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Brief Reports

INTRAVENOUS SODIUM VALPROATE FOR ACUTE PEDIATRIC HEADACHE

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□ **Abstract—Background: Headaches are common in the pediatric population, and increase in prevalence with age. The abortive medications currently used have a number of potential side effects. Sodium valproate (VPA) has been shown to be effective for acute treatment in the adult population, but no data exist in the pediatric population. Objective: The objective of this study was to evaluate the effectiveness of VPA for acute pediatric headache in the emergency department. Methods: This was a retrospective case series of all patients <19 years of age treated in the pediatric emergency department (PED) at two tertiary care pediatric hospitals and with a final diagnosis of migraine or headache who received parenteral VPA. Data collected included patient demographics, pain reduction, length of stay, and final disposition. Results: From July 2010 to February 2014, there were 16 patients who received VPA for acute headache in the PED; 4 were excluded. Eighty-three percent were discharged home. Mean length of stay in the PED before VPA was 395 min, and 120 min after VPA administration. Patients achieved a 17% mean pain score reduction before VPA and approximately an additional 40% mean pain reduction after VPA infusion. Conclusions: VPA appears to be an effective agent for acute pediatric headache in this small series. Patients responded well to VPA in a relatively short amount of time. Further studies are needed to evaluate its effectiveness in combination with other first-line medications or as a single agent.** © 2015 Elsevier Inc.

□ **Keywords—pediatric; migraine; headache; valproate; emergency**

INTRODUCTION

Headaches are common in the pediatric population, with migraine being the most common, and their prevalence increases with age (1). The American Academy of Neurology (AAN) has endorsed clinical guidelines for abortive treatment of pediatric headache and particularly migraine (2). Acute migraine headaches in pediatric patients account for nearly 100,000 emergency department (ED) visits per year in the United States, and general headaches account for almost 500,000 visits. Of the 100,000 ED visits for migraine, a large amount of variability in diagnostic work-up and treatment exists. One study using a national database found high use of narcotics with almost one-third of patients receiving these agents. Previous guidelines and reviews in the pediatric population advise against the use of narcotics for headache management in the ED (1–4). The abortive medications currently recommended have a number of potential side effects, such as drowsiness, dystonic reactions, and potential for prolonged ED length of stay (LOS). Although these medications have shown reasonable efficacy, there continue to be limitations beyond side effects. Prochlorperazine, a dopamine antagonist, has been the most studied in the pediatric migraine population, and the most effective; however, its availability has recently been limited by decreased production. A few recent studies have evaluated alternative agents for migraine,

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including low-dose propofol and intravenous magnesium sulfate, with some success (5,6). These alternatives have shown reasonable efficacy, but have limitations as well. Medications with high efficacy and fewer potential side effects are desired to more effectively and efficiently treat pain, while reducing the use of narcotics in children with this chronic condition.

Intravenous sodium valproate (Depacon®) is effective for migraine headaches in adults, but has limited evidence in children and adolescents <18 years of age. This medication has been studied and used as a prophylactic medication for migraine patients with success (7,8). Literature on its efficacy as a one-time dose in abortive management in the ED setting is also promising. The pathophysiology of migraine is not completely understood. Sodium valproate (VPA) has been theorized to modulate gamma-aminobutyric acid receptors and sodium/calcium neuronal channels that inhibit the excitatory process seen in migraine headaches (9). A recent randomized trial in the adult population showed VPA to be more effective than dopamine antagonists and triptans combined in acute migraine at 2 h without any adverse effects (10). A second adult trial showed significant headache relief within 1 h of VPA infusion, and no adverse effects (9). Due to the limited literature on pediatric migraine treatments in the ED, providers are forced to apply data from adult studies to the child or adolescent in front of them. With shortcomings of current abortive treatments and national shortages, more options need to be available to emergency medicine physicians for treating headaches that have a significant impact on patient and family lives. The objective of this study was to assess the effectiveness of VPA for pediatric headache at two pediatric tertiary care pediatric EDs (PEDs) with the hypothesis that it will improve pain control for refractory headaches. To our knowledge, this is the first report of VPA use in the pediatric population for acute headache management in the PED.

METHODS

This was a retrospective case series from July 2010 to February 2014. All patients <19 years of age with a final diagnosis of migraine or headache who received parenteral VPA in the PED for symptomatic headache relief were included. Data were collected at two pediatric tertiary care centers in close geographical proximity. In both cases, data were collected from the electronic health record after searching on the diagnoses and medications ordered, as mentioned here. Data were collected by a member of the study team who was trained in data abstraction. The Institutional Review Boards at both institutions approved this study.

Data collection included basic demographics of each patient, LOS, pain reduction, need for narcotics, side effects, and final disposition. Pain scores were recorded from the standard pain assessment sheet in the medical record that rates pain from 0 to 10, with 10 being the highest level. Provider notes were reviewed for any side effects documented and vital signs throughout the visit were assessed for significant changes. Patients with missing pain scores before or after VPA administration were excluded from this study. In these centers and in each case presented here, VPA was used as a second-line agent. Therefore, LOS and pain reduction were calculated before VPA administration in the PED and after, in an attempt to isolate its effect from other medications administered. LOS and return visit within 72 h were only analyzed for patients who were discharged. Patients were excluded if full data were not available.

RESULTS

During the study period, 16 patients met inclusion criteria. Of these 16 patients, 3 were missing pain scores before VPA administration and were excluded. One additional patient was excluded because an order was placed for VPA, but the mother refused before the patient received it. The final study cohort consisted of 12 patients. A formal diagnosis of migraine was present in 67% of patients and the remaining had a final diagnosis of headache.

The mean age was 15 years and 50% were female. Seventy-five percent (9 of 12) of patients had a documented history of migraine headaches and 50% (6 of 12) had a family history of migraine headaches. All patients noted trying an abortive medication at home ranging from over-the-counter analgesics to a triptan agent. Sixty-seven percent (8 of 12) of patients were on an oral prophylactic migraine agent at home, with 5 of 12 patients taking topiramate, 2 of 12 patients taking divalproex sodium, and 1 of 12 patients taking amitriptyline. Eighty-three percent (10 of 12) of the cohort were discharged home and 2 patients were admitted to the hospital for pain control. Of the 10 patients discharged, 1 had a return visit within 72 h for headache.

Patients had a mean total LOS of 515 min (standard deviation [SD] = 309 min) (Figure 1). All patients were treated with other abortive headache medications before VPA, including nonsteroidal anti-inflammatories, dopamine antagonists, intravenous fluids, and narcotics. The mean LOS after VPA administration was 120 min (SD = 105 min). Patients admitted to the hospital were excluded from the LOS analysis, as their data were significantly affected by the ability to admit to the hospital; patient number 12 (Table 1) was admitted to PED observation without any improvement in pain before receiving VPA, which increased their LOS significantly. Mean pain reduction from time of presentation to before VPA