician, careful history taking, and examination, leading to a correct diagnosis and appropriate treatment, make migraine controllable. Recent studies show that more effort is needed by all physicians who see headache patients to raise the current level of headache care. Patient education, the identification and elimination of trigger factors, and sharing the responsibility for treatment by the patient optimize the therapeutic setting and increase the likelihood that any medications used are more likely to produce a successful result.

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