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What are effective medical treatments for adults with acute migraine?

EVIDENCE-BASED ANSWER

Medications collectively referred to as "triptans" (eg, sumatriptan, naratriptan, etc) have been shown to be effective for acute migraine (strength of recommendation [SOR]: **A**). Nonsteroidal anti-inflammatory drugs (NSAIDs)—including aspirin, ibuprofen, naproxen sodium, diclofenac potassium, ketoprofen, tolfenamic acid, and ketorolac—are also effective (SOR: **A**). The combination of acetaminophen/aspirin/caffeine is effective (SOR: **B**). Parenteral dihydroergotamine (DHE), when administered with an antiemetic, is as effective as, or more effective than meperidine, valproate, or ketorolac (SOR: **B**). Prochlorperazine is more effective than metoclopramide in headache pain reduction (SOR: **A**). Isometheptene mucate/dichloral-phenazone/acetaminophen is as effective as low-dose oral sumatriptan (SOR: **B**).

CLINICAL COMMENTARY

Inadequate response to medication? Increase dose or change route

For mild to moderate migraine headache attacks, NSAIDs or products containing acetaminophen and/or aspirin with caffeine or isometheptene mucate/dichloral-phenazone/acetaminophen, when used intermittently, are frequently effective. More severe attacks generally respond better to migraine-specific medications such as triptans and ergot derivatives—the latter may be less likely to cause secondary rebound (analgesic overuse) headaches. Inadequate response to migraine-specific medication should prompt the prescriber to increase dose or change route to insure absorption (ie, nasal, rectal, or injectable).

Emerging evidence suggests combining a triptan plus an NSAID may produce higher response rates and more durable responses. Narcotics should generally be avoided. Valproate, ketorolac, IV magnesium, prochlorperazine, and metoclopramide are all somewhat effective for acute migraine, the latter 2 agents having the advantage of helping nausea but with the disadvantage of causing extrapyramidal reactions. A short course of oral steroids may break persistent attacks. Patients with frequent and intense headache patterns should be offered prophylactic therapy and not just abortive treatments.

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Evidence summary

The prevalence of migraine headache is 6% among men and 15% to 17% among women.[1] However, no standardized approach exists for the treatment of acute migraine headache. Systematic reviews of randomized controlled trials (RCTs) summarized that oral sumatriptan (Imitrex),

eletriptan (Relpax), and rizatriptan (Maxalt) reduced migraine headache pain and increased the pain-free response rate for adults when compared with placebo.[2–4] The number needed to treat (NNT) ranged from 3.9 to 9.9 for a given triptan's lower dose to 2.6 to 5.1 for the higher dose.[2–4] RCTs reported superior efficacy of oral almotriptan (Axert), frovatriptan (Frova), and zolmitriptan (Zomig), as well as intranasal sumatriptan and zolmitriptan when compared with placebo.

The following NSAIDs reduced headache severity more than placebo 2 hours after treatment: aspirin (1000 mg; NNT=2.4), ibuprofen (1200 mg; NNT= 1.8), naproxen (750 mg; NNT=2.0), tolfenamic acid (not available in the US; NNT=1.2), and the combination product of acetaminophen/aspirin/caffeine (Excedrin Migraine, et al) (NNT=1.7).[5] Acetaminophen 1000 mg orally has been reported to be superior to placebo for treating pain, functional disability, and photo/phonophobia among patients who did not require bedrest with their headaches and did not vomit more than 20% of the time. However, it was not superior to placebo when given intravenously for more severe acute migraine. No placebo-controlled trials exist for the use of ketorolac (Toradol); there are only comparison studies against other active migraine medications. Ketoprofen (Orudis) has placebo-controlled RCT data supporting its efficacy.

A meta-analysis[6] of RCTs of parenteral metoclopramide (Reglan) revealed significant pain reduction (odds ratio [OR]= 2.84; 95% confidence interval [CI], 1.05–7.68). When compared with other antiemetics (chlorpromazine [Thorazine] and prochlorperazine [Compazine]), metoclopramide was either less effective (OR=0.39; 95% CI, 0.18–0.87) or no different (OR=0.64; 95% CI, 0.23–1.76) than other therapies for reducing migraine pain. No difference was noted between parenteral metoclopramide and subcutaneous sumatriptan (OR=2.27; 95% CI, 0.64–8.11); however, metoclopramide was more effective than ibuprofen in pain reduction scores (standard deviation data missing in this study).

A systematic review[7] revealed that dihydroergotamine (DHE) alone was less effective than subcutaneous sumatriptan in migraine pain reduction (OR=0.44; 95% CI, 0.25–0.77) or headache resolution (OR=0.05; 95% CI, 0.01–0.42). No differences were seen between DHE alone and chlorpromazine or lidocaine. Three studies revealed DHE plus metoclopramide was more effective than or equal to other agents for headache pain reduction at 2 hours: one vs ketorolac IM (OR=7; 95% CI, 0.86–56.89), one vs meperidine (Demerol) plus hydroxyzine (Vistaril, Atarax) IM (OR=47.67; 95% CI, 4.32–526.17), and one vs valproate IV (OR=0.67; 95% CI, 0.19–2.33).[7] Specifically, treatment with DHE plus metoclopramide was superior to ketorolac for pain reduction (P=.03), but patients did not differ in disability scores (P=.06). DHE plus metoclopramide achieved greater reductions in pain scale scores than meperidine plus hydroxyzine (P<.001). No significant difference in pain reduction was noted between DHE plus metoclopramide and valproate (P=.36).

A multicenter, double-blind, randomized parallel group study[8] showed no difference between the combination product isometheptene mucate, dichloralphenazone with acetaminophen (Midrin, Duradrin, etc) (used as recommended in the package insert with a maximum of up to 5 tablets within 24 hours) vs oral sumatriptan (initial dose of 25 mg with a repeat 25 mg dose in 2 hours). No placebo arm was used in this study.

Recommendations from others

The Institute for Clinical Systems Improvement recommends the use of vasoactive drugs over narcotics and barbiturates for treatment of moderately severe migraine headaches.[9] The American Academy of Neurology recommends migraine-specific medications (triptans, DHE) for moderate to severe migraines or those mild to moderate migraines that

FAST TRACK

More severe attacks generally respond better to migraine-specific medications such as triptans and ergot derivatives

responded poorly to NSAIDs or other over-the-counter preparations.[10]

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