Management of Migraine Headache in the Emergency Department

Carrie E. Robertson, M.D.,1 David F. Black, M.D.,2 and Jerry W. Swanson, M.D., F.A.C.P.1

ABSTRACT

Headache is one of the more common reasons for adults to visit an emergency department. Most of these visits are for primary headache disorders, most commonly migraine headache. The authors discuss management options for patients presenting to the emergency department with prolonged, severe, or refractory migraine headaches. Particular attention is given to parenteral treatments and protocols that would not be options as an outpatient. The epidemiology, investigation, and outpatient management of migraine headache are discussed in other articles in this issue.

KEYWORDS: Headache, migraine, status migrainosus, triptan, dihydroergotamine

In the 2006 National Hospital Ambulatory Medical Care Survey, headache accounted for over 3.3 million visits to the emergency department (ED), representing the fourth most common reason adults sought care in an ED.1 Approximately two-thirds of these visits were for primary headache disorders, most commonly migraine headaches.2,3

When treating a patient with headache in the ED, it is first crucial to exclude secondary headache etiologies, such as hemorrhage, infection, or a mass lesion. A patient presenting with a first-ever headache, or a change in the pattern of their headache, deserves careful assessment and further workup. The investigation of a patient with headache, including thunderclap headache, is covered elsewhere in this issue. Migraine headache has also been extensively discussed elsewhere, including outpatient management strategies. Here we will focus primarily on the management options in the ED setting for migraine headache.

ACUTE MIGRAINE TREATMENT IN THE EMERGENCY DEPARTMENT

Patients with a history of migraine presenting to the ED for further management will likely have tried their usual home remedies without success. A prolonged migraine attack with nausea and/or vomiting and poor oral intake may result in volume depletion. Assessment of volume status, followed by intravenous (IV) hydration and treatment of nausea/vomiting should be the first step. Once secondary causes of headache have been eliminated, the patient should be placed in a dark, quiet room to prevent exacerbation of their photophobia and phonophobia. The patient should be given a migraine-specific treatment next, preferably by parenteral route. There are many classes of migraine medications from which to choose, including dopamine (D2) blocking agents, 5-HT receptor agonists, ergotamine, nonsteroidal anti-inflammatory drugs (NSAIDs), other nondependency-producing medications, and opioid drugs. Opioid medications, however, should be avoided if possible as they

1Department of Neurology; 2Department of Radiology, Mayo Clinic, Rochester, Minnesota.

Address for correspondence and reprint requests: Jerry W. Swanson, M.D., F.A.C.P., Professor of Neurology, Department of Neurology, Mayo Clinic, 200 First Street SW, Rochester, MN 55905 (e-mail: jwswanson@mayo.edu).
foster drug-dependence and may not be as effective as migraine-specific treatments.

**Antidopaminergic Agents**

Although initially thought to be useful only for the nausea and vomiting associated with migraine, there is evidence that antidopaminergic medications can be effective in aborting migraine attacks. Side effects of this group include dizziness, somnolence, akathisia, acute dystonia, and other extrapyramidal effects (Table 1). Some of the extrapyramidal side effects can be minimized by premedicating with an anticholinergic drug, such as 1 mg IV/intramuscular (IM) benztropine or 25 mg IV/IM diphenhydramine. Rare but potentially fatal complications of the antidopaminergic drugs include prolongation of the QT interval, ventricular arrhythmias, and sudden cardiac death. For this reason, patients should have an electrocardiogram (ECG) prior to administration of these medications.

**Butyrophenones (Droperidol and Haloperidol)**

The two most studied butyrophenones for migraine headache are droperidol and haloperidol. One small, randomized, double-blind, placebo-controlled trial of 40 patients found 80% of patients treated with 5 mg IV haloperidol achieved significant pain relief, compared with 15% of the placebo group ($p < 0.0001$). Side effects of haloperidol included sedation and akathisia. Of note, 16% of patients found these side effects intolerable, and reported that they would not want to be treated with haloperidol for future migraines. A larger (305 patients) randomized, double-blind trial was performed on droperidol, and found 87% of patients given 2.75 mg droperidol had significant headache relief, compared with 57% of patients given placebo. The side effects of akathisia, somnolence, and anxiety were rated as severe in 30% of patients who experienced them. Another study used droperidol (2.5 mg) every 30 minutes for up to three doses in 25 patients with status migrainosus, and 10 patients with refractory migraine. They found 88% of those with status migrainosus and 100% of those with refractory migraine had little or no headache on this protocol, with a mean improvement time of 40 minutes. Other studies found droperidol to be as effective or more effective than prochlorperazine for migraine treatment in the emergency department. Because of the severity of side effects reported, and the association of prolonged QT syndrome and sudden cardiac death, the butyrophenone group should probably be considered as rescue therapy for patients who have not responded to other therapies.

**Phenothiazines (Prochlorperazine and Chlorpromazine)**

Intravenous prochlorperazine has been shown to be an effective abortive agent for migraine. One randomized
<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Route of Administration</th>
<th>Dosing (mg)</th>
<th>Max Daily Dose (mg)</th>
<th>T max (Hours)</th>
<th>T ½ (Hours)</th>
<th>Side Effects (for all triptans)</th>
<th>Caution (for all triptans)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sumatriptan (Imitrex®, GlaxoSmithKline, Mississauga, Ontario, Canada)</td>
<td>SQ</td>
<td>6; may be repeated 1 h later</td>
<td>12</td>
<td>0.17</td>
<td>2</td>
<td>Chest pressure</td>
<td>Caution</td>
</tr>
<tr>
<td></td>
<td>PO</td>
<td>25, 50, 100</td>
<td>200</td>
<td>1.5</td>
<td>2</td>
<td>Flushing</td>
<td>Pregnancy</td>
</tr>
<tr>
<td></td>
<td>Nasal spray</td>
<td>5, 20</td>
<td>40</td>
<td>1.5</td>
<td>1.8</td>
<td>Tingling</td>
<td>Severe PVD, CAD, cerebrovascular disease</td>
</tr>
<tr>
<td></td>
<td>PR*</td>
<td>25</td>
<td>50</td>
<td>1.5</td>
<td>1.8</td>
<td>Dizziness</td>
<td>Limb heaviness</td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>Tingling</td>
<td>Nausea</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>Dizziness</td>
<td>Basilar or hemiplegic migraine</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Contraindications:</td>
<td>Uncontrolled hypertension</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Use of other triptan or ergot</td>
<td>Previous adverse reaction</td>
</tr>
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<td></td>
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<td></td>
<td></td>
<td></td>
<td>derivative in previous 24 h</td>
<td>Use of MAO-A inhibitor within 2 weeks</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Nausea</td>
<td>Caution in patients taking a SSRI</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Use of other triptan or ergot</td>
<td>because there may be a risk for serotonin syndrome</td>
</tr>
<tr>
<td>Rizatriptan (Maxalt®, Merck &amp; Co., Inc., Whitehouse Station, NJ)</td>
<td>PO</td>
<td>5, 10</td>
<td>30</td>
<td>1.0</td>
<td>2</td>
<td>Use of MAO-A inhibitor within 2 weeks</td>
<td></td>
</tr>
<tr>
<td>Zolmitriptan (Zomig®, AstraZeneca Pharmaceuticals, LP, London, UK)</td>
<td>PO</td>
<td>2.5, 5</td>
<td>10</td>
<td>1.5</td>
<td>3</td>
<td>Caution in patients taking a SSRI</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Nasal spray</td>
<td>2.5, 5</td>
<td>10</td>
<td>3–4</td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eletriptan (Relpax®, Pfizer, New York, NY)</td>
<td>PO</td>
<td>20, 40</td>
<td>80</td>
<td>1.4</td>
<td>6.3 (80 mg dose)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Almotriptan (Axert®, Ortho-McNeil, Inc., Raritan, NJ)</td>
<td>PO</td>
<td>6.25, 12.5</td>
<td>25</td>
<td>2.5</td>
<td>3.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Naratriptan (Amerge®, GlaxoSmithKline, Mississauga, Ontario, Canada)</td>
<td>PO</td>
<td>1, 2.5</td>
<td>5</td>
<td>2</td>
<td>5.5</td>
<td>May have better tolerability, but lower efficacy</td>
<td></td>
</tr>
<tr>
<td>Frovatriptan (Frova®, Elan Pharmaceuticals, South San Francisco, CA)</td>
<td>PO</td>
<td>2.5</td>
<td>7.5</td>
<td>3</td>
<td>25.7</td>
<td>Lower migraine recurrence</td>
<td></td>
</tr>
</tbody>
</table>

*Not available in United States.
SC, subcutaneous; PO, oral; PR, rectal; T max, time it takes to reach peak concentration; T ½, plasma half-life; PVD, peripheral vascular disease; CAD, coronary artery disease; MAO, monoamine oxidase; SSRI, selective serotonin reuptake inhibitor.

Note: T max and T ½ are given for largest dose in the dosing column except for eletriptan, which is given for 80 mg.
double-blind study of 82 patients showed efficacy when compared with placebo.\textsuperscript{11} Other studies have shown significant efficacy of prochlorperazine compared with metoclopramide,\textsuperscript{12,13} valproate,\textsuperscript{14} and ketorolac.\textsuperscript{15} A reasonable dose is 10 mg IV over 2 to 5 minutes. This may be repeated if necessary in 20 to 30 minutes, but the daily maximum dose should not exceed 40 mg/day.\textsuperscript{16} Chlorpromazine has also been found to be an effective migraine abortive agent,\textsuperscript{17} and in one randomized study produced greater relief and less rebound than dihydroergotamine mesylate (DHE).\textsuperscript{18} Chlorpromazine is particularly associated with postural hypotension.\textsuperscript{17} To help minimize this effect, a bolus of 500 cc IV normal saline should be administered.

### Metoclopramide

Metoclopramide appears to be superior to placebo, but may not be as effective as prochlorperazine and chlorpromazine.\textsuperscript{12,19} It may be more effective when used as an adjuvant to other therapy, rather than as primary therapy.\textsuperscript{20,21} Metoclopramide is typically administered as 10 mg IV over a few minutes.\textsuperscript{21,22}

### 5-HT Agonists: Triptans

There are multiple triptan formulations available on the market (Table 2). These differ in their onset of action, bioavailability, lipophilicity, half-life, and tolerability. Sumatriptan, available in subcutaneous form, is able to reach peak concentration in 10 to 12 minutes, with a 97% bioavailability.\textsuperscript{23} This makes it ideal for use in the ED. It also appears to have the highest clinical efficacy, with meaningful migraine relief (as defined by the patient) of 75% at one hour.\textsuperscript{24} Different individuals may respond better to one triptan than another. Therefore, if a patient has tried sumatriptan multiple times in the past without benefit, it may be reasonable to try a different triptan.\textsuperscript{25}

From the limited trials directly comparing triptans, it appears that the oral triptans are broadly comparable in efficacy.\textsuperscript{26,27} Rizatriptan (10 mg) appears to be slightly more efficacious, with more patients achieving headache relief in 2 hours than with oral sumatriptan (50 or 100 mg) or oral zolmitriptan (2.5 mg).\textsuperscript{28,29} Rizatriptan reaches its maximum concentration slightly faster than other oral triptans; frovatriptan has a slower onset of action, but a longer half-life. The longer half-life of frovatriptan may be helpful in patients with longer duration migraines, and may help decrease the recurrence of migraine in the first 24 hours. Naratriptan is better tolerated than other triptans at the low recommended dose of 2.5 mg dose, but is also less efficacious.\textsuperscript{26,29}

Side effects for triptans include chest tightness, paresthesias, flushing, dizziness, and limb heaviness. With all triptans, there is a low but definite potential risk of side effects secondary to vasoconstriction. Hence, they should be avoided in patients with known coronary, peripheral vascular, or cerebrovascular disease.\textsuperscript{29} In some patients, significant nausea and/or vomiting may preclude oral administration of triptans. Sumatriptan and zolmitriptan are also available as nasal sprays.

### Ergotamine and Dihydroergotamine

Ergotamine and its derivative, DHE are well-established treatments for acute migraine, and share effects on adrenergic, dopaminergic, and serotonergic systems.\textsuperscript{30} Side effects for both include nausea, vomiting, diarrhea, abdominal cramps, leg pain, and vasoconstriction (Table 3).

Dihydroergotamine is generally preferred in the ED setting as it is available in multiple parenteral preparations, and is better tolerated than ergotamine, with less nausea and vasoconstriction.\textsuperscript{30} Of the available DHE preparations, including IV, IM, and subcutaneous (SC), the IV form appears to be the best tolerated. Because of the vasoconstrictive effects, DHE is contraindicated in pregnant patients, patients with basilar or hemiplegic migraine, and patients with severe peripheral

### Table 3  Dihydroergotamine Mesylate (DHE)

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosing</th>
<th>Side Effect</th>
<th>Caution</th>
</tr>
</thead>
<tbody>
<tr>
<td>DHE</td>
<td>0.5–1.0 mg IV, followed by 1.0 mg IV in 1 h if necessary*</td>
<td>Nausea/vomiting, Diarrhea, Abdominal cramps, Leg pain, Vasoconstriction</td>
<td>Contraindications: Pregnancy, Severe PVD, CAD, cerebrovascular disease, Basilar or hemiplegic migraine, Uncontrolled hypertension, Previous adverse reaction, Use of other ergot derivative or triptan in previous 24 h</td>
</tr>
</tbody>
</table>

*See Fig. 1 and Table 4 for repetitive and continuous protocol options. IV, Intravenous; PVD, peripheral vascular disease; CAD, coronary artery disease.
vascular disease, coronary artery disease, or cerebrovascular disease. If the patient has uncontrolled hypertension or a history of previous adverse reaction, DHE should not be used. It is probably reasonable to get an ECG prior to the first dose of DHE. More importantly, DHE should not be used if another ergot-alkaloid or 5-HT agonist (triptan) has been used in the previous 24 hours.

About 10 minutes prior to administering DHE in any form, give the patient an antiemetic, such as 10 mg IV prochlorperazine or 10 mg IV metoclopramide. Note that these medications may also require pretreatment with Cogentin (Merck & Co., Inc., Whitehouse Station, NJ) 1 mg IV/IM or diphenhydramine 25 mg IV/IM to prevent extrapyramidal effects. A typical dose for DHE is 1 mg IM/SC, which may be repeated 1 hour later if the patient is tolerating it well.

When giving DHE intravenously, a reasonable approach would be to administer 0.5 mg IV slowly over a few minutes and monitor for chest pain or severe nausea. The patient could then be given another 0.5 mg in a few minutes if no significant nausea or chest pain has developed. The patient may be given another one mg IV dose in 1 hour if necessary. In cases of status migrainosus or truly intractable migraine, the patient will require hospital admission and could be treated with repetitive or continuous DHE, using a protocol such as the ones described by Raskin and Ford (Fig. 1 and Table 4).

In hospitalized patients, a retrospective study comparing nine repeated IV doses over 3 days of either diphenhydramine (average dose 41 mg) or the combination of DHE (average dose 0.79 mg) and metoclopramide (average dose 5.91 mg) found that diphenhydramine reduced head pain perceptibly after each dose more than DHE/metoclopramide, but DHE/metoclopramide reduced the baseline headache more after the final ninth dose. The authors suggested that diphenhydramine may be used alone or in combination with DHE protocols for the treatment of refractory headache. Similarly, when DHE (1 mg) is combined with prochlorperazine (3.5 mg), efficacy and tolerability are both enhanced.

Figure 1  Repetitive (every 8 hours) intravenous (IV) dihydroergotamine mesylate (DHE)–Raskin protocol. PO, orally; IM, intramuscular; BP, blood pressure; PRN, as needed; q, every. (Adapted from Raskin; presented at: Headaches in the ED; AAN Annual Meeting; May 4, 2007; Boston, MA.)
patients who have not responded to sumatriptan.\textsuperscript{35} is an option in the ED, and may be effective even in patients who have not responded to sumatriptan.\textsuperscript{35} Recent trials have demonstrated the combination of oral sumatriptan (50–85 mg) with naproxen (500 mg) as more effective than either agent administered as monotherapy.\textsuperscript{27,36,37} So far studies have been focused on oral rather than subcutaneous sumatriptan.\textsuperscript{35} Recent trials have demonstrated the combination of oral sumatriptan (50–85 mg) with naproxen (500 mg) as more effective than either agent administered as monotherapy.\textsuperscript{27,36,37} So far studies have been focused on oral rather than subcutaneous sumatriptan.\textsuperscript{35} Nonetheless, in severe migraine it may be reasonable to consider the addition of an NSAID to the standard triptan therapy.

**STEREOS**

Early randomized, controlled trials that examined the use of dexamethasone for migraine headache in the ED gave mixed results.\textsuperscript{38–40} However, two recent meta-analyses examined all available randomized, double-blind, placebo-controlled trials of dexamethasone for migraine, and showed a modest but statistically significant benefit when dexamethasone is added to standard abortive therapy.\textsuperscript{41,42} Compared with placebo, these studies showed that the addition of a single parenteral dose of dexamethasone to standard therapy appears to reduce the rate of headache recurrence within 24 to 72 hours. Doses in the trials ranged from 10 to 24 mg IV, given over \( \sim 10 \) minutes. Patients given the dexamethasone tended to experience more dizziness (relative risk [RR] 2.15, 0.98–4.74), but less nausea (RR 0.7, 0.48–1.02) or other adverse events than placebo.\textsuperscript{42} There is some evidence to support the use of IV dexamethasone as an adjunct to other abortive agents for status migrainosus as well.\textsuperscript{34,43,44}

**MADENIUM SULFATE**

The literature regarding magnesium sulfate as a therapy for migraine is somewhat mixed. One study of 113 patients showed 2 g IV magnesium was no better than placebo.\textsuperscript{47} A small study comparing IV metoclopramide combined with magnesium versus IV metoclopramide and placebo, showed patients receiving magnesium actually had a less favorable response than those receiving placebo.\textsuperscript{48} Another randomized placebo-controlled trial of 60 patients showed that 1 g IV magnesium sulfate was better than placebo in migraine with aura, but not in migraine without aura.\textsuperscript{49} Interestingly, there was improvement in photophobia and phonophobia in both groups.\textsuperscript{49} A nonrandomized study showed a beneficial effect of magnesium in both migraine and cluster headache, with a greater chance of improvement if the serum magnesium was less than 0.70 mmol/L.\textsuperscript{50} Although the evidence for magnesium is far from overwhelming, it offers a minimal side effect profile and can be used safely during pregnancy.

**OPIOIDS**

As mentioned previously, one should avoid or limit opioid medications in the treatment of migraine. Not only are they associated with an increased risk of dependency and rebound headache, but they tend to be less efficacious than migraine-directed medicines. Unfortunately, opioids continue to be popular in the ED for acute migraine therapy, and meperidine is the agent most commonly used.\textsuperscript{51} A recent meta-analysis involving 254 patients, found that meperidine was less effective than DHE (odds ratio [OR] 0.30; 95% CI 0.19–1.11), tended to less efficacy than the antiemetics (OR 0.46; 95% CI 0.19–1.11), and was most similar to the efficacy of ketorolac (OR 1.75; 95% CI 0.84–3.61).\textsuperscript{51} Meperidine tended to cause more sedation and dizziness than

| Step 1: Metoclopramide 10 mg IV over 2–3 min q 8 h for 5 doses PRN nausea |
| Step 2: Start DHE 3 mg in 1000 cc normal saline IV at 42 mL/h (may continue up to 7 days) |
| PRN: IF significant nausea: reduce the rate of DHE to 21–30 mL/h |
| IF extrapyramidal symptoms: give benztropine mesylate 1 mg IV/IM/PO |
| IF diarrhea: give diphenoxylate with atropine 1–2 tabs TID |
| PRN, OR give loperamide hydrochloride 1–2 mg TID PRN |

IV, intravenous; IM, intramuscular; PO, orally; q, every; PRN, as needed; TID, three times daily.

Adapted from Ford, 1997; presented at: Headaches in the ED, AAN Annual Meeting; May 4, 2007; Boston, MA.

**VALPROATE**

Intravenous valproate may be a reasonable alternative abortive agent for migraine treatment in the ED. The advantages of sodium valproate are the lack of cardiovascular side effects, no interaction with triptans or ergot alkaloids, lack of sedation, and no dependence formation. Even as a short-term treatment, valproate should probably be avoided in pregnant patients or patients with hepatic disease.

Several preliminary or open-label trials have shown sodium valproate, 300 to 500 mg IV, to result in improvement of migraine within \( \sim 30 \) minutes.\textsuperscript{45,46} One open-label trial involving 106 patients found 300 to 1200 mg IV valproate produced at least 50% improvement in 63% of patients with a mixture of headache types. Randomized placebo-controlled trials need to be performed to confirm the efficacy of sodium valproate in acute migraine management.

**NONSTEROIDAL ANTIINFLAMMATORY DRUGS**

Nonsteroidal analgesics may be quite effective for the acute management of migraine headache, and in some studies have been found to be as effective as triptans (Table 5).\textsuperscript{27} Because it may be given IM or IV, ketorolac offers a minimal side effect profile and can be used safely during pregnancy.

<table>
<thead>
<tr>
<th>Continuous IV Dihydroergotamine (DHE) — Ford Protocol\textsuperscript{22}</th>
</tr>
</thead>
<tbody>
<tr>
<td>Step 1: Metoclopramide 10 mg IV over 2–3 min q 8 h for 5 doses PRN nausea</td>
</tr>
<tr>
<td>Step 2: Start DHE 3 mg in 1000 cc normal saline IV at 42 mL/h (may continue up to 7 days)</td>
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<td>PRN, OR give loperamide hydrochloride 1–2 mg TID PRN</td>
</tr>
</tbody>
</table>

IV, intravenous; IM, intramuscular; PO, orally; q, every; PRN, as needed; TID, three times daily.

Adapted from Ford, 1997; presented at: Headaches in the ED, AAN Annual Meeting; May 4, 2007; Boston, MA.
<table>
<thead>
<tr>
<th>Drug Name</th>
<th>When to Use</th>
<th>Dosing</th>
<th>Side Effect</th>
<th>Caution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Naproxen sodium</td>
<td>Anytime during migraine</td>
<td>550 mg PO; may repeat after 2 h (max 1100 mg in 24 h)</td>
<td>GI distress</td>
<td>Caution with peptic ulcer disease, renal insufficiency, or gastritis</td>
</tr>
<tr>
<td></td>
<td>Preferred to shorter-acting NSAIDS</td>
<td></td>
<td>Dizziness</td>
<td>Contraindicated perioperatively following CABG</td>
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<tr>
<td></td>
<td>May combine with triptan</td>
<td></td>
<td>Hypersensitivity</td>
<td>Avoid in late pregnancy</td>
</tr>
<tr>
<td>Ketorolac</td>
<td>Anytime during migraine</td>
<td>60 mg IM as a single dose OR 30 mg IM every 6 h; max dose, 120 mg/d; max duration, 5 d</td>
<td>GI distress</td>
<td>Hypersensitivity (allergic response/asthma/rash with other NSAID)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Anemia</td>
<td>Bleeding risk</td>
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<tr>
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<td></td>
<td>Dizziness</td>
<td>History of GI bleeding</td>
</tr>
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<td></td>
<td></td>
<td></td>
<td>Edema</td>
<td>Renal impairment (use with diuretic and ACE inhibitor may increase renal toxicity)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Rash</td>
<td>Bleeding risk/GI bleeding</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Bronchospasm</td>
<td>Caution with cardiovascular disease, as thrombotic events have occurred. (Toradol® product info., Roche Laboratories, Nutley, NJ)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Hypersensitivity</td>
<td>Avoid in nursing mothers</td>
</tr>
<tr>
<td>Ibuprofen</td>
<td>Anytime during migraine</td>
<td>600–1200 mg PO initially, then 400 mg PO q 4–6 h (max 2400 mg/24 h)</td>
<td>GI distress</td>
<td>Caution with peptic ulcer disease/gastritis, renal insufficiency</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Rash</td>
<td>Contraindicated perioperatively following CABG</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Dizziness</td>
<td></td>
</tr>
<tr>
<td>Tylenol® (Ortho-McNeil-Jansson Pharmaceuticals, Titusville, NJ)</td>
<td>Anytime during migraine</td>
<td>650 mg–1000 mg (max 4000 mg/24 h)</td>
<td>Hypersensitivity</td>
<td>&gt;4 g/d associated with increased risk of liver toxicity</td>
</tr>
</tbody>
</table>

PO, orally; IM, intramuscular; q, every; GI, gastrointestinal; CABG, coronary artery bypass grafting; ACE, angiotensin converting enzyme.

Note: Dosing is more for the acute setting of the emergency department, and should not continue more than 10 days.
DHE, less akathisia than the antiemetics, and similar sedation and gastrointestinal adverse effects to ketorolac. This review of the literature supports previous guidelines against using meperidine as first-line therapy for migraine.

CGRP Antagonists in the Future?
There are some promising studies assessing the efficacy of oral calcitonin gene-related peptide (CGRP) receptor antagonists for the acute treatment of migraine. The studies have so far demonstrated similar efficacy to some triptans, and these new medications seem to be well tolerated. Liver function may play a limiting role in how frequently these may be used, as one of the phase IIa trials showed asymptomatic elevation of transaminases.

STATUS MIGRAINOSUS
Status migrainosus is an attack of migraine lasting more than 72 hours, with headache-free intervals lasting less than 4 hours. Status migrainosus is often severe and debilitating, and requires aggressive treatment. Status may often be caused by analgesic overuse, and patients may require education regarding the need to limit analgesic medication. Although there are no large trials on the treatment of status migrainosus, most protocols recommend combination therapy. One could start with IV fluids and electrolyte replacement (if indicated), followed by premedication with 25 mg IV/IM diphenhydramine (or 1 mg IV/IM benztropine) and 5 to 10 mg IV prochlorperazine. Some patients require hospital admission to manage their intractable migraine headaches, and in this circumstance, one could utilize a repetitive or continuous DHE protocol as described by Raskin and Ford previously (Fig. 1 and Table 4). As adjunctive therapy, 10 to 20 mg IV dexamethasone, and 5 to 10 mg diazepam could be given. Ketorolac, 30 to 60 mg IM or IV, or sodium valproate, 300 to 500 mg IV (max infusion 20 mg per minute) would be alternatives if DHE or triptan therapy were contraindicated or ineffective.

CLUSTER HEADACHE MANAGEMENT IN THE ED
Cluster headache is considered uncommon among primary headache disorders; nevertheless, the extreme severity and intensity of pain may drive the patient to the ED for further care. There is some evidence supporting oxygen inhalation as effective in aborting a cluster attack as well, with side effects and contraindications similar to those of migraine patients.

SPECIAL CIRCUMSTANCES: THE PREGNANT MIGRAINE PATIENT
Most primary headache syndromes improve during pregnancy; however, the pregnant migraine sufferer may need to come to the ED for management. Tylenol, possibly combined with caffeine, is a good first-line choice for the acute migraine attack. Unfortunately, the patient will likely have tried that prior to coming to the ED. As outlined earlier, treatment should begin with conservative measures, including a dark quiet room, reassurance, and IV hydration if necessary.

Metoclopramide is considered a class B drug by the Food and Drug Administration (FDA; no evidence for risk in humans, but no controlled studies). It has been used in all stages of pregnancy without evidence of fetal harm; therefore, it may be a reasonable option for nausea. Magnesium sulfate is also considered safe for the fetus, and may help with migraine. NSAIDS, such as ibuprofen and naproxen, are considered safe during the second trimester, but should be avoided during the third due to the possibility of premature ductus arteriosus closure. There may also be a small risk of increased spontaneous abortion if NSAIDS are taken during the first trimester.

Opioid medications, such as morphine, meperidine, and oxycodone, are probably not teratogenic and could be considered for very short-term use, during status migrainosus, if necessary. They should not be used for prolonged use, given the risk of drug dependency and rebound headache. This is especially true during the third trimester, when prolonged use could be associated with neonatal addiction and respiratory distress.

Sumatriptan was lethal to rabbit embryos when given in large doses IV, and produced vascular and skeletal abnormalities when given orally. In the pregnancy registry, sumatriptan has been associated with increased preterm delivery and low birth weight. There have also been a small number of recorded birth defects, with an any-trimester exposure proportion of 4.4% with sumatriptan, as compared with the 3.4% estimated birth defects in migraine sufferers. At this point, data on triptan use during pregnancy is still being collected. Due to the limited information, all triptans are considered FDA class C (studies in animals show harm, and limited information in humans). DHE/ergotamine and valproic acid are considered class X, and should be avoided during pregnancy, as there have been cases of fetal toxicity and teratogenicity.
DISMISSAL MEDICATIONS

Over 50% of patients seen in the ED for primary headache disorders will have moderate to severe headache present within 24 hours of discharge.\textsuperscript{69} Furthermore, 23 to 50% will have functional disability within 24 hours of discharge.\textsuperscript{69} Despite this, many patients are dismissed from the ED without a management plan for recurrent pain or nausea. A study of 219 patients seen at a university hospital ED showed fewer than 40% were given a prescription for medication on discharge, and only 40.6% were asked to follow up with a physician.\textsuperscript{70} Without a plan in place, the recurrence of severe pain may lead the patient back to the ED for further care.

As mentioned previously, pooled data from the existing literature suggests a single dose of 10 mg to 24 mg IV dexamethasone, in addition to the standard abortive therapy, may help reduce the rate of recurrent headache, and could therefore be considered prior to dismissal from the ED.\textsuperscript{41,42} A prescription for an antiemetic per rectum would be helpful for patients with nausea, to allow them to tolerate oral medications at home, and to prevent the recurrence of dehydration.

It is reasonable to recommend or even establish a follow-up appointment within 72 hours of the ED visit, especially among patients not obtaining complete headache relief. If a patient is unable to tolerate fluids by mouth, or if the pain is not controlled with oral or rectal medications, it is necessary to admit them for further management.

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