

## Brief Communication

# Inpatient Treatment of Status Migraine With Dihydroergotamine in Children and Adolescents

Marielle A. Kabbouche, MD; Scott W. Powers, PhD; Ann Segers, RN, BSN; Susan LeCates, MSN, CNP; Paula Manning, RN; Shannon Biederman, MSN, CNP; Polly Vaughan, MS, CNP; Danny Burdine, RA; Andrew D. Hershey, MD, PhD

**Objective.**—To assess the effectiveness of aggressive therapy of status migraine in children and adolescents.

**Background.**—Inpatient management of pediatric status migraine and intractable headache is limited because of a lack of studies and guidelines. Adult treatment is often based on anecdotal experience, although a few controlled studies have been reported. Added to that is the discomfort of general pediatricians and neurologists in using available effective treatments in pediatric patients (such as dihydroergotamine: DHE).

**Methods.**—Charts of all patients admitted to the neurology service, at Cincinnati Children's Hospital Medical Center—Department of Neurology, for inpatient treatment for intractable headache/status migraine over a 6-week period were reviewed. Demographics, evaluation, diagnosis, and treatment used were tabulated. Data on the effectiveness of the treatments provided were evaluated. Thirty-two total consecutive charts were retrospectively reviewed during that period.

**Results.**—Upon discharge, 74.4% of the patients were headache-free. The mean severity of the pain upon discharge was  $1.02 \pm 2.22$  (using the 0-10 pain scale).

**Conclusion.**—From our review, DHE is very effective in treating and aborting an episode of status migraine and should be offered to children and adolescent patients who have failed their usual abortive therapy to prevent further severe disability that mainly affects their schooling and social activities.

**Key words:** status migraine, migraine, children and adolescent, dihydroergotamine

**Abbreviations:** DHE dihydroergotamine, ED emergency room department, IV intravenous, SM status migraine

(*Headache* 2009;49:106-109)

Status migraine (SM) is defined as a debilitating continuous unremitting headache of more than

From Cincinnati Children's Hospital Medical Center—Department of Neurology, Cincinnati, OH, USA (M. Kabbouche, A. Segers, S. LeCates, P. Manning, S. Biederman, D. Burdine, and A. Hershey); Cincinnati Children's Hospital Medical Center—Department of Pediatrics, Cincinnati Children's Hospital Medical Center—Department of Psychology, Cincinnati, OH, USA (S. Powers).

Address all correspondence to M. Kabbouche, Cincinnati Children's Hospital Medical Center, Headache Center—Department of Neurology MLC 2015, 3333 Burnet Ave., Cincinnati, OH 45229, USA.

72 hours.<sup>1</sup> The pain during this prolonged attack should be severe in intensity and unremitting for 72 hours or more.<sup>1</sup>

Epidemiological studies on prevalence and incidence of SM are unavailable for the pediatric population. Multiple acute abortive treatments have been used with or without sufficient data on response in the younger population.

The treatment of SM in the pediatric population often poses a challenge in the emergency room or as an inpatient setting because of the lack of controlled data and guidelines, most literature published being

Accepted for publication September 14, 2008.

*Conflict of Interest:* None

on adult population.<sup>2</sup> Added to that is the discomfort of general pediatricians and neurologists in using available effective treatments in pediatric patients. Multiple therapeutic approaches are used in pediatric emergency rooms and in an inpatient setting,<sup>3,4</sup> including intravenous hydration as well as parenteral dopamine antagonist agents: prochlorperazine,<sup>5</sup> metoclopramide,<sup>6,7</sup> droperidol, antiepileptic drugs such as valproic acid: *Depacon*,<sup>8,9</sup> and others such as dihydroergotamine (DHE),<sup>10,11</sup> magnesium sulfate,<sup>12</sup> immunosuppressant therapy: *Solumedrol*<sup>13,14</sup> and even propofol.<sup>15</sup> Most of these approaches have not been studied appropriately in children and their use has been erratic and extrapolated from some reports in the adult population.

The aim of this study was to review retrospectively the treatments made available to all patients admitted on a pediatric neurology ward for SM during a 6-week period. Data on effectiveness of the treatments provided were evaluated.

## METHODS

The charts of all patients admitted to the neurology service for inpatient treatment of intractable headache over a 6-week period between September and October were reviewed. This specific period was considered because of the increase in complaints of headache in children and adolescents around the time when school starts. Demographics, diagnosis, and treatments used were tabulated.

The following data on the effectiveness of the treatments provided were retrospectively evaluated including pain response after each dose of medication, number of doses used to reach 50% and 100% improvement respectively, as well as side effects of the medications. The headache center patients at Cincinnati Children's Hospital Medical Center – Department of Neurology are instructed to call if they failed their outpatient abortive therapy. The outpatient abortive therapy usually includes nonsteroidal anti-inflammatory drugs and/or a triptan. Before deciding on admitting a patient, the outpatient treatment plan is reviewed making sure that these patients maximized their therapy appropriately.

This review specifically focused on the acute therapy with DHE during hospital stay and was a

preliminary evaluation of the effectiveness of inpatient therapy of headache to further expand our acute care service to an independent inpatient headache care unit. Data did not include at this time any details on abortive therapy used prior to admission, preventive medication that patients were on prior to admission or follow-up evaluation at their outpatient visit.

A total of 32 consecutive charts were reviewed. The treatment options were made by the pediatric neurologist covering the service during that period with consultation with the headache center team if the patient was a center patient. All of the patients received aggressive intravenous hydration (load of 20 mg/kg of D5 normal saline) regardless of the specific migraine treatment they were getting. The severity was graded on a scale of 0-10 by the neuro-pediatric nurse before and after each dose of medication given. Any decrease on this pain scale was considered favorable to continue therapy. Response was considered as patient being headache-free.

The DHE protocol used was as follow: all female patients had to have a negative pregnancy test to receive the DHE. A test dose of DHE was first tried (half of the initial dose that is appropriate for age and weight). If the test dose was tolerated the rest was given half an hour later and DHE was then repeated every 8 hours until headache freedom plus one additional dose, or until the maximum of 20 doses were given. The dose of DHE was 1 mg intravenously (IV) over 3 minutes every 8 hours, the dose was decreased to 0.5 mg every 8 hours to children who were less than 25 kg and or 9 years old or younger. All admitted patients were premedicated half an hour prior to the DHE dose with antiemetics: prochlorperazine or metoclopramide for the first 3 doses then ondansetron was used as needed for the rest of the doses to prevent extrapyramidal symptoms that can be seen with repeated doses of the antidopaminergic drugs. Patients should have not used any triptan therapy in the 24 hours prior to receive the first dose of DHE. All the patients were offered a minimum of 5 doses before deciding on unresponsiveness. If there is any noticeable improvement of their headaches, the DHE was continued until they are headache-free. Upon admission, it was relayed to the patients that the headache can feel more annoying with the initial 2-3

doses because of the severe nausea and anxiety that are associated with the DHE. If improvement is noticed, DHE was continued until patient is headache-free or until the maximum of 20 doses was reached.

All patients/guardian signed a Health Information Privacy and Accountability Act (HIPAA) consent for data collection with all patient identifiers removed as approved with the internal review board. This protocol is used as guideline made available by pediatric neurologists board certified in headache medicine but is “off-label” per Food and Drug Administration in children and adolescents.

## RESULTS

A total of 32 consecutive charts were reviewed. The mean age at admission was  $14.52 \pm 1.91$  years. In total, 80% of the patients were female. All the patients had a clinical diagnosis of migraine. Ninety-four percent had a history of migraine consistent with International Classification of Headache Disorders, 2nd edition criteria. The mean severity upon admission was  $8.45 \pm 2.41$ . The mean duration of the headache prior to admission was  $6.21 + 3.61$  days. DHE was used in 97.3% of the patients with a mean total dose of  $7.0 \pm 4.6$  mg, and this interval in dosage depended on the age and weight of the patient admitted as described in the method section.

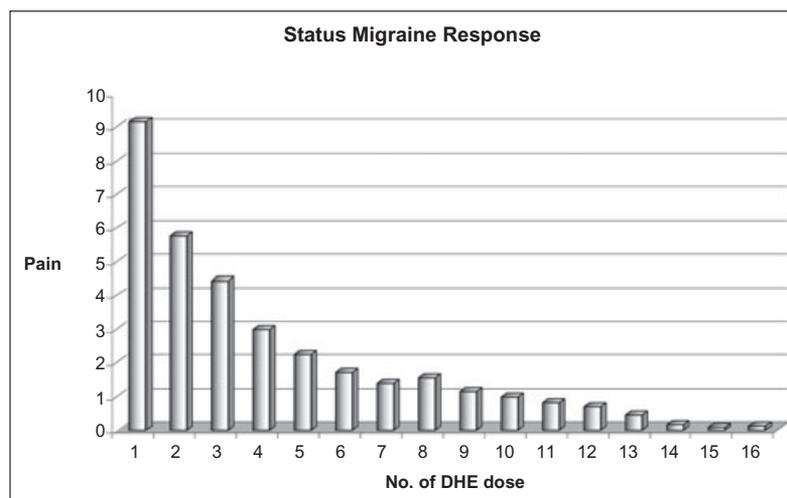
The length of stay for therapy was:  $2.96 + 1.8$  days in the inpatient unit. Side effects from the DHE were

as follows: nausea and vomiting 91.4% (mild to severe were included), chest tightness 6%, hives 2.8%, face flushing 2.8%, increased blood pressure 2.8%, no side effects 8.6%. All the patients who received DHE had local intravenous site discomfort. The DHE treatment was discontinued in the patients with hives and the patient who had an increase in blood pressure; these patients were treated with valproic acid intravenously and were not included in the final review on the effectiveness of therapy.

Upon discharge, 74.4% of the patients were headache-free. The mean severity of the pain upon discharge was  $1.1 + 2.2$  (on the 0-10 pain scale). The improvement from admission to discharge was considered remarkable with an average drop of 7 points on the pain scale. Response to treatment followed a steep angle by the fifth dose with about 40% of the patients being headache-free by that dose, with another drop by the 12th dose. Sixty-seven percent were headache-free by doses 12-13 (Fig.). Only one patient described worsening of her headache with DHE even by dose no. 5 and she was switched to valproic acid as by our inpatient protocol.

## CONCLUSION

Inpatient treatment of intractable headache and SM in the pediatric population can be effective although consistent guidelines are lacking. Patients who are failing all their outpatient acute therapy for a



**Figure.**—Status migraine response to DHE. Gradual improvement of the pain from headache with multiple doses of DHE given every 8 hours. As noticed on the chart, there is a steep response by dose no. 5 followed by another remarkable response by dose nos. 12-13. DHE = dihydroergotamine.

headache should be offered the opportunity of being admitted for further therapy.

Dihydroergotamine is a specific therapy for migraine headache and very effective in children and adolescents as described above. Neurologists should be more comfortable in using it especially in the younger population where medical comorbidities and contraindications are most of the times non-present.

Early aggressive therapy should be our goal to prevent severe disability in this age group and early onset of allodynia. The response to treatment as shown in the Figure may not occur until the fifth dose where the steep angle is seen. All the patients should be offered a minimum of 5 doses before deciding on unresponsiveness. If an improvement is recorded, DHE should be continued until patients are headache-free. It is to be noticed and relayed to the patients that the headache can feel more annoying with the initial 2-3 doses because of the severe nausea and anxiety that are associated with the DHE. If improvement is noticed, DHE should be continued until the patient is headache-free or until a maximum of 20 doses is reached.

It should be emphasized that the described response shows the effectiveness of DHE combined with aggressive IV hydration and initial use of antiemetics in the treatment of prolonged acute headache. Guidelines and protocols need to be evaluated and standardized to optimize effective treatment. These data are only a preliminary review of the effectiveness of inpatient therapy specific to DHE in an inpatient pediatric headache unit. Further studies should review data on headache freedom after discharge and at follow-up to evaluate any rebound after discharge, as well as improvement in the disability scoring.

## REFERENCES

- Olesen J. International Classification of Headache Disorders, 2nd edition. *Cephalalgia*. 2004;24(Suppl. 1):1-160.
- Lipton RB, Reed M, Diamond ML, Stewart WF. Prevalence and burden of migraine in the United States: Data from the American Migraine Study II. *Headache*. 2001;41:646-657.
- Kabbouche MA, Linder SL. Management of migraine in children and adolescents in the emergency department and inpatient setting. *Curr Pain Headache Rep*. 2005;9:363-367.
- Kabbouche MA, Linder SL. Acute treatment of pediatric headache in the emergency department and inpatient settings. *Pediatr Ann*. 2005;34:466-471.
- Kabbouche MA, Bentti Vockell A-L, LeCates SL, Powers SW, Hershey AD. Tolerability and effectiveness of prochlorperazine for intractable migraine in children. *Ped*. 2001;107:E62.
- Coppola M, Leibold RA. Randomized, placebo controlled evaluation of prochlorperazine versus metoclopramide for emergency room treatment of migraine headache. *Ann Emerg Med*. 1996;27:529-530.
- Ellis GL, DeHart DA, Owens A. The efficacy of metoclopramide in the treatment of migraine headache. *Ann Emerg Med*. 1993;22:191-195.
- Mathew NT, Kailaşam J, Meadors L, Chernyshev O, Geutry P. Intravenous valproate sodium (Depacon) aborts migraine rapidly: A preliminary report. *Headache*. 2000;49:720-723.
- Schwartz TH, Karpitskiy VV, Sohn RS. Intravenous valproate sodium in the treatment of daily headache. *Headache*. 2002; 42:519-522.
- Silberstein SD, Hopkins MM, Gebeline-Myers C, Bradley KC. Dihydroergotamine for early and late treatment of migraine with cutaneous allodynia: An open-label pilot trial. *Headache*. 2007;47:878-885.
- Pringsheim T. In-patient treatment of chronic daily headache using dihydroergotamine: A long-term follow up study. *Can J Neurol Sci*. 1998;25:146-150.
- Bigal ME, Tepper SJ, Speciali JG. Intravenous magnesium sulphate in the acute treatment of migraine without aura and migraine with aura. A randomized, double-blind, placebo-controlled study. *Cephalalgia*. 2002;22:345-353.
- Spierings EL. Prednisone as initial treatment of analgesic-induced daily headache. *Cephalalgia*. 2000;20:107-113.
- Rozen TD. Migraine headache: Immunosuppressant therapy. *Curr Treat Options Neurol*. 2002;4:395-401.
- Bloomstone JA. Propofol: A novel treatment for breaking migraine headache. *Anesthesiology*. 2007; 106:405-406.

Copyright of Headache: The Journal of Head & Face Pain is the property of Blackwell Publishing Limited and its content may not be copied or emailed to multiple sites or posted to a listserv without the copyright holder's express written permission. However, users may print, download, or email articles for individual use.