

Anti-emetic for migraine

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- Migraine headache is a common and potentially debilitating disorder often treated by physicians.

- Data comparing different drug classes are relatively scarce. Abortive therapy should be used as early as possible after the onset of symptoms.
- Treating acute migraine is challenging because of substantial rates of nonresponse to medications and difficulty in predicting individual response to a specific agent or dose.

- Effective first-line therapies for mild to moderate migraine are nonprescription nonsteroidal anti-inflammatory drugs and combination analgesics containing acetaminophen, aspirin, and caffeine.

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- Antiemetics, including intravenous (IV) droperidol, IV prochlorperazine, IV metoclopramide, IV ondansetron, IV or intramuscular (IM) prochlorperazine, and IV or IM dexamethasone , are appropriate acute treatment options for migraine and are effective independent of their ability to control nausea.
- These agents are considered primary options for treating acute migraine in the emergency department setting.^{*,**}
- There is no evidence supporting the effectiveness of oral antiemetics in treating migraine, other than for relief of nausea.^{**}

* *Tepper, S.J. and R.C. Spears, Acute treatment of migraine. Neurol Clin, 2009. 27(2): p. 417-27*

** *Gilmore, B. and M. Michael, Treatment of acute migraine headache. Am Fam Physician, 2011. 83(3): p. 271-80.*

- **Metoclopramide** is a D2 receptor antagonist as well as 5-HT3 antagonist and 5-HT4 agonist. Through its anti-dopaminergic and anti-serotonergic effects, it **blocks the communication between the Chemoreceptor Trigger Zone and nucleus tractus solitarius and thereby acts as an potent antiemetic.**

- Evidence supports a role for parenteral antiemetics in acute migraine, independent of their anti nausea effects.
- A meta-analysis of 13 randomized controlled trials concluded that intravenous metoclopramide should be considered a primary agent in the treatment of migraine in emergency departments*.
- Given the potential for rebound and dependence associated with opiates, antiemetics offer a reasonable alternative in acute settings.**
- No evidence supports migraine-specific effects of oral antiemetics, other than relieving nausea.**

*Colman I, Brown MD, Innes GD, Grafstein E, Roberts TE, Rowe BH. Parenteral metoclopramide for acute migraine: meta-analysis of randomised controlled trials. *BMJ*. 2004;329(7479):1369-1373.

** BENJAMIN GILMORE, MAGDALENA MICHAEL. **Treatment of Acute Migraine Headache.** *Am Fam Physician*. 2011 Feb 1;83(3):271-280.

Potentially relevant papers identified by literature search (n=596)

Manuscripts did not contain original data (n=560)

Papers retrieved for more detailed evaluation (n=36)

Not randomised controlled trials (n=5)

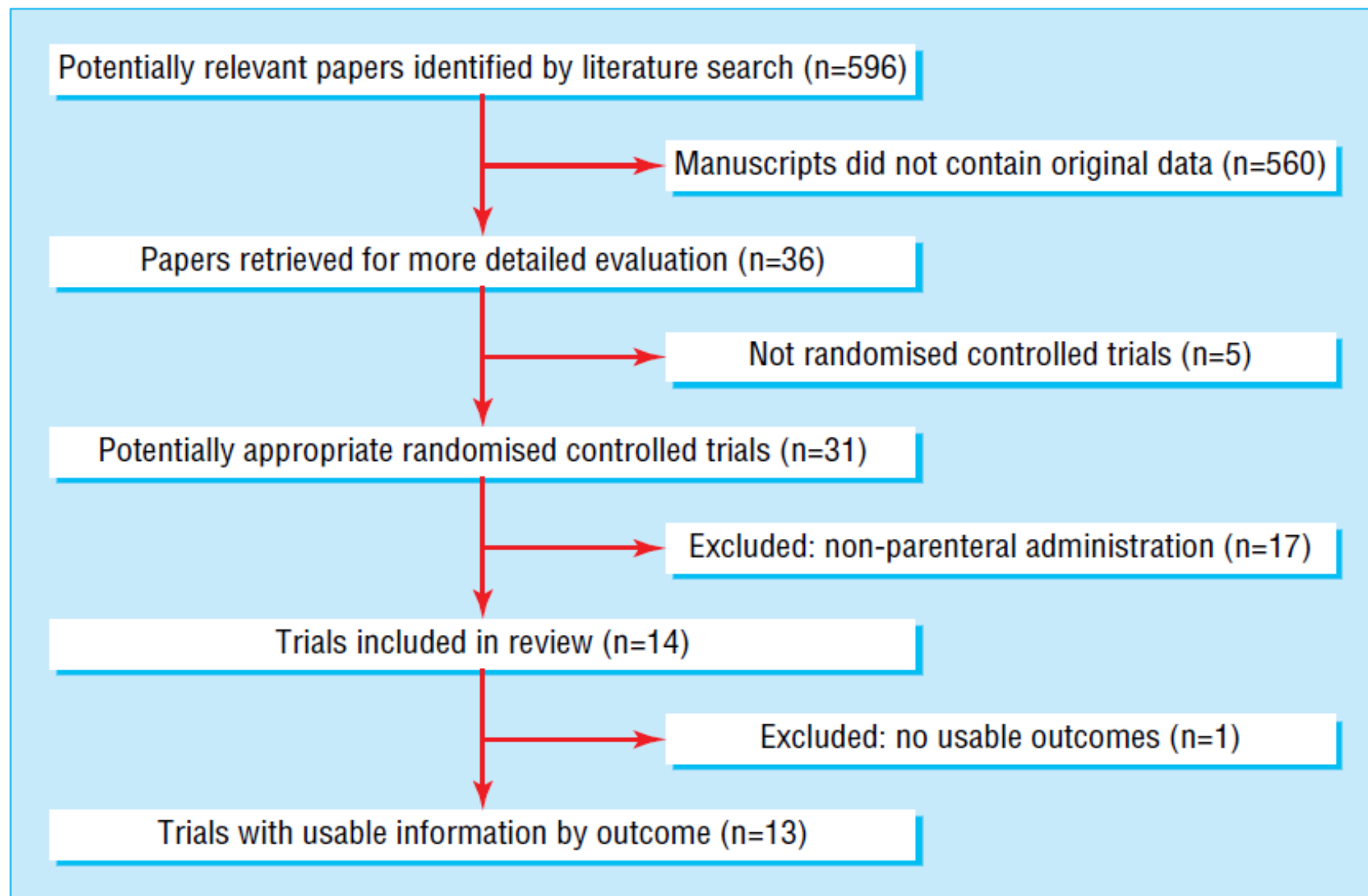
Potentially appropriate randomised controlled trials (n=31)

Excluded: non-parenteral administration (n=17)

Trials included in review (n=14)

Excluded: no usable outcomes (n=1)

Trials with usable information by outcome (n=13)



Metoclopramide versus placebo

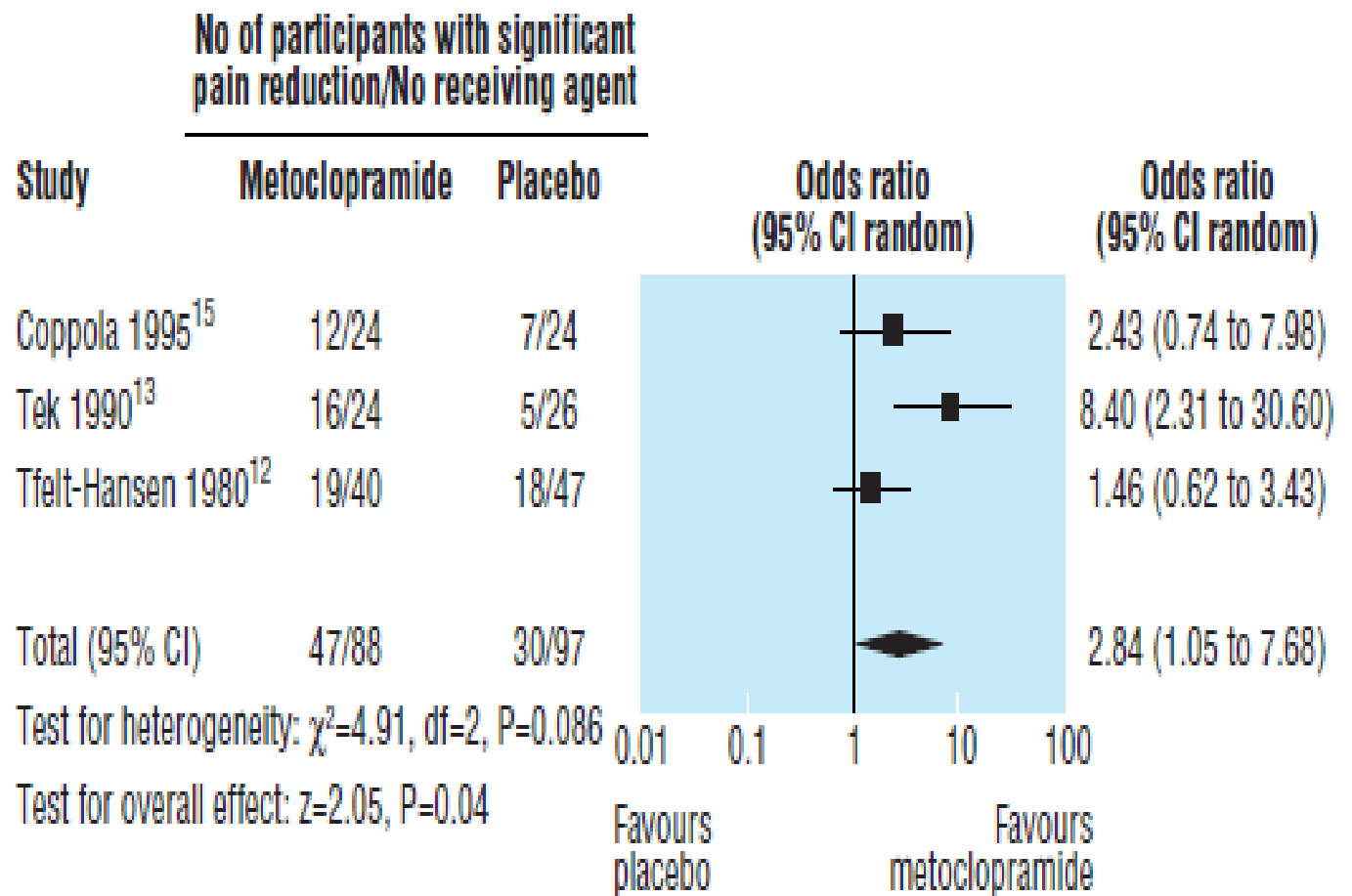
- Five studies, 263 patients compared
- Metoclopramide was superior to placebo for all outcomes related to pain and nausea, although differences were not always statistically significant.
- Pooled data from three studies showed that metoclopramide more often led to significant reductions in headache pain (odds ratio 2.84, 95% confidence interval 1.05 to 7.68), and in these studies, patients who received metoclopramide were significantly less likely to require rescue drugs (0.21, 0.05 to 0.85).

Metoclopramide versus placebo

- Three studies suggested that metoclopramide produced larger improvements in pain scores on a visual analogue scale, but no standard deviations were reported, preventing statistical pooling.
- One study reported that metoclopramide was more likely than placebo to provide complete resolution of migraine; the difference, however, was not statistically significant (2.16, 0.36 to 12.84).

Metoclopramide versus placebo

- Four studies found that metoclopramide was more effective than placebo in reducing nausea (4.20, 1.70 to 10.36), but only two studies reported relapse of migraine, and these found a statistically insignificant advantage favouring metoclopramide (0.30, 0.03 to 3.16).
- Only two studies reported adverse events. One found a statistically insignificant increase in restlessness in the metoclopramide group (2.27, 0.19 to 26.81) whereas the other reported no restlessness, dystonic reactions, hypotension, or seizures in either treatment group.



Metoclopramide compared with placebo in reducing pain from acute migraine

Metoclopramide versus other antiemetics

- Three studies (194 patients) compared metoclopramide with other antiemetics (chlorpromazine and prochlorperazine). These studies suggested that metoclopramide was less effective in relieving pain and nausea, although differences were not always statistically significant.

Metoclopramide versus other antiemetics

- Pooled results from all three studies showed that patients who received metoclopramide were more likely to require rescue drugs (odds ratio 2.08, 1.04 to 4.17). Two studies found no significant differences in relapse of migraine (3.95, 0.88 to 17.66).

Metoclopramide versus other antiemetics

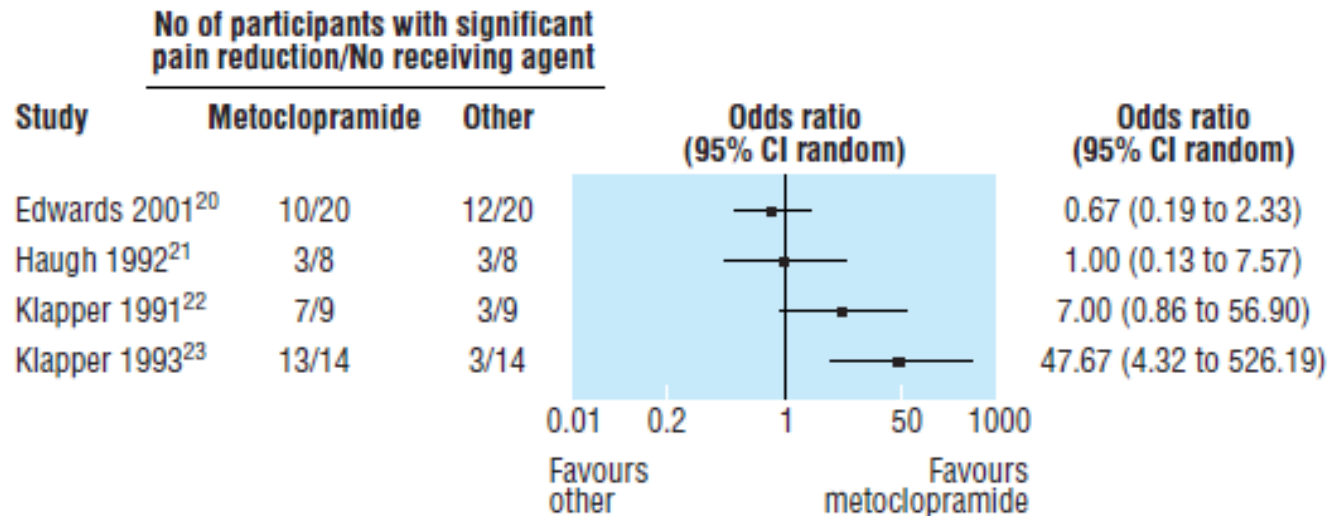
- Metoclopramide was less effective than other antiemetics in reducing nausea, but these differences were not statistically significant.
- Two studies looked at adverse events. One reported no restlessness, dystonic reactions, hypotension, or seizures in either treatment group, whereas the other described several subgroups of adverse events (restlessness, drowsiness, nasal congestion, nausea, dizziness, dry mouth, significant falls in diastolic or systolic blood pressure) but found no statistically significant differences between groups.

Metoclopramide versus non-antiemetics

- Two studies (60 patients) compared metoclopramide with non-antiemetics. The first found no significant differences between metoclopramide and sumatriptan in the rate of complete resolution of migraine (2.27, 0.64 to 8.11), the likelihood of significant reduction of pain (18.38 to 0.96, 352.59).
- In the second study, metoclopramide was compared with ibuprofen on the basis of scores to measure pain and nausea on a visual analogue scale. Metoclopramide produced larger decreases in scores for both outcomes, but standard deviations were not reported, making analysis difficult.

Metoclopramide versus non-antiemetics

- Patients in the metoclopramide group were significantly less likely to require rescue drugs (0.05, 0.00 to 0.56). Neither study reported adverse events, no common outcomes were reported, and no statistical pooling was possible.



Metoclopramide combinations versus other agents

- Seven studies (211 patients) compared metoclopramide combinations (usually metoclopramide with dihydroergotamine) with other antimigraine regimens (hydroxyzinemepерidine, dihydroergotamine alone, valproate, ibuprofen, ketorolac, promethazine-mepерidine).
- Owing to significant heterogeneity in study methods (see table), particularly for comparison treatments, studies were not pooled statistically.

Metoclopramide combinations versus other agents

- One study showed that complete resolution of migraine was significantly more likely in patients who received metoclopramide (7.79, 1.79 to 33.86), and results from four studies suggested that patients who received metoclopramide were equally, or more, likely to have “significant reductions” in headache pain.

Metoclopramide combinations versus other agents

- Two studies showed that patients who received metoclopramide had equivalent, or larger, reductions in pain scores on the basis of a visual analogue scale.
- One study found no significant differences between groups in requirement for rescue drugs (0.22, 0.04 to 1.12).
- Three studies reported that patients who received metoclopramide were equally, or less, likely to have relapse of migraine

Metoclopramide combinations versus other agents

- Reporting for adverse events was inconsistent. Four studies found no significant differences for nausea between groups.
- One study found restlessness, dysphoria, and flushing more common among patients treated with metoclopramide and dihydroergotamine compared with those treated with hydroxyzine and meperidine or butorphanol, and no significant differences for dizziness.
- Another study found that drowsiness, dizziness, and an orthostatic blood pressure response were less common among patients treated with metoclopramide and dihydroergotamine compared with those treated with promethazine and meperidine.

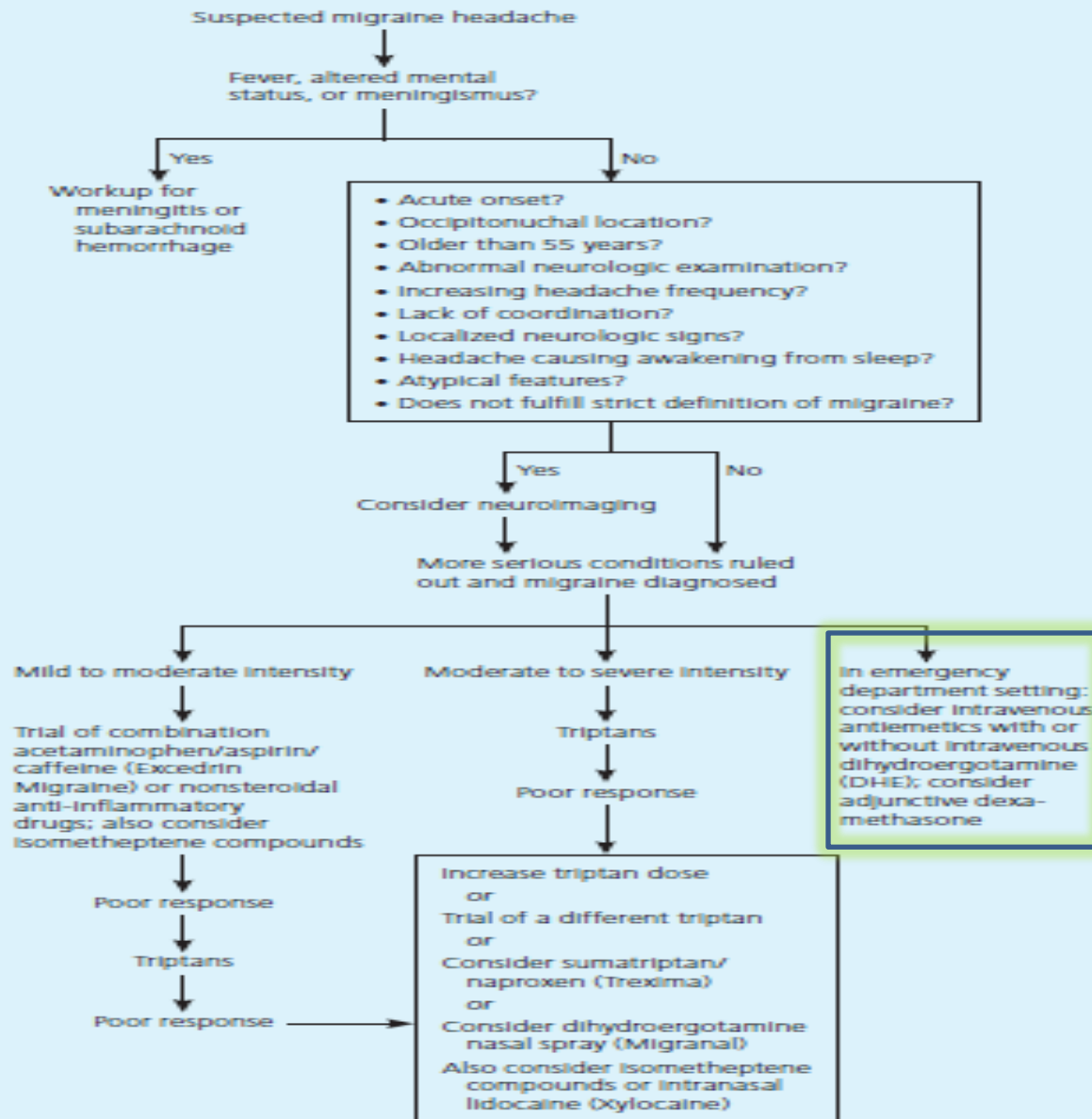
SORT: KEY RECOMMENDATIONS FOR PRACTICE

<i>Clinical recommendation</i>	<i>Evidence rating</i>	<i>References</i>
Triptans are effective and safe for treatment of acute migraine.	A	8
Abortive therapy should be used as early as possible in the course of a migraine.	B	19
Combination analgesics containing aspirin, caffeine, and acetaminophen are an effective first-line abortive treatment for migraine.	A	7, 9
Ibuprofen at standard doses is effective for acute migraine treatment.	A	21
Intravenous metoclopramide (Reglan) is effective for acute migraine treatment.	B	11
Parenteral dexamethasone is useful as an adjunctive treatment in the emergency department to help prevent short-term headache recurrence.	A	12, 18
Opiates and barbiturate-containing compounds should not be routinely used for abortive treatment of migraine.	C	14, 34

A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to <http://www.aafp.org/afpsort.xml>.

11. Colman I, Brown MD, Innes GD, Grafstein E, Roberts TE, Rowe BH. Parenteral metoclopramide for acute migraine: meta-analysis of randomised controlled trials. *BMJ*. 2004;329(7479):1369-1373.

Management of Acute Migraine Headache



NOTE: Abortive migraine therapy should be used as soon as possible after symptom development for maximum benefit; if abortive therapy is unsuccessful or used more than twice weekly, consider adding prophylactic therapy. Patients with nausea and vomiting may require nonoral medication. For all medications, consider patient comorbidities and contraindications.

- Metoclopramide & placebo
 - patients who received metoclopramide were significantly less likely to require rescue drugs
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- Metoclopramide & other antiemetics
- studies showed that patients who received metoclopramide were more likely to require rescue drugs

- Intravenous antiemetics, with or without intravenous dihydroergotamine, are effective therapies in an emergency department setting.*

- * BENJAMIN GILMORE, MAGDALENA MICHAEL. **Treatment of Acute Migraine Headache.** *Am Fam Physician.* 2011 Feb 1;83(3):271-280.

Be alone in the crowd



- Thank you for your patience