Effective Health Care Program

Brain and Nerve Conditions
Acute Migraine Treatments

Acute Migraine Treatment in Emergency Settings

Research Focus for Clinicians

In response to a request from the public about treatment of adults with migraines in emergency departments (EDs) or other emergency settings, the Agency for Healthcare Research and Quality (AHRQ) funded the University of Alberta Evidence-based Practice Center to develop a systematic review of the literature to summarize the evidence regarding the comparative effectiveness of parenteral medicines for adults who present to the ED with migraine. The systematic review included 71 clinical studies published through January 5, 2012. This summary is provided to assist in decisionmaking along with a patient's values and preferences. Reviews of evidence should not be construed to represent clinical recommendations or guidelines. An online version of this summary provides links directly to the sections of the full report with references for individual findings, inclusion criteria for the studies, and an explanation of the methods for rating the studies and determining the strength of evidence for individual findings. The online version of this summary and the full report are available at *www.effectivehealthcare.ahrq.gov/migraine-emergency.cfm*.

Background

Acute migraine headaches can last from 4 hours to 3 days if untreated. Migraines often require bed rest, pain medications, and time off from work and other activities, thus reducing an individual's productivity and quality of life. Seven percent of U.S. migraine patients reported using an ED or urgent care center for treatment within the previous 12 months. Of patients who use an ED for migraine treatment, 19 percent make multiple visits over the course of 1 year. Practice patterns of migraine treatment in the emergency setting vary in the United States. As many as 20 different agents are commonly used to treat acute migraines in the ED. A synthesis of the evidence from the clinical literature may inform treatment choices based on the balance of benefits and adverse effects of parenteral agents for treating acute migraine.

Conclusions

- Several common parenteral treatments for migraine pain (e.g., sumatriptan, metoclopramide, neuroleptics, and nonsteroidal anti-inflammatory drugs [NSAIDs]) in EDs are effective at reducing pain intensity and/or achieving pain-free status within 1–2 hours of administration.
- Direct head-to-head comparisons are very limited; however, moderate-strength evidence suggests that droperidol may provide full headache relief better than prochlorperazine.
- Low-strength evidence from indirect comparisons made across trials using statistical techniques to assess pain reduction suggests that dihydroergotamine (DHE), in combination with either prochlorperazine or metoclopramide, and neuroleptic monotherapy are the most effective (approximately a 40-mm reduction on a 100-point visual analog scale [VAS]).
- Patients who receive dexamethasone plus abortive therapy are less likely to have a recurrence.
- Most adverse effects are minor and self-limiting; however, the data on pain relief must be weighed carefully with the data on side effects, especially akathisia, which is associated more with the neuroleptics and metoclopramide.

Clinical Bottom Line

Ability To Achieve Pain-Free Status

- Neuroleptics, NSAIDs, and sumatriptan improve the likelihood of achieving pain-free status at various time points after administration versus placebo. ●●○
  - Sumatriptan at 30 to 120 minutes: RR = 4.73 (95% CI 3.77 to 5.94)
  - Neuroleptics at 60 minutes (prochlorperazine, chlorpromazine, or droperidol): RR = 3.38 (95% CI 1.16 to 9.83)
  - NSAIDs at 60 to 120 minutes: RR = 2.74 (95% CI 1.26 to 5.98)
- More patients report full relief from headaches with droperidol when compared with prochlorperazine (RR = 0.81; 95% CI 0.68 to 0.98). ●●○
- The evidence is insufficient to permit conclusions about the likelihood of achieving pain-free status with other treatments. ○○○

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Strength of Evidence Scale

High:	●●●	High confidence that the evidence reflects the true effect. Further research is very unlikely to change our confidence in the estimate of effect.
Moderate:	●●○	Moderate confidence that the evidence reflects the true effect. Further research may change our confidence in the estimate of effect and may change the estimate.
Low:	●○○	Low confidence that the evidence reflects the true effect. Further research is likely to change our confidence in the estimate of effect and is likely to change the estimate.
Insufficient:	○○○	Evidence either is unavailable or does not permit a conclusion.

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Clinical Bottom Line *(Continued)*

Ability To Provide Significant Headache Relief (Complete or Partial Relief)

Neuroleptics and sumatriptan provide significant headache relief at various time points versus placebo. ●●○

- Neuroleptics at 60 minutes (haloperidol, chlorpromazine, prochlorperazine, and droperidol):
  RR = 2.69 (95% CI 1.66 to 4.34)
- Sumatriptan at 60 minutes:
  RR = 3.03 (95% CI 2.59 to 3.54)
- Sumatriptan at 120 minutes:
  RR = 2.61 (95% CI 2.09 to 3.26)

Ability To Reduce Pain Intensity

Pain intensity measurements at time points after administration are reported as the mean difference (MD) versus placebo on a 100-point VAS (in mm)*.

- Neuroleptics, metoclopramide, opioids, and sumatriptan significantly improve pain intensity at various time points versus placebo. ●●○
  - Neuroleptics at 30 minutes to 4 hours (chlorpromazine, haloperidol, and prochlorperazine):
    MD = -46.59 mm (95% CI -54.87 to -38.32)
  - Metoclopramide at 30 to 60 minutes:
    MD = -21.88 mm (95% CI -27.38 to -16.38)
  - Opioids at 45 to 60 minutes (pethidine, nalbuphine, tramadol, and hydroxyzine + nalbuphine):
    MD = -16.73 mm (95% CI -24.12 to -9.33)
  - Sumatriptan at 30 minutes:
    MD = -15.45 mm (95% CI -19.49 to -11.41)
- Neuroleptics (chlorpromazine and prochlorperazine) as a group reduce pain intensity more than metoclopramide (MD = 16.45 mm; 95% CI 2.08 to 30.83); however, there are no differences in the reduction of pain intensity when metoclopramide and prochlorperazine are compared alone. ●○○
- There are no significant differences in the reduction in pain between prochlorperazine and droperidol. ●○○
- The evidence is insufficient to permit conclusions about the ability of other interventions to reduce migraine headache pain (see the full report). ○○○

Strength of Evidence Scale

High:	●●●	High confidence that the evidence reflects the true effect. Further research is very unlikely to change our confidence in the estimate of effect.
Moderate:	●●○	Moderate confidence that the evidence reflects the true effect. Further research may change our confidence in the estimate of effect and may change the estimate.
Low:	●○○	Low confidence that the evidence reflects the true effect. Further research is likely to change our confidence in the estimate of effect and is likely to change the estimate.
Insufficient:	○○○	Evidence either is unavailable or does not permit a conclusion.

Ability To Prevent Recurrence**

- Patients receiving dexamethasone plus standard abortive therapy are less likely to report recurrence of pain or headache up to 72 hours after discharge when compared with placebo plus standard abortive therapy (RR = 0.68; 95% CI 0.49 to 0.96). ●●○
- The rate of headache recurrence within 24 hours is lower with sumatriptan than with placebo (RR = 0.72; 95% CI 0.57 to 0.90). ●○○
- Additional evidence on recurrence rates is too limited to guide clinical decisionmaking.

Indirect Comparisons Performed Across Controlled Clinical Trials Using Statistical Methods

- Combination therapy with DHE plus either prochlorperazine or metoclopramide, as well as neuroleptic monotherapy, decrease pain intensity by about 40 mm on the VAS (95% CIs ranging from -60.9 to -22.1). ●○○
- Metoclopramide, opioids, and NSAIDs decrease pain intensity by about 24 mm on the VAS (95% CIs ranging from -38.8 to -12.0). ●○○
- DHE monotherapy, sumatriptan, and orphan agents† decrease pain intensity by about 12 to 16 mm on the VAS (95% CIs ranging from -32.6 to -0.5). ●○○
- No statistically significant difference in effect on pain intensity is noted for other antinauseants. ●○○

Adverse Effects

- The evidence is insufficient to conclude which active treatment results in more or fewer adverse effects. ○○○
- The odds of developing akathisia after a neuroleptic agent or metoclopramide is about 10 times greater than with placebo.
- The risk of sedation is common after receiving metoclopramide or prochlorperazine treatment (17% for both).
- The most common adverse effects from DHE included pain or swelling at the injection site, IV site irritation, sedation, digestive issues, nausea or vomiting, and chest symptoms (palpitations, arrhythmia, or irregular heartbeat).
- The most common adverse effects of triptans are local reactions. According to the FDA, there is a risk of coronary vasospasm if sumatriptan is given to patients with known or unknown coronary or vascular risk factors.
- NSAIDs and opioids are associated with few short-term side effects.

* All pain scales are subjective, numerical, and anchored by "severe" and "none" extremes. Pain scores in any format other than the VAS (in mm) were converted to a 100-point scale for comparative purposes across studies.

**Recurrence is defined as the return of headache in the followup period after successful initial treatment in the ED.

† This group of drugs were not easily classified and were infrequently studied (i.e., hydroxyzine, lidocaine, magnesium sulfate, octreotide, and sodium valproate).

95% CI = 95-percent confidence interval; FDA = U.S. Food and Drug Administration; IV = intravenous; RR = relative risk

Gaps in Knowledge

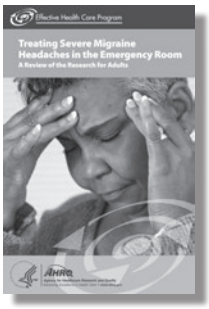
- More head-to-head comparisons are needed to determine which treatments are most effective in quickly reducing migraine pain, achieving pain-free status, and reducing the likelihood of recurrence.
- The effects of sex, race, or duration of headache on the response to treatment should be investigated.
- The differences in effectiveness between the various parenteral delivery routes (intravenous, intramuscular, and subcutaneous) should be further explored.

What To Discuss With Your Patients

- The effectiveness of chosen treatments
- Evidence of adverse effects
- Reasons for using combination therapy
- Use of dexamethasone to prevent relapse
- The availability of treatments for chronic migraine to prevent recurrent emergency treatment

Resource for Patients

Treating Severe Migraine Headaches in the Emergency Room, A Review of the Research for Adults is a free companion to this clinician research summary. It can help patients talk with their health care professionals about treatment options. It provides information about:



- Migraine headaches
- When to visit the emergency room
- Benefits and possible side effects of migraine headache treatments
- Questions to discuss with their doctor

Ordering Information

For electronic copies of *Treating Severe Migraine Headaches in the Emergency Room, A Review of the Research for Adults*, this clinician research summary, and the full systematic review, visit *www.effectivehealthcare.ahrq.gov/migraine-emergency.cfm*. To order free print copies, call the AHRQ Publications Clearinghouse at 800-358-9295.

Source

The information in this summary is based on *Acute Migraine Treatment in Emergency Settings*, Comparative Effectiveness Review No. 84, prepared by the University of Alberta Evidence-based Practice Center under Contract No. 290-2007-10021-I for the Agency for Healthcare Research and Quality, November 2012. Available at *www.effectivehealthcare.ahrq.gov/migraine-emergency.cfm*. This summary was prepared by the John M. Eisenberg Center for Clinical Decisions and Communications Science at Baylor College of Medicine, Houston, TX.

AHRQ Pub. No. 12(13)-EHC142-3
September 2013