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Acute Treatment of Pediatric Migraine
A Review of the Updated Guidelines

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Abstract
The purpose of the Research to Practice column is to review and critique current research articles that directly affect the practice of the advanced practice nurse (APN) in the emergency department. This review examines the findings of M. Oskoui et al. (2019) from their article, "Practice guideline update summary: Acute treatment of migraine in children and adolescents: Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology and the American Headache Society." The authors completed an extensive literature review and created eight recommendations for the acute treatment of pediatric migraine focusing on medication selection, dosing, patient education, and patient counseling. By applying the evidence-based guidelines presented in this study, the urgent care or emergency department APN can confidently recognize and treat acute migraine symptoms and reduce patient risks from unnecessary testing and overuse of acute migraine medications. **Key words:** headache, medication-overuse headache, migraine, pediatrics, triptans

SAMMIE, A 12-YEAR-OLD African American boy, accompanied by his mother, presents to the urgent care clinic with a severe headache. Sammie has had other similar severe headaches in the past. His current symptoms are not new. His mother brought him to urgent care because his pain and associated vomiting quickly become uncontrollable when he gets a severe headache. Last month she had to take him to the emergency department (ED) with the same type symptoms, and she does not want to end up there again. Last month, at ED discharge, they were instructed to use ibuprofen at home for pain and to follow up with a neurologist; however, the wait time for a new patient neurology visit was 3 months from their ED visit.

Sammie describes his headache as throbbing and worse on the right side than the left. He vomited twice at home since the headache started and once in the car on the way over. He did have an aura prior to having head pain that he describes as zigzagging lines in his visual field that lasted about 10 minutes. His vision is back to normal now, but he says light makes his headache worse. His headache is rated as an 8/10 and consistent with his last three attacks. He also tells you that he is very stressed out at school and staying up late at night studying hard to make sure he is able to test into

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advanced placement classes next year. He denies any tingling, numbness, weakness, dizziness, autonomic symptoms, such as unilateral facial sweating, redness of the face, lacrimation of the eye, nasal congestion, or neck pain or stiffness. He and his mother deny any recent upper respiratory symptoms or fever. Except for his headaches his medical history is negative, and his vaccinations are up-to-date. His surgical history includes a tonsillectomy at age 6. He denies any drug, alcohol, or tobacco use and lives in a smoke-free home with his mother and father and two younger sisters. He is not sexually active. His mother states that she works part time as a paraprofessional at his school, and his father works full time as an economics professor at the local state university. His mother does have a history of migraine. They deny any family history of cardiovascular disease, hypertension, diabetes, or cancer.

On examination, the patient appears in moderate distress holding an emesis basin. Vitals signs include temperature 37.1°C, heart rate 99, blood pressure 120/75, and respiration rate 19. His body mass index is 20, and he appears well nourished. He is alert and oriented to person, place, time, and situation. His skin is warm, dry, with no rash. Pupils are equal, round, reactive to light, with normal conjunctiva. His mucous membranes are dry; he has no sinus tenderness pharyngeal erythema or nuchal rigidity. His tympanic membranes are pearly gray. His musculoskeletal examination reveals no neck tenderness with full range of motion without meningeal signs. His neurological examination reveals intact cranial nerves II-XII, no papilledema, normal cerebellar function, normal sensation, and normal gait. All other physical examination findings were within normal limits.

A basic metabolic panel and complete blood count were ordered revealing no acute electrolyte abnormalities, anemia, or leukocytosis. The patient vomited twice in the waiting and examination rooms since arrival. He notes that his pain is increasing. You decide to initially treat his symptoms with ondansetron 4-mg oral disintegrating tablet and oral sumatriptan/naproxen sodium 10-/60-mg tablet. The sumatriptan/naproxen 10-/60-mg table was called into the pharmacy next door enabling Sammie's mother to pick it up and administer it to him as a trial dose while in the clinic to avoid a costly ED visit.

Tiered differential diagnoses include tier one, migraine with aura; tier two, meningococcal disease; and tier three, tension-type headache. Less likely, but possible, differential diagnoses include seizure, viremia, gastroenteritis, influenza, and strep pharyngitis. You wonder, should you expose him to radiation and order a computed tomography (CT) of the head? He has no focal neurological deficits, and you want to avoid unnecessary tests, but you also do not want to miss a potentially life-threatening emergency. You also have limited diagnostic laboratory capabilities in your clinic. So far his rapid strep and flu tests are negative.

RESEARCH ARTICLE

Oskoui, M., Pringsheim, T., Holler-Managan, Y., Potrebic, S., Billinghurst, L., Gloss, D., . . . Mack, K. (2019). Practice guideline update summary: Acute treatment of migraine in children and adolescents: Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology and the American Headache Society. *Neurology*, *93*(11), 487–499. doi:10.1212/WNL.0000000000008095

Purpose and Methods

The purpose of Oskoui et al.'s study was to update the American Academy of Neurology (AAN)'s 2004 clinical guidelines for the acute treatment of pediatric migraine (Lewis et al., 2004). In January 2015, the AAN assembled a multidisciplinary expert panel including 12 physicians and three patient representative members to review the current evidence on self-administered pharmaceutical interventions for treatment of migraine. Studies evaluating pharmaceutical interventions administered in an ED or infusion center setting

were excluded from review. The purpose of the study was to develop revised guidelines and recommendations based on new evidence in the acute treatment of pediatric migraine (Oskoui et al., 2019).

To evaluate the evidence, the panel conducted a systematic review of all randomized controlled trials (RCTs) evaluating the effectiveness of acute and preventative self-administered pharmaceutical agents for treatment of pediatric migraine using MEDLINE and Embase databases from December 1, 2003, to February 15, 2015, and from January 2015 through August 25, 2017 (Oskoui et al., 2019). The start search date was selected to evaluate all the evidence since publication of the 2004 clinical guidelines. Study inclusion criteria included (1) RCTs of at least 20 participants, (2) RCTs that compared self-administered pharmaceutical therapies to a placebo-controlled comparison group, and (3) studies in which at least 90% of study participants, aged 0–18 years, had a prior diagnosis of migraine (Oskoui et al., 2019).

After the literature search was completed 2,482 abstracts were found to be relevant to the clinical question. Of those, the panel reviewed 313 full-text articles. After this review only 10 studies met all inclusion criteria for the current guidelines. The panel also reviewed the studies used in the development of the 2004 guidelines and additionally incorporated six of the previously used studies.

After selecting the studies for inclusion in the review, a modified GRADE process was used in the analysis to reduce the potential for bias in the panel's conclusions (Oskoui et al., 2019). The GRADE process is a standardized tool for guideline development that ranks evidence in four levels (high, moderate, low, or very low) by evaluating the risk for error, including limitations of the study, inconsistency of results, indirectness of evidence, imprecision, and reporting bias (Guyatt et al., 2008).

Following the review and GRADE process analysis, the panel created practice recommendations based on the strength of evidence assigning an evidence level to each recommendation using a modified Delphi process or a structured communication technique between experts to achieve consensus (Oskoui et al., 2019). The panel's aim was to create recommendations that answered the clinical question of whether acute self-administered treatments, compared with placebo, reduce headache pain and associated symptoms (nausea, vomiting, photophobia, and phonophobia) and maintain headache freedom in children and adolescents with migraine (Oskoui et al., 2019).

RESULTS AND CONCLUSIONS

The panel's systematic review and analysis resulted in eight recommendations focused on appropriate headache diagnosis, first-line treatment for acute, access to various treatment options, patient counseling, treatment for associated symptom reduction, and contraindications to triptan use. Methods to engage patients and caregivers within their care plan were included to ensure the goals of evidence-based practice are achieved, combining best clinical evidence with provider and patient choice. The major updates to the 2004 guidelines are as follows.

Establish a Specific Headache Diagnosis

Establishing a specific headache diagnosis can be difficult, as many migraine patients are misdiagnosed (Al-Hashel, Ahmed, Alroughani, & Goadsby, 2013). However, for optimal treatment to be achieved it is essential that the patient be diagnosed with the correct headache disorder. The AAN recommends first establishing whether the headache is of a primary or secondary (caused by another condition) origin. This is achieved by obtaining a complete headache history (see Figure 1) including headache semiology, determining whether the patient has aura symptoms and, if so, how the aura presents, associated migraine symptoms, and defining the degree of disability during the attack (Oskoui et al., 2019). This recommendation aligns with the International Headache Society (IHS) headache classification clinical

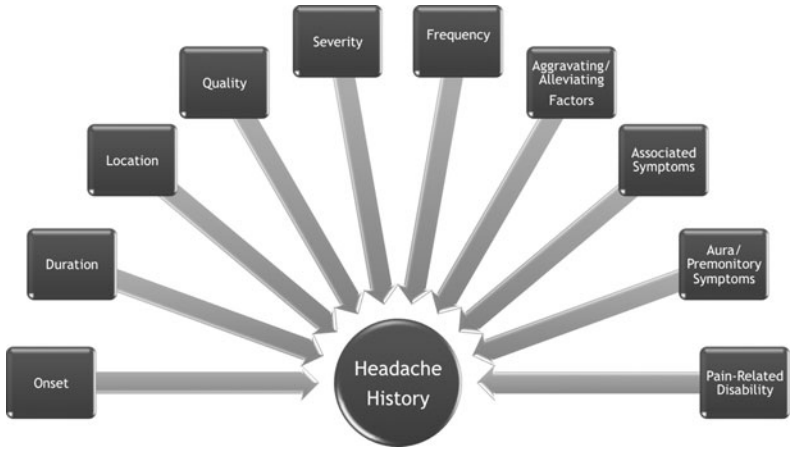

Figure 1. Components needed for complete headache history.

criteria for migraine diagnosis (Headache Classification Committee of the International Headache Society, 2018). The IHS (2018) defines a migraine headache as including at least five attacks that last 4–72 hr (untreated), with two of the following characteristics: unilateral location, pulsating, moderate/severe pain intensity, and/or aggravated by routine physical activity, as well as nausea and/or vomiting and photophobia and phonophobia. These key elements in the patient's history are necessary to determine an accurate headache diagnosis as recommended by the AAN (Oskoui et al., 2019)

Acute Migraine Treatment

The goal of acute migraine treatment is quick relief of migraine pain and associated symptoms, allowing the child or adolescent to return to his or her normal activities. Symptomatic relief is best achieved when acute treatment is given soon after migraine pain occurs. Early treatment is essential in the treatment of both pediatric and adult migraine, but there are treatment differences in pediatric patients when compared with adults.

The AAN's practice recommendations for acute migraine treatment in pediatrics focus on quick initiation of treatment. The first-line medication for acute migraine treatment in pediatrics is ibuprofen oral solution 10 mg/kg (Oskoui et al., 2019). In adolescents with migraine, combination therapy with sumatriptan and naproxen is superior compared with monotherapy with a triptan or nonsteroidal anti-inflammatory drug (NSAID) at reducing migraine pain (Derosier et al., 2012). Although not completely understood, the combination of triptans with NSAIDs has been found to better reduce the pathophysiological mechanisms that cause acute migraine pain (Derosier et al., 2012). However, there are certain cases where NSAIDs may not be well tolerated such as a drug allergy and individual use of a triptan is needed. In those cases, zolmitriptan and sumatriptan nasal spray, rizatriptan ODT, and almotriptan tablets are effective at reducing pediatric migraine pain (Oskoui et al., 2019).

Due to multiple drug administration routes, some migraine medications are preferred based on a patient's associated symptoms. Therefore, it is important to consider all of a patient's migraine symptoms. Specifically, in patients with significant nausea and vomiting, alternative medication routes such as nasal sprays and orally dissolving tablets should be considered. Patients should also have access to different triptan agents, because patients can have varying degrees of migraine symptoms and should be empowered to select the best triptan dosing

route based on migraine severity, adverse effects, and patient preference. For example, the treatment of severe migraine attacks that reach peak intensity quickly might require agents with a quick onset of action, like nasal sprays; however, patients may prefer an oral triptan route with fewer adverse effects, such as postnasal drip and nasal tingling, for typical migraine attacks.

Because migraine attacks can vary in degree of severity, a previously effective triptan may not be effective if the migraine has quickly reached peak intensity. This does not represent a triptan failure but suggests that a different triptan agent should be tried (Oskoui et al., 2019).

In addition to selecting the best triptan for the patient, clinicians should assess for migraine return within 24 hr. For patients experiencing a return in his or her migraine, they should be advised to take a second triptan dose 2 hr after the initial dose. Improvement in 24-hr migraine attack return with two triptan (one at onset and repeated in 2 hr) doses has been observed in adult patients and should be considered in the pediatric population, although ensuring that patients and caregivers do not exceed the maximum daily dosing recommendations is an important consideration with this strategy (Buse et al., 2013; Oskoui et al., 2019).

Treatment of Associated Symptoms

Although migraine pain can be debilitating, many patients also have severe associated symptoms that affect their quality of life. For treatment of migraines in adults, triptan agents can improve many associated migraine symptoms, including nausea and vomiting. Although triptans do improve photophobia and phonophobia in pediatric patients, these agents are not effective at reducing migraine-associated nausea and vomiting (Oskoui et al., 2019). The AAN recommends that migraine-associated nausea and vomiting in pediatrics should be treated with antiemetic agents in addition to triptan or NSAID use (Oskoui et al., 2019).

Counseling

Migraine is a chronic disease and requires patient education to reduce symptoms. Nurses play a key role in patient education. Patients with migraine should receive ongoing counseling on lifestyle modifications including sleep hygiene, migraine triggers, and the importance of exercise in reducing their migraine symptoms (Oskoui et al., 2019).

Contraindication to Triptan Use

Although triptans are a valuable treatment option for many patients suffering from migraine attacks, there are specific instances when triptans should be avoided. Based on the Food and Drug Administration (FDA)'s recommendations, the AAN recommends that clinicians avoid use of triptans in patients with a history of ischemic vascular disease or accessory conduction pathway disorders such as Wolff-Parkinson-White syndrome (Oskoui et al., 2019).

AREAS FOR FUTURE RESEARCH

Although the authors of this review did not discuss strengths and limitations to their analysis, the authors did suggest several areas for future research. First, there is a high placebo response in pediatric migraine RCTs, and although the pathophysiology of migraine is presumed to be the same in adult and pediatric patients, further study of the placebo response in pediatrics may offer a safer alternative to treatment of headaches in the pediatric population (Oskoui et al., 2019). Drug metabolism differences and the pathophysiology underlying pediatric migraine presentations, such as duration of attack, should also be considered when designing clinical trials in pediatrics to reduce biases and the risk of error when interpreting results (Oskoui et al., 2019).

AUTHOR COMMENTS

Headache is the third leading cause of pediatric ED visits (Kabbouche, 2015). The

recommendations from Oskoui et al.'s systematic review and treatment guidelines aim to improve the acute treatment of pediatric migraine and decrease the negative effect migraines can have on pediatric patients. Oskoui et al.'s recommendations provide improved treatment options for acute migraine treatment based on current best evidence. The strengths of these recommendations are rooted in the guideline review process that was thorough, specific to the targeted population, and aimed to decrease the risk of reviewer bias by utilization of the modified GRADE process for evidence ranking. These factors are essential in creating high-level evidence-based practice guidelines. However, the weakness of these recommendations is the need for additional evidence on the treatment pediatric migraine. Additionally, further recommendations are needed to ensure best practices in the treatment of acute migraine in the ED setting.

Although the ED treatment of acute pediatric migraine was outside the scope of the current treatment guidelines, consensus on migraine management in these settings should be studied. Standardized ED headache treatment algorithms to ensure that pediatric patients are receiving the best treatment for acute migraine could decrease ED revisits and throughput times. For instance, prochlorperazine, effective at reducing migraine pain as well as associated migraine symptoms such as nausea and vomiting, appears to be superior—when compared to other medications including metoclopramide and opioids—at preventing ED return visits (Bachur, Monuteaux, & Neuman, 2015; Friedman et al., 2017). Although prochlorperazine, dosed at 0.15 mg/kg with a maximum dose of 10 mg, is generally well tolerated, it may be given with diphenhydramine to reduce dystonic effects. Prophylactic treatment of akathisia with diphenhydramine in patients receiving dopamine receptor antagonists such as prochlorperazine and metoclopramide should be used cautiously in pediatric populations, as these symptoms are rare, generally mild, and the use of diphenhydramine has been found to be associated with increased return visits to the ED in pediatric populations (Bachur et al., 2015).

Interestingly, although triptan/NSAID use is strongly recommended for acute migraine treatment, many pediatric patients are not prescribed these agents and may not be used in the ED setting (Bachur et al., 2015; Kabbouche, 2015). Despite FDA approval for use of almotriptan, sumatriptan/naproxen, and zolmitriptan nasal spray in children 12 years and older and the approval of rizatriptan for use in children 6 years and older, providers may not be aware that these drugs are safe and effective in pediatrics. There is some evidence that adults receiving triptans in the ED may have reduced migraine pain; however, this has only been studied in adult populations (Meredith, Wait, & Brewer, 2003). If prescribing combination therapy including a triptan at discharge, it is important to discuss the risk of medication-overuse headache with the patient and family.

Medication-overuse headache is defined in the International Classification of Headache Disorder, 3rd edition (ICHD-3) as a headache occurring more than 15 days per month for 3 months with associated overuse of acute migraine medications on more than 10 or 15 days per month depending on the offending agent (ICHD-3, 2018). All patients should be cautioned about this syndrome.

Although acute medication selection and dosing is important, attention should also be given to the use of neuroimaging in pediatric patients with headache. The American College of Radiology recently released their appropriateness criteria for neuroimaging in pediatric headache and suggested that neuroimaging is generally not appropriate in children with primary or uncomplicated headache (Hayes et al., 2018). Patients with red flag symptoms such as abnormal neurological examination, papilledema, history of neoplasm, fever, or posttraumatic headache may need further evaluation to rule out secondary causes (Do et al., 2019). Patients and caregivers should be included in shared decision-making and educated on the risks

and low value of neuroimaging in this population because headache is relatively common in the pediatric population.

Patient education and counseling is key in the management of headaches in the pediatric population, as strong placebo effects have caused clinical trials to end early due to headache improvement with placebo treatment. Pediatric patients are thought to be more compliant with treatment plans suggested by role models such as parents and clinicians (Faria, Linnman, Lebel, & Borsook, 2014). Furthermore, clinical trials focusing on behavioral interventions, such as cognitive-behavioral therapy, have shown positive results in children. For example, nonpharmacological interventions studied in pediatric populations have been shown to improve the effect of pharmacological intervention (Powers et al., 2013). This combined approach is essential to migraine treatment and clinicians should utilize their training in patient education to ensure that patients are aware of the importance of nonpharmacological as well as pharmacological treatment options.

Pediatric migraine is a common medical condition that affects many children and families. Evidence-based treatment guidelines such as the AAN's can improve treatment effectiveness, reduce costs, and ensure patients receive the most appropriate care. Specifically, improved access to effective treatments that can be initiated at home may reduce costly and stressful ED visits and improve patient quality of care. Additionally, standardization of the ED treatment of pediatric migraine could reduce ED return visits, improve throughput times, and reduce unnecessary diagnostic imaging and radiation exposure burden.

CONCLUSION

You return to reassess Sammie and find that he is doing much better. He denies any vomiting since receiving the ondansetron and notes that his migraine pain has decreased to a 4/10. Differentials include but are not limited to migraine with aura, meningococcemia, strep pharyngitis, seizure, and tension headache. By applying the new pediatric migraine guidelines and based on his response to treatment, headache presentation, and history, you decide that his most likely differential diagnosis was acute migraine with aura. This diagnosis is consistent with a primary headache syndrome due to lack of red flag symptoms or concerning neurological examination findings including papilledema, cranial nerve dysfunction, and/or seizures.

After 2 hr you give Sammie a second dose of sumatriptan naproxen 10/60 mg by mouth and recheck his pain, now a 2/10. Through shared decision-making, you discuss the risks and benefits of neuroimaging, including the American College of Radiology's appropriateness use criteria for neuroimaging in pediatric patients with headache (Hayes et al., 2018). As a team, Sammie, his mother, and you decide to discharge him home to rest and defer sending him to the ED for diagnostic imaging. You explain that migraines can be managed with proper treatment. You encourage him and his mother to keep their appointment with the pediatric neurology group. You agree to send an encrypted e-mail to the neurology provider with your notes attached to see whether his appointment can be expedited. You prescribe sumatriptan/naproxen 10/60 mg by mouth as needed for migraine and ondansetron 4 mg by mouth as needed for nausea/vomiting. You discuss the importance of not using the sumatriptan/naproxen more than 10 days per month to reduce the potential for increased headaches from medication overuse (Headache Classification Committee of the International Headache Society, 2018). You and Sammie discuss the importance of getting enough sleep, avoiding migraine triggers, and trying to find an activity he enjoys that can help to reduce his stress. You instruct him to go to the ED if symptoms worsen or if he develops any neurological deficits such as dizziness, vision changes, tingling/numbness, weakness, slurred speech, confusion, or fever. You agree to follow up with a phone

call to the mother tomorrow to check on his condition and to have the mother call you with any concerns tonight. Both Sammie and his mother are satisfied with the plan of care, and his mother feels as if she can now confidently initiate home treatment if he has another headache recurrence before his visit to the neurologist. She agrees to let you know if there are any new recommendations for his care after he sees the neurologist.

Pediatric migraine is common and impacts the quality of life of many children. Acute treatment of migraine can reduce pain and associated migraine symptoms allowing children to return to their normal activities quicker. Appropriate diagnosis, treatment, and counseling are essential for best outcomes. The AAN's acute treatment guidelines for pediatric migraine help clinicians to deliver high-quality care that enables children to return to school and play, decreasing the negative impact migraine has on their lives.

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