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Original Article

Outcome and Cost of Inpatient Hospitalization for Intravenous Dihydroergotamine Treatment of Refractory Pediatric Headache

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ABSTRACT

BACKGROUND: To determine the cost and efficacy of admitting patients for intravenous dihydroergotamine treatment and to identify factors associated with a higher likelihood of response to treatment. **METHODS:** We performed a retrospective review of all pediatric hospitalizations from 2001 to 2010 for intravenous dihydroergotamine therapy for headache. Data were collected using the REDcap database and consisted of multiple variables, including pre-admission demographics, headache duration, use of prophylactic medications, inpatient therapies including dihydroergotamine dosing, procedures, consultations, total hospital cost, and headache severity at discharge and at follow-up. **RESULTS:** Seventy-four percent of the 145 individuals who were hospitalized were female. Mean age was 14.9 years. Headache was described as chronic or daily in almost all patients and 28 (19%) had status migrainosus. Sixty-six percent had a first-degree relative with migraine. The average length of stay was 3.7 days, and the average cost was $7569 per hospitalization. Patients received an average of eight doses of dihydroergotamine. At the time of discharge, 63% of patients reported improvement. Follow-up information was available for 68% of the cohort at a median of 42 days after discharge, and 21 of 99 patients (21%) experienced sustained relief of headache. Response to dihydroergotamine was correlated with a lower rate of comorbid diagnoses, lumbar puncture, and outpatient neuroimaging. Response also correlated to less expensive hospitalizations with an average cost of $5379 per hospitalization versus $7105 per hospitalization without positive response. Response was also correlated with a patient receiving more doses of intravenous dihydroergotamine. **CONCLUSIONS:** Although intravenous dihydroergotamine is an effective abortive medication for intractable migraine, it may provide only short-term headache relief in many pediatric patients. Hospitalization is relatively costly with only modest long-term benefit, especially in patients with chronic migraine or chronic daily headache.

Keywords: headache, migraine, dihydroergotamine, chronic daily headache, cost

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Introduction

Migraine headache occurs in 10% to 20% of children and adolescents and chronic daily headache (headaches present on 15 or more days per month for at least three months) occurs in 1% to 4%. The prevalence is higher in female patients.[1-3] Headaches constitute one of the most common pediatric neurological problems seen by pediatricians and child neurologists,[4] and 34% to 60% of patients present to a headache clinic with chronic daily headache.[3,5] Headache is the second most common reason, after seizures, for referral to our pediatric neurology practice.

Management of headaches in children and adolescents consists of lifestyle changes to identify and avoid triggers (such as stress, dehydration, and certain foods), abortive medications to treat acute headaches, preventative medications to decrease the frequency and intensity of headaches, and complementary treatments that may include guided imagery, acupuncture, herbals, or chiropractic. Fortunately, the vast majority of children and adolescents with a normal neurological examination do not have serious underlying causes for headaches, such as central nervous system tumors[6-8] or chronic systemic conditions.

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Despite optimum outpatient management, some children and adolescents continue to have chronic headaches that interfere greatly with their quality of life or school attendance.

Many options exist for the treatment of intractable headaches. Some children and adolescents require hospitalization to break the headache cycle. Therapy during hospitalization often involves intravenous dihydroergotamine (IV DHE) and additional medical consultations and treatments. Ergot derivatives were historically used to treat migraine, but the formulation of DHE created a better-tolerated compound equipotent to previous ergot derivatives.[9] IV DHE has been shown to be effective in treating intractable headaches in children, including chronic migraine[10] and status migrainosus,[9,11-13] but no studies have identified the factors associated with improvement with DHE or evaluated the cost of hospitalization for this therapy. Data on the long-term outcomes of hospitalizations for IV DHE treatment are also limited.[14,15] Patients are often electively admitted but are also frequently admitted after presenting to the emergency department because of severe migraines or worsened chronic daily headaches, which has a lower response to IV DHE in adult patients,[14] with no studies showing efficacy in pediatric patients.

Methods

Setting and study population

Primary Children's Hospital, owned and operated by Intermountain Healthcare, a not-for-profit health care system in the Intermountain West, is a 289-bed hospital that serves as the tertiary care center for children living in the Intermountain region, a large geographic area that includes Utah, Western Colorado, and portions of Idaho, Wyoming, and Nevada. Approximately 2 million children aged 18 years and younger live within the region served by Primary Children's Hospital. We conducted a review of the medical records of children hospitalized at Primary Children's Hospital between January 1, 2001 and December 31, 2010. The institutional review board of the University of Utah and Primary Children's Hospital approved this study.

Treatment protocol

Patients with episodic migraine and intractable chronic daily headaches or status migrainosus were eligible for IV DHE using a protocol based on the article by Linder, 1994.[10] As this protocol did not exclude patients based on duration of headache, most of our patients had migraine with or without aura and chronic daily headache. All patients were managed using a treatment protocol, which consists of insertion of a percutaneous catheter for IV DHE administration. This protocol was based on institutional experience before the initiation of the protocol that peripheral IV (PIV) administration of DHE led to repeated IV placements and considerable difficulty obtaining IV access after initiation of IV DHE because of the systemic vasoconstriction. Sedation was performed by a nurse practitioner sedation team per institution practice, and sedation was introduced with either midazolam or ketamine, if needed. IV DHE administration for more than 2 to 3 days, antinausea medications, and consultations with physical therapy, behavioral medicine, and integrative medicine were performed. DHE was administered with a test dose of 0.1 mg IV and incremental increases to a maximum of 0.5 to 1 mg per dose based on age (see Table 1). Patients were premedicated 30 minutes before each dose with appropriate weight-based dosing of metoclopramide, promethazine, or ondansetron to decrease nausea or vomiting. Patients were carefully followed for evidence of cardiovascular or hemodynamic changes before and after each dose. An electrocardiogram was also obtained before the first dose of DHE. For female patients of child-bearing potential, a negative urine beta-human chorionic gonadotrophin hormone (b-hCG) was required before administering IV DHE. The neurology service actively participated in the management of all patients admitted for IV DHE therapy. The protocol allows for variation based on attending preference, and this can affect the total dosing of IV DHE and other minor variations in application of the protocol, such as use of consulting services and choice of antinausea medications.

Selection criteria and chart review

All hospitalizations of patients aged less than 18 years for IV DHE treatment of headache were compiled and reviewed for inclusion in this study. Records were randomly reviewed by one of the three authors (G.R.N., J.F.B., L.M.K.), and all REDcap entries were rechecked for accuracy by G.R.N. Hospitalizations were excluded if the primary reason for admission was not IV DHE administration, if headache was secondary to another diagnosis, or if documentation did not confirm administration of IV DHE. A small number of hospitalizations were initiated for IV DHE treatment but were aborted because of the identification of cardiovascular contraindications to DHE. These hospitalizations were included in this intention-to-treat analysis. Each hospitalization was counted as an independent event, and some patients were admitted multiple times in the time period studied.

Demographics as well as prehospital characteristics including previous evaluation by neurology, use of migraine preventative medications, and previous brain imaging were collected. Procedures and consultations performed were noted. Follow-up was available for patients who were seen within the Intermountain Healthcare system by a child neurologist. When available, records of follow-up visits were reviewed for medication use, headache frequency and intensity, medical visits because of headache, and any interval changes in diagnosis.

Outcome assessment

Response was defined as patient-reported or medical record documentation of improvement or resolution in headache by discharge. When available, improvement in pain scores was used to determine improvement or resolution of headache. If outcome was not documented, the hospitalization was counted as a lack of response ($n = 4$). Response at follow-up was defined in the same manner.

Statistical analysis

Information extracted from the electronic medical record was compiled using the REDcap[16] database. Data were analyzed by the Study Design and Biostatistics Center at the University of Utah, using mean and standard deviation for descriptive data. Logistic regression was performed using univariate and multivariate analyses. P value was set at <0.05 for significance. Analysis was performed using SAS 9.2 (Cary, North Carolina).

Results

Study population

The record search yielded 167 hospitalizations. Twenty-two hospitalizations were excluded because of insufficient data to evaluate the hospital course or a diagnosis of secondary headache. Finally, 145 hospitalizations for used for review, corresponding to 124 unique patients. Seventy-four percent of hospitalizations involved female patients. Age of hospitalized patients ranged from 6 to 19 years, with a median age of 14 years (mean of 14.9 ± 2.4 years). Headache was described as chronic or daily in almost all patients. All patients met criteria for migraine with or without aura. No patients were admitted with new persistent daily headache. Twenty-eight hospitalizations were for headache that met criteria for status migrainosus, but only seven had headache