Implementing AHRQ Effective Health Care Reviews

Helping Clinicians Make Better Treatment Choices

Acute Migraine Treatment in Emergency Settings

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The Agency for Healthcare Research and Quality (AHRQ) conducts the Effective Health Care Program as part of its mission to organize knowledge and make it available to inform decisions about health care. A key clinical question based on the AHRQ Effective Health Care Program review is presented, followed by an evidence-based answer and an interpretation that will help guide clinicians in making treatment decisions. For the full review, clinician summary, consumer summary, and CME activity, go to http://effectivehealthcare.ahrq.gov/search-for-guides-reviews-and-reports/?pageaction=displayproduct&productid=1758.

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This clinical content conforms to AAFP criteria for continuing medical education (CME). See CME Quiz Questions on page 708.

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Key Clinical Issue

What are the comparative benefits and adverse effects of parenteral treatments for adults who present to the emergency department with migraine headaches?

Evidence-Based Answer

Parenteral sumatriptan, metoclopramide, neuroleptics, and nonsteroidal anti-inflammatory drugs (NSAIDs) effectively reduce or eliminate migraine headache pain within two hours. (Strength of recommendation [SOR]: A, based on consistent, good-quality patient-oriented evidence.) Droperidol may provide complete relief better than prochlorperazine. (SOR: B, based on inconsistent or limited-quality patient-oriented evidence.) Migraine recurrence is less likely in patients receiving dexamethasone with abortive therapy. Most adverse effects are minor and self-limiting; however, akathisia is associated with neuroleptics and metoclopramide.

Practice Pointers

Migraine headaches affect about one in five adults in the United States and rank fifth among all reasons for emergency department visits.[1] They can last from four to 72 hours, and are usually described as pulsing, unilateral, and moderate to severe. They are aggravated by activity and usually accompanied by nausea or vomiting and photo- or phonophobia.[2] Migraine headaches are associated with $17 billion in direct and indirect health care costs annually.[3]

This Agency for Healthcare Research and Quality review included 69 randomized controlled trials and two other studies examining the comparative effectiveness of parenteral interventions for adults presenting to the emergency department with migraine headache. Of the agents studied, neuroleptics (prochlorperazine, chlorpromazine, and droperidol), NSAIDs, and sumatriptan improved the likelihood of achieving pain-free status at 30 to 120 minutes compared with placebo. Neuroleptics (haloperidol, chlorpromazine, prochlorperazine, and droperidol) also were associated with complete or partial relief at 60 minutes compared with placebo. Sumatriptan was similarly associated with significant relief at 60 and 120 minutes.[4]

Neuroleptics (chlorpromazine, haloperidol, and prochlorperazine) were associated with reduced pain intensity as measured on a 100-point visual analog scale. Metoclopramide, opioids (meperidine, tramadol, nalbuphine, and nalbuphine plus hydroxyzine), and sumatriptan were also associated with reduced pain intensity. Co-administration of dexamethasone with standard abortive therapy decreased the risk of symptom recurrence over the following 72 hours compared with placebo plus standard abortive therapy (number needed to treat = 9).[4]

The evidence was insufficient to determine the risks of adverse effects, although there was some indication of increased akathisia in patients taking a neuroleptic agent or metoclopramide and increased sedation in patients taking metoclopramide or prochlorperazine.[4]

Clinical practice guidelines recommend a stepwise escalation of medical management of migraine headaches in the emergency setting. The Institute for Clinical Systems Improvement suggests a graduated response

Clinical Bottom Line: Acute Migraine Treatment in Emergency Settings

Ability to achieve pain-free status

Neuroleptics, NSAIDs, and sumatriptan improve the likelihood of achieving pain-free status at various time points after administration vs. placebo. ●●○

Sumatriptan at 30 to 120 minutes (RR = 4.73; 95% CI, 3.77 to 5.94)

Neuroleptics (prochlorperazine, chlorpromazine, and droperidol) at 60 minutes (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 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.

Ability to provide significant headache relief (complete or partial)

Neuroleptics and sumatriptan provide significant headache relief at various time points after administration vs. placebo. ●●○

Neuroleptics (haloperidol, chlorpromazine, prochlorperazine, and droperidol) at 60 minutes (RR = 2.69; 95% CI, 1.66 to 4.34)

Sumatriptan at 60 minutes (RR = 3.03; 95% CI, 2.59 to 3.54) and 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 vs. placebo on a 100-point visual analog scale (in mm).*

Neuroleptics, metoclopramide, opioids, and sumatriptan significantly improve pain intensity at various time points vs. placebo. ●●○

Neuroleptics (chlorpromazine, haloperidol, and prochlorperazine) at 30 minutes to four hours (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 (meperidine; nalbuphine; tramadol; and hydroxyzine plus nalbuphine) at 45 to 60 minutes (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.

From indirect comparisons (not head-to-head trials), there is limited evidence that monotherapy with dihydroergotamine or dihydroergotamine in combination with either prochlorperazine or metoclopramide can reduce pain intensity. ●○○

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 compared with patients receiving 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 decision making.

Adverse effects

The evidence is insufficient to conclude which active treatment results in more or fewer adverse effects.

The odds of developing akathisia after treatment with a neuroleptic agent or metoclopramide are about 10 times greater than with placebo.

The risk of sedation is common after treatment with metoclopramide or prochlorperazine (17% for both).

The most common adverse effects from dihydroergotamine include pain or swelling at the injection site, intravenous 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 U.S. Food and Drug Administration, 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 adverse effects.

Strength of evidence scale

High: ●●● There are consistent results from good-quality studies. Further research is very unlikely to change the conclusions.

Moderate: ●●○ Findings are supported, but further research could change the conclusions.

Low: ●○○ There are very few studies, or existing studies are flawed.

Insufficient: ○○○ Research is either unavailable or does not permit estimation of a treatment effect.

CI = confidence interval; MD = mean difference; NSAIDs = nonsteroidal anti-inflammatory drugs; RR = relative risk.

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

†—Recurrence is defined as the return of headache in the follow-up period after successful initial treatment in the emergency department.

Adapted from the Agency for Healthcare Research and Quality, Effective Health Care Program. Acute migraine treatment in emergency settings. Clinician research summary. Rockville, Md.: Agency for Healthcare Research and Quality; September 2013. http://effectivehealthcare.ahrq.gov/ehc/products/289/1717/migraine-emergency-clinician-130919.pdf. Accessed February 20, 2014.

to severe migraine headache symptoms starting with triptans and NSAIDs, progressing to dihydroergotamine and ultimately neuroleptics, with the reservation of opiates and dexamethasone as adjuncts in refractory cases.[5] The European Federation of Neurological Societies likewise suggests starting with aspirin, with or without metoclopramide or sumatriptan. Dihydroergotamine is recommended for severe attacks, and corticosteroid therapy is recommended for status migrainosus.[6]

Based on this review, a reasonable approach for physicians in emergency settings would be to use parenteral NSAIDs, sumatriptan, metoclopramide, or neuroleptics for initial symptom control, and to consider dihydroergotamine for severe cases and dexamethasone for possible prophylaxis against recurrence. The addition of opioids may be considered for severe headaches that do not respond to other therapies.

EDITOR'S NOTE: *American Family Physician* SOR ratings are different from the Agency for Healthcare Research and Quality Strength of Evidence (SOE) ratings.

The opinions and assertions contained herein are the private views of the authors and are not to be construed as official or as reflecting the views of the U.S. Army Medical Department or the U.S. Army Service at large.

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