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Original Article

Predictors of Triptan Response in Pediatric Migraine

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ABSTRACT

BACKGROUND: Migraine is common in children and adolescents and can be disabling. Being able to predict which patients will respond to triptans based on their clinical phenotype would be helpful. Adult data suggest cranial autonomic symptoms and aura predict triptan response. This study examined clinical predictors of triptan response in pediatric migraineurs. **METHODS:** This chart review study included all patients less than 18 years old with migraine who were seen at the University of California, San Francisco Headache Center in 2014. Univariate χ^2 analyses were performed, followed by multivariate logistic regression modeling. **RESULTS:** Of 127 pediatric migraineurs, 70 (55%) had chronic migraine and 24 (19%) had aura. The majority (55%) had at least one cranial autonomic symptom. Of 65 with triptan outcome data, 47 (73%) benefitted from a triptan. In univariate analyses, triptan benefit was seen in 65% with chronic migraine versus 88% with episodic migraine ($P = 0.048$), 67% with aura versus 74% without ($P = 0.66$), and 70% with cranial autonomic symptom versus 74% without ($P = 0.76$). In a multivariate logistic regression model, chronic migraine, aura, and cranial autonomic symptom were not statistically significant predictors of triptan benefit: chronic migraine: 0.25 (0.06-1.04); aura: 0.65 (0.09-4.45); cranial autonomic symptom: 0.75 (0.22-2.52). **CONCLUSIONS:** In univariate analysis, individuals with chronic migraine were less likely to benefit from triptans. In contrast to what has been documented in adults, cranial autonomic symptoms and aura did not predict triptan response, although our small sample size limited the study's power. Larger pediatric studies are needed, and future pediatric triptan trials should provide response rates stratified by clinical variables such as aura.

Keywords: migraine, pediatrics, triptan, aura, cranial autonomic symptoms

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Introduction

Migraine is both common and disabling in children and adolescents. Prevalence of migraine is approximately 5% by age 10 years and increases across adolescence, approaching adult prevalence rates by late adolescence.[1] Chronic migraine, meaning migraine occurring on 15 days or more per month for at least the last three months,[2] is also common in the pediatric population, affecting 0.6% of 5- to 12-year-olds and 0.8% to 1.8% of 12- to 17-year-olds.[3,4] Over half of pediatric patients with chronic migraine are severely disabled by their headaches,[4] and many miss or perform poorly in school.[3] Ten percent of children and adolescents with migraine missed at least one day of school over a two-week period.[5] Therefore, with the goal of achieving rapid return to normal function, it is important to diagnose

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migraine accurately and to treat attacks in children and adolescents.

Being able to predict which acute migraine treatments will be effective for a given child based on the clinical phenotype would be helpful. In adult studies, the presence of unilateral cranial autonomic symptoms (CAS) predicts a better response to triptans compared with the absence of CAS.[6,7] In addition, there is recent evidence in adults that the presence of aura predicts a lower triptan response rate compared with those who have migraine without aura.[8] This study aims to evaluate the impact of CAS and aura on triptan efficacy in pediatric migraine.

Methods

The University of California, San Francisco Committee for Human Research approved this retrospective chart review study (CHR 15-15938). The study population consisted of patients (1) age <18 years, (2) who were seen at the University of California, San Francisco Headache Center between January and December 2014, and (3) who met International Classification of Headache Disorders third edition (beta) criteria[2] for migraine. Analysis of triptan benefit was performed on that subset that had had at least one adequate triptan trial.

Definition of an adequate triptan trial

For a trial to be considered adequate, the patient had to have tried the triptan, at an appropriate dose for weight (Table 1), three or more times for headache. We selected this definition because it can be difficult to assess efficacy after just one or two trials of a medication and because underdosing may impair efficacy. For the two triptans that were US Food and Drug Administration–labeled for pediatric use at the time of the study design, we considered the labeled doses to be appropriate: i.e., rizatriptan oral or melt, 5 mg for <40 kg, 10 mg for ≥40 kg, and almotriptan 12.5 mg orally for adolescents 12-17 years (presumably over 40 kg). For the others, appropriate doses were determined through a combination of reviewing published data of studied dosing in this age group and consensus expert opinion of the authors.

Because we generally counsel patients to take triptans with a nonsteroidal anti-inflammatory drug (NSAID) for best efficacy[13,22,23] (unless there is an NSAID contraindication), we did not differentiate whether the triptan was taken in isolation or along with an NSAID. However, all patients who were prescribed a triptan had had inadequate relief with NSAIDs alone (or NSAIDs were contraindicated).

TABLE 1.
Definition of Adequate Pediatric and Adolescent Dosing of Triptans

	<40 kg	≥40 kg
Sumatriptan NS[9–11]	≥5 mg	20 mg
Sumatriptan PO[12,13]	≥25 mg	≥50 mg
Sumatriptan SC[14,15]	≥0.1 mg/kg	≥4 mg
Zolmitriptan PO[16]	≥2.5 mg	5 mg
Zolmitriptan NS[17]	NA	5 mg
Naratriptan PO[18]	≥1 mg	2.5 mg
Frovatriptan PO	2.5 mg	2.5 mg
Eletriptan PO	20 mg	40 mg
Rizatriptan PO, MLT[19,20]	5 mg	10 mg
Almotriptan PO[21]	≥6.25 mg	12.5 mg

Abbreviations:
MLT = Melt
NA = Not applicable
NS = Nasal spray
PO = Per os
SC = Subcutaneous

Definition of outcomes

Benefit was defined as any degree of improvement as noted in the medical chart. If there was no comment on triptan efficacy in the chart, the patient was not included in the efficacy analysis.

Determination of migraine subtype diagnosis

Definition of migraine with aura and migraine without aura was made based on International Classification of Headache Disorders third edition (beta) criteria,[2] as was determination of episodic versus chronic migraine. As per criteria, if a patient was experiencing more than 14 days of headache per month, but that pattern had not yet been present for at least three months, they were still considered to have episodic migraine. Some patients fluctuated between episodic and chronic migraine throughout their treatment; for the analysis, the diagnosis during the 2014 examination year was used. NSAID overuse was defined as NSAID use on 15 or more days per month. Triptan overuse was defined as triptan use on 10 or more days per month.

Determination of cranial autonomic symptoms

Patients were interviewed with at least one parent present as part of our standard semistructured interview for all new patients. They were explicitly asked whether they ever experience each of the following symptoms with their headaches:

(1) Conjunctival injection
(2) Lacrimation
(3) Sense of grittiness or scratchiness in the eye
(4) Nasal congestion
(5) Rhinorrhea
(6) Eyelid edema
(7) Ptosis
(8) Sense of ear fullness or pressure
(9) Facial sweating/flushing

If at least one symptom was present with at least some attacks, patients were categorized as having CAS. The frequency of each of these symptoms was not recorded.

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)[24] database.

Data analysis

Data were analyzed using STATA v.13 (College Station, TX). Descriptive statistics were calculated, including demographics and clinical features.

The primary predictor of interest was the presence of CAS and aura. The effects of chronic migraine status, sex, and age were also analyzed given their general clinical importance and a possible effect of age on triptan response in adults.[25] Age was examined as a binary variable: preadolescent (≤11 years) versus adolescent (12 to 17 years). Given the relative infrequency of medication overuse in the sample, the absence of any opioid or barbiturate overuse, and the relatively small study sample size that limits the number of predictors that can be studied, we did not examine the effect of medication overuse on triptan benefit. The primary outcome measure was headache benefit. This was a binary outcome measured as any benefit versus no benefit.

First, univariate analysis was performed using χ^2 or Fisher exact test, as appropriate. Subsequently multivariate logistic regression modeling was performed. Age and sex were not retained in the multivariate regression model given the relatively small number of outcomes, and that they were not significant in univariate analyses. Chronic migraine was retained because it was significant in univariate analysis, as were aura and CAS because they were the primary predictors of interest.