

Managing Migraine

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Editor's Note: *The Expert Clinical Management series consists of shorter, practical review articles focused on the optimal approach to a specific sign, symptom, disease, procedure, technology, or other emergency department challenge. These articles—typically solicited from recognized experts in the subject area—will summarize the best available evidence relating to the topic while including practical recommendations where the evidence is incomplete or conflicting.*

OVERVIEW

Migraine is a recurrent headache disorder that afflicts 18% of US women and 9% of US men.¹ It causes at least 1.2 million visits to US emergency department (EDs) annually; the actual number is probably substantially larger because many migraine patients are assigned nonspecific headache diagnostic codes.² Migraine severity, as measured by the frequency with which it disrupts a patient's life, ranges from minimal to severe. On one end of this spectrum are patients who have occasional headaches that are rapidly and effectively treated with over-the-counter therapies. On the other end are patients with chronic migraine. They have headache on more days than not and their work and social life is detrimentally affected.

An aura is one of several reversible neurologic phenomena that precede the headache and resolve completely. Most commonly, these are visual or sensory, although they may involve motor function or speech. Migraine patients also frequently report neurologic phenomena including dizziness, sensory disturbances, and visual symptoms during the acute attack. Because they occur during the headache, these latter symptoms are not typically referred to as aura. The migraine prodrome is a constellation of symptoms that precede the acute migraine attack by several days and include changes in mood,

alertness, and appetite. Allodynia, an alteration of nociception that causes typically non-noxious sensory stimuli (such as brushing one's hair or shaving one's face) to be perceived as painful, develops as acute migraine duration increases. This is thought to indicate involvement of higher-order central nervous system sensory relay stations, notably, the thalamus.

Migraine was once believed to be a vascular headache. Advanced imaging studies do not support this description and indicate that migraine is a neurologic disorder involving dysfunctional nociceptive processing.³ Abnormally activated sensory pathways turn non-noxious stimuli into headache, photophobia, phonophobia, and osmophobia. Cortical spreading depression, a slow wave of brain depolarization, underlies migraine aura but has not been demonstrated clearly in migraine patients without aura.

DIAGNOSIS

Migraine is a clinical diagnosis. There are currently no laboratory or imaging findings available to confirm this diagnosis. The International Headache Society's *International Classification of Headache Disorders*, currently in its third iteration, is used to standardize the diagnosis for both research studies and clinical practice.⁴ The specific criteria for migraine are somewhat cumbersome (Figure 1) and may be difficult to ascertain during a severe acute attack. ID-Migraine (Figure 2), a 3-item screening instrument that has been validated against expert diagnosis in the outpatient setting, seems apropos to ED patients with recurrent headaches.⁵

Some question the need to establish a specific primary headache diagnosis among ED patients. Central to this argument is the observation that other primary headaches (cluster and tension-type headache) respond to many of the same medications as does migraine, including triptans,^{6,7} antidopaminergics,^{8,9} and nonsteroidal anti-inflammatory drugs. There is truth to this argument, and it is reasonable to delay diagnosis until the end of the ED visit. However, before discharge, providing patients with a specific headache diagnosis will allow them to access resources and discuss their headache disorder knowledgeably.

Recurrent headache disorder manifesting in attacks lasting 4-72 hours. Typical characteristics of the headache are unilateral location, pulsating quality, moderate or severe intensity, aggravation by routine physical activity, and association with nausea or photophobia and phonophobia.

Diagnostic criteria:

- A. At least 5 attacks fulfilling criteria B to D
- B. Headache attacks lasting 4-72 hours (untreated or unsuccessfully treated)
- C. Headache has at least 2 of the following characteristics:
 1. unilateral location
 2. pulsating quality
 3. moderate or severe pain intensity
 4. aggravation by or causing avoidance of routine physical activity (eg, walking, climbing stairs)
- D. During headache at least 1 of the following:
 1. nausea or vomiting
 2. photophobia and phonophobia
- E. Not attributed to another disorder

Figure 1. *International Classification of Headache Disorders* migraine without aura criteria.⁴

With the exception of a pregnancy test, which may be used to guide treatment, routine laboratory tests are unlikely to contribute to clinical management and should not be ordered. Similarly, neuroimaging is not indicated for patients who present with a typical migraine exacerbation. It is unknown whether patients who present with a headache that is somewhat different from their typical migraine require neuroimaging. These latter patients may present with a migraine that did not respond as it usually does to standard medication, one that is longer or more intense than usual, or one that occurs in a different location than usual. In the author's experience, absent typical red flags (thunderclap onset, focal neurologic findings, fever, head trauma, or altered mental status), these patients are at low risk for pathologic findings. In these latter patients, decisions on neuroimaging should be delayed until after treatment. For many patients, successful treatment provides a better perspective on the similarity of the headache to the patient's previous headaches. This is not to say that response to treatment can exclude a malignant cause of headache. Rather, in my experience, a patient who is now headache free is better able to contextualize the acute headache in regard to previous headaches and may report that in fact the acute headache was not much different than previous headaches.

When compared with expert opinion, this instrument demonstrated sensitivity of 0.81 (95% confidence interval [CI] 0.77 to 0.85) and a specificity of 0.75 (95% CI 0.64 to 0.84) in a primary care setting. It has not been evaluated in an acute care setting.

During the last 3 months, did you have any of the following with your headaches?

1. You felt nauseated or sick to your stomach when you had a headache.
2. Light bothered you (a lot more than when you do not have headaches).
3. Your headaches limited your ability to work, study, or do what you needed to do for at least 1 day.

A positive result is an affirmative response to 2 of these 3 questions.

Figure 2. ID-Migraine.⁵

TREATMENT

Three classes of medication have emerged as first-line parenteral treatment of acute migraine: the antidopaminergics, the triptans, and nonsteroidal anti-inflammatory drugs (Table).

During the last 3 decades, compelling clinical evidence has emerged to support the use of antidopaminergics as monotherapy for acute migraine.¹⁰ These medications work not just for migraine-associated nausea and gastroparesis but also to relieve the acute headache itself. This is true for various types of antidopaminergics, including metoclopramide,¹¹⁻¹³ prochlorperazine,¹⁴⁻¹⁶ droperidol,¹⁷⁻¹⁹ and haloperidol.^{20,21} Unfortunately, clinical science has outpaced basic science and a mechanism of action is not clear. Some data suggest that migraine is a dopaminergic phenomenon, but these data are neither robust nor consistent.²² Because metoclopramide has a favorable pregnancy rating, it should be considered the primary parenteral therapy for pregnant migraineurs.

Although highly effective, intravenous antidopaminergics are accompanied by extrapyramidal symptoms, most commonly akathisia, a distressing syndrome of restlessness and agitation that may occur in one third of patients who receive these medications.²³ Akathisia is usually short-lived, but patients who experience it once report that they do not want to receive the same antidopaminergic medication again. Some use a strategy of akathisia prophylaxis by coadministering diphenhydramine, an anticholinergic. This is a strategy that is effective for prochlorperazine²³ but

Table. First-line parenteral treatment of migraine.

Agent	Dose, Route	Frequent Adverse Effects	Cautions/Contraindications
Triptans			
Sumatriptan	6 mg SC	Flushing, dizziness, palpitations, drowsiness, injection site reactions	Use cautiously in patients with cardiovascular risk factors. Use cautiously in those who have already received triptans within 24 h.
Antidopaminergics			
Metoclopramide	10 mg IV	Akathisia, drowsiness, dizziness, generalized weakness	Diphenhydramine not indicated to prevent akathisia
Prochlorperazine	10 mg IV	Akathisia, drowsiness	Diphenhydramine should be used to prevent akathisia
Nonsteroidal anti-inflammatory drugs			
Ketorolac	30 mg IV or 60 mg IM	Well tolerated	

does not seem to be needed for metoclopramide.²⁴ A slower rate of medication administration is associated with less frequent akathisia.²⁵ Once it develops, akathisia should be treated with diphenhydramine or midazolam.²⁶ Dystonic reactions are relatively uncommon. Tardive dyskinesia, an irreversible involuntary motor disorder, has never been reported after an isolated dose of an antidopaminergic.²⁷

The triptans are serotonin receptor agonists that, during the last 30 years, have revolutionized the outpatient treatment of migraine.²⁸ Although originally developed as vasoconstrictors, these medications decrease nociceptive transmission within the trigeminal pathway.²⁸ Subcutaneous sumatriptan, the only available parenteral triptan, has a number needed to treat of 2.5 versus placebo for meaningful headache relief in the ED setting and a median time to headache relief of 34 minutes.²⁹ In actual clinical practice, this means a migraine patient could be placed in a chair, could be administered a subcutaneous dose of medication, and likely will be ready for discharge in less than an hour. Unfortunately, sumatriptan comes with a number of unpleasant adverse effects (number needed to harm=4), including chest symptoms, flushing, and worsening of the headache.²⁹ Also, two thirds of patients who receive sumatriptan report recurrence of headache within 24 hours.²⁹ Sumatriptan is more likely to be effective in patients who have not developed allodynia and those who have had a favorable response to it previously. In head-to-head studies, intravenous antidopaminergics tended to be more efficacious and better tolerated than subcutaneous sumatriptan.^{12,13,15,30}

Ketorolac is the specific parenteral medication used most commonly to treat migraine in US EDs, although high-quality data supporting its use are less robust.³¹ Ketorolac can be combined with either the antidopaminergics or the triptans, a strategy that is intuitively appealing, although one that has not been subjected to clinical trials.

The evidence supporting other parenteral medications is less compelling. Antihistamines such as diphenhydramine and hydroxyzine probably are not efficacious in acute migraine.²⁴ Ketamine³² and propofol^{33,34} seem to work acutely, but it is unclear what happens to the headache after the medication wears off. Magnesium has not consistently shown benefit.³⁵⁻³⁸ Dihydroergotamine, an older medication, has mostly been supplanted by sumatriptan. Parenteral ondansetron and other serotonin-receptor antagonists have not been well studied in acute migraine.

Intravenous fluid is commonly used for acute migraine but it is unclear whether it is of benefit.³⁹ Fluids are best reserved for patients with overt signs of dehydration.

Because they are generally well tolerated, various nerve blocks are sometimes used to treat acute migraine, although evidence supporting efficacy does not yet exist.⁴⁰

Parenteral opioids have a complicated relationship with acute migraine. This class of medication is the most common one used to treat migraine in US EDs.² Led by hydromorphone, opioids are used in slightly more than 50% of all migraine visits.⁴⁰ Low-quality studies (nonexperimental design) have linked ED use of parenteral opioids to a variety of negative outcomes, including repeated ED visits and less responsiveness to triptans.⁴¹ Regardless of whether these associations are true, opioids seem less likely to achieve the goals of sustained headache freedom and return to work and so should not be offered as first-line therapy to patients who present de novo to an ED with acute migraine and without contraindications to the therapies discussed above. Strategies for patients who insist on treatment with opioids are discussed elsewhere.⁴²

The author's stepwise approach for treatment of refractory acute migraine is presented in [Figure 3](#).

DISCHARGE

Migraine is a recurrent headache disorder. Patients are very likely to continue to experience headaches in the days,

Metoclopramide 10 mg IV drip lasting 15 minutes (OR prochlorperazine 10 mg IV drip lasting 15 minutes + diphenhydramine 25 mg IV OR droperidol 2.5 mg IV drip lasting 15 minutes ± diphenhydramine 25 mg IV).



A second dose of antidopaminergic from step 1* + ketorolac 30 mg IV



A third dose of antidopaminergic from step 1* + dihydroergotamine 1 mg IV drip lasting 15 minutes



Bilateral greater occipital nerve block using bupivacaine 0.5%



Oral opioid combination such as oxycodone/acetaminophen

Consider administering dexamethasone 10 mg IV to all acute migraine patients to mitigate the very frequent recurrence of headache after ED discharge. Other agents to consider include: acetaminophen 1 mg IV; ketamine 0.1 mg/kg IV; propofol 30-40 mg IV with 10-20 mg bolus every 3-5 minutes up to 120 mg; haloperidol 5 mg IV + diphenhydramine 25 mg IV.

I wait one hour between successive treatments. Local practice determines how many of these treatments should be administered in the ED versus the inpatient setting. Consider neurology or pain management consult for patients with chronic migraine, concomitant medication overuse headache, or frequent ED visits for migraine. Admission to the hospital is appropriate for patients with persistent pain or those who are unable to tolerate liquids by mouth.

*In 1 ED-based randomized controlled trial, successive 20 mg of IV metoclopramide were administered to migraine patients every 30 minutes as needed for persistence of pain. Some patients received 80 mg of metoclopramide during 2 hours. This regimen was well tolerated and highly efficacious.¹²

Figure 3. The author's stepwise approach to treatment of refractory acute migraine.

weeks, months, and years after ED discharge. Two thirds of ED patients with migraine experience headache during the 24 hours after discharge. Many of these headaches are functionally impairing or severe in intensity.⁴³ Parenteral dexamethasone is modestly effective at mitigating recurrence of moderate or severe headache within 72 hours of ED discharge (number needed to treat=9).⁴⁴ Naproxen 500 mg or sumatriptan 100 mg, to be used to treat the postdischarge headache, will improve some but not all of these headaches.⁴⁵ An ED-based headache education program with specialist referral did not improve long-term headache outcomes among a general population of ED migraineurs.⁴⁶ This type of intervention is best reserved for patients with more complicated disease, including those with chronic migraine, psychiatric comorbidities, and concomitant medication overuse headache, a disorder defined by an upward spiral of increasing headache frequency in the setting of increased usage of analgesic or migraine medication, including nonsteroidal anti-inflammatory drugs, acetaminophen, opioids, and triptans.⁴⁷ Preventive medications, such as the β -blockers propranolol and metoprolol or the antiepileptic topiramate, are often considered for patients who continuously experience several days or more of migraine per week.⁴⁸

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