

Tolerability and Effectiveness of Prochlorperazine for Intractable Migraine in Children

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ABSTRACT. *Objective.* To study the effectiveness of prochlorperazine in aborting severe, intractable migraines in children.

Study Design. Patients for this study were drawn from the population seen and evaluated in the Headache Center at Cincinnati Children's Hospital Medical Center. All patients were diagnosed with migraine headache by both clinical and International Headache Society criteria. The effectiveness of intravenous prochlorperazine in 20 consecutive patients referred to the emergency department for severe, prolonged migraines was retrospectively reviewed.

Results. Patients evaluated in this study presented with a mean headache severity of 8.4 on a 0- to 10-point scale and an average duration of 54 hours. At 1 hour, 90% of the patients reported feeling better with 50% becoming pain-free. A 50% or greater reduction in severity occurred in 75% of patients at 1 hour and in 95% at 3 hours. At 3 hours, 95% of the patients reported feeling better, and 60% were pain-free. Only 1 patient failed to respond to prochlorperazine.

Conclusion. Prochlorperazine was shown to be highly effective in aborting intractable migraines in children. It was well tolerated with no significant side effects. Additional large, double-blinded, randomized, placebo-controlled studies are needed to further investigate its effectiveness. *Pediatrics* 2001;107(4). URL: <http://www.pediatrics.org/cgi/content/full/107/4/e62>; headache, emergency department, abortive therapy, intractable headache, status migrainosis.

ABBREVIATIONS. ED, emergency department; IV, intravenous; IHS, International Headache Society.

Headache is a common problem in children and adolescents. More than 10% of children 5 to 15 years of age have recurrent headaches,¹ with the percentage even higher for older adolescents.² This creates a significant impact on daily life. Ten percent of children with migraines missed 1 day of school over a 2-week period and nearly 1% missed 4 days. This translates into 164 454 missed school days in any 2-week period in the United States.³

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Treatment of childhood headaches involves both acute abortive therapy as well as long-term management. The use of pharmacological agents for abortive therapy is often limited to over-the-counter medication, with ibuprofen shown to be an effective medication for childhood migraines.⁴ However, at times, children can develop severe migraine attacks, intractable migraines, or status migrainosis. Status migrainosis is often characterized as a migraine headache that is refractory to standard treatment. This term has also been applied to a state of intractable, debilitating pain that can intensify progressively and is accompanied by the usual characteristics of acute migraine. In older teenagers the incidence of status migrainosis in patients with migraine may be as high as 14% in girls, while lower in boys of the same age.² During intractable migraines, parenteral intervention may be required. Patients may require emergency department (ED) treatment with intravenous (IV) medication and IV hydration or hospital admission.

One therapy that has been observed to be effective for intractable headaches in adults is prochlorperazine.⁵ It was first used to control nausea in migraine headaches, but the possibility of a dopaminergic mechanism in migraines has highlighted its potential usefulness as a direct treatment of migraines.⁶

A controlled study has shown that IV prochlorperazine is effective in reducing adults' headaches in the ED setting.⁵ Seventy-four percent of the patients had complete relief of their headaches 60 minutes after a 10-mg dose of IV prochlorperazine. Fourteen percent of these patients had partial relief, with an overall response of 88%, compared with 45% in the placebo group. Prochlorperazine has been shown to be most effective when administered intravenously compared with other routes of administration,⁷ with superiority compared with metoclopramide⁸ or ketorolac.⁹

In children, prochlorperazine has been primarily evaluated for its efficacy as an antiemetic. In one study, it was shown to be well tolerated and to have good to excellent results in 90% of the 116 patients treated for nausea and vomiting who received a dose of 0.2 to 0.4 mg/kg.¹⁰ Its efficacy in treating child and adolescent headaches, however, has not been established. The use of an abortive medicine in children presenting to the ED with severe, intractable migraines has not been studied. In this article, we report our results on the effectiveness and tolerability

of IV prochlorperazine in a retrospective review of 20 consecutive children seen in the ED for a severe, intractable migraine attack.

METHODS

At Children's Hospital Medical Center in Cincinnati, Ohio, the Headache Center has been established to study the clinical characteristics and treatment of childhood headaches. All of the patients were evaluated by a board-certified child neurologist and pediatric psychologist. The patient's headaches were diagnosed by both clinical impression and International Headache Society (IHS) criteria. An individual treatment plan was developed for each patient using standardized protocols. These protocols included abortive therapy, oral hydration during a headache, prophylactic therapy when indicated, and biobehavioral therapy. Children with an intractable migraine or status migrainosus were advised to call the Headache Center nurse practitioner if their home regimen was ineffective. Children and their parents determined when their headaches reached the point of unresponsiveness to their home treatment regimen. Therefore, the definition of intractability was determined individually. Information on 20 consecutive patients who were treated in the ED was gathered by the Headache Center nurse practitioners and the data were analyzed for this study.

Treatment Protocol

Before referral, the patients were asked about the features of their current headache. This included their headache duration, severity, and abortive medication use or hydration taken during this headache. On arrival to the ED, therapeutic interventions were discussed with the staff. A complete history and physical examination were obtained to exclude alternate diagnoses that might have been related to the prolonged headache. A ~0.15-mg/kg dose of prochlorperazine and IV hydration were then administered. Patients were contacted ~24 hours after discharge from the ED and asked about their overall responsiveness at 1 hour, 3 hours, and 24 hours after administration of prochlorperazine and about side effects and impression. ED records were reviewed for dosing and impression in the ED. Response was graded by severity on a scale of 0 to 10, with response defined as any improvement, as well as by subjective response (better, same, or worse). Resolution was defined as elimination of the headache, with the severity going to 0. The times of response, resolution, and disposition were recorded.

Statistical Analysis

Student's *t* tests for paired comparisons were used to compare the effectiveness of prochlorperazine on the severity of migraine headache, using time 0 as the baseline severity in comparison to both 1 and 3 hours later.

RESULTS

Patient Demographics

Twenty consecutive patients were evaluated and treated. The mean age of the patients was 12.9 years (± 2.9 ; range: 8–17). There were 11 girls and 9 boys. All patients were white. Seventeen (85%) met the IHS criteria for migraine (1 migraine with aura, 15 migraine without aura, and 1 migrainous disorder). The remaining 3 patients (15%) had a clinical diagnosis of migraine but did not meet the IHS criteria for migraine. This was attributable to the lack of associated symptoms in 2 patients and a continuous headache with episodic worsening in 1 patient. Fourteen patients were treated with prophylactic medication. Thirteen patients had treated their headache before referral without success. Twelve patients had treated their headache with ibuprofen and 2 patients had treated the headache with a triptan. Nineteen of the patients reported orally hydrating themselves. The patients reported for all their headaches a mean fre-

quency of 20.2 (± 11.3) headaches per month, a mean duration of 10.2 (± 11.6) hours, and a mean severity of 6.7 (± 1.2) on a 0- to 10-point scale.

Headache Characteristics

All of the patients reported the same headache features as their typical migraine with the exception of the headache's intractability. On presentation to the ED, the mean headache severity was 8.4 (± 1.6) on a 0- to 10-point scale. The mean duration of the current, prolonged headache was 54 (± 75) hours. If the patient with a 336-hour headache was excluded, the mean headache duration was 38.7 (± 35.0) hours. The most commonly reported associated symptoms were nausea (85%), vomiting (55%), photophobia (80%), and phonophobia (80%). Seventy-five percent of the patients reported a throbbing quality to their headache.

Prochlorperazine Response (Table 1)

The mean dose of prochlorperazine administered was 0.13 (± 0.03) mg/kg. The mean volume of IV hydration with normal saline was 17.4 (± 10.2) mL/kg. At 1 hour, 18 patients stated that they were better (90%), whereas 2 patients were the same (10%). Their mean headache severity was diminished from 8.4 (± 1.6) to 1.6 (± 2.5 ; $P < .0001$). Twelve patients (60%) reported that their headache had resolved at 1 hour. Of the remaining 8 patients, the mean severity was reduced from 8.3 to 3.9. There were 15 patients (75%) with a 50% or greater reduction in their headache severity. At 3 hours, 19 patients (95%) were better, whereas 1 patient reported no response. The patient with no response at 3 hours did have a slight response at 1 hour (severity from 9 to 8). The severity at 3 hours continued to diminish to a mean of 1.1 (± 2.2 ; $P < .0001$). There were 19 patients (95%) with a 50% or greater reduction in their headache severity by 3 hours. Thirteen patients reported that their headaches had resolved by this time. Two patients who continued to have a headache at 1 hour were admitted to the hospital: 1 received dihydroergotamine as an abortive treatment (patient 2), the other patient (patient 20) became pain-free without further intervention. The patient receiving dihydroergotamine had chronic daily headaches and did respond to the dihydroergotamine. The remaining 18 patients (90%) were discharged from the hospital from the ED. The mean time of response was 91 (± 130) minutes for all of the patients.

24-Hour Response

Eighteen patients (90%) were pain-free 24 hours after discharge from the ED. Of the 2 remaining patients, 1 was continuing treatment with dihydroergotamine (patient 2), whereas the other patient had a headache recurrence at 9 hours (patient 4). Patient 4 had a history of chronic daily headaches and the headache severity returned to its baseline severity at 9 hours. This results in an overall pain-free rate of 90% at 24 hours. In 1 patient, the headache recurred 4 days later, and in another patient, the headache recurred in 36 hours. The patients with recurrences had daily headaches.

TABLE 1. Response Pattern to IV Prochlorperazine

Patient Number	Headache Duration (Hours)	Prochlorperazine Dose (mg/kg)	IV mL/kg	Severity at Time Zero	Severity at 1 Hour	Subjective at 1 Hour	Severity at 3 Hours	Subjective at 3 Hours	Time to Complete Response (Minutes)	Perceived Benefit
1	1	0.16	15.6	10	5	Better	1	Better	120	Good
2	24	0.17	17.2	9	8	Same	9	Same	30	Some
3	96	0.16	24.5	10	0	Better	0	Better	5	Good
4	24	0.14	28.2	10	2	Better	NA	Better	120	Great
5	48	0.13	13.5	6	1	Better	1	Better	15	Good
6	12	0.13	17.6	9	3	Better	3	Better	30	Good
7	0.5	0.08	16.3	5	0	Better	0	Better	60	Good
8	336	0.07	14.9	8	1	Better	1	Better	60	Great
9	28	0.13	0	10	0	Better	0	Better	60	Good
10	26	0.06	11.5	10	0	Better	0	Better	15	Great
11	24	0.17	33.2	8	0	Better	0	Better	30	Great
12	10	0.19	2.5	10	NA	Better	0	Better	180	Good
13	72	0.13	26.7	9	NA	Better	0	Better	120	Good
14	96	0.12	11.6	7	0	Better	0	Better	45	Good
15	12	0.12	12.4	8	0	Better	0	Better	30	Good
16	48	0.17	16.9	9	0	Better	0	Better	60	Great
17	8	0.11	11.2	9	0	Better	0	Better	30	Great
18	96	0.13	44.9	9	6	Better	3	Better	600	Good
19	14	0.15	15.2	7	0	Better	0	Better	30	Great
20	96	0.15	14.5	5	5	Same	2	Better	180	Moderate
Mean	54	0.13	17.4	8.4	1.7		1.1		91	

NA indicates not applicable.

DISCUSSION

This study demonstrates that prochlorperazine was a useful therapeutic approach in the treatment of intractable migraines and status migrainosis in children. It has been shown to be effective in adults in a randomized, double-blinded study with 88% response, compared with 45% in the placebo group.⁵ Previously, value in the pediatric group has been mostly reported for nausea and vomiting.¹⁰

Children in this study tolerated prochlorperazine well with no reported side effects. All but 1 patient had a reduction in the severity of their pain, with a majority becoming headache-free. IV prochlorperazine acted rapidly and effectively to decrease the intensity of the migraine headache in 90% of the patients at 1 hour and 95% at 3 hours, despite the long duration of the pain before treatment. The values of the 0- to 10-point scale are subjective for the individual patients but clearly demonstrate a positive response in the majority of patients. In general, the patients' subjective response was positive, with the majority rating the benefit from prochlorperazine as good (55%) or great (35%). These features make this approach ideal for the acute treatment of intractable migraines and headaches in childhood.

IV hydration was also used in our management to minimize the potential side effects and to assist with the headache treatment. Its role was not studied separately. Although fluid hydration is often promoted as useful in migraine management, its degree of effectiveness has not been determined. A controlled study delineating this treatment modifier

would be interesting to examine in acute migraine headache management.

Children presenting with a severe migraine attack responded well to IV prochlorperazine and IV fluids. Additional randomized, placebo-controlled studies would be useful to further define the benefit that we demonstrated and to assist with our understanding of this useful treatment strategy.

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