A Randomized Controlled Trial of Prochlorperazine Versus Metoclopramide for Treatment of Acute Migraine

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Study objective: We compare prochlorperazine 10 mg intravenously versus metoclopramide 20 mg intravenously for the emergency department (ED) treatment of acute migraine.

Methods: This was a randomized, double-blind, clinical trial comparing 2 parenteral dopamine antagonists. Both drugs were administered during 15 minutes with 25 mg intravenous diphenhydramine. Pain scores on a numeric rating scale were assessed at baseline, every 30 minutes for 2 hours, and by telephone 24 hours after discharge. The primary endpoint was the between-group difference in change in numeric rating scale from baseline to 1 hour postbaseline. Secondary endpoints included mean differences in change in numeric rating scale at 2 and 24 hours, headache relief, adverse effects, and desire to receive the same treatment for future migraines.

Results: Of 152 patients screened, 97 were eligible and 77 were randomized. The mean change in numeric rating scale scores at 1 hour was 5.5 and 5.2 in subjects receiving prochlorperazine and metoclopramide, respectively (difference = 0.3; 95% confidence interval [CI] = –1.0 to 1.6). Findings were similar at 2 hours and 24 hours. Forty-six percent (18/39) of prochlorperazine and 32% (12/38) of metoclopramide subjects reported adverse events (difference = 15%; 95% CI = –6% to 36%). Seventy-seven percent (26/34) of prochlorperazine and 73% (27/37) of metoclopramide subjects wanted to receive the same medication in future ED visits (difference = 4%; 95% CI = –16% to 24%).

Conclusion: Either prochlorperazine 10 mg intravenously or metoclopramide 20 mg intravenously, combined with diphenhydramine 25 mg intravenously, is an efficacious treatment for ED patients with acute migraine. Three quarters of subjects in both arms would want the same medication for their next migraine. [Ann Emerg Med. 2008;52:399-406.]

INTRODUCTION
Background

A mounting body of evidence has demonstrated the efficacy of the antiemetic dopamine antagonists as primary parenteral treatment for acute migraine.1-7 These agents are at least as efficacious as parenteral triptans,8-10 dihydroergotamine,2 and nonsteroids11 and are well tolerated. There is no consensus as to the optimal choice among the members of this class.
Editor’s Capsule Summary

What is already known on this topic
Prochlorperazine and metoclopramide are commonly used to treat migraine headache. Neither agent is clearly superior.

What question this study addressed
Prochlorperazine (10 mg) was compared to metoclopramide (20 mg), with diphenhydramine coadministered to all patients.

What this study adds to our knowledge
In this 77-patient trial, neither agent was clearly superior. Although pain outcome trends favored prochlorperazine, adverse events trends favored metoclopramide. More than 70% of patients in both groups wanted to receive the same medication in future emergency department visits for migraine.

How this might change clinical practice
Although the study cannot tell us which agent to use for all patients, it suggests that clinicians incorporate patient preferences for adverse events in choosing between agents and that higher-than-typical doses of metoclopramide can be used.

However, metoclopramide and prochlorperazine are often used because, unlike other medications in their class, they do not cause significant orthostatic changes or require cardiac monitoring. Although previous trials have concluded that prochlorperazine is superior to metoclopramide for the treatment of acute migraine, the 10-mg dose of metoclopramide used in those studies may have been insufficient. The optimal dose of metoclopramide for the acute treatment of migraine is unknown because dose-finding studies have not been conducted. However, 20 mg of intravenous metoclopramide is efficacious and well tolerated.

Importance
There is substantial practice variation in the emergency department (ED) – based treatment of acute migraine. Two dozen parenteral agents, alone or in combination, are commonly used in US EDs. Yet, ED migraine care remains suboptimal. Incomplete pain relief, need for rescue medication, adverse medication effects, functional disability, and recurrence of headache after ED discharge continue to plague individuals with migraine, independent of the primary treatment. This study addressed the efficacy and tolerability of a 20-mg dose of metoclopramide versus a 10-mg dose of prochlorperazine, with the intent of helping emergency physicians decide whether one of these 2 dopamine antagonists is superior as a primary treatment for acute migraine.

Goals of This Investigation
Our primary goal was to compare the 1-hour efficacy of metoclopramide + diphenhydramine with that of prochlorperazine + diphenhydramine. Specifically, we compared the mean change in a previously validated and reproducible 11-point pain scale between baseline and 1 hour. Secondary outcome measures included pain scores 2 and 24 hours after medication administration, achievement of pain-free status, sustained headache relief, functional status, development of adverse event (particularly akathisia), need for rescue medication, and the desire of patients to receive the same medication for acute migraine in the future.

MATERIALS AND METHODS
Study Design
This was a randomized, double-blind, clinical trial comparing 2 parenteral antiemetic/dopamine-antagonist medications, prochlorperazine 10 mg intravenously and metoclopramide 20 mg intravenously, for the treatment of acute migraine. For ethical reasons, there was no placebo arm. This trial was approved by the institutional review boards of Montefiore Medical Center and Columbia University Medical Center. It was registered online at http://www.clinicaltrials.gov (identifier-NCT00364806).

Setting
This study was performed in 2 academic EDs in discrete neighborhoods of New York City. Montefiore, an urban ED serving the communities in and around the Bronx, NY, receives 80,000 adult visits annually. The Montefiore ED is staffed around the clock by salaried, trained, technician-level research associates who execute research studies under the supervision of the principal investigators. The Columbia University ED is located in upper Manhattan, serves 70,000 patients annually, and is staffed by volunteer research associates who were specifically trained for this study. These individuals staff the ED around the clock during the academic year.

Selection of Participants
Adult patients who presented to the ED with a primary headache disorder were screened by research associates. Any patient with migraine with or without aura, as defined by the International Headache Society’s International Classification of Headache Disorders (ICHD), were eligible for inclusion. Also eligible were patients with probable migraine (ICHD-2: 1.6) lasting longer than 72 hours, which resulted in the inclusion of patients who met all migraine-without-aura criteria except duration of headache. Our unpublished data have shown that these patients constitute 20% of all patients who meet undifferentiated migraine criteria (ICHD category 1.0). We chose to include these patients to increase the generalizability of our findings to a larger cohort of patients treated for migraine in the ED. Patients were excluded for concomitant secondary headache, if the patient was to receive a lumbar puncture in the
ED, allergy or intolerance to study medication, pregnancy, or previous enrollment.

**Interventions**

The intervention consisted of administration of 10 mg intravenous prochlorperazine or 20 mg intravenous metoclopramide, both accompanied by 25 mg of intravenous diphenhydramine. The dose of prochlorperazine, 10 mg, is standard and has known efficacy in migraines.4,14,22 When unaccompanied by diphenhydramine, 10 mg of prochlorperazine is complicated by a substantial rate of akathisia.23 We did not use more than 10 mg of prochlorperazine for fear of an increased rate of akathisia with a larger dose.24

Although the standard dose of metoclopramide is 10 mg, the optimal dose of metoclopramide for the acute treatment of migraines is unknown because dose-finding studies have not been conducted. According to previous work in which 20-mg doses of metoclopramide were used, repeated as necessary for persistent migraine pain, up to a total of 80 mg during 2 hours,9 we chose 20 mg as the dose of metoclopramide most likely to represent a fair comparison with the standard 10-mg dose of prochlorperazine.

Investigational medication packages were prepared by a research pharmacist in blocks of 6 in an order determined by a random-number table generated online (http://www.randomization.com). These packages were then used consecutively by the research associates. Assignment was known only by the pharmacist. Each research package in the metoclopramide arm contained 20 mg of metoclopramide hydrochloride. Each package in the prochlorperazine arm contained prochlorperazine edisylate 10 mg. Prochlorperazine and metoclopramide appear the same to the naked eye. The metoclopramide dose required more volume, so the prochlorperazine was diluted with normal saline solution so that a comparable volume of investigational medication was delivered to the clinical nurse. The investigational medication was inserted into a 50-mL bag of normal saline solution, along with 25 mg of diphenhydramine by the nurse, who was blinded to assignment, and administered as an intravenous drip during 15 minutes. If subjects required more pain medication after 1 hour, they were administered rescue medication at the discretion of the treating physician.

**Methods of Measurement**

The research associates performed a baseline pain assessment and then returned every 30 minutes to ascertain the subject’s pain level. Subjects were contacted by telephone 24 hours after ED discharge to ascertain pain status, approval of the treatment, and presence of adverse effects.

The primary measure of pain intensity was a standard, validated, reproducible, 11-point, numeric rating scale.20 Subjects are asked to assign their pain a number between 0 and 10, with 0 representing no pain and 10 representing the worst pain imaginable. Secondary measurement tools included a standard 4-point pain-intensity categorical scale, in which subjects describe their pain as “severe,” “moderate,” “mild,” or “none” and a 4-point functional disability scale, as recommended by the International Headache Society.25 A patient-oriented assessment of treatment was performed by asking each subject, 24 hours after medication administration, whether he or she would want to receive the same medication at the next ED visit for an acute migraine. This latter question allowed subjects to weigh for themselves the overall relative efficacy and tolerability of the medication.

Adverse effects were assessed 1, 2, and 24 hours after medication administration. Because akathisia is a known and common adverse effect of these medications,23,26 this reaction was assessed specifically using a brief akathisia rating scale 1 hour after medication administration. On this validated instrument, akathisia is diagnosed by an increase of 1 point on a 10-point objective scale and an increase of 2 points on a 12-point subjective scale.23,27

**Data Collection and Processing**

Data acquisition was performed by the research associates, supervised by the site investigators. Data were entered directly onto a standardized data collection instrument used in 3 previous migraine clinical trials.3,9,28 Twenty-four-hour telephone follow-up was performed by the research associates. All data were entered into SPSS Data Entry V.4.0 (SPSS, Inc., Chicago, IL) by a research secretary and then double checked for accuracy by the principal investigator, who remained blinded during this process.

**Outcome Measures**

The primary outcome for this study was the between-group difference in change in numeric rating scale score between baseline and 1 hour. Although 2 hours is a more standard endpoint for outpatient migraine trials,25 our previous work found that many subjects feel well enough to be discharged before the 2-hour endpoint has arrived. Therefore, 1 hour may be a more appropriate primary endpoint for ED-based migraine research. Because recurrence or persistence of headache is common after initial treatment of migraine in the ED, we also report the between-group difference in change in numeric rating scale score between baseline and the worst pain experienced within 24 hours of ED discharge.

Secondary outcomes include sustained pain-free (achieving a pain-free state within 2 hours of medication administration and maintaining it for 24 hours without use of additional medication), sustained headache relief (achieving headache intensity of “mild” or “none” within 2 hours of medication administration and maintaining it for 24 hours), sustained normal functioning, and need for rescue medication.25 For the “headache relief” outcome (headache becoming mild or none), subjects are required to have a baseline pain level of “moderate or severe.”25

According to previous work, we assumed a normal distribution and a numeric rating scale SD of 3.0.15,29 With a
2-sided $\alpha=0.05$, a sample size of 38 subjects in each group would give us a power of 0.8 to detect a difference of 2.0 in the primary outcome (numeric rating scale baseline–numeric rating scale 1 hour). We chose a numeric rating scale change of 2.0 as a worthwhile cutoff for our study because it has been previously shown to have robust clinical significance.

### Primary Data Analysis

Once patients were randomized, their pain scores were included in the analysis regardless of whether or not they required rescue medication. A Student’s $t$ test for independent samples was used to compare mean differences in pain scores. $\chi^2$ Analyses was used to compare rates. Between-group differences are expressed as means or proportions, bounded by 95% confidence interval (CI). Analyses were performed using SPSS V.13 (SPSS Inc.).

### RESULTS

This study was conducted from August 2006 through March 2007. During this time, 152 patients were screened for participation in the study, 97 were eligible, and 77 were ultimately randomized (CONSORT diagram; Figure 1).

Baseline characteristics are listed in Table 1. Changes in pain intensity between baseline and each endpoint are listed in Table 2. The primary outcome, the between-group difference between baseline and 1-hour pain scores, favored prochlorperazine by 0.3 (95% CI $-1.0$ to $1.6$), a result that did not achieve statistical significance or a prespecified criterion for clinical importance. These data deviated somewhat from a normal distribution; however, a nonparametric analysis using the Mann-Whitney U test came to the same conclusion: no statistically significant difference between the 2 arms ($P=0.64$).

Dichotomous pain and functional outcomes are presented in Table 3. Overall, there is a consistent but statistically nonsignificant difference favoring prochlorperazine.

One hour after medication administration, nausea was reported by 5% (2/38) of prochlorperazine and 6% (2/35) of metoclopramide subjects. As shown in Table 1, about 90% of subjects in both arms reported nausea or vomiting before investigational medication administration.

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**Table 1. Baseline characteristics.**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Prochlorperazine (n=39)</th>
<th>Metoclopramide (n=38)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female sex, %</td>
<td>85</td>
<td>95</td>
</tr>
<tr>
<td>Ethnicity, %</td>
<td>62</td>
<td>68</td>
</tr>
<tr>
<td>Hispanic/Latino</td>
<td>38</td>
<td>32</td>
</tr>
<tr>
<td>Not Hispanic/Latino</td>
<td>51</td>
<td>53</td>
</tr>
<tr>
<td>Race, %</td>
<td>36</td>
<td>42</td>
</tr>
<tr>
<td>White</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Black</td>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td>Asian</td>
<td>34 (10)</td>
<td>38 (12)</td>
</tr>
<tr>
<td>Age, y, mean (SD)</td>
<td>48 (9, 96)</td>
<td>72 (24, 99)</td>
</tr>
<tr>
<td>Nauseated or vomited, %</td>
<td>90</td>
<td>92</td>
</tr>
<tr>
<td>Baseline pain intensity, %</td>
<td>62</td>
<td>57</td>
</tr>
<tr>
<td>Severe</td>
<td>69</td>
<td>79</td>
</tr>
<tr>
<td>Moderate</td>
<td>26</td>
<td>21</td>
</tr>
<tr>
<td>Mild</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>Baseline numerical rating scale, mean (95% CI)</td>
<td>8.4 (7.8–9.0)</td>
<td>8.8 (8.3–9.2)</td>
</tr>
</tbody>
</table>

**Table 2. Change in pain intensity between baseline and each endpoint.**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Prochlorperazine (n=39)</th>
<th>Metoclopramide (n=38)</th>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline – 1 h*</td>
<td>5.5 (4.6 to 6.3)</td>
<td>5.2 (4.2 to 6.1)</td>
<td>0.3 ($-1.0$ to $1.6$)</td>
</tr>
<tr>
<td>Baseline – 2 h</td>
<td>6.4 (5.6 to 7.3)</td>
<td>5.9 (5.0 to 6.8)</td>
<td>0.6 ($-0.6$ to $1.8$)</td>
</tr>
<tr>
<td>Baseline – 24 h</td>
<td>6.3 (5.3 to 7.3)</td>
<td>5.3 (4.1 to 6.5)</td>
<td>1.0 ($-0.6$ to $2.5$)</td>
</tr>
</tbody>
</table>

Reported as mean with 95% CI.
*Primary outcome.
Adverse medication effects were reported by 46% (18/39) of prochlorperazine patients and 32% (12/38) of metoclopramide patients (95% CI for difference of 15%, –6% to 36%). The frequency of akathisia, as measured by the brief akathisia rating scale, was similar in the 2 groups (Table 4). Similarly, an assessment of off-protocol use of additional diphenhydramine or lorazepam as rescue medication for treatment of akathisia was comparable between the groups (Table 4).

Other than symptoms attributable to akathisia, the only adverse event that occurred with some frequency within the ED was drowsiness, which occurred in 15% (6/39) of prochlorperazine subjects and 13% (5/38) of metoclopramide subjects. Of the 2 metoclopramide subjects who reported specific adverse effects after ED discharge, one reported generalized weakness and one reported lightheadedness. Ten prochlorperazine subjects reported 12 specific adverse effects after discharge, including rash, nausea, neck stiffness, restlessness, nervousness, sleepiness, and weakness.

Subjects were asked to remain in the ED until the 1-hour endpoint was completed. At the 1-hour point, 35% (13/37) of prochlorperazine subjects were ready for discharge versus 25% (9/36) of metoclopramide subjects (95% CI for difference of 10%, –10% to 30%). These percentages had increased to 40% (15/38) for prochlorperazine and 33% (12/36) for metoclopramide by 90 minutes.

Twenty-four hours after receiving the investigational medication, subjects were asked whether they wanted to receive the same medication the next time they visited the ED with a migraine. Affirmative responses were recorded in 77% (26/34) of prochlorperazine subjects and 73% (27/37) of metoclopramide subjects (95% CI for difference of 4%, –16% to 24%). Of the 10 metoclopramide subjects who would not want the same medication again, 9 provided a reason for their answer. Eight of these 9 cited lack of efficacy as their rationale. Of the 8 prochlorperazine subjects who would not want the medication again, 7 provided a reason for their answer. All of these subjects cited adverse medication effects as their rationale.

The effect of baseline duration of headache on the primary analyses was tested by creating a linear regression model with the primary outcome (change in numeric rating scale score at 1 hour) as the dependent variable and study medication as the independent variable. Duration of headache was then added to the model and the effect on the coefficient examined. This analysis showed that duration of headache did not influence the 1-hour outcome ($R^2=0.00$; $P=.73$).

**LIMITATIONS**

The optimal dose of metoclopramide and prochlorperazine for the treatment of acute migraine is unknown. Doses were chosen that were thought to be clinically sensible, acceptable to emergency physicians, and likely to be efficacious. Dose-finding studies, particularly of metoclopramide, which was well tolerated at this dose, are a reasonable next step.

This trial was powered to detect a clinically important difference in the continuous outcome, change in numeric rating scale score, but was underpowered to detect clinically important differences in categorical outcomes, such as sustained pain free or need for rescue medication. Although dichotomous outcomes are recommended for use by the International Headache Society, the preferred outcome in ED-based headache research is less clear. We followed the example of the emergency medicine headache researchers who have published before us, most of whom used this continuous outcome.
**DISCUSSION**

We did not find a clinically important or statistically significant difference between the 2 groups in change in pain intensity 1, 2, or 24 hours after medication administration. Therefore, either of these medication regimens is a reasonable treatment option for patients who present to an ED with acute migraine. This conclusion is further supported by the similarly high proportion of subjects in both arms who would want to receive the same medication in future ED migraine visits.

With regard to the dichotomous outcomes, prochlorperazine consistently outperformed metoclopramide, though never with a magnitude large enough to achieve statistical significance, which raises the possibility that prochlorperazine may demonstrate superiority in larger studies using a different primary endpoint. A clinical trial would require 1,040 subjects to be adequately powered for the sustained pain-free outcome, substantially more than we enrolled. Even if statistically significant, the clinical relevance of the between-group difference is likely to be small: using the absolute risk reduction in sustained pain-free rate of 6%, the best estimate of number needed to treat is 17. For 2-hour headache relief, the best estimate of number needed to treat is 11.

Results of the 2 previous prochlorperazine versus metoclopramide clinical trials differed from our primary outcome. Coppola et al13 compared prochlorperazine 10 mg intravenous to metoclopramide 10 mg intravenous. By 30 minutes, 82% of 22 prochlorperazine subjects and 48% of 24 metoclopramide subjects experienced substantial pain relief and satisfaction with the treatment (95% CI for difference of 34%, 8% to 60%). Jones compared prochlorperazine 10 mg intramuscularly to metoclopramide 10 mg intramuscularly. By 60 minutes, 32% of 28 prochlorperazine subjects and 14% of 29 metoclopramide subjects had experienced complete relief of pain (95% CI for difference of 18%, –3% to 39%).14 It is plausible that the difference in outcomes is due to dose effect. We used 20 mg of metoclopramide, twice the dose used in these other trials. Despite the higher dose of metoclopramide, adverse medication effects tended to occur less frequently than in the prochlorperazine arm.

The near-complete elimination of nausea in both arms of this study is noteworthy. Although it is not surprising that antiemetic medications were successful at eliminating nausea, this additional benefit should influence emergency physicians choosing among parenteral migraine medications. Subcutaneous sumatriptan, intramuscular dihydroergotamine, and intramuscular meperidine, though somewhat effective at combating nausea, left 20% to 30% of ED migraine patients nauseated 1 hour after medication administration.17,18

Despite administration of diphenhydramine to all subjects, akathisia did occur on occasion. In 5% of prochlorperazine subjects and 8% of metoclopramide subjects, development of akathisia required the administration of additional medication. With both these medications, rapid administration is more likely to result in nausea. Left 20% to 30% of ED migraine patients nauseated 1 hour after medication administration.17,18

**Table 3. Dichotomous pain and functional outcomes.**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Prochlorperazine, % (n/N)</th>
<th>Metoclopramide, % (n/N)</th>
<th>Difference, % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sustained pain-free*</td>
<td>17 (6/35)</td>
<td>11 (4/38)</td>
<td>6 (–10 to 22)</td>
</tr>
<tr>
<td>Sustained headache relief†</td>
<td>65 (22/34)</td>
<td>47 (17/36)</td>
<td>18 (–5 to 41)</td>
</tr>
<tr>
<td>Sustained normal functioning‡</td>
<td>47 (15/32)</td>
<td>36 (13/36)</td>
<td>11 (–12 to 34)</td>
</tr>
<tr>
<td>Two-hour pain free</td>
<td>57 (21/37)</td>
<td>41 (15/37)</td>
<td>16 (–6 to 38)</td>
</tr>
<tr>
<td>Two-hour headache relief‡</td>
<td>87 (32/37)</td>
<td>78 (29/37)</td>
<td>9 (–8 to 26)</td>
</tr>
<tr>
<td>Requested rescue medication§</td>
<td>9 (3/34)</td>
<td>17 (6/36)</td>
<td>8 (–8 to 24)</td>
</tr>
</tbody>
</table>

Two subjects with mild baseline pain are not included in this table, because the “headache relief” outcome requires a baseline pain level of moderate or severe. Discrepant denominators are due to missing data.

*Pain-free state achieved within 2 hours in the ED and maintained for 24 hours without need of additional medication.
†Pain level of mild or none achieved and maintained for 24 hours.
‡No functional impairment by ED discharge and no functional impairment reported for the 24-hour follow-up period.
§Pain level of mild or none achieved within 2 hours of investigational medication administration.
¶Requested additional medication by clinical attending physician.

**Table 4. Adverse events.**

<table>
<thead>
<tr>
<th>Adverse event</th>
<th>Prochlorperazine, % (n/N)</th>
<th>Metoclopramide, % (n/N)</th>
<th>Difference, % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any adverse event</td>
<td>46 (18/39)</td>
<td>32 (12/38)</td>
<td>15 (–6 to 36)</td>
</tr>
<tr>
<td>Akathisia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brief akathisia rating scale at 1 h</td>
<td>8 (3/39)</td>
<td>5 (2/38)</td>
<td>2 (–8 to 14)</td>
</tr>
<tr>
<td>Required rescue medication for akathisia*</td>
<td>5 (2/39)</td>
<td>8 (3/38)</td>
<td>2 (–8 to 14)</td>
</tr>
<tr>
<td>Drowsiness</td>
<td>15 (6/39)</td>
<td>13 (5/38)</td>
<td>2 (–14 to 18)</td>
</tr>
</tbody>
</table>

*Additional diphenhydramine or lorazepam administered off-protocol by clinical attending physician.
administered prophylactically with metoclopramide is an unresolved issue.

Although the results did not achieve statistical significance, the adverse event data trended toward a greater frequency of adverse effects in the prochlorperazine arm. This trend was mirrored in the reasons subjects offered for not wanting to receive the same medication on return visit to the ED; subjects not wanting metoclopramide cited lack of efficacy, in contrast to the disapproving prochlorperazine subjects, all of whom cited adverse medication effects as their reason.

In conclusion, administration of either prochlorperazine 10 mg intravenously or metoclopramide 20 mg intravenously, in conjunction with diphenhydramine 25 mg intravenously, will effectively relieve headache in most migraine patients presenting to the ED. Secondary outcomes and review of the literature suggest prochlorperazine may be slightly more efficacious, though this is balanced by a suggestion that metoclopramide is better tolerated and may have been used in subtherapeutic doses in past trials. Three quarters of subjects in both arms would want the same medication for the next migraine.

**Supervising editor:** Knox H. Todd, MD, MPH

**Author contributions:** BWF, DE, CS, EC, MH, JP, PB, and EJG conceived the study and designed the trial. BWF, RBL, and EJG obtained research funding. BWF, ND, PG, RR, and TV supervised the conduct of the trial and data collection. BWF, TV, ND, PG, and RR undertook recruitment of participating centers and patients. BWF, CC, and AA managed the data, including quality control. BWF, PB, RBL, and EJG provided statistical advice on study design and analyzed the data. BWF drafted the article, and all authors contributed substantially to its revision. BWF takes responsibility for the paper as a whole.

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**REFERENCES**


18. Carleton SC, Shesser RF, Pietrzak MP, et al. Double-blind, multicenter trial to compare the efficacy of intramuscular dihydroergotamine plus hydroxyzine versus intramuscular meperidine plus hydroxyzine for the emergency department...


CORRECTION

In the July 2008 issue, in the article by Roslund et al (“The Role of Oral Ondansetron in Children With Vomiting as a Result of Acute Gastritis/Gastroenteritis Who Have Failed Oral Rehydration Therapy: A Randomized Controlled Trial”, pages 22-29), there were several errors in the Abstract and Main Results sections. In the Abstract/Results it says, “If a subject vomited or refused to drink, he or she was considered a failed oral rehydration therapy and received acute gastroenteritis. It should have read, “. . . received IV hydration.” Also, “We used the x2 test to compare the proportions of subjects requiring acute gastroenteritis in each group.” should have read, “. . . requiring IV hydration in each group.” In the Main Results, page 26, “Data were analyzed using intention to treat. Of the subjects who received oral ondansetron, 11 of 51 (21.6%; 95% CI 11.3% to 35.3%) of subjects who received ondansetron required acute gastroenteritis and 30 of 55 (54.5%; 95% CI 40.6% to 68.0%) of placebo subjects required acute gastroenteritis (P.001), for a difference of 32.9% (95% CI 14.5% to 48.37%).” - the two instances of “required acute gastroenteritis” should have said “required IV hydration.” We regret these errors.