# The Use of a Pediatric Migraine Practice Guideline in an Emergency Department Setting

*Courtney R.J. Kaar, BS, James M. Gerard, MD, and Albert K. Nakanishi, MD, MPH*

**Objective:** The aim of the study was to evaluate the safety and efficacy of a standardized pediatric migraine practice guideline in the emergency department (ED).

**Methods:** Migraine Clinical Practice Guideline (MCPG) was created in collaboration with the Division of Pediatric Neurology and Pediatric Emergency Medicine. The MCPG was established on evidence-based data and best practice after a review of the literature. The MCPG was implemented for patients with a known diagnosis of migraine headaches and a verbal numeric pain score (VPS) greater than 6 on a 0 to 10 scale. Patients received intravenous saline, ketorolac, diphenhydramine, and either metoclopramide or prochlorperazine. After 40 minutes, another VPS was obtained, and if no improvement, a repeat dose of metoclopramide or prochlorperazine was administered. If after 40 minutes and minimal pain relief occurred, a consult to neurology was made. A chart review of patients enrolled in the MCPG from April 2004 to April 2013 was conducted. We recorded demographic data, vital signs, ED length of stay, initial VPS, last recorded VPS, adverse events, and admission rate. Nonparametric statistics were performed.

**Results:** A total of 533 charts were identified with a discharge diagnosis of migraine headache of which 266 were enrolled in the MCPG (179 females and 87 males). Mean (SD) age was 13.9 (3.1). Mean (SD) initial VPS was 7.8 (2.0). Mean (SD) discharge VPS was 2.1 (2.8), representing a 73% reduction of pain. Twenty patients (7.5%) were admitted for status migrainosus; mean (SD) age was 14.0 (3.5) years and mean (SD) VPS was 6.3 (2.8). Mean (SD) length of stay in ED was 283 (107) minutes. No adverse events were identified.

**Conclusions:** Our MCPG was clinically safe and effective in treating children with acute migraine headaches. Our data add to the dearth of existing published literature on migraine treatment protocols in the ED setting. We recommend additional prospective and comparative studies to further evaluate the effectiveness of our protocol in this patient population.

**Key Words:** migraine headaches, migraine practice guideline, medication adverse events

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Migraines are one of the most common causes of recurrent pain in children.[1,2] Migraine headaches are a significant source of disability, with a prevalence of 1% to 3% in ages 3 to 7 years, 4% to 11% in ages 7 to 11 years, and 8% to 23% by the age of 15 years.[3,4] Disabilities experienced by children include the inability to get out of bed, poor performance in school, and the failure to attend school.[5–7] In addition, it has been suggested that migraines play a role in childhood depression.[8–11]

Despite sometimes effective outpatient treatment, many children present to the emergency department (ED) after 2 to 3 days of headaches when home-based migraine abortive therapies have failed.[12] Migraine headaches do not always respond to treatment in the ED, and intractable cases can require inpatient hospital admission for pain and other associated symptoms. Inpatient admission rates for pediatric migraine patients are reported as ranging from 3% to as high as 32%.[8,13]

In the ED, pain care for children with migraine headaches is often varied and evidence-based treatment is inconsistently applied.[13–15] To our knowledge, currently there is no universally accepted treatment protocol for use in the ED setting.

We developed a migraine protocol at our institution as a collaborative undertaking of the Departments of Pediatric Neurology and Pediatric Emergency Medicine to standardize treatment of pediatric migraines in our ED. We report our experience with implementing the evidence-based clinical practice guideline for a 4-year period. Our study's goal was to evaluate its safety and efficacy. Our hypothesis was that our protocol would standardize migraine care and improve patients' pain scores, resulting in low rates of hospital admission and few adverse effects.

## METHODS

At our institution, a pediatric Migraine Clinical Practice Guideline (MCPG) was established in collaboration between the Divisions of Pediatric Neurology and Pediatric Emergency Medicine at Cardinal Glennon Children's Medical Center/Saint Louis University School of Medicine (Fig. 1). The protocol was first implemented in April 2009. The protocol was used for any patient who was treated in our ED with an established diagnosis of migraine and a verbal numeric pain score (VPS) of greater than 6 on a 0 to 10 scale. In our scale, 0 is no pain, 5 is moderate pain, and 10 is the worst possible pain.

Patients received intravenous (IV) normal saline (up to 1000 mL bolus), ketorolac (0.5 mg/kg; max, 30 mg), diphenhydramine (2 mg/kg; max, 50 mg), and either metoclopramide (0.2 mg/kg; max, 20 mg) or prochlorperazine (0.1 mg/kg; max, 10 mg). The choice between metoclopramide or prochlorperazine was left to the discretion of the treating ED physician. After 40 minutes, another VPS was obtained, and if no improvement, a repeat dose of metoclopramide or prochlorperazine was administered. If after another 40 minutes there was still no improvement in the patients' VPS, a neurology consultation was obtained. With the approval of the neurology consult service, IV dihydroergotamine (0.2 mg/kg; max, 0.75 for 3 minutes) was infused with cardiac monitoring. A repeat dose of dihydroergotamine (up to 0.5 mg) could be administered after 30 minutes. If after this time the neurology team felt that the patient required further monitoring, the patient was admitted to the hospital on the inpatient neurology service.

A retrospective emergency medical record (ED-EMR, EPIC systems) review was performed on all ED patients with a discharge diagnosis of migraine headache from April 2009 through April 2013. We obtained Saint Louis University School of Medicine Institutional Review Board approval for our study. Inclusion criteria were any ED patient with a discharge diagnosis of migraine headache. We excluded any patient whose treatment did not follow the MCPG's protocol. Data on each patient were

From the Department of Pediatrics, Division of Emergency Medicine, Saint Louis University School of Medicine, Saint Louis, MO.
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Reprints Albert K. Nakanishi, MD, MPH, Saint Louis University School of Medicine, Cardinal Glennon Children's Medical Center, 1465 S, Grand Blvd, St. Louis, MO 63104 (e-mail: nakanimk@slu.edu).

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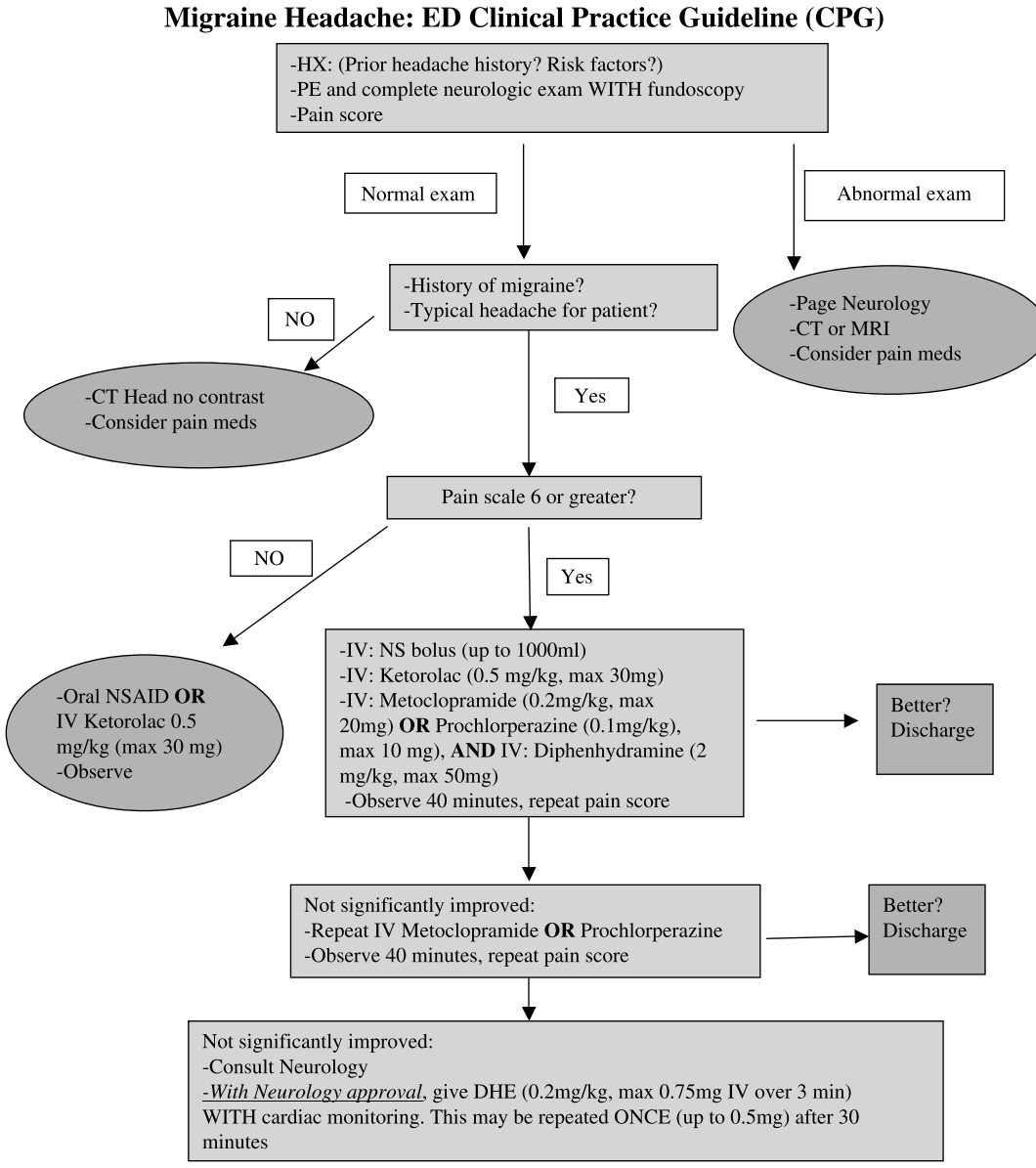


**FIGURE 1.** Migraine headache: ED Clinical Practice guideline (CPG).

recorded and included demographics, vital signs, ED length of stay, initial VPS, last recorded VPS, any adverse effects that were identified (eg, akathisia, dystonia, or any evidence of medication intolerance), and disposition status.

Summary data analysis was performed with SPSS Version 21.0 (SPSS Inc, Chicago, Ill). We calculated the mean (SD) age, the mean (SD) initial and discharge VPSs, the percent of reduction of pain at discharge, and the mean (SD) length of stay in the ED. The admission rate to the hospital was also calculated.

## RESULTS

Between April 2009 and April 2013, a total of 533 ED patients were identified with the diagnosis of migraine headache. Of these, 271 patients were not treated according to the protocol's guidelines and were excluded from the data analysis. Therefore, 266 patients were enrolled in the MCPG. There were 179 females (67.3%) and 87 males (32.7%). Age of the patients ranged from 5 to 20 years with a mean (SD) age of 13.9 (3.1) years.

The mean (SD) initial VPS was 7.8 (2.0) and the mean (SD) discharge VPS was 2.1 (2.8). This represented a 73% reduction of the patients' pain. The mean (SD) total length of stay in the ED was 283 (107) minutes for patients not admitted. Thirty-three patients required a second dose of metoclopramide or prochlorperazine, 13 (0.05%) were comfortable enough for home discharge with 20 patients admitted to the hospital neurology service for status migrainosus, for an admission rate of 7.5%. The mean (SD) age of this group of patients was 14 (3.5) years with a mean (SD) admission VPS of 6.3 (2.8). There were no recorded medication-related complications in any of the 266 patients studied.

## DISCUSSION

In our retrospective study, we found that our MCPG was effective for decreasing pain in pediatric patients who presented to our ED for migraine headache relief. Our MCPG included treatment with IV saline, ketorolac, diphenhydramine, and either metoclopramide or prochlorperazine and resulted in a large

decrease in pain scores. There was a low hospital admission rate involving patients with status migrainosus. We were unable to identify any adverse medication-related events.

The assessment of headache intensity was essential in determining the choice of treatment in our patients.[16] Patients with known migraine headaches and a VPS greater than 6 were enrolled into our MCPG. There is controversy in the literature on the accurate reportage of acute pain. Because VPSs have fewer increments (ie, 1–10) versus a visual analogue scale (VAS, 0–100), they are often considered less sensitive.[17,18] However, in a study by Herr et al,[19] VPS was determined to be superior to VAS and faces pain scale when compared with internal validity, reliability, sensitivity, and patient preference.[19,20] Acute pain may be more easily assessed by description than a mark on a continuous scale without definitions or numbers. There is also greater intraindividual agreement using VPS than using VAS for assessing the subjective nature of pain.[20]

Despite the commonality and disturbances in a child's life due to migraines, few studies have been conducted to determine efficacy of treatments, especially in an ED setting.[4,8,21] Many published studies focus on treatments in the outpatient setting, for example, an outpatient clinic or at home[3,15,22–25] despite the estimates that migraines represent 8% to 18% of all headaches seen in EDs.[15,26,27] In addition, many guidelines for the treatment of pediatric migraines are based on adult protocols.[4,15]

The prevalence of migraines in children may be underestimated because of the fact that some children are likely treated outside the ED. These treatments commonly involve acetaminophen and ibuprofen.[1,15,28,29] Other first-line therapies include the use of sumatriptan.[15,30–38] In a study by Hamalainen et al,[1] ibuprofen was more effective at reducing pain than acetaminophen. However, acetaminophen had a faster onset than ibuprofen. Both were shown to be significantly more effective than a placebo.[1] In our study, we used IV ketorolac, which has been previously demonstrated to provide a 55% pain relief when used alone.[21] In addition, our patients received IV saline. Because renal function is a concern with the usage of NSAIDS, the IV saline likely provided a measure of renal protection[4,39] and improved hydration in nauseated and potentially dehydrated children.

Dopamine receptor antagonists (DRAs) such as prochlorperazine and metoclopramide treat nausea often accompanying migraine headaches in addition to providing pain relief. In the only randomized, double-blinded trial of pediatric migraine therapy in the ED setting, IV prochlorperazine was effective when outpatient treatment failed.[15,21] Furthermore, prochlorperazine was superior at providing pain relief than IV ketorolac. Pain relief occurred after 1 hour in 85% of children given IV prochlorperazine compared with only 55% treated with ketorolac.[21] In an adult study by Lane et al,[40] migraine patients were able to give themselves repeated doses of chlorpromazine (0.1 mg/kg, up to 3 doses) for their headache relief after receiving metoclopramide. No significant hypotensive or dystonic reactions were reported.[40] In a study comparing chlorpromazine and sumatriptan, patients could receive up to 3 doses of chlorpromazine (12.5 mg) for their pain relief, all patients received metoclopramide at baseline. No adverse reactions were noted.[41]

Failure rates of treatment, commonly defined as the need for a second rescue drug, headache recurrence within 48 hours, and readmission, range from 10% to 50% with the use of DRAs.[9,11,13,21,41–45] The admission rates of pediatric patients with migraine headaches are reported in the literature from 3% to 32%.[8,13] We had an admission rate of 7.5%, although we did not evaluate the relapse rate or readmission rate for our patients discharged from the ED. We believe that our low rate of admission is due to the successful treatment of migraines with our MCPG.

Significant adverse effects of DRAs include extrapyramidal symptoms, such as akathisia and dystonia. In our study, no cases of extrapyramidal symptoms were noted. However, other studies demonstrate a higher prevalence of adverse effects. In a prospective cohort study using prochlorperazine and diphenhydramine, 5% had a definitive diagnosis of akathisias and 34% was suspected to have akathisia.[46] In a study comparing the effectiveness of chlorpromazine versus prochlorperazine and metoclopramide, there was a rate of 12% of akathisia in patients treated with prochlorperazine. However, with subsequent treatment with diphenhydramine, all of the patients' symptoms improved.[13]

Recommendations exist for minimizing the possibility of extrapyramidal symptoms with DRAs. They include the use of diphenhydramine, which may be responsible for why we found no cases of akathisias in our patient population.[13,46,47] Another recommendation is decreasing the DRA infusion rate. For metoclopramide, doing so decreases sedation and akathisias while not affecting the treatment of nausea and headache.[4,48–51] In contrast, decreasing the infusion rate of prochlorperazine does not decrease the prevalence of akathisias.[4,52]

Triptans have been studied in pediatric patients as an alternative to DRAs when treating migraines; however, no triptan is approved by the US Food and Drug Administration for treatment of adolescent migraines.[38] Studies have shown that the tritpans, most notably sumatriptan, may be successful at treating migraines and there is a dose-dependent effect.[35,37,38] Winner et al[31,36,38] demonstrated that 20 mg of sumatriptan nasal spray was significantly superior than placebo at 30 minutes and 2 hours after treatment, but not for sustained headache relief. However, 5 mg of sumatriptan was not superior to placebo. Sumatriptan is relatively safe and the most commonly noted adverse effect was taste disturbance.[33,35,38] Studies of rizatriptan show that it is more effective than placebo,[33] but not significantly so until 3 hours postdose during which time other medications may need to be administered.[31] The literature is not clear about the effectiveness of zolmitriptan. In 1 study, there was no statistically significant improvement between treatment with zolmitriptan versus placebo for migraine pain relief.[34] However, in another study, patients treated with zolmitriptan had significant pain relief compared with placebo and the effect was similar to ibuprofen.[29] We did not use triptans in our protocol because to be effective, triptans need to be started early in the headache course and many patient who arrive to the ED for relief of their migraine pain often have had symptoms for days.[12]

The use of codeine by itself or in combination with other medications has been used to treat patients with intractable migraines.[53] However, no studies specifically address codeine use in pediatric migraine patients, and current national guidelines recommend against its use in the ED.[54] Codeine was not part of our MCPG, due to concerns regarding opioid toxicity. Codeine is metabolized through the CYP3A4 subfamily and CYP2D6 subfamily of cytochrome P450 enzymes. Most codeine metabolism is through CYP3A4 subfamily, but 10% of the conversion is through CYP2D6 with morphine as its metabolite.[55] Different genotypes of CYP2D6 are associated with variable rates of drug metabolism.[56,57] The genetic variant of having 2 or more copies of CYP2D6 is associated with abnormally high plasma concentrations of certain drugs and greater production of morphine from codeine.[55,58] For individuals who are ultrarapid metabolizers, the use of codeine comes with a high risk of toxicity resulting in life-threatening situations or even death.[58]

There have been 2 previous retrospective studies on treating patients in the ED for migraine headaches with a standardized protocol.[8,10] Trottier et al[10] used ibuprofen for mild headaches and ibuprofen or naproxen for moderate headaches. For severe

headaches in patients younger than 8 years, they used codeine, and they used prochlorperazine and diphenhydramine for patients 8 years or older. They evaluated for the number of patients treated in the ED as well as which specific drugs were used for a 10-year time span. They did not evaluate for the clinical effectiveness of their protocol.[10]

Leung et al[8] evaluated an ED migraine protocol, which consisted of an IV saline bolus, ketorolac, and either prochlorperazine or metoclopramide with diphenhydramine. Patients who did not improve within 1 hour were admitted to the hospital. Of note, odansetron was also used at the discretion of the treating physician. Their protocol group (87 patients) had decreased pain scores, ED length of stay, and rate of hospital admission compared with a nonprotocol group (165 patients). Of note, they did not evaluate for medication complications.[8]

The limitations of our study are similar to those of any single institution retrospective case series. This design may have affected our ability to identify the occurrence of all medication adverse effects. Just more than half of the patients presenting with migraines did not receive the full MCPG protocol and were therefore excluded from the study. Patient's pain scores may have been lower and were relieved with other analgesics or providers may not have elected to use the MCPG. Furthermore, we do not have data on readmission rates as well as follow-up data from outpatient visits. Lastly, there were no comparison groups to determine whether there was any benefit of our protocol for treatment in patients who received other medications and dosing regimens.

In conclusion, our standardized migraine protocol was found to be clinically safe and effective in treating pediatric migraine patients presenting to the ED. Our data add to the lack of existing published literature on acute migraine treatment in children. We recommend additional prospective and comparative clinical trials to further evaluate the effectiveness of our protocol in this patient population.

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