Chronic headache: Stop the pain before it starts

Familiarity with the risks associated with medication overuse and the importance of headache prophylaxis is key to easing your patient’s pain.

CASE

Eric K, age 25, is in your office, seeking help for chronic headache—which he’s had nearly every day for the past 9 months. He says that the headaches vary in quality and intensity. Sometimes the pain is in the right temporal area; has a throbbing, pulsating quality; and is accompanied by nausea and photophobia. These headaches are incapacitating, with an intensity of 10 on a scale of one to 10. When they occur, the patient reports, all he can do is take migraine medication and lie down in a darkened room for several hours, until the pain goes away. He cannot identify any triggers.

He also gets headaches that are not incapacitating, but occur almost daily, the patient says, describing a dull bilateral pressure that usually begins in the afternoon and worsens until he takes headache medication. He denies any fever, chills, weight loss, visual changes, or tinnitus. His medical history is significant only for obesity, but a system review is positive for depression and insomnia. Physical examination reveals normal vital signs; normal head, eyes, ears, nose, and throat (HEENT); and normal fundoscopic and neurological exams.

Patients like Mr. K can be challenging for primary care physicians, but referral to a neurologist is indicated only in the most intractable cases. For the vast majority of patients with frequent headaches, family physicians can perform the diagnostic work-up and oversee treatment. This review will help with both.

What kind of headache?

While most headaches are sporadic in nature, the prevalence of “chronic daily headache” ranges from 3% to 5% worldwide.1-3

Chronic daily headache is not a diagnosis, however, nor is it an indication that a patient has a headache every day. According to the International Classification of Head-
Acute headache medications should follow the “one and done” rule, eliminating the pain with a single dose.

Pinpointing the type of headache
An accurate diagnosis requires a thorough headache history and a HEENT and neurological examination. The history should include questions about the characteristics of the headache, including the location, intensity, frequency, timing, associated symptoms, previous headache diagnoses, and triggers, and address comorbidities, medication use, caffeine intake, and family history. In the absence of red flags—age >50 years, history of headache or systemic illness, sudden onset, or papilledema, among other findings that may indicate more serious conditions
A definitive diagnosis of chronic migraine is possible only in the absence of overuse of abortive headache medications.

Migraine or tension headache?

**Chronic migraine.** To be classified as CM, the headache must have occurred ≥15 days a month for 3 months or more and have features of migraine, such as unilateral location, pulsating quality, and moderate to severe intensity. Migraines are aggravated by physical activity and associated with nausea and/or vomiting, photophobia, and phonophobia, and may or may not be preceded by aura. Common triggers include stress, menstruation, alcohol, skipped meals, dehydration, and chocolate. Migraines typically respond to ergots and triptans.

**Partial treatment.** Patients with CM often take medication early in the course of a headache. This sometimes results in a partially treated migraine that develops into a headache with tension-type features, such as a bilateral location, a pressing quality, and mild-to-moderate intensity, as well as a possible transformation to MOH. This is most likely to occur in patients who have migraines without an aura.

To avoid partial treatment, medications for acute migraine should be taken within 30 minutes of an attack, in a dose that’s sufficient to relieve the pain within 2 hours, with no need for a second dose—a protocol known as “one and done.” Efficacy of a triptan can be improved by adding a nonsteroidal anti-inflammatory drug (NSAID).

A definitive diagnosis of CM is only possible in the absence of medication overuse.

**Chronic tension-type headache.** In addition to traits common to tension headaches, CTTH may be associated with mild nausea, photophobia, or phonophobia (but typically only one such feature at a time). There may also be tenderness to palpation of the pericranial muscles. Unlike migraine, CTTH is not affected by physical activity.

Here, too, overuse of headache medication is often a factor and should be stopped, if possible, before a definitive diagnosis of CTTH can be made.

**Headache with overlapping features.** It is possible for a patient to have chronic headache with features of both migraine and tension headache. Advise patients whose headaches have varying characteristics to keep a headache journal to determine which features are more prominent. Patients with smart phones can download a free app, such as iHeadache or My Headache Log Pro, to be used for this purpose.

**When to suspect medication overuse headache**

MOH is sometimes referred to as a rebound headache or drug-induced headache. Headaches associated with medication overuse have variable intensity. Patients with MOH often awaken from sleep with a headache, and neck pain is highly prevalent.

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**TABLE 1**

Diagnosing and treating chronic headache

<table>
<thead>
<tr>
<th>Type of headache</th>
<th>ICHD-II diagnostic criteria</th>
<th>First-line treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Chronic migraine</strong></td>
<td>1. Headache fulfilling criteria for migraine without aura ≥8 days/month &lt;br&gt;2. Headache occurs ≥15 days/mo for ≥3 mo &lt;br&gt;3. No overuse of medication &lt;br&gt;4. No secondary headache</td>
<td>Prophylactic therapy: &lt;br&gt;• TCAs &lt;br&gt;• SNRIs &lt;br&gt;• Anticonvulsants &lt;br&gt;• Beta-blockers &lt;br&gt;• Botulinum toxin A &lt;br&gt;Limit acute medication; avoid triggers; initiate lifestyle modification</td>
</tr>
<tr>
<td><strong>Chronic tension-type headache</strong></td>
<td>1. Headache fulfilling criteria for tension-type headache &lt;br&gt;2. Occurs ≥15 days/mo for ≥3 mo &lt;br&gt;3. No overuse of medication &lt;br&gt;4. No secondary headache</td>
<td>Prophylactic therapy: &lt;br&gt;• Amitriptyline &lt;br&gt;• Venlafaxine &lt;br&gt;• Mirtazapine &lt;br&gt;Limit acute medication; avoid triggers; initiate lifestyle modification</td>
</tr>
<tr>
<td><strong>Medication overuse headache</strong></td>
<td>1. Headache occurs ≥15 days/mo &lt;br&gt;2. Single abortive medication use ≥10 days/mo or combination therapy ≥15 days/mo for ≥3 mo &lt;br&gt;3. Headache developed or worsened during medication overuse</td>
<td>Discontinue overused acute meds; provide headache education; bridge with NSAIDs, prednisone, or botulinum toxin A; begin prophylactic medication</td>
</tr>
<tr>
<td><strong>Hemicrania continua</strong></td>
<td>1. Headache for ≥3 mo &lt;br&gt;2. All of the following characteristics:  &lt;br&gt;• Unilateral pain without side shift &lt;br&gt;• Daily and continuous, without pain-free periods &lt;br&gt;• Moderate intensity, but with exacerbations of severe pain &lt;br&gt;3. At least one of the following on the same side as the pain:  &lt;br&gt;• Conjunctival injection and/or lacrimation &lt;br&gt;• Nasal congestion and/or rhinorrhea &lt;br&gt;• Ptosis and/or miosis &lt;br&gt;4. Complete response to therapeutic doses of indomethacin</td>
<td>Indomethacin</td>
</tr>
<tr>
<td><strong>New daily persistent headache</strong></td>
<td>1. Headache for ≥3 mo &lt;br&gt;2. Characteristics of tension-type headache (but migrainous features are common) &lt;br&gt;3. Unrelenting from onset or within 3 days of onset &lt;br&gt;4. No medication overuse</td>
<td>Rule out secondary causes; treat according to migrainous or tension features of headache</td>
</tr>
</tbody>
</table>

ICHD-II, International Classification of Headache Disorders; NSAIDs, nonsteroidal anti-inflammatory drugs; SNRIs, serotonin-norepinephrine reuptake inhibitors; TCAs, tricyclic antidepressants.
able to recall, to the day, when the headache started. More than 50% report a precipitating event, such as a viral illness, a stressful experience, or surgery. ICHD-II defines NDPH as having the characteristics of a tension headache. Notably, however, migrainous features are also common, and neurologists often diagnose NDPH with either migrainous or tension-type features.

The sudden onset of NDPH is a red flag and, like other red flags, always warrants further work-up. Magnetic resonance imaging with gadolinium is preferred to computed tomography. Magnetic resonance venography or lumbar puncture may also be considered.

**Beyond headache: Red flags warrant additional testing**

<table>
<thead>
<tr>
<th>Red flag</th>
<th>Condition(s) to rule out</th>
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<tbody>
<tr>
<td>Age of onset &gt;50 y</td>
<td>Giant cell arteritis, mass lesion, stroke</td>
</tr>
<tr>
<td>No prior history of headache OR change in characteristic from prior headaches</td>
<td>Cancer, aneurysm, stroke, cerebral sinus thrombosis, infection</td>
</tr>
<tr>
<td>“Thunderclap” headache</td>
<td>Ruptured aneurysm</td>
</tr>
<tr>
<td>Signs or symptoms of systemic illness (eg, fever, chills, weight loss)</td>
<td>Meningitis, encephalitis, cancer</td>
</tr>
<tr>
<td>History of systemic illness, such as cancer, autoimmune disease, or HIV</td>
<td>Brain metastasis, mass lesion, autoimmune meningitis, thrombosis</td>
</tr>
<tr>
<td>Headache brought on by change in head position or Valsalva maneuver</td>
<td>Spontaneous CSF leak or Chiari malformation</td>
</tr>
<tr>
<td>Occipital location of headache (in children)</td>
<td>Brain tumor</td>
</tr>
<tr>
<td>Neurological symptoms</td>
<td>Mass lesion, encephalitis</td>
</tr>
<tr>
<td>Papilledema</td>
<td>Idiopathic intracranial hypertension, cerebral sinus thrombosis</td>
</tr>
</tbody>
</table>

CSF, cerebrospinal fluid; HIV, human immunodeficiency virus.

**TREATING CHRONIC HEADACHE: WHICH DRUGS ARE BEST?**

A multimodal approach combining pharmacologic and nonpharmacologic therapies is usually required for patients with chronic headache. The particular therapy and prognosis depend on the type of headache a patient has and the presence of comorbidities (TABLE 3).

**CHOICE FOR MIGRAINE PROPHYLAXIS? HERE’S WHAT THE EVIDENCE TELLS US**

Although most studies of the benefits of prophylaxis have involved patients with episodic or frequent migraine rather than CM, extrapolation of the findings to patients with CM is not unreasonable. And, although dozens of pharmacologic and complementary therapies have been studied for migraine prophylaxis and certain classes of drugs have been identified as effective, there are very few head-to-head trials comparing agents.


Key findings: The types of medication with the most evidence to support their use as first-line agents for CM are antidepressants, anticonvulsants, and beta-blockers.
Antidepressants, especially tricyclics (TCAs) and serotonin-norepinephrine reuptake inhibitors (SNRIs), have been found to be effective. Chief among them are amitriptyline, a TCA, which is inexpensive and may be beneficial for patients with coexisting insomnia due to its sedating effect, and venlafaxine, an SNRI, which may help treat comorbid depression.23 Amitriptyline is associated with weight gain and can prolong the QT interval at higher doses. There is insufficient or conflicting evidence of the value of selective serotonin reuptake inhibitors for migraine prophylaxis.

Anticonvulsants that have been studied most extensively for migraine are topiramate and sodium valproate. Both have level A ratings for established efficacy.23 Topiramate has also been shown to be noninferior to amitriptyline in reducing migraine frequency and is associated with weight loss, rather than weight gain.25 (Topiramate and valproic acid should be avoided in women who are hoping to become pregnant.) Gabapentin has conflicting evidence and is not recommended for migraine.

Beta-blockers that appear to be most effective as prophylaxis for CM are propranolol, metoprolol, and timolol.23,26 Any of these would be the obvious choice for a patient with comorbid hypertension. Beta-blockers can take several months to have an effect on migraines, however. Their use as CM prophylaxis may be limited by their adverse effect profile, which includes erectile dysfunction, bradycardia, and hypotension, although the lower dosage needed for migraine prophylaxis may be a mitigating factor. Calcium channel blockers are commonly prescribed for migraine, but there is little evidence to support their use for CM.23

Other medications that are likely effective for migraine prophylaxis include naproxen24 and tizanidine27 (a muscle relaxant). Complementary and alternative treatments that appear to be effective include magnesium, feverfew, butterbur, and riboflavin, although the benefits may not be noticeable for several months.24

Botulinum toxin A is the only medication approved by the US Food and Drug Administration for prevention of CM. It is generally considered to be a second-line agent because of its high cost and the need for training and expertise to administer it. Botulinum toxin A is not effective as prophylaxis for EM.28

Treating other headache syndromes
Chronic tension-type headache. Treatment of CTTH applies similar principles to those of CM, and amitriptyline and venlafaxine—as well as mirtazapine, a sedating SNRI—have evidence to support their use for this type of headache.29 Overall, however, CTTH therapies have not been studied as extensively as those for migraine. There is conflicting evidence of the value of anticonvulsants.
Beta-blockers are an obvious choice for headache prophylaxis in patients with hypertension, but their use may be limited by their adverse effects profile.

**Medication overuse headache.** Prophylactic medications are not effective in patients who are overusing acute headache medications, and patients with MOH should be instructed to stop the offending drugs. Withdrawal of triptans, simple analgesics, and ergots—either cold turkey or with a slow wean over 4 to 6 weeks—is fairly safe and can be done in an outpatient setting. Concomitant use of prednisone, long-acting NSAIDs, or botulinum toxin A can be used as “bridge therapy” to relieve acute pain. Start the patient on a prophylactic medication based on the best estimate of his or her baseline headache and comorbidities.

Most patients with MOH will improve with drug withdrawal, but some will be left with the same disabling headaches that caused them to overuse medication in the first place. For such patients, weekly office visits during the withdrawal period may be helpful. After completion of the bridge therapy, they will likely require abortive headache treatment, but its use must be limited to no more than twice a week. Referral to a specialty headache clinic may be appropriate for such patients.

**Hemicrania continua.** The treatment for HC is indomethacin. A 2- to 5-day course typically results in complete recovery.

**New daily persistent headache.** For patients with NDPH, the first step is ruling out secondary causes. Once that has been done, most experts recommend trying to characterize the headache as having features of either migraine or tension and treating accordingly with preventive therapy. If acute headache medication is still needed, limit the quantity you prescribe and stress the importance of taking it no more than twice a week.

**CASE** Mr. K receives a diagnosis of MOH and probable CM. You explain the way MOH develops and how his medication use has contributed to the escalation of his headaches, and ask him to stop all the headache medications he has been using and to keep a headache journal. You prescribe meloxicam as a short-term bridge therapy and low-dose venlafaxine, which is increased to 150 mg/d over the next 4 weeks; recommend riboflavin 400 mg/d; and refer Mr. K to a neurologist for botulinum toxin A.

You ask him to return in 4 weeks and explain that because he has successfully stopped the overuse of acute headache medications, he can begin taking them again—provided he limits their use to no more than twice a week.

**Nonpharmacologic measures can help, too**

Lifestyle modification can play an important role in the treatment of chronic daily headache. Advise patients of the importance of proper sleep hygiene, regular exercise, stress reduction, and a healthy diet, as well as avoiding known triggers and minimizing intake of caffeine. Tell patients that biofeedback, cognitive behavioral therapy, and physical therapy may play a role in conjunction with pharmacotherapy, especially for CTTH, but that hypnosis, acupuncture, chiropractic manipulation, transcutaneous electrical nerve stimulation, and hyperbaric oxygen have too little evidence to recommend for or against their use.

In discussing treatment for chronic headache and the goals of therapy with a patient with chronic headache, it is important to be frank. Explain that while a complete cure is not always possible, a decrease in both the frequency and severity of headaches and an improvement in the quality of life and the patient’s ability to function are realistic goals.

**CASE** At the 3-month follow-up, Mr. K reports that his headaches are down to less than twice a week, and that he is undergoing cognitive behavioral therapy for depression. For acute headache pain, he takes sumatriptan 100 mg with ibuprofen 800 mg, and is careful not to do so more than twice a week.
References