Headaches in Adults in Primary Care

Evaluation, Diagnosis, and Treatment

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KEYWORDS

• Headache • Tension-type headache • Migraine headache • Abortive therapy
• Preventive therapy

KEY POINTS

- Headaches are traditionally classified as primary (tension-type headaches, migraines, cluster headaches) or secondary headaches (intracranial pathology, vascular disease, medication overuse headaches).
- Headaches can be diagnosed with a careful history and physical with attention to red flag symptoms.
- Treating migraine headaches has 2 components: treating the acute headache (abortive therapy) and preventing the onset of later headaches (prophylactic therapy).
- Early treatment of acute symptoms is important with careful attention to avoiding overtreatment to prevent overuse headaches.
- Prophylactic therapy for for either Tension-type headaches or migraine headaches is indicated if the headaches are frequent, long lasting, or are associated with significant functional impairment.

INTRODUCTION

Headache is one of the most common symptom presentations in primary care[1] with more than 90% of all primary headaches falling into 2 categories, tension-type headache and migraine headache.[2] It is estimated that more than 3 billion individuals worldwide suffer from headaches, with 1.89 billion patients with tension-type headaches and 1.04 billion with migraine headaches. Although tension headaches are more common in the population than migraine headaches, migraine is the most frequent etiology of headaches in patients seeking treatment because of the increased disability of migraine headaches. Migraine headaches are the second most disabling medical condition worldwide, impacting all domains of life. Given the prevalence of headaches in the population and frequency with which patients with headaches present in primary care settings, an understanding of the different headache syndromes and their management should be a part of every primary care physician's repertoire.

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This review focuses on the 2 most common headache syndromes encountered in primary care practice—tension-type headache and migraine headaches.

CLASSIFICATION OF HEADACHES

Headaches are traditionally classified as primary (tension-type headaches, migraines, cluster headaches) or secondary headaches (intracranial pathology, vascular disease, medication overuse headaches) and can be diagnosed with a careful history and physical examination with attention to red flag symptoms. Important historical features include location, characteristics of the headache, degree of functional impairment, duration, and associated symptoms. The physical examination should focus on discriminators of secondary etiologies: vital signs (blood pressure and pulse), bruits of the head and neck, palpation of the temporal arteries, and palpation of the head, neck, and shoulder muscles, with a detailed neurologic examination, including cranial nerve testing, funduscopy, and symmetry of motor, reflex, cerebellar, and sensory testing. Patient characteristics with low risk for secondary disease include: age 50 years or younger, features typical of a primary headache syndrome, history of similar headache with no change in usual pattern, and a normal physical examination (**Table 1**). Patients who meet these criteria and have no red flag symptom do not require imaging. Red flag symptoms include[3] onset after age 50; pattern change (eg, worst headache of your life); positional headache or headache precipitated by sneezing, coughing, or exercise; symptoms such as fever or history of neoplasm or trauma; and papilledema or neurologic deficit. The presence of any red flag symptoms should trigger further evaluation including brain imaging (**Table 2**).

TENSION-TYPE HEADACHE

Pathophysiology and Headache Characteristics

Tension-type headache is the most common headache in the general population and the second-most prevalent disorder in the world[4] (**Table 3**). Tension-type headache presents as an undifferentiated headache syndrome that is characterized by a bilateral headache of mild to moderate intensity that is nonthrobbing and has no associated symptoms such as sensitivity to light or sound or nausea or vomiting. The pain is described as pressure or bandlike. The pain is not aggravated by routine physical activity, such as walking or climbing stairs. The physical examination may demonstrate increased pericranial muscle tenderness of the head, neck, or shoulders. The diagnosis is clinical and neuroimaging is not required in the absence of red flag findings, as discussed elsewhere in this article. The headache can last days and patients can usually function through their headaches.

There are 3 main subtypes recognized by the International Headache Classification:

- Infrequent episodic tension-type headache: headache less than 1 day per month (63.5% of tension-type headache patients)
- Frequent episodic tension-type headache: headache 1 to 14 days per month (21.6% of tension-type headache patients)
- Chronic episodic tension-type headache: headache 15 or more days per month (0.9% of tension-type headache patients)

A population-based study in the United States found that the prevalence of episodic tension-type headache peaked in the fourth decade with a decreasing prevalence with advancing age.[5] Women and whites have a slightly higher prevalence of tension-type headache than men and black patients. The societal impact is high for patients with

Table 1
Characteristic of common primary headache syndromes

Characteristic	Tension Type	Migraine	Headache
Demographics	Slightly more common in women; 1 year prevalence for episodic tension-type headache 38.3%, chronic tension-type headache 2.2%; higher prevalence in white patients		
Patient appearance	Variable; generally patient remains active and functional or may retreat	Uncomfortable; prefers dark and quiet room; function is impaired	Generally remains functional
Location	Unilateral in 70%; bilateral or global in 30%;	Bilateral, usually temporal but rarely generalizes to the entire head	Always unilateral; classically begins in the eye or around the temple
Duration	4–72 h; may be evident all day (present upon awakening and there when going to sleep)	30 min to 7 d	15 min to 3 h
Characteristics	Mild to moderate intensity; bilateral; nonthrobbing	Pressure; tightness; often described as band-like	Acute onset—reaches maximum intensity within minutes; pain is severe and incapacitating
Associated symptoms	None	May have associated aura (visual or other neurologic deficit); Nausea and/or vomiting; Photophobia or phonophobia;	Tearing and eye redness on the same side as the headache; rhinorrhea; seating; Horner syndrome; sensitivity to alcohol

Table 2
Red flag symptoms requiring further evaluation

Symptom	Example
Age	After 50
Pattern change	Worst headache of your life
Positional headache	Exacerbated with change
Precipitating factors	Sneezing, coughing, exercise
High risk history	Fever, neoplasm, trauma
Physical examination findings	Papilledema, neurologic deficit

episodic tension-type headache reporting an average of 9 lost work days and 5 reduced effectiveness days per year.[5]

The pathophysiology of tension-type headache is unclear, but probably multifactorial. Current models propose that activation of myofascial pain receptors is the underlying cause of episodic tension-type headache, whereas sensitization of pain pathways in the central nervous system owing to prolonged stimuli from pericranial myofascial tissues is responsible for the conversion from episodic to chronic tension-type headache. Studies of pain tolerance in these patients have suggested generalized hyperalgesia in patients with chronic tension-type headache. Thus, increased sensitivity to pain in both the central and the peripheral nervous systems is thought to play a critical role in the pathogenesis of tension-type headache.[6] Spasm of the pericranial muscles was long thought to be important in the pathophysiology of tension-type headache, but this construct is no longer considered a factor. There are minimal if any genetic predispositions to tension-type headache.

Treatment of Acute Tension-Type Headache

Most patients with tension-type headache self-treat using over-the-counter medications without consulting a medical provider. When managing tension-type headache, several principles (albeit not evidence based) are thought to guide therapy.

Table 3
Recommended pharmacologic treatment of tension-type headaches

Medication	Dose	Caveats
Acute treatment		
Pain medications		
Acetaminophen	1000 mg	Enhanced with caffeine
Ibuprofen	400 mg	
Ketoprofen	25 mg	
Aspirin	1000 mg	Enhanced with caffeine
Chronic treatment		
Antidepressants		
Amitriptyline	10–25 mg	Many side effects
Anticonvulsants		
Topiramate	25–00 mg	Reduction at 3 mo

- Because abortive therapy is more effective for migraine headache when given early, it is generally presumed to be more effective for tension-type headache when given as soon as possible after headache onset, although no evidence is available to support that belief.
- Similarly, recommendations are to start with a maximum initial medication dose with the hope of eliminating later doses; the effectiveness of analgesics decreases with increasing headache duration and frequency.
- Chronic tension-type headache is often associated with stress, anxiety, and depression,[7] and analgesics are usually of limited benefit in this setting.
- Avoiding medication overuse headache is a crucial goal of therapy and requires extensive patient education and counseling. The recommendations are that over-the-counter combination medications should be limited to 9 treatment days per month and nonsteroidal anti-inflammatory drugs (NSAIDs) should be limited to 15 or fewer days per month.
- Opioids and butalbital containing analgesics should be avoided owing to their high potential for misuse, including inducing medication overuse headaches.

Clinical trial evidence supports using simple analgesic agents like acetaminophen, aspirin, and NSAIDs as initial therapy.[8] A systematic review of randomized controlled trials concluded that acetaminophen 1000 mg, ibuprofen 400 mg, and ketoprofen 25 mg were more effective than placebo for achieving a pain-free state at 2 hours. Aspirin (1000 mg) was less effective but better than placebo with its effectiveness modest at best with pain-free rates at 2 hours ranging from 16% to 37%. Overall, NSAIDs are preferred because they are less likely to lead to medication overuse headaches than acetaminophen. The role of combination agents is also unclear. Several studies have suggested that adding caffeine to either aspirin or acetaminophen was superior to either agent alone.

Prevention of Tension-Type Headaches

Prophylactic therapy for tension-type headache is indicated if the headaches are frequent, long lasting, or are associated with significant functional impairment. Generally, a frequency of more than 10 headache days per month warrants preventive treatment. Evidence for pharmacologic therapy is limited, but a recent review[9] suggested that the evidence is most robust for tricyclic antidepressants. Other suggested medications include mirtazapine, venlafaxine, topiramate, and gabapentin and the muscle relaxant tizanidine.

Antidepressants

A 2017 meta-analysis[10] supported the contention that tricyclics are therapeutic for tension-type headache prevention. Headache frequency was reduced by 4.8 headaches per month in patients with very frequent headaches (21 headaches per month) and analgesic use was decreased. However, given the headache frequency, this effect was modest at best. Recommendations for starting tricyclic therapy include starting at the lowest dose (10 mg of amitriptyline) and waiting at least 2 weeks before increasing the dose. A maximum dose of 100 to 125 mg of amitriptyline is recommended. Benefits may continue to be seen for up to 3 months after initiating therapy. Nortriptyline and protriptyline are alternatives if amitriptyline is poorly tolerated. Side effects limit the usefulness of this medication and include dry mouth, constipation, palpitations, orthostatic hypotension, weight gain, blurry vision, and urinary retention. Confusion is also common in the elderly. In addition, these medications are associated with an increased risk of cardiac conduction abnormalities and preexisting conduction system disease precludes their use. There are less robust data supporting the use of

mirtazapine and venlafaxine; in contrast, evidence suggests that selective serotonin reuptake inhibitors are only effective for the treatment of tension-type headache in patients with depression.[11]

Anticonvulsants

There is 1 open-label study of 51 patients with tension-type headache treated with topiramate (starting at 25 mg/d increasing to 100 mg/d), which reported a decrease in headache frequency after 3 months.[12] The medication is generally well-tolerated, but there are many side effects that include paresthesia, anorexia, weight loss, fatigue, difficulty with memory and concentration, nausea, and alterations in taste. Side effects are more common at higher doses and 30% of patients on 200 mg/d had to have the drug withdrawn. It is also a teratogenic, so birth control is critical in women of reproductive age. There is very little evidence to support the use of gabapentin for the treatment of tension-type headache. The 1 study that evaluated the use of gabapentin in tension-type headache prevention was limited by the fact that 58 of the 95 patients studied had a combination of migraine and tension-type headache. High-dose gabapentin (2400 mg) was associated with a significant decrease in headache-free days, but it is unclear if the benefit was due to migraine reduction.[13]

Other pharmacologic interventions

The muscle relaxant tizanidine has been evaluated in several small studies with conflicting results. Trigger point injections with lidocaine may be promising; several small trials suggest a reduction in headache frequency and acute medication use[14] but the studies are small and more data is needed. There is little data to support the use of botulinum toxin injections. A 2012 meta-analysis evaluated onabotulinumtoxin A (botulinum toxin type A) as a preventive treatment for tension-type headache and found no statistically significant decrease in headache frequency.[15]

Behavioral therapies

Given the lack of benefit of pharmacologic interventions in the prevention of tension-type headache, behavioral treatments should be a part of every headache prevention strategy despite limited data showing efficacy. Recommended behavioral modifications include the following: regulation of sleep, exercise, and meals; cognitive-behavioral therapy; relaxation techniques; biofeedback; and stress management.[16] Studies suggest that stress and mental tension are the most frequently identified triggers for tension-type headache and developing coping skills is an important part of any behavioral therapy. The analysis of the effectiveness of behavioral interventions is limited with small studies, many of which lack of methodologic rigor. The most robust data is for biofeedback. A 2008 meta-analysis concluded that biofeedback was more effective than headache monitoring alone, and that this benefit was increased by adding relaxation therapy.[17] A combination of stress management therapy and tricyclic medication has been shown to be more effective than either therapy alone.[18] There are limited studies that support both Tai Chi[19] and yoga.[20] One randomized controlled trial of 15 weeks of Tai Chi in 47 patients with tension-type headache found a reduction in both headache impact and an increase in quality of life. There is 1 randomized controlled trial that suggests that yoga may be beneficial, but the numbers are small. It is unclear whether headache frequency and/or intensity improved or if overall coping and overall perception of wellness was enhanced.

Other therapies

Both acupuncture and physical therapies (including exercises, traction, spinal manipulation, transcutaneous electoral nerve stimulation, electromagnetic therapy, and

ultrasound therapy) have all been proposed. Several meta-analyses have tried to look at the benefit of such therapies,[21] but the trials are small and have methodologic problems. Results are heterogeneous with inconsistent benefit reported. Although there is a lack of clear benefit in well-done studies, these treatments are low risk and may offer a decrease in some patients and should be considered as alternative therapies.

MIGRAINE HEADACHE

Pathophysiology and Headache Characteristics

The traditional understanding that the pathophysiology of migraine headache is secondary to vasodilation and that the aura of migraine is cause by vasoconstriction is no longer considered accurate[22] (**Table 4**). The current understanding underlying migraine suggests that the primary insult is a neuronal aberration that leads to a

Table 4
Recommended pharmacologic treatment of migraine headaches

Medication	Dose	Caveats
Acute treatment		
Pain medications		
Acetaminophen	1000 mg	Do not underdose!
Ibuprofen	400–600 mg	
Naproxen	275–825 mg	
Diclofenac	50–100 mg	
Aspirin	1000 mg	
Triptans		
Sumatriptan	50–100 mg	Oral, nasal, SQ injection
Rizatriptan	10 mg	Oral only
Eletriptan	80 mg	Oral only
Almotriptan	12.5 mg	Oral only
Antiemetics		
Metoclopramide	10 mg PO or IV	Give with antihistamine
Prochlorperazine	10 mg IV	Give with antihistamine
Chronic treatment		
Beta-blockers		
Metoprolol	5 mg BID to 200 mg/d	
Propranolol	40 mg BID to 160 QD	
Timolol	5 mg QD to 30 mg/d	Higher doses BID
Antidepressants		
Amitriptyline	10 mg up to 50 mg	Titrate every 2–4 wk
Venlafaxine	25 up to 150 mg	
Anticonvulsants		
Topiramate	25 mg to 200 mg BID	Teratogenic
Valproic acid	500–1500 mg	Teratogenic
Calcitonin gene-related peptide antagonist		
Erenumab	70−140 mg q month	Last resort

Abbreviations: BID, 2 times per day; IM, intramuscularly; IV, intravenously; PO, by mouth; SQ, subcutaneously; QD, daily.

spreading of self-propagating depolarization that spreads across the cortex.[23] This spreading depolarization is thought to both cause the aura and to activate the trigeminovascular system, which then leads to inflammatory changes in the pain receptors of the meninges, subsequently leading to the pain of migraine headache. Vasoactive peptides are released in response to the neurogenic inflammation, which in turn then cause vasodilation and plasma protein extravasation. When vasodilation occurs it is thus thought to be a secondary phenomenon. Although the use of serotonin-augmenting agents is the mainstay in the treatment of acute migraine headaches, the role of serotonin in the initiation of migraine headaches remains uncertain. There is some evidence that baseline low levels of serotonin may enhance the activation of the trigeminovascular nociceptive pain pathways owing to a deficit in the serotonin-mediated descending pain inhibitory system.[24,25] There is also a complex genetic component underlying the etiology of migraines. The risk of migraine headaches is 3 times greater in relatives of migraineurs than the population at large.[26] No specific Mendelian pattern of inheritance has been identified. It is thought that the familial basis of migraine headaches is due to a different genetic threshold between excitatory and inhibitory channels in the nervous system that makes patients more susceptible to a migraine attack.

Migraine is a recurrent headache disorder that classically has 4 phases[27,28]. (1) Prodrome (prevalence 77%): These symptoms may occur 24–48 hours before the onset of headache and consist of a wide variety of symptoms including depression, euphoria, irritability, and food cravings. (2) Aura (prevalence 25%): A typical migraine aura is characterized by the gradual development of either positive and negative neurologic symptoms lasting no longer than 1 hour and having complete resolution. Positive symptoms are classically visual (bright lines, shapes, objects) or auditory (tinnitus, noises, music) but can also be somatosensory or motor (paresthesia, jerking). Negative symptoms include loss of vision, hearing, feeling, or body movement. Patients may also experience auras without headache, known as a migraine equivalent. Negative symptoms or auras without headache are often confused with transient ischemic attacks. (3) Migraine headache: The details of the headache are the most important diagnostic consideration in approaching a patient with a headache syndrome. Classically, migraine headaches are described as unilateral, throbbing, and moderate to severe in intensity. Associated symptoms include photophobia, phonophobia, and nausea and vomiting. Symptoms increase over a course of 1 to 2 hours and can last 4 hours to several days. Commonly attacks with resolve with sleep. (4) Postdrome: After resolution there may be a postdromal phase characterized by pain owing to sudden head movement in the area of the previous headache. Patients may feel either exhausted or have euphoria.

A careful history and physical examination is the most important diagnostic tool for the diagnosis of migraine headaches. Careful attention to the timing, location, nature, and associated features of the headache is critical. The neurologic examination should be nonfocal. Yet, despite clear guidelines, many migraine headaches are misdiagnosed. For example, a significant number of migraine headaches are accompanied by nasal congestion and are misdiagnosed as sinus headaches.[26] Given the challenges in diagnosis, a number of diagnostic questionnaires have been developed and validated. The easiest to remember is the ID Migraine.[29] Patients with 2 or more headaches in the previous 3 months were asked the following: (1) *P*hotophobia: Did light bother you? (2) *I*ncapacity: Did your headaches limit your ability to work, study, or do what you needed to do for as least 1 day? (3) *N*ausea: Did you feel nauseated or sick to your stomach? This diagnostic screen is considered positive if 2 of the questions are answered yes. In a systematic review of more than 500 studies the

pooled sensitivity of this 3-question tool was 0.84 and the pooled specificity was 0.76.[30] The mnemonic PIN (Pain, Incapacity, Nausea) is an easy way to remember the questions used in this screen. Another commonly used screening tool is the POUND mnemonic asking 5 yes or no questions: pulsatile, onset 4 to 72 hours, unilateral, nausea/vomiting, and disabling. If 3 questions are answered yes, the likelihood ratio for a migraine is 3.5; if 4 questions are answered yes, the likelihood ratio is 24. Interestingly adding associated symptoms of photophobia/phonophobia did not enhance performance criteria.[31] An even easier screen is asking if the headache was disabling. In 1 study, this simple question identified migraine in 136 or 146 patients (93%) with episodic migraine headaches.[32]

Treatment of Acute Migraine Headache

Treating migraine headaches has 2 components: treating the acute headache (abortive therapy) and preventing the onset of later headaches (prophylactic therapy). This section reviews commonly used measures for the acute treatment of migraine. Several observations guide therapeutic recommendations: (1) abortive therapies are more effective the earlier they are administered in the course of the headache, (2) a single large dose of a medication is more effective than repeated smaller doses of medications, and (3) many oral medications are of limited effectiveness because migraine induces gastric stasis, which leads to poor absorption. Treatment options consist primarily of simple analgesics, migraine-specific agents, and antiemetics.

Simple analgesics

Both acetaminophen and NSAIDs including aspirin have been show to be efficacious. A randomized, placebo-based trial of acetaminophen at a dose of 1000 mg in patients with self-reported migraines demonstrated relief in both pain and functional disability.[33] Many NSAIDs have reported efficacy in acute migraine treatment and include aspirin (900–1000 mg), ibuprofen (400–600 mg), naproxen (275–825 mg), and diclofenac (50–100 mg) among others. This suggests that all NSAIDs may be effective in treating migraine patients both with and without aura if appropriately high doses are used. One of the most common mistakes is the underdosing the initial dose of NSAIDs. Head-to-head comparisons are limited, so if 1 medication does not work then another medication should be tried. Remember also that acetaminophen can be used in combination with NSAIDs. The over-the-counter combination of acetaminophen, aspirin, and caffeine has also been shown to be effective.[34] Parenteral ketorolac (30 mg intravenously [IV] or 60 mg intramuscularly [IM]) can be considered in patient with significant nausea or vomiting.

Triptans

Triptans are 1 b/1d serotonin agonists and are effective migraine-specific treatments to stop acute migraine headaches.[35] Two available preparations have both oral and nonoral administrations: sumatriptan (oral, nasal spray, or subcutaneous injection) and zolmitriptan (oral and nasal). The remaining agents include naratriptan, rizatriptan, almotriptan, eletriptan, and frovatriptan and are only available for oral use. There is a paucity of trials comparing the triptans head to head, so the choice of an initial agent may be influenced by availability and desired route of administration. A meta-analysis of the oral agents suggested that the most effective agents were rizatriptan (10 mg dose), eletriptan (80 mg dose), and almotriptan (12.5 mg dose).[36] Naratriptan and frovatriptan were found to be slower in onset and less efficacious overall. Dosing is important and these medications are often underdosed. For example, oral sumatriptan is given at a starting dose of 50 to 100 mg, which may be repeated once after 2 hours

(maximum dose in 24 hours is 200 mg). The 100-mg dose of sumatriptan is more effective but has more side effects. Subcutaneous sumatriptan dosing (6 mg) has a more rapid onset and is more effective than oral sumatriptan, but has more adverse effects including injection site reactions, chest heaviness, flushing, dizziness, and paresthesia. Because head-to-head trials are lacking, the choice of triptan can be individualized; delivery routes may help to guide the decision making. Early administration of the medication and adequate dosing are the factors most likely to predict success. Concern has been raised about triptan use and subsequent cardiovascular events, but a systematic review of observational studies found no association,[37] although these medications were prescribed to lower risk patients. It is also recommended that triptans not be prescribed in patients with hemiplegic migraines, basilar migraines, a history of ischemic strokes or myocardial infarction, angina, uncontrolled hypertension, or pregnancy.[38] A final important note is that, although the combination of a triptan with a serotonin reuptake inhibitor has raised concerns about the possibility of precipitating serotonin syndrome, this risk is so low to nonexistent[39] that most headache experts recommend using triptans in combination with serotonin reuptake inhibitors when indicated.

Antiemetics

Metoclopramide (IV), chlorpromazine (IM), and prochlorperazine (IM) can all be used both as monotherapy for acute migraine headaches or as adjunctive therapy with NSAIDs. Metoclopramide seems to be slightly less effective than either of the other agents but is better tolerated with less risk of QT prolongation than the other medications. Intravenous diphenhydramine (12.5–25.0 mg every hour for 2 hours) is commonly given with these medications to prevent the acute dystonic reactions, which are common and distressing with these medications. In contrast to IV or IM preparations, oral antiemetics are less likely to be effective. Ondansetron for use in acute migraine treatment is less studied, and has a high incidence of headache as a side effect.

Other agents

Less commonly used agents that are poorly defined in their place in the treatment of migraines include lasmiditan (selective serotonin IF receptor agonist), calcitonin-gene related peptide antagonists, and ergotamines. Parenteral treatment with dexamethasone in addition to other abortive therapies has been shown to reduce the rate of early migraine recurrence after initial treatment[40] and may be considered for patients requiring emergency room treatment. Finally, just a reminder that opioids and barbiturates should never be used for the acute treatment of migraines because of limited efficacy, high risk of rebound headaches, and a risk of developing dependence.

Summary

The severity of the attack along with the presence of nausea or vomiting should guide the initial therapy. For milder attacks with no gastrointestinal symptoms, simple analgesics such as acetaminophen or NSAIDs may suffice. They are preferred both because they are cost effective and because they are less likely to cause side effects than the migraine-specific agents. In addition, antiemetics should be considered if there is nausea or vomiting. For moderate attacks with no gastrointestinal symptoms, oral migraine specific agents are first line with or without NSAIDs. The timing and dosage of the initial medications chosen are critical for effective intervention.

Prevention of Migraine Headaches

Prophylactic therapy for migraineurs is recommended for patients with frequent and/or disabling migraines that do not respond adequately to abortive therapy. More than 4 headaches per month or headaches that last longer than 12 hours are considered indications for preventive therapy.[41] The goals of therapy are to decrease the frequency and severity of the attacks and to improve responsiveness to acute therapy to decrease the associated disability and to help prevent progression to chronic migraines. There are 2 mainstays to preventive therapy. The first is to identify and modify any and all migraine triggers whenever possible; the second is pharmacologic therapy for the prevention of migraines.

In 1 retrospective study, 75% of patients reported at least 1 migraine trigger.[42] Common migraine triggers include emotional stress (80%), estrogen-related changes in women (65%), skipping meals (57%), weather changes (53%), and sleep disturbances (50%). Other common triggers include alcohol (especially wine) and specific foods (especially those including nitrates and aspartame). Asking patients to keep a headache diary to identify individual triggers and then providing counseling and education about trigger factor modification is a critical and often overlooked management strategy for preventing migraines. Avoiding overuse of acute headache therapies such as analgesics and triptans to prevent rebound headaches is also a key component of preventive therapy.

With regard to pharmacologic therapy, 4 classes of drugs have been shown to be effective in the prevention of migraines: beta-blockers, antidepressants, anticonvulsants, and calcitonin gene-related peptide antagonists. General principles of preventive therapy, regardless of the medication chosen, include starting at a low dose increasing gradually until benefit, side effect, or maximum dosage is achieved. Studies have suggested that the benefit of any drug or dosage is unlikely to be noted before 4 weeks and may continue to increase for up to 3 to 6 months for any given medication. Patient education and counseling regarding the extended time needed to assess the benefit of any preventive therapy is critical to avoid patient discontinuation of medications before an effective therapeutic trial has been achieved. Initial treatment should be individualized with attention to comorbid disorders to help with choice of agent; in general, calcitonin gene-related peptide antagonists are not considered to be first-line agents. Approximate 50% to 75% of patients given any of these 3 classes of drugs with have a 50% decrease in headaches.[43]

Beta-blockers

Data from randomized, controlled trials has established the efficacy of metoprolol, propranolol, and timolol for migraine prevention.[44] Lesser evidence suggests but does not establish the efficacy of calcium channel blockers, angiotensin-converting enzyme inhibitors, and angiotensin receptor blockers. Recommended doses for commonly used beta-blockers include the following options: propranolol twice daily starting at a daily dose of 40 mg, with a dose range of 40 to 160 mg/d; metoprolol twice daily starting at a daily dose of 5 mg, with a dose range of 50 to 200 mg/d; and timolol 5 mg starting once daily, with a dose range of 10 to 30 mg/d in 2 divided doses. It can take several weeks for headache improvement to manifest and each dose should be maintained for 3 months before either titrating the medication up or deciding that the medication has failed. There are many comorbid conditions that limit the use of beta-blockers, including bradycardia, hypotension, peripheral vascular disease, depression, and reactive airways disease.

Antidepressants

A 2012 guideline from the American Academy of Neurology concluded that amitriptyline and venlafaxine were effective for migraine prevention.[44] Amitriptyline is started at a dose of 10 mg at bedtime with a titration to a daily dose of up to 50 mg at bedtime. Although nortriptyline, doxepin, and protriptyline are commonly used for migraine prevention, only amitriptyline has data supporting its use. Tricyclic side effects were discussed elsewhere in this article.

Anticonvulsants

Both topiramate and valproate have been established to be more effective for migraine prevention than placebo.[44] Gabapentin has been used, but data are lacking. The starting dose of topiramate is 25 mg/d with a slow titration by 25 mg weekly to a maximum dose of 200 mg twice daily (or the highest tolerated dose). Randomized trials showed that a minimum of 100 mg of topiramate daily was required for symptoms reduction. About 50% of patients demonstrated a 50% decrease in headache frequency. Valproate is also effective at doses ranging from 500 to 1500 mg/d. Higher doses are associated with more side effects that include nausea, lethargy, tremor, dizziness, weight gain, and hair loss. It is also teratogenic, so again birth control is critical.

Calcitonin gene-related peptide antagonists

Erenumab is a human monoclonal antibody that binds to and inhibits the calcitonin gene-related peptide receptor. The medication is modestly effective to prevent migraines; in a study of patients who had failed other medications randomized to 140 mg subcutaneously or placebo, 30% had a 50% or greater decrease in headache days.[45] The starting dose is 70 mg subcutaneously once monthly, which can be increased to 140 mg monthly if needed. The most common side effect is site injection reactions.

Other agents

A host of other agents have been used for migraine prevention. The 2012 American Association of Neurology review[44] concluded that feverfew, magnesium riboflavin, and certain NSAIDS (including ibuprofen and naproxen) may be effective. In addition, several randomized placebo-controlled trials have concluded that botulinum toxic type A injection therapy is effective for the treatment of chronic migraine only ($\geq$15 headache days per month).

SUMMARY

Headaches are common in primary care practices with 90% of primary headaches being either tension-type headache or migraine headache. The diagnosis is made by a careful history and physical with particular attention to the identification of red flag signs and symptoms. Imaging is generally not warranted unless concerning findings are identified. Several general principles underlie the acute treatment of either type of headache with early initiation of therapy and adequate dosing at first dose. Careful attention to avoid too frequent administration of acute therapy is important to minimize medication overuse headaches. Opioids should always be avoided. Preventive treatment is indicated for frequent headaches of either type, but the data are better to support the prevention of migraine headache. Successful treatment requires the initiation of low-dose medication with careful titration and monitoring of headache frequency over months. Finally, behavioral strategies are important in both types of headache and should be a part of any comprehensive headache management plan.

CLINICS CARE POINTS

- Approximately 90% of all primary headache syndromes are tension-type headache or migraine headache; chronic sinus problems, hypertension, and eye strain are commonly diagnosed as causes of headaches. Headaches may worsen with these conditions, but they are rarely the primary cause. Many of these are migraine headaches.
- Both tension-type headache and migraine headache are diagnosed by history and physical diagnosis; in the absence of red flag signs and symptoms, imaging is rarely indicated.
- Abortive therapies for both tension-type headache and migraine headache are more effective the earlier they are administered in the course of the headache and a single large dose of a medication is more effective than repeated smaller doses of medications.
- Avoiding medication overuse headache is a crucial goal of therapy and requires extensive patient education and counseling; episodic treatment medications should be limited to 9 treatment days per month with NSAIDs being limited to 15 or fewer days per month.
- Tricyclic antidepressants are effective in preventing both tension-type headache and migraine headache and in the absence of contraindications should be considered first line. Start low and titrate slow realizing benefit can take up to 3 months.
- Behavioral strategies should be a part of any headache management plan.

DISCLOSURE

The authors have nothing to disclose.

REFERENCES

1. Finley CR, Chan DS, Garrison S, et al. What re the most common conditions in primary care? Can Fam Physician 2018;64:832–40.
2. GBD 2016 Headache Collaborators. Global, regional and national burden of migraine and tension-type headache, 1990-2016: a systematic analysis for the Global Burden of Disease Study 016. Lancet Neurol 2017;17(11):954–76.
3. Do TP, Remmers A, Schytz HW, et al. Red and orange flags for secondary headaches in clinical practice: SNNOOP10 list. Neurology 2019;92:134.
4. Martelli P, Birbeck GL, Katsarava Z, et al. The Global Burden of Disease survey 2010: lifting the burden and thinking outside-the-box on headache disorders. J Headache Pain 2013;14:13.
5. Schartz BS, Stewart WF, Simon D, et al. Epidemiology of tension-type headache. JAMA 1998;279:381.
6. Jensen R. Peripheral and central mechanism in tension-type headache: an update. Cephalalgia 2003;23(Supple 1):49.
7. Rasmussen BK. Epidemiology of headache. Cephalalgia 1995;15:45.
8. Moore Ra, Derry S, Wiffen PJ, et al. Evidence for the efficacy of acute treatment of episodic tension-type headache: methodological critique of randomized trials for oral treatments. Pain 2014;155:2220.
9. Verhagen AP, Damen L, Berger MY, et al. Lack of benefit for prophylactic drugs of tension-type headache in adults: a systematic review. Fam Pract 2010;27:151.
10. Jacson JL, Mancuso JM, Nickoloff S, et al. Tricyclic and tetracyclic antidepressants for the prevention of frequent episodic or chronic tension-type headaches

in adults: a systematic review and meta-analysis. J Gen Intern Med 2017;32:1351.
11. Lenaerts ME. Pharmacoprophylaxis of tension-type headache. Curr Pain Headache Rep 2005;9:442.
12. Lampl C, Marecek S, May A, et al. A prospective, open-label, long-term study of the efficacy and tolerability of topiramate in the prophylaxis of chronic tension-type headache. Cephalalgia 2006;26:1203.
13. Gobel H, Hamouz V, Hansen C, et al. Chronic tension type headaches: amitriptyline reduces clinical headache-duration and experimental pain sensitivity but does not alter pericranial muscle activity readings. Pain 1994;59:241.
14. Karadas O, Gul HL, Inan LE. Lidocaine injection of pericranial myofascial trigger points in the treatment of frequent episodic tension-type headache. J Headache Pain 2013;14:44.
15. Jackson JL, Kuriyama A, Hayashino Y. Botulinum toxin A for prophylactic treatment of migraine and tension headaches in adults: a meta-analysis. JAMA 2012;307:1736.
16. Penzien DB, Rains JC, Lipchik GL, et al. Behavioral interventions for tension-type headache: overview of current therapies and recommendations for a self-management model for chronic headache. Curr Pain Headache Rep 2004;8:489.
17. Nestoriuc Y, Rief W, Martin A. Meta-analysis of biofeedback for tension-type headache: efficacy, specificity, and treatment moderators. J Consult Clin Psychol 2008;76:379.
18. Holrod KA, O'Donnell FJ, Stensland M, et al. Management of chronic tension type headache with tricyclic antidepressant medication, stress management therapy, and their combination: a randomized controlled trial. JAMA 2001;285:2208.
19. Abbott RB, Hui K, Hayes R, et al. A randomized trial of Tai Chi for tension headaches. Evid Based Complement Alternat Med 2007;4(1):107.
20. Kim S. Effects of yoga exercises for headaches: a systematic review of randomized controlled trials. J Phys Ther Sci 2015;27:2377.
21. Chaibi A, Russell MB. Manual therapies for primary chronic headaches: a systematic review of randomized controlled trials. J Headache Pain 2014;15:67.
22. Charles A. Vasodilation out of the picture as a cause of migraine headache. Lancet Neurol 2013;12:419.
23. Cutrer FM. Pathophysiology of migraine. Semin Neurol 2006;26:171.
24. Hamel E. Serotonin and migraine: biology and clinical implications. Cephalalgia 2007;27:1293.
25. Panconesi A. Serotonin and migraine: a reconsideration of the central theory. J Headache Pain 2008;9:267.
26. Lance JVV, Anthony M. Some clinical aspects of migraine. A prospective survey of 500 patients. Arch Neurol 1966;15:356.
27. Charles A. The evolution of a migraine attack—a review of recent evidence. Headache 2013;53:413.
28. Barbanti P, Fabgrini G, Pesare M, et al. Unilateral cranial autonomic symptoms in migraine. Cephalalgia 2002;22:256.
29. Rapoport AM, Bigal ME. ID-migraine. Neurol Sci 2004;25 Supple 3:S258.
30. Cousins G, Hijazze S, Van de Laar FA, et al. Diagnostic accuracy of the ID Migraine: a systematic review and meta-analysis. Headache 2011;51.
31. Niere K. The presence of four simple history features can diagnosis migraine accurately. Australian J of Physiology 2006;52(4):304.
32. Maizels M, Burchette R. Rapid and sensitive paradigm for screening patients with headache in primary care settings. Headache 2003;43:441.

33. Derry S, Moore RA. Paracetamol (acetaminophen) with or without an antiemetic for acute migraine headaches in adults. Cochrane Database Syst Rev 2013;(4):CD008040.
34. Lipton RB, Steward WF, Ryan RE Jr, et al. Efficacy and safety of acetaminophen, aspirin, and caffeine in alleviating migraine headache pain; three double blind, randomized, placebo-controlled trials. Arch Neurol 1998;55:210.
35. Tfelt-Hansen P, Knight YE, Goadsby PJ. Triptans in migraine; a comparative review of pharmacology, pharmacokinetics and efficacy. Drugs 2000;60:1259.
36. Ferrari MD, Roon KL, Lipton RB, et al. Oral triptans (serotonin 5-HT (1B/1D) agonists) in acute migraine treatment: a meta-analysis of 53 trials. Lancet 2001; 358:1668.
37. Roberto G, Raschi E, Piccinni C, et al. Adverse cardiovascular events associated with triptans and ergotamines for treatment of migraine: systematic review of observational studies. Cephalalgia 2015;35:118.
38. Jamieson DG. The safety of triptans in the treatment of patients with migraine. Am J Med 2002;112:135.
39. Evans RW. Concomitant triptan and SSRI or SNRI use: what is the risk for serotonin syndrome? Headache 2008;42:1692.
40. Colman I, Friedman BW, Brown MD, et al. Parenteral dexamethasone for acute severe migraine headaches: meta-analysis of randomized controlled trials for preventing recurrence. BMJ 2008;336:1359.
41. MacGregor EA. In the clinic. Migraine. Ann Intern Med 2013;159:ITC5.
42. Kelman L. The triggers or precipitants of the acute migraine attack. Cephalalgia 2007;27:394.
43. Goadsby PJ, Lipton RB, Ferrari MD. Migraine—current understanding and treatment. N Engl J Med 2002;346:257.
44. Silberstein SD, Holland S, Freitag F, et al. Evidence-based guideline update: pharmacologic treatment for episodic migraine prevention in adults: report of the Quality Standards Subcommittee of the American Academy of Neurology and the American Headache Society. Neurology 2012;78:1337.
45. Reuter U, Goadsby PJ, Lanteri-Minet M, et al. Efficacy and tolerability of erenumab in patients with episodic migraine in whom two-to-four previous preventive treatments were unsuccessful: a randomized, double-blind, placebo-controlled phase 3b study. Lancet 2018;392:2280.