Review: Intravenous metoclopramide is better than placebo for reducing pain in acute migraine in the emergency department

Colman I, Brown MD, Innes GD, et al. **Parenteral metoclopramide for acute migraine: meta-analysis of randomised controlled trials.** BMJ. 2004;329:1369-73.

QUESTION

In patients with acute migraine, is metoclopramide more effective than a control intervention for reducing symptoms?

METHODS

Data sources: MEDLINE, EMBASE/Excerpta Medica, LILACS, CINAHL, and the Cochrane Central Register of Controlled Trials; neurology, headache, and emergency medicine conference proceedings (1998 to 2004); clinical practice guidelines for the management of acute migraine; hand-searching Web sites, theses or dissertations, and the bibliographies of relevant studies; and contacting authors and experts in the field.

Study selection and assessment: Randomized controlled trials (RCTs) that compared parenteral metoclopramide with control (placebo, other antiemetics [AEs], non-AEs, or other antimigraine [AM] regimens) in adults with an acute migraine, distinguished migraine from other types of headaches, and were done in an emergency department (ED) or headache clinic. Study quality was assessed using the 5-point Jadad scale.

Outcomes: Complete relief of headache, significant reduction in headache pain, and reduction in headache pain on the basis of a 10-cm visual analogue scale (VAS). Secondary outcomes included relapse of migraine within 48 hours of treatment, nausea, number of rescue drugs required, functional status, and adverse events.

MAIN RESULTS

13 RCTs (n = 655) met the selection criteria. 7 RCTs (54%) were high-quality (Jadad score ≥ 3). Through use of a random-effects model, meta-analysis of 3 RCTs showed that metoclopramide reduced headache pain (Table), nausea (odds ratio [OR] 4.20, 95% CI 1.70 to 10.36), and the need for rescue drugs (OR 0.21, CI 0.05 to 0.85) more than placebo. The groups did not differ for complete relief of headache (Table), relapse of migraine, or restlessness. 2 RCTs found that metoclopramide reduced headache pain less than other AEs (chlorpromazine and prochlorperazine) (Table). The groups did not differ for complete relief of headache (Table), pain scores on the VAS, relapse of migraine, nausea, or adverse events. Pooled results showed that patients in the metoclopramide groups were more likely to require rescue drugs than those in the other AE groups (OR 2.08, CI 1.04 to 4.17). Of the 2 RCTs that compared metoclopramide with non-AEs, 1 RCT showed no difference between metoclopramide and sumatriptan for complete relief of headache (Table), reduction in headache pain (Table), or nausea (OR 19.74, CI 1.00 to 390.32). In another RCT, metoclopramide reduced the need for rescue drugs more than ibuprofen (OR 0.05, CI 0.00 to 0.56). In studies comparing drug combinations, more patients achieved complete headache relief with metoclopramide combination than other AM regimens (Table).

CONCLUSIONS

In patients with acute migraine, metoclopramide reduces headache pain more than placebo. Compared with other single agents, metoclopramide shows variable effectiveness for other migraine symptoms.

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For correspondence: Dr. B.H. Rowe, University of Alberta, Calgary, Alberta, Canada. E-mail brian.rowe@ualberta.ca.

Metoclopramide vs placebo, other antiemetics (AEs) (chlorpromazine, prochlorperazine), non-AEs, and other antimigraine (AM) regimens for acute migraine at 1 week*

Outcomes	Number of trials (n)	Comparisons	Weighted event rates	RBI (95% CI)	NNT (CI)
Reduction in headache pain	3 (185)	Metoclopramide vs placebo	56% vs 31%	80% (1 to 221)	4 (3 to 44)
				Odds ratio (CI)	
	2 (161)	Metoclopramide vs other AEs		0.39 (0.18 to 0.87)	
	1 (40)	Metoclopramide vs non-AEs		18.38 (0.96 to 352.59)†	
Complete relief of headache	1 (86)	Metoclopramide vs placebo		2.16 (0.36 to 12.84)†	
	2 (177)	Metoclopramide vs other AEs		0.64 (0.23 to 1.76)†	
	1 (40)	Metoclopramide vs non-AEs		2.27 (0.64 to 8.11)†	
	1 (62)	Combination metoclopramide vs other AMs		7.79 (1.79 to 33.86)	

*Abbreviations defined in Glossary; weighted event rates, RBI, NNT, and CI calculated from data in article using a random-effects model.
†Not significant.

COMMENTARY

Metoclopramide avoids many perceived or actual liabilities of other current treatment choices for acute migraine. It also provides relief of pain and other such migraine-associated symptoms as nausea and vomiting. These virtues explain the enduring popularity of metoclopramide for treating migraine in the ED setting.

Colman and colleagues provided a good summary of evidence of the effect of metoclopramide. Although the results show a reduction in pain that favors metoclopramide over placebo, the duration of effect and rate of headache relapse are not known. However, metoclopramide alone does provide definitive treatment for some patients; 3 of 4 patients on average will require alternative or adjunctive treatment. The severity of the migraine should dictate the approach to treatment in the ED. Nonsteroidal antiinflammatory drugs, ketorolac, sumatriptan, dihydroergotamine, chlorpromazine, prochlorperazine, and dexamethasone—with or without metoclopramide—can be considered for treatment of migraine in the ED.

Whether metoclopramide might outperform sumatriptan remains unanswered because the single study that reached this conclusion was low-quality and lacked a placebo group. Some evidence supports the use of oral metoclopramide for acute migraine (1); however, the FDA recently rejected an application for an oral sumatriptan–metoclopramide combination product, stating concerns about long-term safety (2). This should temper enthusiasm for wide-scale use of metoclopramide.

Elizabeth W. Loder, MD
Spaulding Hospital
Boston, Massachusetts, USA

References

1. **Pryse-Phillips WE, Dodick DW, Edmeads JG, et al.** CMAJ 1997;156:1273-87.
2. Prozen announces receipt of not-approvable letter for MT 100. Accessed January 28, 2005 at: www.pozen.com/product/mt100.asp