CLINICAL REVIEW

Headache Treatment Options

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Family medicine physicians often see headache as the chief complaint when meeting patients within their practice. The goal is to try different treatment modalities without having to send the patient to a specialist. Headaches affect different individuals during their lifetime. Before any treatment begins, it is best that one rules out possible causes of the headache, for example, drug interactions or structural cerebrum conditions. Nonpharmacological treatment is recommended first before attempting a stepwise approach to cost-effective pharmacological treatment options. Pharmacological treatment options should include preventive and on-demand options. A family physician has all the resources to assist patients with different types of headaches. (J Am Board Fam Med 2024;37:737–744.)

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Prevalence

Headache disorders affect approximately 90% of individuals during their lifetime.[1] The Center for Disease Control (CDC) estimated in the ambulatory setting headache only visits accounted for 0.1% whereas migraines accounted for 0.4%.[2] There are 2 major subsets of headache disorders: primary and secondary headaches. Primary headache disorders are not caused by an underlying medical condition and are categorized into 3 different types: migraine, tension-type, and cluster headaches. Of these, the most common are tension-type (38%) and migraine (12%). Secondary headaches are caused by an underlying medical condition.[3]

Pathophysiology

Multiple head and neck structures are sensitive to pain (meninges, intracranial and cervical arteries, and cranial nerves), resulting in head or neck discomfort caused by structural pressure, traction, or inflammation. Headaches involve the release of vasoactive inflammatory chemicals such as pituitary adenylate cyclase-activating peptide and calcitonin gene-related peptide.[3]

Tension-Type Headaches

Tension-type headaches are the most common headache with an occurrence slightly higher in women. The diagnosis of tension-type headaches relies solely on clinical presentation and symptoms. Tension-type headaches are characterized by bilateral, nonpulsatile pain with mild to moderate intensity typically described as a tightening or pressing sensation with a duration from 30 minutes to 7 days. Patients may describe the headache feeling like a band is surround their head. These headaches are not accompanied by nausea or vomiting but may have either phonophobia or photophobia. Twenty percent of patients may complain of mild anorexia with tension-type headaches. Unlike migraine headaches, tension-type headaches are not worsened by physical activity. On physical examination patients may have tenderness of the paracervical muscles. Tension-type headaches often have precipitating factors such as reduced sleep, increased stress, or missed meals. There are 3 subtypes of tension headaches: infrequent episodic (less than

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1 headache day per month), frequent (up to 14 headache days per month), and chronic (greater than 15 headache days per month).[4] Although tension-type headache is the most prevalent headache type, its diagnosis is based mostly on not having the features found in other headache types such as unilaterality, aggravated by physical activity, nausea, and vomiting. If a patient presents with an atypical history or clinical presentation, further workup is indicated with either magnetic resonance imaging or computed tomography of the head.[5]

Cluster Headaches

Cluster headaches are an uncommon debilitating headache disorder (prevalence 0.12%) characterized by severely intense and painful unilateral headaches, typically located in the supraorbital, retroorbital, or temporal region.[6] Associated diagnostic symptoms include ipsilateral lacrimation, conjunctival injection, nasal, rhinorrhea, miosis, ptosis, or facial swelling. Cluster headaches occur at any age, but the typical onset is between 20 and 40 years of age with a male predominance.[6,7] Eighty percent of cluster headaches are the episodic subtype, where the attacks occur during a period of weeks to months with pain-free remission greater than 3 months. With the chronic subtype, attacks occur throughout the year without remission longer than 3 months.[6]

Migraine Headaches

Migraine headaches are the most disabling of the primary headache disorders and affect women 3 times more than men.[3] Migraine headaches are distinguished from other headache types by the following features: unilateral; pulsating quality; lasting 4 to 72 hours; aggravated by physical activity; and associated with phonophobia, photophobia, nausea, or vomiting.[8]

Medication Overuse Headache

Medication overuse headache (MOH) is one of the most common chronic headache disorders with a worldwide prevalence of 1 to 2%.[9] MOH is a chronic daily headache and a secondary disorder in which acute medications are used excessively that cause headache in headache-prone individuals. Aspirin, acetaminophen, and NSAIDs may contribute to rebound headaches especially when the patient exceeds the recommended daily dosages. Over the counter pain relievers that contain a combination of caffeine, aspirin, and acetaminophen or butalbital commonly cause medication overuse as well.[10] All these medications are high risk for MOH if taken for 10 or more days per month. Triptans and ergotamines also have a moderate risk of causing MOH when used for 10 or more days per month. Opioids cause MOH when used 1 or more days per month. Caffeine intake of more than 300 mg per day increases the risk of MOH. Patients must be educated about the risk of rebound headaches with medication overuse. Breaking a MOH headache cycle may take up to 6 months.[11]

Headache Triggers

Headaches can be triggered by food, stress, hormones (particularly for migraine with aura combined oral contraceptive pills (OCPs) are contraindicated), environmental factors, and change in activity level. A regular sleep cycle should be all week long, including the weekends. Eating regular meals 3 times a day can help prevent low blood sugars. In addition, foods that can cause a spike in blood glucose, which can trigger a headache. Caffeine, a stimulant, can induce headaches when the caffeine levels have a rapid fluctuation in the body. Alcohol, citrus fruits, cured meats, chocolate, and salty food and monosodium glutamate can also be triggers for headaches. Having a patient keep a headache diary will help identify triggers, such as certain food, weather changes, and hormone changes. This will help guide therapy for the patient and to prevent avoidance of the triggers. Phone apps are available to help identify triggers, manage headache pain, and connect with other users with the same condition. Data suggests that tracking in an electronic diary allows users to capture more real-time data than tracking in article diaries.[3,12]

Non-Pharmacologic Treatments

Behavioral Therapies

The biopsychosocial model of chronic headache is a multidirectional relationship between the biologic, psychological, and social or environmental factors. This poses a challenge, as well as an opportunity for family physicians caring for these patients.[13] Although numerous processes can affect headache and disability it is only by recognizing all aspects of the patient- their biological, psychological, and social circumstances - that we can affect better treatment recommendations.

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Patient beliefs about pain can influence how a patient reacts to chronic headache.[14] Pain catastrophizing can be associated with hopelessness, rumination, and migraine-related disability. Individuals with chronic headache pain are often found to have concomitant increased risk for depression and anxiety due to the patient being unable to control their symptoms and headache outcomes.[15] Inadequate coping with environmental stressors, for example, career, finances, or relationships can contribute to increased anxiety that is in turn linked to increased headache intensity and more frequent headaches.

In addition, there is also some current standardized neuropsychological testing research demonstrating that migraine attacks can be associated with poor cognitive performance.[16] Despite these findings the cognitive difficulties are not noted during the headache-free period. Tension-type headache was also associated with reversible cognitive impairment as were cluster headaches. There is no current evidence that patients with chronic headaches or migraines were at increased risk of overall cognitive decline. Regardless, with regards to patients with chronic headaches and cognitive changes more studies are required to determine the impact of medications and the confounding associated psychiatric disorders.[16]

In general, family physicians need to be aware that patients with chronic migraines may experience poor sleep quality, increased anxiety sensitivity, and other psychiatric symptoms. However, whether migraine or chronic headaches precedes psychiatric changes or that these underlying psychiatric conditions are exacerbated or triggered by the headaches is difficult to tease out.[14] Because these conditions can be tightly intertwined and overall decrease patients' well- being this may increase their demand for medications in treating pain.

Several behavioral therapies have grade A evidence in headache treatment. Behavioral therapies can be useful for patients who cannot or prefer not to use pharmacologic management or who have identified specific psychological or behavioral factors that may precipitate or exacerbate headaches (eg, poor stress coping skills, untreated psychological disorders). Relaxation and biofeedback training help individuals learn to recognize and decrease sympathetic arousal. Cognitive behavioral therapy (CBT) or stress management training targets unhelpful thoughts and behaviors and seeks to enhance a patient's response to stressors. Promotion of healthy lifestyle behaviors (eg, avoiding migraine triggers, practicing mindful relaxation) may be incorporated into CBT. CBT also can be used to treat comorbid psychological disorders (eg, depression, anxiety, insomnia). Finally, there is emerging evidence for the use of mindfulness-based therapies (eg, mindfulness-based stress reduction).[17,18]

Family physicians can mitigate the difficulty of using behavioral strategies by integrating them with ongoing pharmacologic care and/or connecting the patient with a behavioral specialist. In addition, family physicians can help the patient recognize and manage triggers, encourage patients with chronic headaches to take their medications as prescribed for maximum efficacy, and assist the patient with normalizing their need for managing stress.[15] Using a self-management model whereby the patient and physician partner on goals for pain management and functioning, treatment benefits can be maximized by allowing the patient a more active role in managing their chronic headaches as has been used successfully in other chronic disease management.[13]

Osteopathic Manipulative Treatment

Manipulative Treatments (OMT) may be a beneficial adjunct in headache treatment to decrease intensity and frequency. Particularly effective may be cranial OMT for migraine heachache.[19] It uses the primary respiratory mechanism, which is synchronous with the cranial rhythmic impulse, a 2-phase rhythmic cycle that represents a dynamic metabolic exchange with each stage of the body. This cycle is indicated as loops between 7 and 14 per minute. Cranial OMT is utilized to affect the movements of the skull bones, sacrum, dural membranes, and cerebrospinal fluid in the central nervous system.[20] Other evidence based OMT techniques consist of myofascial release, a type of soft tissue therapy where an examiner uses manual force to lengthen shortened fascial tissue.[21] Myofascial release OMT often is combined with trigger point injection and stretching. Some studies adjunctively included cranial OMT whereas most studies compared cranial OMT to myofascial OMT and trigger point injection with stretching. Fascial mobilization increases energy use in segments as impacted by the mechanical changes induced by cranial or myofascial OMT.[22] These treatments help to reduce the spasm in the layers as they extend facially to

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dissolve adhesions and to increase the range of motion.

Mild adverse effects of OMT can consist of muscle stiffness and soreness and can occur in up to 50% of people who undergo this therapy.[23] Serious events secondary to OMT are rare, and in the case of treatments for headache or cervicogenic pain would consist of vertebrobasilar injury.[23] Most of the articles that have been reviewed for the use of OMT in migraine headaches enrolled a low number of patients, were usually not randomized controlled trials, and demonstrated a high risk of bias. In many studies, the impact of the migraine headache was assessed with the Headache Impact Test (HIT-6). Migraine headache disability was assessed by the Migraine Disability Assessment Score (MIDAS) along with quality of life evaluated by the Short Form Health Survey (SF-36).[24] Overall, the findings of these studies determined that OMT may be as effective as amitriptyline and can reduce the frequency and intensity of headache pain. OMT also demonstrated a significant amount of change in the HIT-6 and MIDAS scores by 11% in conjunction with usual care, sham therapy, or muscle relaxation techniques along with 21 fewer days of migraines per month.[25]

Overall, given the small risk of serious adverse events, OMT can be a valid adjunctive, and possibly an alternative preventive therapy for headaches. However, additional high quality and adequately powered studies will be needed before definitively recommending this as sole treatment for migraine headaches.[23]

Acupuncture

The most recent Cochrane Systematic Review[26] of acupuncture for migraine headaches found acupuncture to be a useful alternative treatment reducing frequency and duration of chronic and episodic migraines. There is moderate evidence for acupuncture being at least noninferior to pharmacologic therapy; one study proposes superiority of acupuncture over propranolol based on an indirect comparison analysis.[27] Acupuncture is a safe, helpful, and often readily available option for patients who have not responded to (or complied with) pharmacotherapy. Acupuncture therapy is primarily effective after 6 to 8 sessions; the most effective timing and frequency of visits has not been determined.[28–30]

Neuromodulators

Neuromodulators are an option for those who have failed previous treatments, do not want to take medications, or are pregnant. The neuromodulators may be used for acute and/or preventative treatment. Several types of neuromodulators have been approved by the US Food and Drug Administration (FDA); some are available over the counter.[31]

Transcutaneous electric nerve stimulation (TENS) is a therapy that uses low voltage electric current to provide pain relief. A TENS unit consists of a battery-powered device that delivers electric impulses through electrodes placed on the surface of the skin. The electrodes are placed at or near nerves where the pain is located or at trigger points. Currently there are no FDA approved TENS units approved for treatment of migraines; however, one study of TENS use in the emergency department setting for acute migraine indicated effective pain reduction in the first 20 minutes after treatment with decreased effectiveness after that time.[32]

An external trigeminal nerve stimulation (e-TNS) delivers a specific level of micro impulses by using a device that is placed on the head when an attack is coming on or during a migraine to decrease pain. This type of device is available both over the counter and by prescription for ages 18 and up. Evidence suggests that users have fewer migraine attacks, fewer headache days per month, and need less migraine medications.[31] In 2014, the FDA approved Cefaly Dual®. It uses reusable electrodes that are adhered to magnets. They are placed on the forehead once daily for 20 minutes for prevention or 60 minutes for a migraine attack. Relivion® is another noninvasive e-TNS device that delivers pulses to stimulate the occipital and trigeminal nerves. The 2 sensors sit on either side of the nose and are to be put on at the onset of a migraine. The amount and type of modulation are controlled via application on a paired smartphone. This device requires a prescription from a physician. Based on a randomized clinical trial, 42% of users reported pain freedom and 67% reported freedom of bothersome symptoms (nausea, light sensitivity, or sound sensitivity) at 2 hours.[33]

Noninvasive vagus nerve stimulation (nVNS) is another approach to relieve migraine. A systematic review and meta-analysis found that nVNS was effective in achieving a pain-free status within 30 minutes, pain-relief status within 30 minutes and at 1 hour, a

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reduction in abortive medication use, and pain-free status in more than 50% of treated attacks compared with sham-device treatment.[33] GammaCore Saphire® is a nVNS that was approved for adults by the FDA in 2015; in 2021, the FDA expanded the use for acute and preventative migraine treatment for those ages 12 to 17. It is a rechargeable handheld device used to treat cluster headaches and migraines. Patients apply conductive gel to the 2 stimulators and then hold the device against the side of their neck below the jaw line. It delivers small electric pulses to the vagus nerve at 2-minute increments. The patient controls the intensity of the pulses.[35]

Remote Electric Neuromodulation (REN) is used to stimulate peripheral nerves in the upper arm. It activates pain control centers in the brainstem which blocks the pain signaling in migraines. 74% of people who have REN experienced pain relief by 2 hours with minimal side effects reported.[36] Nerivio® is FDA- approved REN wireless remote armband for ages 12 and older for the acute treatment of migraine with and without aura. The device is controlled by an app and features a migraine diary to track sessions and migraine attacks. Nerivio is available by prescription only; each device delivers twelve 45-minute treatments.[37]

Single-pulse transcranial magnetic stimulation (sTMS) delivers short magnetic pulses that target the layers of the scalp, skull, meninges, and superficial layers of the cortex. One study showed that sTMS reduced migraine symptoms and the need for rescue medications. SAVI Dual® is FDA- approved battery powered handheld device that delivers a magnetic pulse to treat and prevent migraine attack in ages 12 and up; it has a cloud-based diary that can help improve migraine management.[38]

These different neuromodulators are effective and well tolerated; however, they can be expensive and often are not covered by insurance. People with epilepsy or with pacemakers should avoid this technology.[38]

Pharmacologic Treatment

When considering pharmacological treatment options, setting realistic goals is important. Headache treatments typically are divided into acute versus preventative strategies. Acute treatment goals are rapid (within 2 hours), offer consistent freedom from pain and associated symptoms, restoration in functioning, reduced need for repeat medication dosing or rescue medications, and include minimal to no adverse effects from the medication. Preventative treatments aim to reduce headache frequency, severity, duration, and disability, as well as improve responsiveness to and avoid escalation in the use of acute treatments.[30] The standard of therapy for migraine prevention is a 50% reduction in monthly migraine days or headache intensity.[39] Effective treatment should result in a reduction in headache-related disability and psychological distress and improved function in important areas of life and health related quality of life.[1] See Tables 1 and 2 for a summary of acute and preventative pharmacologic treatments for migraine.

A consensus statement integrating treatments into practice calls for a stepwise approach that starts with nonsteroidal anti-inflammatory drugs for mild to moderate headaches.[30] These oral agents include aspirin, diclofenac, ibuprofen, and naproxen. Acetaminophen is a nonsteroidal analgesic. Some patients require caffeinated analgesic combinations. Therapy escalation should limit acute medication use to an average of 2 headache days per week.[1] If a patient requires more medications, then preventative treatment should be offered. Preventative treatment dose may be increased, or acute therapy should be changed if migraine consistency persists.

For migraine headache, triptans are first line treatment.[29] They are selective agonists for 5- hydroxytryptamine 1B (5-HT1B) and 5- hydroxytryptamine 1 Days (5-HT1D) receptors by causing vasoconstriction and reducing neurogenic inflammation associated with antidromic neuronal transmission correlating with the relief of migraines. Triptans are contraindicated in patients with coronary artery disease.

The Calcitonin Gene-related peptide (CGRP) receptor antagonists are a newer class of medications on the market for both prevention and acute treatment of migraines.[40] They are considered second line therapy after trialing triptans. Access to these medications may be limited by financial and insurance constraints. CGRP levels in the cranial circulation have been found to be elevated during migraine attacks. The anti-CGRP antibodies that bind to the CGRP ligand and block its binding to the receptor are eptinezumab (Vyepti®), fremanezumab (Ajovy®), and galcanezumab (Emgality®). The anti-CGRP receptor antagonists that directly antagonize the receptor are atogepant (Quilipta), rimegepant (Nurtec), and ubrogepant (Ubrelvy). The anti-CGRP receptor monoclonal antibody that directly blocks CGRP receptor activity is erenumab (Aimovig®). Their longer half-life corresponds to

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Table 1. Treatment for Acute Migraines

Class	Formulation	Relative Contraindications	Reduction in Migraine Attacks per Month vs Placebo	Other
Triptans	PO ODT, spray, SQ, nasal spray	Concomitant ergot or MAOI use Cerebrovascular syndrome Significant cardiovascular disease Hemiplegic or basilar migraine	N/A	Triptans are first-line treatment for severe migraines as they are generally highly effective, with a low risk of side effects Failure of one triptan does not indicate failure of the entire class of medication. Consider trying a second triptan medication if the first one does not improve symptoms
CGRP receptor antagonists	PO, SQ, Intranasal		N/A	
Seratonin 5-HT1F receptor antognists	PO		N/A	Side effects: dizziness, fatigue
Aspirin & NSAIDs (contraindicated if history of GI bleeding)	PO		N/A	May be used with triptans, caffeine increases efficacy
Antiemetics	PO, IM, IV, suppositories	People at risk for extrapyramidal syndromes (EPS)	N/A	Used as adjunctive treatment
Ergots	Sublingual tablets, suppositories	Safety/efficacy not established in pediatrics Pregnancy Hemiplegic or basilar migraine Ischemic heart disease Severe hepatic or renal impairment	N/A	Rebound associated with overuse of this class Oldest therapy for migraines Side effects: nausea and anxiety are very common

Abbreviations: IV, intravenously; IM, intramuscularly; PO, Oral; ODT, orally dissolving tablet; SQ, subcutaneous.

treating migraines up to 48 hours.[40] Zavegepant (Zavzpret®) 10 mg was approved in 2023 as the first CGRP nasal spray for the acute treatment of migraine with or without auras in adults.[42]

Selective serotonin (5-HT1F) receptor agonists are hypothesized to decrease stimulation of the trigeminal system and treat migraine pain without causing vasoconstriction. Lasmiditan is the only

Table 2. Prophylaxis for Migraines

Class	Formulation	Relative Contraindications	Reduction in Migraine Attacks per Month vs Placebo	Other
Beta blockers	PO	Asthma Depression CHF Raynaud's disease Diabetes Bradycardia	1.26[37]	
Calcium channel blockers	PO	Constipation Hypotension Sick sinus syndrome Second- or third-degree AV block without pacemaker Severe left ventricular dysfunction		May be combined with NSAIDs
Ace inhibitors	PO	Pregnancy Hereditary or idiopathic angioedema	1.5[38]	
Antiepileptics	PO	Pregnancy Kidney stones Bleeding disorders Weight loss concerns	2[39]	Sedative and confusion
Tricyclic antidepressants	PO		6.9[46]	
Anti-CGRP antibody	IV	Avoid in pregnancy and in adults with cardiovascular risks or vascular malformations	N/A	

Abbreviations: IV, intravenously; PO, Oral.

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FDA-approved medication in this class. It is very sedating and considered third line therapy.[1] It should be administered early during a migraine attack, at the first sign of pain, to improve response to treatment.

Ergot alkaloids are fourth line option for moderate to severe headaches.[1] They are often used in combination with caffeine for faster absorption. They cause blood vessels in the body to constrict; this can cause decreased blood flow to other parts of the body that can lead to adverse effects.

Parenteral options for chronic migraine include CGRP mAbs and botulinum toxin. Injectable CGRP mAbs should be trialed for 3 months for those administered monthly and 6 months after the start of quarterly treatments.[1] Botulinum toxin is approved for chronic migraine, which is 15 or more headaches per month.[1]

Other oral, multi-function medications that have established efficacy in migraine prevention include β blockers, ACE inhibitors, ARBs, anticonvulsants, tricyclic antidepressants, NMDA receptor antagonists, and SNRIs. When starting these medications, a minimum of 8 weeks at the target dose is recommended. If a partial response is seen, a cumulative benefit may occur over 6 to 12 months. If no response is seen, another preventative treatment is recommended.[1]

Conclusion

For family physicians, headache is one of the most common presenting chief complaints. With migraine and tension-type headache accounting for most of those, making the diagnosis and developing a cost-effective plan is key. Stepwise approach to treatment—after a holistic history review and confirmation of optimized lifestyle factors—can begin with nonpharmacologic treatment approaches then, if needed, with nonsteroidal anti-inflammatory medications. Beyond that, stepwise care can involve acute and preventive pharmacological treatments when deemed necessary by the clinical scenario. It may be prudent to refer to neurology or a headache specialist physician for novel approaches presented herein, and/or nonpharmacologic complementary approaches offered beyond the walls of a family medicine clinic.

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