Treatment of acute migraine in the emergency department

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Case description
Erica, a healthy 24-year-old medical student, presents to your emergency department (ED) during your evening shift with a severe headache that she has had for the past 6 hours. She has had similar headaches once a term that keep her from her clinical duties for 1 or 2 days if untreated. After a careful history and physical examination you decide she has a migraine.

What is the best treatment for her in the ED?

Migraine is a common presentation in the ED. Migraines are characterized by recurrent, unilateral, throbbing headache associated with photophobia and nausea. Diagnosis is made clinically using tools such as the POUND (pulsatile, one-day duration, unilateral, nausea or vomiting, and disabling) mnemonic. While our understanding of the pathophysiology of migraine continues to evolve, it is hypothesized that the pain of migraine results from a cyclic propagation of neural dysfunction and vasospasm in the brain. Purported therapies for the ED treatment of acute migraine are legion and of mixed efficacy. Some ED therapeutic strategies might even increase ED recidivism. This article aims to provide an evidence-based and effective strategy for treating acute migraine in the ED.

Discussion
Nonsteroidal anti-inflammatory drugs. Multiple, different nonsteroidal anti-inflammatory drugs (NSAIDs) have been shown in randomized, placebo-controlled trials to be effective for acute migraine. Given its parenteral formulation, ketorolac is a reasonable option in the ED. The recommended ketorolac dosage is a 60-mg intramuscular dose or 30-mg intramuscular or intravenous (IV) doses every 6 hours (maximum daily dose of 120 mg). The incremental benefit of NSAIDs combined with other therapies remains unclear, but it is reasonable to prescribe NSAIDs alone given their consistent efficacy when studied as monotherapy.

Acetaminophen. Acetaminophen is frequently taken by patients before ED presentation. A Cochrane meta-analysis estimated the number needed to treat to be 12 for acetaminophen in acute migraine. Given the low cost, wide availability, and safe side effect profile of acetaminophen, it is a useful first-choice drug for acute migraine. No studies have been undertaken to see whether the addition of acetaminophen to the standard abortive migraine therapy provides substantial incremental benefit.

Triptans. Abortive therapy using serotonin 1B or 1D agonists (triptans) for migraine is now a well-accepted strategy for acute migraine in the outpatient setting. Several medications have been developed that can be delivered by oral, nasal, or subcutaneous routes. Evidence suggests that subcutaneous delivery is fastest and most effective, although there is no clear superiority of one triptan over another. Common side effects include injection site reactions, dizziness, and paresthesias. Triptans are contraindicated in cardiovascular disease, pregnancy, basilar migraines, Prinzmetal angina, and ischemic stroke, and with the use of ergotamines within the previous 24 hours. Studies have also suggested that triptan therapy is less effective in patients with prolonged and severe migraine. Given the side effect profile, lack of efficacy in severe migraine, and relative contraindications, triptan use in the ED is of limited value.

Ergotamines. Traditionally, dihydroergotamine (DHE) has been used for abortive therapy in migraine, as it acts on serotonin 1B and 1D receptors, similar to triptans. There is some evidence that DHE combined with an antiemetic medication is as effective as meperidine, valproate, or ketorolac in relieving migraine and preventing relapse. However, studies comparing the efficacy of DHE monotherapy with antiemetic therapy are small and favour non-DHE therapies. Contraindications to DHE use are similar to those of triptans. Given the potential side effect profile and lack of superiority compared with common treatment modalities, ergotamine use is not a preferred strategy for ED patients.

Intravenous fluids. Dehydration is a known trigger of migraine. Persistent nausea and vomiting further
exacerbates the migraine. Although there is a relative paucity of strong evidence for the administration of IV fluids, adequate hydration might improve patient malaise and could prevent some of the adverse cardiovascular effects seen with many migraine therapies.19,20

**Antiemetic medications.** Parenteral metoclopramide, chlorpromazine, and prochlorperazine all have demonstrated efficacy in randomized trials as monotherapy for acute migraine.21-23 While metoclopramide has been the most studied, there is some evidence that chlorpromazine and prochlorperazine might be more effective in reducing pain and nausea.23,24

The most common adverse reactions are sedation and postural hypotension. True and clinically relevant akathisia and acute dystonic reactions have been difficult to interpret from the literature but appear rare.25 Akathisia was more commonly associated with prochlorperazine than metoclopramide, and adjuvant diphenhydramine reduced the relative risk of akathisia induced by prochlorperazine by 61%.26

Antiemetic medications are efficacious and are recommended for acute migraine in the ED. To reduce the risk of akathisia, diphenhydramine should be included.

**Butyrophenones (haloperidol and droperidol).** Randomized controlled trials have demonstrated efficacy of haloperidol and droperidol monotherapy compared with placebo for acute migraine.27-29 However, these drugs have been associated with frequent side effects (somnolence, akathisia, anxiety) and have a black-box warning for QT prolongation. As a result, these medications are generally reserved for rescue therapy in refractory migraine.

**Opioids.** When compared with NSAIDs, DHE, and antiemetic medications, opioids are less effective for migraine.30,31 Unfortunately, most of the literature about the use of opioids for migraine was published when meperidine was commonly used.

Use of opioids for migraine control has also been associated with higher recurrence rates, greater functional disability, and an increased likelihood of ED recidivism.32

While these data cannot demonstrate causation, they indicate that opioids are not an effective first-line strategy for patients with severe migraines.3 However, there are circumstances in which using opioids in the ED as a second-line treatment for an individual patient with an acute migraine is entirely appropriate, and it would be cruel to do otherwise.

**Dexamethasone.** The role of dexamethasone in treating the inflammatory processes of acute migraine has been investigated.33 Adjunctive parenteral dexamethasone (10 to 25 mg intravenously or intramuscularly) did not reduce acute pain scores in the ED, but did reduce the likelihood of migraine recurrence within 72 hours when added to standard abortive therapy.34 Dexamethasone was shown to have a number needed to treat of 9 and an adverse event profile equal to placebo. Oral administration of dexamethasone was not studied.

**Sequence and combination of therapies.** Stepped care within attacks is a treatment plan in which medications are added depending on patient response. Stratified care based on severity is a treatment plan in which all of the anticipated medications are given up front. Patients have improved outcomes with stratified care.34

Until we have further evidence to guide our medication combinations, treating the patient with multiple medications that have independently been found to be efficacious at the onset of his or her ED visit is recommended over stepped care (Box 1).

<table>
<thead>
<tr>
<th>Box 1. Suggested prescription for severe migraine</th>
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<tbody>
<tr>
<td>1-L bolus of IV normal saline solution</td>
</tr>
<tr>
<td>10 mg of IV prochlorperazine</td>
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<tr>
<td>25 mg of IV diphenhydramine</td>
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<tr>
<td>30 mg of IV ketorolac</td>
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<tr>
<td>10 mg of IV dexamethasone</td>
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**Case resolution**

Erica’s severe migraine was treated with parenteral prochlorperazine, diphenhydramine, and ketorolac after a bolus of normal saline solution. She also received a dose of parenteral dexamethasone. Her discharge instructions included a handout on migraines (widely available online), a family physician referral, and a prescription for triptan therapy to be used early for future migraines. The next time you see her, she is doing her emergency medicine rotation during residency.


**BOTTOM LINE**

- Acute migraine is a common presentation in the emergency department (ED).

- Opioids are, at best, a second-line treatment for acute migraine in the ED.

- Nonsteroidal anti-inflammatory drugs, antiemetic medications, diphenhydramine, dexamethasone, and intravenous fluids all have shown benefit for treating acute migraine in the ED. Their effect is greater when they are all administered up front as opposed to being delivered in a stepwise pattern throughout the ED stay.

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