Acute Migraine Management in Children

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Abstract: Migraines are common, incapacitating, and often stress inducing for pediatric patients and parents alike. According to the Agency for Healthcare Research and Quality, more than 1 million Americans seek emergency care every year due to migraines, with increasing frequency among adolescents. The disease can vary in severity and character, often mimicking life-threatening conditions, requiring prompt nuanced recognition by emergency personnel and implementation of an effective treatment strategy. Development of emergency department guidelines for the management of pediatric migraines should be based on up-to-date evidence supporting safe, appropriate therapies for children.

Key Words: migraine, headache, migraine management

(*Pediatr Emer Care* 2015;31: 722–730)

TARGET AUDIENCE

The target audience for this review includes pediatric emergency physicians, general emergency physicians, general pediatricians, and family practice physicians working in emergency departments (EDs).

LEARNING OBJECTIVES

After completion of this article, the reader should be able to:

1. Understand current epidemiology of pediatric migraines.
2. Diagnose pediatric patients with migraines and variants.
3. Formulate a migraine-specific treatment plan for children.

When evaluating children with headaches in the ED, it is challenging to tease out the nagging and noxious from the nefarious. However, prompt identification of pediatric migraine should lead to expedient relief of patient discomfort and parental anxiety while preventing prolonged lengths of stay and unnecessary hospital resource utilization. The differential diagnosis of pediatric headache is vast, involving numerous etiologies, including infectious, vascular, hematologic, neoplastic, toxic, dental, ophthalmic, nutritional, allergic, and traumatic causes, to name a few. Among the causes of headaches in children, it is important to note that primary headaches (migraine, tension type, and cluster) significantly outnumber secondary headaches (meningitis, encephalitis, subarachnoid hemorrhage) but are ultimately a diagnosis of exclusion.

Migraine Epidemiology

Headache is the third most common cause of referral to a pediatric ED, and migraines are the most common cause of headache among children.[1] Among school-aged children, the prevalence of major headache ranges from 37% to 51%, whereas it increases to 57% to 82% by adolescence. In a 2009 national sample of children and adolescents, frequent or severe headaches (including migraines) were reported by 17% of participants.[2] A migraine can occur at any age, ranging from case reports as early as a few months of age (as an alternative cause of colic) to rates of 2.7% in early childhood and 11% during puberty, increasing with age.[3,4] In a large meta-analysis of over 25,000 cases, Lewis et al[5] found the incidence of migraine to be 2% by ages 3 to 7 years, 7% by ages 7 to 11 years, and 20% by ages 11 to 15 years. In terms of sex differences, prepubertal males outnumber females (3:2), while adolescent females surpass postpubescent males (3:1).[6]

Classification of Migraine

The International Headache Society (IHS) publishes a standardized classification system that provides diagnostic criteria and a classification scheme for headaches in general, and its most recent update was released in July 2013, the International Classification of Headache Disorders, Third Edition, Beta Version (ICHD-III). Unlike adult migraine presentation, pediatric migraines may be characterized by unilateral or bilateral head pain, lacking throbbing character, and shorter duration (2-72 hours). Typically, patients report a family history of migraine and patients endorse relief with sleep. Migraine can be divided into 2 groups: migraine with aura and migraine without aura (historically "classic" and "common" migraines, respectively, but this terminology is now outdated). For detailed diagnostic criteria for migraines, see Tables 1 and 2.

Migraines with aura prove particularly troubling in the ED setting, as they are accompanied by transient neurologic symptoms, which may occur immediately before, during, or after a headache of varying severity, imitating a major neurologic event such as a stroke, which must be excluded.[7] Migraine with aura accounts for less than one third of pediatric migraines, though its true incidence remains in doubt since some patients may be too young to reliably verbalize aura symptoms. Onset of the aura (visual, sensory, and/or verbal) is gradual and usually lasts no more than 60 minutes. For a full listing of rare migraine forms and atypical migraine variants, see Table 3.

Emergency Department Evaluation

A complete and thorough history and physical examination of a child presenting with a headache should identify patients who require further diagnostic testing (eg, computed tomography scan, or preferably magnetic resonance imaging where readily available, and lumbar puncture) to eliminate less common but worrisome diagnoses. For most primary headaches, including migraines, the physical examination will be normal. While obtaining a nuanced history from a young child may prove challenging, parental observations and patient illustrations may be revealing. Key red flags that warrant further investigation for secondary headache causes include the following[9]:

- Preschool age
- Occipital location or unable to describe
- First/worst headache with sudden "thunderclap" onset
- Progressively increasing severity or frequency

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TABLE 1. IHS Diagnostic Criteria Migraine Without Aura (Taken From PEMP Article)

A. At least 5 attacks fulfilling criteria B-D
B. Headache attacks lasting 4-72 h (untreated or unsuccessfully treated)*
C. Headache has at least 2 of the following characteristics:
  1. Unilateral location†
  2. Pulsating quality
  3. Moderate or severe pain intensity
  4. Aggravation by or causing avoidance of routine physical activity
D. During headache, at least 1 of the following:
  1. Nausea and/or vomiting
  2. Photophobia and phonophobia
E. Not better accounted for by another ICHD-III diagnosis

*In children and adolescents (aged <18 years), attacks may last 2 to 72 hours.

†Migraine in children and adolescents (aged <18 years) is more often bilateral than is the case in adults; unilateral pain usually emerges in late adolescence or early adult life. Migraine is usually frontotemporal. Occipital headache in children is rare and calls for diagnostic caution. Headache Classification Committee of the International Headache Society (IHS). International Classification of Headache Disorders, 3rd edition (beta version). *Cephalalgia*. 2013;33(9):645. Copyright © 2013 by Sage Publications.

- Sharp change in headache character or unable to describe quality for children who should be able to given their developmental stage
- Sleep arousal from headache; exclusive early morning or late night occurrence
- Association with severe vomiting, particularly in the early morning
- Association with straining during Valsalva
- Poor response to ongoing therapy
- Abrupt alteration in mental status
- Papilledema
- Focal neurologic deficit
- High-risk populations (sickle cell disease, immunodeficiency, malignancy, coagulopathy, pregnancy, neurocutaneous syndromes, congenital heart disease, or recent head trauma)
- Persistent vital sign derangement (fever, hypertension with bradycardia)
- Petechial rash or lesions associated with neurocutaneous disease (ash-leaf spots or café au lait spots)
- Nuchal rigidity or meningismus
- Seizure

Treatment

General Principles

The armamentarium for managing headaches in the ED is vast, but management should be tailored by current evidence. However, regardless of medication choice, the following interventions are universal:

- Provide abortive medications as soon as possible
- Optimize age- and weight-based analgesic doses
- Avoid opioids and benzodiazepines (due to likelihood of rebound effects)
- Provide hydration and antiemetics as needed
- Address underlying triggers
- Treat comorbidities (somatic or psychiatric)
- Outline goals of care for patient and parent(s)
- Create a low-stimulation environment within the examination room
- Provide age-appropriate education
- Encourage stress reduction
- Support regular healthy routines (attention to nutrition, exercise, sleep, and adequate fluid intake)
- Review healthy coping strategies
- Caution about medication overuse headache
- Recommend maintenance of a headache diary for follow-up review

Abortive Pharmacological Interventions For Migraine[10]

Clinical practice varies widely as results from large, randomized control, pediatric ED-based research is scarce, requiring extrapolation from small pediatric studies, adult trials, and non-ED research.[11] As a result, there are significant limitations to the recommendations for pediatric migraine management by the American Academy of Neurology, whose practice parameter was last updated in 2004.[12] A suggested treatment algorithm is outlined in Figure 1.

Nonsteroidal Anti-inflammatory Drugs

Nonsteroidal anti-inflammatory drugs inhibit cyclooxygenase, reducing prostaglandin and thromboxanes synthesis. They are contraindicated with active gastrointestinal bleeding and to children aged younger than 6 months.

- Ibuprofen 10 mg/kg per dose (maximum, 800 mg) given orally every 6 hours as needed.
  - Evidence review: recommended by the American Academy of Neurology, based on class I, level A evidence. Two notable studies demonstrated superior pain relief among children with ibuprofen over acetaminophen (Hämäläinen et al,[13] randomized double-blind placebo-controlled trial; 88 patients) and placebo (Lewis et al,[14] prospective double-blind placebo-controlled parallel group randomized study; 138 patients).
- Ketorolac 0.5 mg/kg intravenously (maximum, 30 mg) given every 6 hours as needed.
  - Evidence review: class IV, level U. In a small double-blind study of 62 children, Brousseau et al[15] showed pain relief with

TABLE 2. IHS Diagnostic Criteria Migraine With Aura

A. At least 2 attacks fulfilling criteria B–D
B. One or more of the following fully reversible aura symptoms:
  1. Visual
  2. Sensory
  3. Speech and/or language
  4. Motor
  5. Brainstem
  6. Retinal
C. At least 2 of the following:
  1. At least 1 aura symptom spreads gradually over ≥5 min and/or 2 or more symptoms occur in succession
  2. Each individual aura symptom lasts 5-60 min
  3. At least 1 aura symptom is unilateral
  4. The aura is accompanied, or followed within 60 min, by a headache
D. Not better accounted for by another ICHD-III diagnosis, and transient ischemic attack has been excluded.

Headache Classification Committee of the International Headache Society (IHS). International Classification of Headache Disorders, 3rd edition (beta version). *Cephalalgia*. 2013;33(9):646. Copyright © 2013 by Sage Publications.

TABLE 3. Rare Migraine With Aura Subtypes and Atypical Migraine Variants

Migraine with aura subtypes	
Familial hemiplegic migraine	More common among children than adults
	Sudden onset of hemiparesis or hemianesthesia, followed by headache
	Genetically heterogeneous, associated with disorders including episodic ataxia and generalized epilepsy with febrile seizures
Basilar artery migraine	More common among females
	Characterized by ≥2 of the following: dysarthria, tinnitus, diplopia, hypoacusia, decreased loss of consciousness, vertigo, ataxia, or visual disturbances
Ophthalmoplegic migraine	Characterized by ≥2 headache episodes with weakness of ≥1 of cranial nerves III, IV, and/or VI
Retinal migraine	Characterized by brief (seconds to 60 min), sudden, monocular blackouts/grayouts or bright, blinding episodes of visual disturbance before, during, or after headache
Alice in Wonderland syndrome	Characterized by unusual visual illusions and spatial distortions (micropsia, macropsia, metamorphopsia, and/or teleopsia) that precede headaches
Acute confusional migraine	Typically lasts 4-24 h
	Associated with agitation, lethargy, and impaired sensorium
	Focal neurologic deficits include aphasia, anisocoria, and memory impairment
Migraine equivalents (without headache)[8]	
Cyclic vomiting	More typical among school-aged children
	Characterized by predictable, stereotypical high-frequency vomiting episodes (>4/h), duration 1 h to 10 d, with interval return to normalcy
Abdominal migraine	Precursor to more typical migraines
	Recurrent episodes of moderate-severe periumbilical or diffuse abdominal pain lasting 2-72 h, with associated anorexia, nausea, vomiting, and/or pallor, with interval return to baseline normalcy
Benign paroxysmal vertigo	More typical among young children
	Characterized by sudden episodic dizziness (seconds to hours) with interval resolution
Benign paroxysmal torticollis	More typical among infants or young children
	Characterized by intermittent episodes of head tilt, associated with crying, irritability, pallor and/or malaise, lasting minutes to days, with interval resolution

ketorolac, but a greater response rate when combined with prochlorperazine.

Acetaminophen

Acetaminophen inhibits prostaglandin synthesis, but the specific mechanism of action is unclear. They are contraindicated with hepatic failure.

- Acetaminophen 15 mg/kg per dose (maximum, 1000 mg) given orally every 4 to 6 hours as needed (maximum daily dose, 75 mg/kg or 4 g).
  - Evidence review: recommended by the American Academy of Neurology based on class I, level B evidence. A 2005 systematic review by Damen et al[16] best highlights several small studies that showed symptomatic relief among children.

Dopamine Receptor Antagonists

Dopamine receptor antagonists (DRAs) treat pain and nausea, but also have antihistaminic and anticholinergic effects. Concurrent use of diphenhydramine has been associated with some increased rates of recidivism but may be necessary to treat extrapyramidal adverse effects, such as dystonia and akathisia.

- Prochlorperazine 0.1 to 0.15 mg/kg given intramuscularly or intravenously (maximum daily dose, 7.5-20 mg based on weight) for children aged older than 2 years; associated with QTc prolongation.
- Chlorpromazine 0.25 to 0.55 mg/kg given orally, intramuscularly, or intravenously (maximum daily dose, 40-75 mg based on weight) for children aged older than 6 months; associated with QTc prolongation and hypotension; included for completeness; recent data suggests poor effectiveness among children.[17]
- Metoclopramide 0.1 to 0.2 mg/kg per dose (maximum dose, 10 mg).
  - Evidence review: all DRAs are class IV, level U. Among DRA use, the retrospective review of Bachur et al[18] shows that prochlorperazine is more effective than metoclopramide for acute treatment of migraine in children in an ED setting and is associated with lower ED return rates.

Triptans

Triptans are vascular serotonin 5-HT1 receptor agonists, producing vasoconstriction, which may be efficacious if used early. They are contraindicated in patients with a history of stroke, cardiovascular disease, uncontrolled hypertension, and hemiplegic migraine; in pregnancy, it is a category C drug. They may not be used within 24 hours of ergot preparations or previous triptan use.

- Almotriptan 6.25 to 12.5 mg tablet orally for children aged older than 12 years.
- Eletriptan 40 mg tablet orally for children aged older than 12 years.
- Rizatriptan 5 to 10 mg tablet or melt away orally for children aged older than 6 years.
- Sumatriptan 5 to 20 mg intranasally or 6 mg subcutaneously for children aged older than 12 years; Food and Drug Administration–approved for adolescents.
- Zolmitriptan 2.5 to 5 mg tablet or melt away orally, 5 mg nasal spray for children aged older than 12 years.
  - Evidence review: Sun et al[19] offers a thorough systematic analysis of available evidence for the multitude of triptan

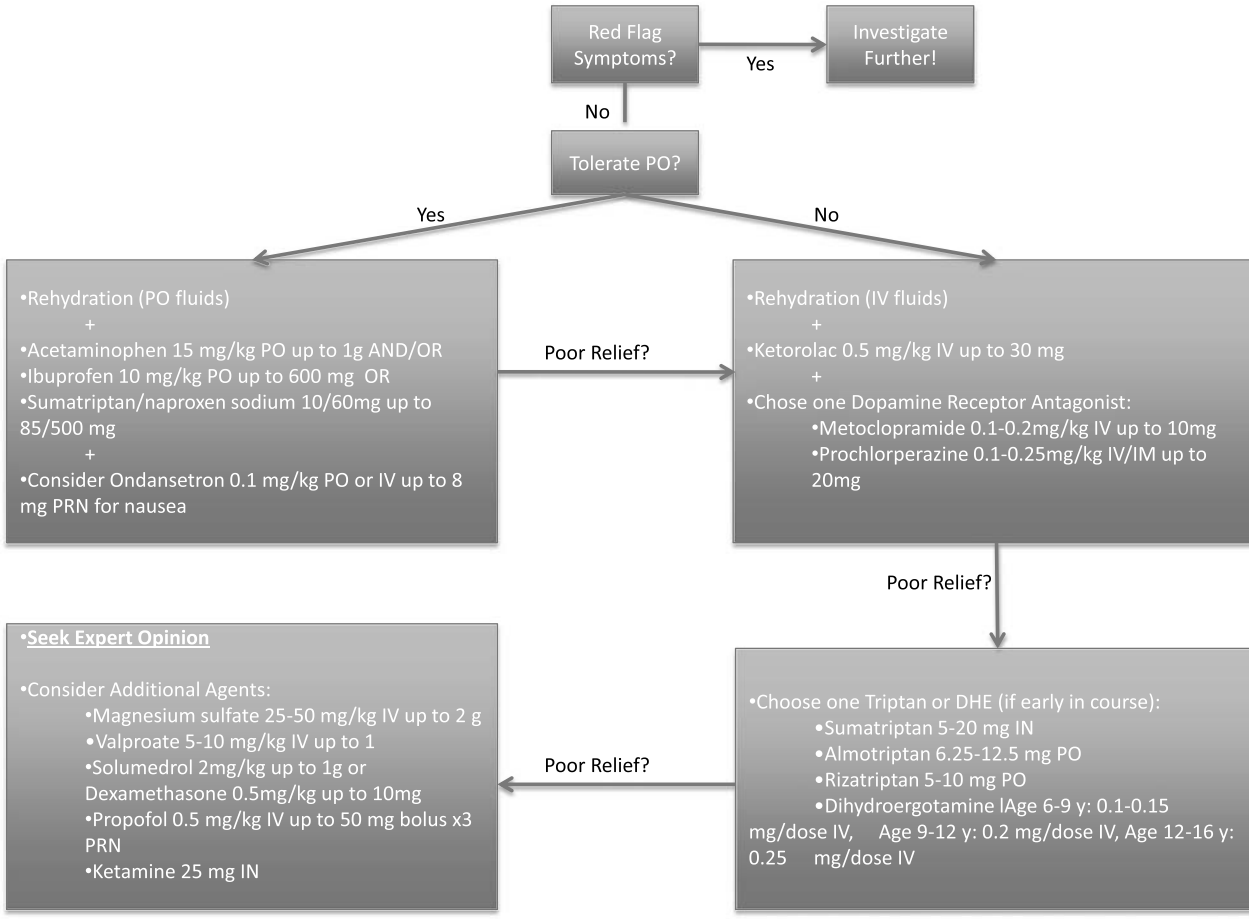

FIGURE 1. Migraine treatment algorithm.

adolescent trials. To date, the best quality evidence supports intranasal sumatriptan (class I, level A, recommended by the American Academy of Neurology), oral almotriptan (class I, level A), and oral rizatriptan (class I, level B) among children. Oral eletriptan, oral/subcutaneous sumatriptan, and zolmitriptan have class IV, level U evidence.

Dihydroergotamine

Dihydroergotamine (DHE) is an ergot alkaloid that functions as an effective intravenous abortive vasoconstrictor; contraindicated in patients with uncontrolled hypertension, pregnancy, cardiovascular disease, and stroke. Common adverse effects include nausea and anxiety.

- Low-dose DHE 0.1 to 0.2 mg given intravenously every 6 hours (maximum, 16 doses) or high-dose DHE 0.5 to 1 mg given intravenously every 8 hours (maximum, 20 doses), along with intravenous rehydration and antiemetic pretreatment; may require multiple doses for effect.
  - Evidence review: class IV, level U. A retrospective review by Kabbouche et al[20] demonstrates the effective use of DHE among 32 pediatric inpatients with status migrainosus.

Botulinum Toxin A (Botox)

Botulinum toxin A injections of head and neck muscles is FDA approved for management of chronic migraine (>15 headache days per month). Adverse side effects include local pain and redness at injection sites.

- Botulinum toxin A 150 IE injected IM.
  - Evidence review: class IV, level U. There has been evidence for use among adults and more recently a small, promising case series by Bernhard et al[21] of 10 adolescent chronic migraineurs treated effectively by neurology with Botox injections.

Propofol

Low-dose subanesthetic propofol has not been widely studied among children. Adverse side effects include apnea, hypoventilation, hypoxia, or hypotension.

- Propofol 0.5 mg/kg per bolus, ranging from 10 to 50 mg per bolus, up to 3 boluses.
  - Evidence review: there is 1 small case-control study of 7 pediatric patients by Sheridan et al[22] supporting its role for intractable migraine in the pediatric ED.

Combination Therapies

- Standardized treatments often consist of intravenous therapy with normal saline fluid bolus, ketorolac, DRA, and diphenhydramine (1 mg/kg per dose to a maximum of 50 mg).
  - Evidence review: class IV, level U. According to a retrospective study by Leung et al,[23] 87 pediatric patients who received standard combination therapy experienced a significant decrease

in pain score, length of stay, and hospital admission rate without changes in the ED return rates; however, concurrent use of diphenhydramine among children has been associated with a modest increase in revisit rates.

- Sumatriptan/naproxen sodium (10/60 mg, 30/180 mg, 85/500 mg) oral combination therapy for adolescents.
  - Evidence review: Winner et al[24] offers a randomized placebo-controlled, cross-over study, which demonstrates efficacy for 2-hour relief for the acute treatment of migraine in adolescents outside the hospital setting, but clinically and statistically insignificant pain-free relief after 24 hours compared with placebo.

Prophylactic Pharmacological Interventions for Migraine

The ED treatment should focus on abortive therapies, as long-term and preventive management of migraine belongs under the guidance of outpatient neurology, who may prescribe prophylaxis for patients who report 4 or more migraines per month. Medications (such as amitriptyline, cyproheptadine, flunarizine, gabapentin, nimodipine, propranolol, sodium valproate, and topiramate), nutraceutical supplementation (including butterbur root, coenzyme Q10, magnesium, riboflavin, vitamin B12), and nonpharmacologic techniques (such as relaxation, biofeedback, and cognitive behavioral therapy) have been used, but data remains inconclusive. Topiramate (2-4 mg/kg per day or 25 mg/d to 100 mg twice a day) is the only drug available in the United States with FDA approval for migraine prophylaxis.[8]

Adult Therapies Not Yet Proven Effective for Children

- Magnesium—the role of magnesium sulfate remains unclear, unless known deficiency. Replacement may benefit patients with migraine with aura. Adverse effects include diarrhea, hypotension, and gastrointestinal discomfort; contraindicated in combination with metoclopramide due to cerebral vasodilatory effects.
- Valproate—it has been proven effective among adults, but there remains a paucity of literature support for pediatric use.
- Corticosteroid—No pediatric data supporting corticosteroid use in the management of migraine. Among adults, a short course of corticosteroids may prevent headache recurrence for headaches that have lasted for more than 72 hours.[25–27]
- Intranasal Ketamine—25 mg of intranasal ketamine has demonstrated relief of aura among adult migraineurs, but it has not been explored among pediatric migraineurs.
- Aspirin, acetaminophen, and caffeine combinations have not been proven effective for children, may worsen chronic headaches, and put patients at undue risk for Reye syndrome.

Complicated headache patterns that fail to respond to treatment may require a pediatric neurology consultation in the ED, while chronic recurrent sufferers should be referred to a pediatric neurologist for further outpatient management. While most pediatric migraineurs are successfully discharged from the ED, approximately 15% require inpatient management and 6% require a return visit.[18] Admission is indicated for headaches that require continuous intravenous medications, chronic daily headaches that have failed aggressive outpatient treatment, analgesic rebound headache, or headaches of unclear etiology that are severe, worsening, or associated with an abnormal neurologic examination.

Patient Education

For more free resources about pediatric migraines, patients and parents may consult the National Headache Foundation (www.headaches.org) and the American Headache Society Committee for Headache Education (www.achenet.org).

SUMMARY

Headache is a common complaint among pediatric ED patients, most of which are caused by migraines. Prompt recognition and management may improve patient outcomes and decrease length of stay. When approaching the pediatric headache patient, the most important step is diagnosis, as missing evidence of increased intracranial pressure or neurovascular derangement could be life threatening. Treatment should be tailored to current evidence-based interventions, with the caveat that most studies currently guiding therapy were not performed in the pediatric ED setting and were performed with adults. To date, there remains few large, prospective, randomized control trials guiding therapy, leaving significant opportunity for further research.

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CME EXAM
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CME EXAMINATION
October 2015

Please mark your answers on the ANSWER SHEET.

Acute Migraine Management in Children, *Chen and Alfonzo*

1. A 10-year-old boy presents to the pediatric emergency department with the chief complaint of headache. All of the following are "red flags" prompting further investigations except
   A. Disconjugate gaze
   B. History of hemoglobinopathy
   C. Aphasia
   D. Unilateral headache
   E. Meningismus

2. A 6-year-old girl presents to the pediatric emergency department from summer camp with headache and photophobia. She has a history of recurrent migraines. Because she was at camp, she had not received any treatments. After a careful history and physical examination to exclude other causes of headaches, what's the most appropriate next step in treating her migraine?
   A. Intravenous morphine
   B. Oral nonsteroidal anti-inflammatory drug
   C. Intravenous ketorolac
   D. Ondansetron by oral route
   E. Intravenous metoclopramide

3. A 3-year-old presents to the pediatric emergency department in shock. His frantic mother says he got into her pills. She is prescribed a medicine for "migraines," but she cannot remember what it is. You suspect one of the following, institute appropriate therapy, and stabilize the patient.
   A. Topiramate
   B. Sumitriptan
   C. Ibuprofen
   D. Amitriptyline
   E. Caffeine

4. A 13-year-old boy with a history of migraine headaches presents with sudden onset of splitting headache upon exertion. On examination, he has dysarthria and facial asymmetry. The most appropriate next step in management is
   A. Intravenous ketorolac
   B. Oral nonsteroidal anti-inflammatory drug
   C. Intravenous morphine
   D. Placing patient in a quiet and dark environment
   E. Neuroimaging

5. The prevalence of headaches in adolescents is thought to be closest to:
   A. 5%
   B. 10%
   C. 20%
   D. 30%
   E. 50%

ANSWER SHEET FOR THE *PEDIATRIC EMERGENCY CARE* CME PROGRAM EXAM October 2015

Please answer the questions on page 728 by filling in the appropriate circles on the answer sheet below. Please mark the one best answer and fill in the circle until the letter is no longer visible. To process your exam, you must also provide the following information:
Name (please print): _____
Street Address _____
City/State/Zip _____
Daytime Phone _____
Specialty _____

1. (A) (B) (C) (D) (E)
2. (A) (B) (C) (D) (E)
3. (A) (B) (C) (D) (E)
4. (A) (B) (C) (D) (E)
5. (A) (B) (C) (D) (E)

Your completion of this activity includes evaluating them. Please respond to the following questions below.

Please rate this activity (1 - minimally, 5 - completely)	1	2	3	4	5
Was effective in meeting the educational objectives	○	○	○	○	○
Was appropriately evidence-based	○	○	○	○	○
Was relevant to my practice	○	○	○	○	○

Please rate your ability to achieve the following objectives, both before this activity and after it:
1 (minimally) to 5 (completely)

	Pre					Post				
	1	2	3	4	5	1	2	3	4	5
1. Understand current epidemiology of pediatric migraines.	○	○	○	○	○	○	○	○	○	○
2. Diagnose pediatric patients with migraines and variants.	○	○	○	○	○	○	○	○	○	○
3. Formulate a migraine-specific treatment plan for children.	○	○	○	○	○	○	○	○	○	○

How many of your patients are likely to be impacted by what you learned from these activities?

○ <20% ○ 20%–40% ○ 40%–60% ○ 60%–80% ○ >80%

Do you expect that these activities will help you improve your skill or judgment within the next 6 months? (1 - definitely will not change, 5 - definitely will change)	1	2	3	4	5
	○	○	○	○	○

How will you apply what you learned from these activities (mark all that apply):

- In diagnosing patients ○
- In monitoring patients ○
- In educating students and colleagues ○
- As part of a quality or peformance improvement project ○
- For maintenance of board certification ○
- To consider enrolling patients in clinical trials ○
- In making treatment decisions ○
- As a foundation to learn more ○
- In educating patients and their caregivers ○
- To confirm current practice ○
- For maintenance of licensure ○

Other _____

Please list at least one strategy you learned from this activity that you will apply in practice:

How committed are you to applying these activities to your practice in the ways you indicated above? (1 - minimally, 5 - completely)	1	2	3	4	5
	○	○	○	○	○

Did you perceive any bias for or against any commercial products or devices?	Yes	No
	○	○

If yes, please explain:
How long did it take you to complete these activities? _____ hours _____ minutes
What are your biggest clinical challenges related to pediatric emergency care?
[ ] Yes! I am interested in receiving future CME programs from Lippincott CME Institute! (Please place a check mark in the box)

Mail by January 15, 2016 to
Lippincott CME Institute, Inc.
Wolters Kluwer Health
Two Commerce Square
2001 Market Street, 3rd Floor
Philadelphia, PA 19103

CME EXAM ANSWERS
Answers for the Pediatric Emergency Care CME Program Exams

Below you will find the answers to the examination covering the review article in the July 2015 issue. All participants whose examinations were postmarked by October 15, 2015 and who achieved a score of 80% or greater will receive a certificate from Lippincott CME Institute, Inc.

EXAM ANSWERS
July 2015

1. C
2. D
3. C
4. D
5. D