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Original Article

Outcomes of Greater Occipital Nerve Injections in Pediatric Patients With Chronic Primary Headache Disorders

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ABSTRACT

BACKGROUND: Chronic migraine is common in pediatrics and generally disabling. In adults, infiltration of the area around the greater occipital nerve can provide short- to medium-term benefit in some patients. This study reports the efficacy of greater occipital nerve infiltrations in pediatric patients with chronic primary headache disorders. **METHODS:** Retrospective chart review of patients <18 years with a chronic primary headache disorder undergoing a first-time injection. Infiltrations were unilateral and consisted of a mixture of methylprednisolone acetate, adjusted for weight, and lidocaine 2%. **RESULTS:** Forty-six patients were treated. Thirty-five (76%) had chronic migraine, 9 (20%) new daily persistent headache (NDPH), and 2 (4%) a chronic trigeminal autonomic cephalalgia. Medication overuse was present in 26%. Ages ranged from 7 to 17 years. Follow-up data were available for 40 (87%). Overall, 53% (21/40) benefitted, and 52% (11/21) benefitted significantly. Benefit onset ranged from 0 to 14 days, mean 4.7 (SD 4.3), with mean benefit duration of 5.4 (SD 4.9) weeks. In chronic migraine, 62% (18/29) benefitted, and 56% (10/18) significantly benefitted. In NDPH, 33% (3/9) benefitted; 33% (n = 1) significantly. Neither child with a chronic trigeminal autonomic cephalalgia benefitted. In logistic regression modeling, medication overuse, age, sex, and sensory change in the distribution of the infiltrated nerve did not predict outcome. There were no serious side effects. **CONCLUSIONS:** Greater occipital nerve injections benefitted 53% of pediatric patients with chronic primary headache disorders. Efficacy appeared greater in chronic migraine than NDPH. Given the benign side effect profile, a greater occipital nerve infiltration seems appropriate before more aggressive approaches.

Keywords: pediatric migraine, pediatric headache, NDPH, medication overuse headache

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Introduction

Chronic migraine is common in pediatric patients, affecting 0.8-1.75% of adolescents 12-17 years of age[1] and 0.6% of children 5-12 years of age.[2] Children with chronic migraine have experienced headache at least 15 days per month for at least the previous 3 months.[3] Pediatric patients with migraine are often highly disabled by their headaches[1] and miss or perform poorly in school.[2,4] Rarer primary headache disorders such as chronic trigeminal autonomic cephalalgias and the primary new daily persistent headaches (NDPH) also affect children and can be highly disabling.

There are no therapies approved by the Food and Drug Administration for chronic primary headache prophylaxis in pediatric patients, and treatment is often challenging. In adults, onabotulinum toxin type A injections are approved by the Food and Drug Administration for chronic migraine, and topiramate has been studied for chronic migraine. However, both of these agents often provide only partial relief even weeks to months into therapy.[5-8] Waiting this long for relief from pain in pediatric patients with chronic headache is challenging. Therapies with more rapid onset are urgently needed.

In adults with chronic primary headache disorders, infiltration around the greater occipital nerve with methylprednisolone and lidocaine 2% has been shown to be

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beneficial in 53% of patients, with a mean latency of onset of benefit of two days.[9] The greater occipital nerve provides sensory innervation over most of the occipital region and derives its innervation predominantly from the C_2 spinal root.[10] At the level of second order neurons, C_2 spinal afferents overlap with trigeminal afferents in the trigeminocervical complex, an area of the brain important in headache disorders.[11,12] In this study we report the open-label efficacy and tolerability of greater occipital nerve infiltrations in pediatric patients with chronic primary headache disorders, and examine predictors of benefit.

Methods

The University of California San Francisco Committee for Human Research approved this retrospective chart review. The study population consisted of patients <18 years of age who were seen at the University of California San Francisco Headache Center between October 2008 and June 2012 and were treated with a first-time greater occipital nerve infiltration for a chronic primary headache disorder: chronic migraine, NDPH, or a chronic undifferentiated trigeminal autonomic cephalalgia (TAC). Given that tenderness to palpation over the greater occipital nerve predicts a beneficial response in adults,[9] only those pediatric patients who had tenderness at the time of initial evaluation were offered a greater occipital nerve injection.

Headache disorder definitions

Chronic migraine, NDPH, and chronic undifferentiated TAC were defined by the use of International Classification of Headache Disorders-III-beta criteria.[3] Medication overuse was determined to be present if the patient was currently using ≥4 days/month of barbiturate containing compounds, ≥10 days per month of opioids or triptans, or if they had been using nonsteroidal anti-inflammatory drugs or other nonspecific analgesics for ≥15 days/month for the last 3 months. Patients with medication overuse were not withdrawn before the injection, as one of the treatment goals was that headache benefit from the injection would make it easier for the child to withdraw from the overused acute medication(s). Patients had generally not responded to at least one adequate trial of a headache prophylactic medication before the injection. To be clear whether a side effect is secondary to the injection or a new medication, our clinic practice is to start a new prophylactic medication 1 week after the injection.

Administration of greater occipital nerve injections

The injections were performed by 1 of 2 headache neurologists (A.A.G. and P.J.G.). The clinician palpated over the greater occipital nerves and injected the side that was most tender. Children weighing ≥40 kg received a mixture of 80 mg of Depo-medrol (methylprednisolone acetate, Pharmacia & Upjohn Co, a division of Pfizer, New York, NY) and 40 mg of 2% lidocaine (APP Pharmaceuticals, Schaumburg, IL) and children <40 kg received 40 mg of methylprednisolone acetate and 20 mg of 2% lidocaine.

Definitions of outcomes

The definitions for "some benefit" and "significant benefit" were determined *a priori*. "Significant benefit" was defined as when the notes documented one or more of the following: (1) decrease in headache frequency by at least one third for at least 1 month, (2) decrease in headache intensity by at least one third for at least 1 month, (3) decrease in headache duration by at least one third for at least 1 month, or (4) notes document a "significant" or "substantial" improvement in headache for a period of at least 1 month. "Some benefit" was defined as when some degree of improvement was documented in the notes, but the criteria for "significant benefit" were not met. Ascertainment of treatment response was performed by one of the headache neurologists as part of routine clinical care before the conceptualization of the study and recorded in the medical record at the first clinic follow-up visit after the injection.

Side effects and adverse events

Side effects and adverse events noted in the medical records were collected and reported. Side effects are assessed for routinely at follow-up visits per clinic protocol.

Data collection

Data were collected from the medical records onto a standardized abstraction form and then entered into a secure web-based electronic REDCap (Research Electronic Data Capture)[13] database.

Data analysis

Data were analyzed using STATA v.12 (College Station, TX). Descriptive statistics were calculated, including demographics and clinical features, percent of total patients who benefitted, percent of patients with NDPH and chronic migraine who benefitted, and percent that benefitted significantly.

The primary predictor of interest in this study was headache diagnosis. Because there were only 2 patients with a chronic TAC, this was ultimately simplified to a binary predictor: chronic migraine vs. NDPH.

The primary outcome measure for this study was headache benefit. For most analyses this outcome was dichotomized such that having a benefit included both those patients who had some benefit and those who had significant benefit, as defined above.

First, the proportion of patients with chronic migraine and the proportion with NDPH who benefitted from the injections were calculated, and a Fisher's exact test was performed to assess whether these proportions differed in a statistically significant way.

Recognizing that factors other than diagnosis may also influence response to treatment and therefore need to be controlled for to understand better the implication of diagnosis on treatment benefit, univariate and then multivariate logistic regression modeling also were performed. Medication overuse was included in the logistic regression model as a confounding variable given its influence on the development of chronic migraine[14] and response to treatment.[6] Age and sex were also included in the logistic regression model as potential confounders.[15,16] Age was examined in 2 ways: (1) as a continuous variable, (2) as a binary variable: preadolescent (≤11 years) vs adolescent (12-17 years). The continuous age variable was used in the multivariate logistic regression model.

Finally, sensory change (ie, numbness and/or tingling) in the ipsilateral occipital region after the injection was included in the model as it was considered a possible mediator on the causal pathway and the goal of the analysis was to measure the direct effects of headache diagnosis on benefit. The presence of sensory change objectively indicates accurate targeting of the nerve and underlying diagnosis conceivably could influence how susceptible the nerve is to sensory change when injected. All variables were entered into the logistic regression model and then removed one by one to allow the detection of unmasked negative confounding.

Two other regression models were also generated to examine whether results differed from the logistic regression model (1) an ordinal logistic regression model (3 outcome categories: no benefit, some benefit, and significant benefit), and (2) an exact logistic regression model given the relatively small sample size in the study.

Results

Forty-six pediatric patients were treated with greater occipital nerve injections during the study period. Their diagnoses and demographics are shown in Table 1. Follow-up information was available on 40 (87%). The six patients missing follow-up data did not return to the clinic for care. Overall, 53% (21/40) of children with a chronic primary headache disorder benefitted from the injection. Of those