Review Article

Treatment of Pediatric Migraine in the Emergency Room

Amy A. Gelfand MD\textsuperscript{a,b,*}, Peter J. Goadsby MD, PhD\textsuperscript{b}

\textsuperscript{a}Division of Child Neurology, Department of Neurology, University of California, San Francisco, San Francisco, California
\textsuperscript{b}Headache Center, Department of Neurology, University of California, San Francisco, San Francisco, California

Abstract

Migraine constitutes a relatively common reason for pediatric emergency room visits. Given the paucity of randomized trials involving pediatric migraineurs in the emergency department setting compared with adults, recommendations for managing these children are largely extrapolated from adult migraine emergency room studies and trials involving outpatient home pediatric migraine therapy. We review current knowledge about pediatric migraineurs presenting at the emergency room and their management, and summarize the best evidence available to guide clinical decision-making.

Introduction

Migraine is common in children, with a prevalence of 1-3\% in 3-7-year-olds, 4-11\% in 7-11-year-olds, and 8-23\% by age 15 years [1]. Headache constitutes a frequent pediatric complaint in the emergency room, and migraine comprises the most common primary headache disorder in these children [2,3]. We review the epidemiology of pediatric migraine in the emergency room and how it is currently treated, and we then outline the evidence base for managing acute migraine in children and adolescents in the emergency room setting. The differential diagnosis of acute headache in a pediatric patient is beyond the scope of this article, and was recently reviewed elsewhere [4,5].

Because, to the best of our knowledge, only one controlled trial of pediatric migraine patients in the emergency room has been reported, acute therapy trials in other clinical settings will be discussed. How the findings of these studies compare with emergency room outcomes is unknown. All pediatric migraine therapies described here refer to an off-label indication, except where otherwise specified.

Epidemiology of Pediatric Migraine in the Emergency Room

Adolescents are more likely than younger children to come to the emergency department for migraine. At least in part, this fact is likely a reflection of the higher prevalence of migraine [1] in this older age group. Across several studies, the mean ages of pediatric migraineurs presenting at the emergency room ranged from 12.1-13.6 years [6-8], with a median age of 14.0 years (standard deviation, 2.4 years) reported in one study.

Girls predominate in some [6,8,9] but not all [3,7] studies of pediatric migraine in the emergency room. In one study, the ratio of children seeking treatment for status migrainosus was 64.2\% female and 35.8\% male [9]. In another study, 57.4\% of children presenting to the emergency room for migraine were female [8]. Given that migraine is more common in females from adolescence onward [1], this sex difference is likely explained by the underlying prevalence rates.

Typically the headache has been ongoing for a couple of days by the time the child or adolescent comes to the emergency room [7-9]. In one study, children presented an average of 2.2 days after their migraine had begun [8]. In another study of pediatric “status migrainosus” in the emergency department, where “status” simply meant that abortive intravenous therapy was required, the mean duration of headache at presentation was 72 hours [9].

Only a minority of children who present to the emergency room for migraine has chronic migraine (i.e., migraine ≥15...
days per month) [10]. In one study, these children constituted 14.5% of the group [8]. However, this percentage may be an underrepresentation, because detailed headache histories may not always be taken in the emergency room setting, and most chronic migrainers demonstrate exacerbations that seem no less troublesome in practice than those experienced by episodic migrainers.

Most pediatric patients (62.6-71%) have already tried a migraine-abortive medication before presenting to the emergency room [7,8]. Most often they have used a nonspecific oral analgesic such as acetaminophen or ibuprofen [7,8]. In one study, 2.2% had used a triptan before presenting, whereas 4.7% had used an opioid, suggesting either that children are more likely to receive an opioid for their outpatient migraine therapy than a migraine-specific triptan, or that those who treated home attacks with triptans were less likely to need emergency room treatment [8].

Current Treatment of Pediatric Migraine in the Emergency Room

Treatment in a pediatric emergency room, as opposed to a mixed-population emergency room, appears to influence the management of pediatric migraine. In one study, pediatric emergency physicians were more likely to prescribe dopamine receptor antagonists and less likely to prescribe opioids than physicians practicing in a mixed environment. Notably, treatment in a pediatric emergency room was also predictive of complete headache resolution [3].

In pediatric emergency rooms in Canada, dopamine receptor antagonists are prescribed most commonly for pediatric migraine [8,9], and metoclopramide comprises the most commonly used agent. Opioids are second most common, and are prescribed in 5.5% of cases [8]. Triptans are used only rarely, in 0.5% of cases [8]. Providing an intravenous fluid bolus is relatively common [8]. In nearly a third of pediatric migrainers, no treatment may be administered [3]. These patients’ visits may have been focused on diagnosis, as evidenced by the relatively high use of neuroimaging (a computed tomography scan rate of 16.3-20.9%) in the evaluation of pediatric patients who are ultimately diagnosed as having migraine. Serious intracranial pathology that altered management was not evident in any of the children imaged in these two studies [8,9]. Cranial imaging has not been demonstrated to decrease the likelihood of a return visit, and in one pediatric study was actually a risk factor for further visits to the emergency room [9].

Principles and Evidence Regarding Pediatric Migraine Therapy in the Emergency Room

Treatment environment

After a diagnosis of migraine has been made, reassuring the patient and family about the benign etiology of the headache, and that the pain and associated signs can be controlled, are important. If possible, the patient should be put in a dark, quiet area of the emergency room. Sleep should be encouraged [11]. Imaging is generally not indicated in those with normal results of a neurologic examination [1], particularly when a child has a well established history of episodic headaches. In multiple studies of children presenting at the emergency room with headache, all with serious intracranial pathology displayed red flags in their history or objective neurologic signs on examination, e.g., loss of consciousness, optic disc swelling, ataxia, hemiparesis, abnormal reflexes, or abnormal eye movements [2-13]. In addition, in a study of more than 3000 children with brain tumors, of those who presented with headache, less than 1% reported headache as their only symptom, and 97.7% demonstrated at least one objective abnormality on neurologic examination [14].

Hydration

Children with migraine may have been vomiting before their emergency room presentation, and their oral intake may have been poor secondary to nausea. The main downside of intravenous rehydration is the need for catheter placement, although about half of pediatric migrainers (48.4%) will be treated with intravenous therapy in the emergency room, and hence will require intravenous insertion regardless [8]. In these patients, fluid replacement is unlikely to be harmful, and may be beneficial. Assuring good hydration can also provide renal protection before treatment with an nonsteroidal anti-inflammatory drug (NSAID) such as ketorolac, which is important because higher-dose ketorolac has been associated with acute renal failure [15]. Fluids can also help prevent postural hypotension [16] after treatment with a phenothiazine such as chlorpromazine.

Opioids

The American Academy of Neurology practice parameter for migraine treatment advises against the use of opioids as first-line therapy for acute migraine in adults [17], although they are often prescribed for this purpose [18]. In adults, opioids exert limited efficacy for acute migraine, compared with more specific agents [19-21], and involve more side effects [22,23] and potential for dependence [24]. Their use is associated with an increased risk of developing chronic migraine [25]. Opioids can also precipitate medication-overuse headache [26], and appear to decrease the efficacy of other acute rescue medications [27]. Although no controlled trials, to the best of our knowledge, have compared the efficacy of opioids with that of other agents for acute migraine in children, opioids are generally not favored in the treatment of acute migraine in children [11], and their use is considered to be out of keeping with the evidence base [8]. This message appears to be reaching pediatric emergency physicians, because they are significantly less likely to prescribe opioids for pediatric migraine than physicians working in a mixed emergency department environment (6.8% vs 12.9%, P = 0.044) [3].

Dopamine receptor antagonists

Dopamine receptor antagonists are useful for treating both migraine head pain and the accompanying nausea. The most commonly used agents include chlorpromazine, prochlorperazine, and metoclopramide. Chlorpromazine and prochlorperazine are both phenothiazines, whereas metoclopramide exists in its own class. Many dopamine receptor
antagonists exert other pharmacologic effects, e.g., anti-histaminic or anticholinergic, which may also play a role in their therapeutic effect.

The adult practice parameter of the American Academy of Neurology recommends treating the significant nausea that accompanies migraine, even without vomiting [28]. Dopamine receptor antagonists have been used extensively in children to treat nausea and vomiting from a variety of etiologies [29-33], and they are commonly used for this purpose in the emergency room setting [30,31]. Chlorpromazine has also been used to treat children with psychiatric disorders [34,35], and even to provide systemic vasodilation in neonates undergoing cardiac surgery [36]. With regard to pediatric migraine, intravenous dopamine receptor antagonists comprise the parenteral agents prescribed most frequently in pediatric emergency rooms [8].

Although metoclopramide is used most often for pediatric migraine in the emergency room setting [8,9], the evidence for prochlorperazine in children is somewhat stronger [7,37,38]. In an adult migraine trial in an emergency room setting, prochlorperazine was superior to placebo, whereas metoclopramide was not [39]. Furthermore, in the only randomized trial of treatment for pediatric migraine in an emergency department setting, intravenous prochlorperazine provided relief at 1 hour in 84.8% of children, compared with only 55.2% of those treated with ketorolac [37].

Multiple placebo-controlled trials [40,41] of chlorpromazine have supported its efficacy in adults, and it has been used clinically in pediatric emergency rooms for migraine [8].

The main side effects of dopamine receptor antagonists include sedation and extrapyramidal signs, such as dystonia and akathisia. In adults, treatment with diphenhydramine decreases the likelihood of akathisia, but increases sedation [42]. Even with the coadministration of diphenhydramine, at least 5% of children will experience akathisia after receiving prochlorperazine [7]. Slowing the infusion of metoclopramide to involve more than 15 minutes decreases sedation [43] and akathisia [43-46], and does not influence the benefits regarding headache [45] and nausea [45,46]. However, slowing the infusion does not appear to decrease the akathisia from prochlorperazine [47]. Phenothiazines can also prolong the QT interval, and therefore it may be prudent to perform a screening electrocardiogram before administration.

**NSAIDs and other nonspecific analgesics**

Ibuprofen (7.5-10 mg/kg) [48,49] and acetaminophen (15 mg/kg) [49] were demonstrated in randomized, double-blind placebo controlled trials [49] to be effective in the home treatment of acute migraine among children as young as age 4 years. However, the majority of pediatric migraineurs in the emergency room will have already received one of these nonspecific oral analgesics before presentation [9].

Ketorolac was evaluated in the one pediatric migraine trial performed in an emergency room setting. Dosing was 0.5 mg/kg intravenous to a maximum of 30 mg, and efficacy was reported as 55.2% at 1 hour [37]. Pretreatment with intravenous fluids can provide renal protection, particularly if a child is dehydrated on presentation.

A parenteral form of naproxen is available for pediatric use in Canada [8], whereas in the United States, an oral formulation is available. Naproxen 500 mg is effective in treating headache recurrence after emergency room discharge in adults [50]. Diclofenac 75 mg by intramuscular injection was useful in an emergency room setting in adults [51]. A placebo-controlled trial of intravenous aspirin supports its use in acute migraine among adults [52]. However, it is not easily obtained in the United States because it is not approved by the Food and Drug Administration. Aspirin is generally avoided in children less than 15 years of age because of concerns regarding Reye syndrome [28].

Combining an NSAID with a triptan exerts greater efficacy than either agent alone in adults [53], and the safety of this combination has been studied in adolescents [54]. Using an NSAID in conjunction with a dopamine receptor antagonist may also constitute a useful strategy, particularly for those with significant nausea.

**Triptans**

Triptans are most efficacious when taken while the head pain is still mild, which tends to be early in an attack [55,56]. Because the average duration of pediatric migraine exceeds 24 hours by the time children are presenting at the emergency room, and because they have come to the emergency room, they are less likely to be experiencing only mild pain. Therefore, the response rate of triptans when used in the emergency room is likely to be decreased in the emergency room setting. Indeed, when used within 6 hours of migraine onset, subcutaneous sumatriptan demonstrated 91.2% efficacy in adults [52], whereas in the emergency room setting, it demonstrated 75% efficacy [57]. Nonetheless, multiple trials in adults [57,58] support the use of triptans in the emergency room setting for acute migraine, and although no pediatric-specific trials have been performed in this setting, triptans remain a potentially useful option. The choice of which route of administration to use (injection, oral, or nasal-spray triptan) often depends on the severity of the child’s nausea, and on the child’s willingness to try an injection or nasal spray medication.

Table 1 summarizes the results of positive, randomized acute migraine treatment trials in pediatric patients, including randomized pediatric triptan trials.

**Oral triptans**

Several oral triptans, including almotriptan, rizatRIPTAN, and zolmitriptan, have undergone positive, placebo-controlled, randomized, double-blind trials supporting their efficacy in pediatric migraineurs. Almotriptan is approved by the Food and Drug Administration for acute migraine therapy in patients aged 12-17 years, and rizatRIPTAN is approved for 6-17-year-olds. In a placebo-controlled parallel group study of almotriptan in adolescents, the rate of 2-hour pain relief was reported as 71.8% with 6.25 mg, and 72.9% with 12.5 mg [59].

A recent randomized, double-blind, placebo-controlled trial of rizatRIPTAN in 6-17-year-olds (dosing 5 mg for <40 kg, 10 mg for ≥40 kg), two hour pain freedom rate was higher in the rizatRIPTAN group (30.6%) vs placebo (22%), \( P = 0.03 \) [60]. In another study of rizatRIPTAN, a trial with a placebo-controlled crossover design, rizatRIPTAN demonstrated a rate of 2-hour pain relief of 73-74% [61]. In a study of oral zolmitriptAN involving a three-way crossover design, the rate of...
pain relief at 2 hours was 62% for zolmitriptan, 69% for ibuprofen, and 28% for placebo \( (P < 0.05 \) for the difference between zolmitriptan and placebo) \[62\]. The study of zolmitriptan included a post hoc analysis of children under age 13 years, wherein the rate of pain relief with zolmitriptan at 2 hours was 64% in this age group, demonstrating that it was similarly effective in younger children and in adolescents \[62\].

Oral sumatriptan was no different from placebo in a pediatric crossover study \[63\]. A second study of pediatric oral zolmitriptan produced negative results, which were thought attributable to the very high placebo response rate (58%) among adolescents in this parallel-group study \[64\].

**Table 1. Positive randomized trials of acute therapies in pediatric migraineurs**

<table>
<thead>
<tr>
<th>Agent</th>
<th>Trial Design</th>
<th>Clinical Setting</th>
<th>Ages Studied (Years)</th>
<th>Dose</th>
<th>Pain Relief</th>
<th>Contraindications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonspecifc analgesics</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acetaminophen [49]</td>
<td>Double-blind, placebo-controlled, crossover</td>
<td>Home</td>
<td>4-15</td>
<td>15 mg/kg PO</td>
<td>54% at 2 hours</td>
<td>Liver failure</td>
</tr>
<tr>
<td>NSAIDs</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ibuprofen [48,49]</td>
<td>Double-blind, placebo-controlled, crossover [49]</td>
<td>Home</td>
<td>4-15</td>
<td>10 mg/kg PO</td>
<td>68% at 2 hours</td>
<td>Active GI bleeding</td>
</tr>
<tr>
<td>Ketorolac [37]</td>
<td>Double-blind parallel group [48]</td>
<td>Home</td>
<td>6-12</td>
<td>7.5 mg/kg</td>
<td>76% at 2 hours</td>
<td>Significant renal impairment</td>
</tr>
<tr>
<td>Dopamine receptor antagonists</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prochlorperazine [37]</td>
<td>Double-blind; no placebo</td>
<td>Emergency</td>
<td>7-18</td>
<td>0.15 mg/kg IV; maximum, 10 mg</td>
<td>84.8% at 1 hour</td>
<td>Long QT syndrome Movement disorder</td>
</tr>
<tr>
<td>Triptans</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Almotriptan *</td>
<td>Double-blind, placebo-controlled, parallel-group</td>
<td>Home</td>
<td>12-17</td>
<td>6.25 or 12.5 mg PO</td>
<td>71.8-72.9% at 2 hours</td>
<td>History of stroke or cardiovascular disease</td>
</tr>
<tr>
<td>Rizatriptan [61]</td>
<td>Double-blind, placebo controlled</td>
<td>Home</td>
<td>6-17</td>
<td>20-39 kg; 5 mg PO &gt;40 kg; 10 mg</td>
<td>73-74% at 2 hours</td>
<td>Uncontrolled hypertension</td>
</tr>
<tr>
<td>Zolmitriptan [62,71]</td>
<td>Double-blind, placebo-controlled, crossover [62]</td>
<td>Home</td>
<td>6-18</td>
<td>2.5 mg PO</td>
<td>62% at 2 hours; 64% in those &lt;13 years old</td>
<td>Hemiplegic migraine</td>
</tr>
<tr>
<td>Sumatriptan [65-67]</td>
<td>Double-blind, placebo-controlled, crossover [65]</td>
<td>Home</td>
<td>12-17</td>
<td>5 mg NS</td>
<td>58.1% at 1 hour</td>
<td></td>
</tr>
<tr>
<td>Rizatriptan [62,71]</td>
<td>Double-blind, placebo-controlled [67]</td>
<td>Home</td>
<td>8-17</td>
<td>20-39 kg; 10 mg NS &gt;40 kg; 20 mg</td>
<td>64% at 2 hours</td>
<td>Pregnancy (?)</td>
</tr>
</tbody>
</table>

Abbreviations:

- GI = Gastrointestinal
- IV = Intravenous
- NS = Nasal spray
- NSAIDs = Nonsteroidal anti-inflammatory drugs
- PO = Oral

* Almotriptan is approved by the Food and Drug Administration for acute migraine treatment in patients aged 12-17 years and rizatriptan is approved for the 6-17-year-old age group.

† The 2004 practice parameter of the American Academy of Neurology recommends the consideration of nasal-spray sumatriptan for acute migraine in pediatric patients, and it is approved in Europe for adolescents.

**Nasal-spray triptans**

Sumatriptan nasal spray is the best-studied triptan in children, with three positive randomized, placebo-controlled trials. In two studies, children were selected for their “treatment resistance to commonly used antimigraine drugs” \[65\] such as acetaminophen (paracetamol) or NSAIDs \[66\]. This detail is pertinent to treating children in the emergency room setting, because many of them present after their headache proves refractory to an over-the-counter analgesic. In a small randomized, double-blind, placebo-controlled study of prepubertal children (aged 6.4-9.8 years), an improvement of two grades in pain intensity was evident in 86% at 2 hours, compared with 43% in the placebo group \( (P = 0.031) \), and total headache relief was evident in 64% vs 14% \( (P = 0.016) \) \[65\]. In a somewhat larger study in patients aged 8-17 years, nasal-spray sumatriptan demonstrated a 2-hour efficacy of 64% vs 39% \( (P = 0.003) \) \[66\]. In a much larger trial involving adolescents, 56% of those receiving 10 mg or 20 mg sumatriptan nasal spray demonstrated headache relief at 1 hour, compared with 41% in a group receiving placebo \( (P < 0.05) \). At 2 hours, complete relief was significantly greater in the 20-mg dose group than in the group receiving placebo (36% vs 25%). In all three trials, no serious adverse events were observed, and the most common side effect was taste disturbance \[65-67\].

Intranasal sumatriptan is approved for use among adolescents in Europe \[68\]. The Joint 2004 practice parameter of the American Academy of Neurology and Child Neurology Society regarding the treatment of migraine in children states, “Sumatriptan nasal spray is effective and should be considered for the acute treatment of migraine in adolescents” \[28\].
Zolmitriptan nasal spray exhibits superior absorption compared with sumatriptan [69,70]. In a double-blind, randomized, placebo-controlled study of adolescents (aged 12-17 years), the group treated with zolmitriptan (5-mg dose) demonstrated a higher 1-hour response rate than the group receiving placebo (58.1% vs 43.3%, respectively; \( P < 0.05 \)) [71].

**Injectable triptan**

Sumatriptan is the only triptan available in an injectable form. It is also the oldest triptan, with clinical use in the United States since 1993. Subcutaneous sumatriptan has been studied in an open-label fashion in children. In the office setting, 78% of children (aged 6-18 years) responded within 2 hours to a dose of 0.06 mg/kg [72]. A second small open-label study (with patients aged 6-16 years) used doses of 3-6 mg subcutaneously [73]. The two smaller children who had received 3 mg were headache-free at 2 hours, and eight of 15 who received 6 mg experienced headache relief by 2 hours. No major adverse events were observed, and side effects such as unusual sensations in the neck were brief and mild.

**Triptans combined with NSAIDs**

In adults, the efficacy of sumatriptan 85 mg/naproxen 500 mg in combination for the home treatment of acute migraine attacks is greater than with either agent alone [53]. Such comparative efficacy has not been studied in the pediatric population. However, in open-label home use of sumatriptan 85 mg/naproxen 500 mg for 12 months, 622 adolescents (aged 12-17 years) were treated for more than 12,000 migraine attacks without any serious adverse events related to the study drug. The overall 2-hour pain-free rate was 42% [54]. This result provides a reassuring safety assessment for the use of this combination in the adolescent age group. The synergistic efficacy is thought to involve a triptan/NSAID class effect [74], and thus other triptans such as almotriptan could be substituted for providers who prefer to prescribe the Food and Drug Administration-approved triptan to adolescents. In fact, some evidential basis was reported for using an NSAID/almotriptan combination in adults [75].

**Dihydroergotamine**

Dihydroergotamine, an ergot alkaloid or tetracyclic ergoline derivative, is effective for acute migraine in adults intravenously, intramuscular, and intranasal formulations [76]. Although multiple placebo-controlled trials involved the use of dihydroergotamine in adults, most were performed in an outpatient setting [76]. In an emergency room setting, 0.75 mg intravenous dihydroergotamine was effective at 1 hour in 60% of adult patients in a placebo-controlled study [77].

Among pediatric migraineurs, the repetitive dosing of intravenous dihydroergotamine has been used on an inpatient basis to treat “status migraine” [78,79]. In one study, 74.4% of children on discharge were headache-free, and the majority of those who responded began to improve within the first five doses. However, we note that the patients were also being treated with intravenous hydration and dopamine receptor antagonists before the first three doses. Hence these other measures may account for some of the benefits observed with the first few doses of intravenous dihydroergotamine [79]. Nonetheless, this strategy of administering a dopamine-receptor antagonist followed by several doses of intravenous dihydroergotamine could easily be adapted to treat pediatric migraine in the emergency room setting. The dose administered in the previous study comprised 1 mg intravenously every 8 hours, with children under 25 kg or under age 10 years receiving 0.5 mg [79]; weight-based dosing has also been used [80]. In an emergency room setting, a second dose could be administered an hour after the first if needed [76].

Oral dihydroergotamine, which demonstrates very poor bioavailability, was no more effective than placebo at 2 hours in a small (\( n = 12 \)) pediatric double-blind, placebo-controlled, crossover home-treatment trial [81].

Although dihydroergotamine does exert vasoconstrictive effects, serious cardiovascular adverse events in appropriately selected adult patients are rarely observed at recommended doses. Nonetheless, contraindications for dihydroergotamine include uncontrolled hypertension, cardiovascular disease, stroke, and pregnancy. Nausea is the most common side effect. Although intravenous dihydroergotamine requires pretreatment with an antiemetic, almost certainly because of an emetogenic activation of the dopamine D2 receptor [82], intramuscular administration is notably less nauseating [76], likely because of its lower \( C_{\text{max}} \).

**Sodium valproate**

In an open-label retrospective study performed in the clinic setting, 78% of pediatric migraineurs (mean age, 15 years) achieved the desired pain relief after a 1000-mg infusion of sodium valproate at approximately 1 hour [83]. Although these results are encouraging, we note that sodium valproate has never been studied in a placebo-controlled trial for acute migraine in adults or children, and the results of randomized studies [84,85] indicate efficacy rates notably lower than in open-label series [86-89]. Hence the role of sodium valproate in the treatment of acute migraine remains unclear.

**Summary of Treatment Recommendations for Pediatric Migraine Patients in the Emergency Room**

After a diagnosis of migraine has been established, adequate hydration should be provided, either orally or intravenously, if needed. Stimulation (e.g., sounds and light) in the child’s treatment environment should be minimized. If substantial nausea accompanies the head pain, a dopamine receptor antagonist would be the most useful, because these agents treat both pain and nausea. Prochlorperazine is the best-studied agent in this class. If nausea is not a significant component, then triptans, dihydroergotamine, or dopamine receptor antagonists are all reasonable first-line options. Ketorolac and sodium valproate represent additional options. Opioids should be avoided if at all possible. The clinician’s choice will be guided by the patient’s comorbidities (e.g., hypertension, or pregnancy in adolescent girls), the classes of treatment the patient has already received before presenting at the emergency room, and side-effects profiles.
Strategies for Managing the Patient at Emergency Department Discharge

If a child is headache-free at emergency room discharge, the therapeutic focus shifts to ensuring the family has the necessary tools to treat the next migraine attack effectively at home, thus preventing a repeat emergency room visit. This focus involves ensuring that a follow-up visit is scheduled, ideally with a provider experienced in managing pediatric headache. Observational data suggest that pediatric patients who are monitored at a headache center are unlikely to come to the emergency department for an acute attack, although this finding remains to be studied in a prospective fashion [13].

At discharge, patients must be provided with at least one rescue treatment option that is appropriate for their level of migraine severity. By virtue of presenting at the emergency room, these children have usually demonstrated that they are capable of experiencing at least moderately severe migraine attacks, and hence receiving only nonspecific analgesics for home rescue options may not be appropriate. The practice parameter of the American Academy of Neurology and Child Neurology Society recommends the use of “migraine-specific agents in patients whose headaches respond poorly” to NSAIDs or acetaminophen [28]. Triptans comprise migraine-specific therapies that are appropriate for the treatment of moderate and severe migraine attacks. Clinicians may still be uncomfortable prescribing triptans to children, insofar as pediatric migraineurs leaving pediatric emergency rooms receive opioids 5.4% of the time, but triptans only 1% of the time [8]. However, the evidence base in the medical literature supporting the use of triptans in children has grown, and treatment should reflect this finding. Almotriptan is approved for adolescents by the Food and Drug Administration for acute migraine and rizatriptan is approved in 6-17-year-olds. Therefore these triptans should not be withheld in the absence of a medical contra-indication. For younger children, or for those among whom nausea makes an oral medication untenable, nasal-spray sumatriptan and zolmitriptan have proven efficacious and safe in randomized, placebo-controlled trials. Sumatriptan is available in a generic form, and some insurance carriers may require a trial of this medication before granting approval for newer triptans. Combining triptans with NSAIDs improves efficacy and reduces rebound headache after emergency department discharge in adults [90]. The efficacy and safety of the combination of sumatriptan and naproxen in adolescents have been established [54]. Dihydroergotamine is also a migraine-specific therapy that can be administered at home via nasal spray or injection. Dopamine receptor antagonists represent another option for home use, particularly with those children with significant nausea or vomiting. If a clinician has any concerns regarding possible cardiac effects at home, checking an electrocardiogram to exclude long-QT syndrome would be noninvasive and reassuring. Prochlorperazine can be administered at home orally, by injection, or per rectum.

Recent emergency room visits for pediatric migraine are not uncommon. In one study, 12% of pediatric migraineurs returned to the emergency department within 7 days [7], and in another, 11.2% returned within a month of their initial visit [9]; nearly half (42.9%) of this 11.2% ultimately returned for a third visit [9]. Clearly, strategies for preventing returns to the emergency room are required, although no such strategies have been specifically studied in children.

Some data in adults suggest that a single parenteral dose of corticosteroids at emergency department discharge, although not helpful in treating migraine acutely, may decrease the likelihood of headache recurrence at 24 hours. Some clinicians have adopted this practice in children, and 2.4-10% of children with migraine are apparently prescribed corticosteroids on discharge from the emergency room [8,9]. However, many returns to the emergency department for migraine occur after the initial 24 hours, and no data, to the best of our knowledge, suggest that corticosteroids prevent these visits. In fact, corticosteroids did not decrease the likelihood that a child would return to the emergency department within a month [9]. Moreover, if the practice were to become widespread, some children could accumulate a significant exposure to corticosteroids with repeated emergency room visits. Although rare, cases of avascular necrosis of the bone have been reported after relatively short courses of oral corticosteroids [91-94].

If a child is not headache-free at discharge, a course of standing naproxen may be useful. Although naproxen is most often used as acute migraine therapy, several positive trials demonstrated its efficacy as a preventive agent [95-98], including a positive trend in a small-scale adolescent study wherein patients were treated with 250 mg naproxen twice daily for 6 weeks [99]. One pediatric emergency room incorporates standing naproxen for 7 days after discharge as part of its treatment protocol [7]. The potential for NSAIDs to cause medication-overuse headache is unresolved [26], and in moderate use, they protect against conversion to chronic migraine in adults [25]. Suitable gastric protection, e.g., a proton-pump inhibitor or H₂ blocker, can be added if necessary.

Admission to the hospital for acute migraine involves many downsides, including significant sleep disruption and likely exacerbations of photophobia and phonophobia. Furthermore, admitting the patient provides no guarantee that the headache will resolve in the hospital. In one report, 25.6% of pediatric patients admitted acutely for “status migraine” were still not headache-free after 20 doses of dihydroergotamine, a treatment course that would have taken nearly 7 inpatient days to administer [79]. Evidence from adults informs us that the benefit of an inpatient course of intravenous dihydroergotamine is cumulative through the first month after discharge, with headache freedom achieved in the first few weeks after discharge rather than during hospitalization in a significant subset of patients [80]. Therefore, the goal of any admission for migraine should involve providing an adequate dose of dihydroergotamine, safely and with good nausea control, with the clearly set expectation that the headache will not necessarily abate during the admission.

Conclusions

Migraine constitutes a common pediatric problem in the emergency room. Direct trial evidence for the treatment of pediatric migraine in the emergency room is quite limited, and therefore clinical decision-making is largely guided by adult data and pediatric data collected in the outpatient
setting. More pediatric migraine treatment trials in the emergency department setting are clearly required.

References