Headaches in Children

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ABSTRACT

Purpose of Review: This article provides an overview of the differences in epidemiology, presentation, and treatment of pediatric headache compared to adult headache.

New Findings: New proposals are presented regarding the classification of pediatric migraine and ophthalmoplegic migraine. The distinction between basilar migraine and migraine with aura is reconsidered.

Summary: Pediatric headache is a common but underdiagnosed condition. Primary headache syndromes, in particular migraine, can present differently in children than in adults. Diagnosis can be problematic, especially in young children, because standard criteria used for classification are often incomplete. Treatment focuses on biobehavioral modification and adapted use of standard adult medication management.

Continuum Lifelong Learning Neurol 2012;18(4):853–868.

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Relationship Disclosure: Dr Babineau reports no disclosure. Dr Green has served as a speaker for Zogenix, Inc., and has performed malpractice reviews.

Unlabeled Use of Products/Investigational Use Disclosure: All of the medications that Drs Babineau and Green discuss for the treatment of headache in children are unlabeled except for almotriptan, which is approved for people aged 12 years and older, and rizatriptan, which is approved for people aged 6 years and older.

INTRODUCTION

Headache is one of the most common concerns reported by children. Recurrent headaches are reported in one-third to one-half of children and adolescents and occur daily or near daily in about 2% to 6% of young patients.[1–3] However, after the evaluation for secondary causes of headache is completed, most children with a primary headache syndrome are left untreated or undertreated. Pharmaceutical studies often exclude individuals under the age of 18 from clinical trials. Several studies have observed that medication is often only a small part of the treatment plan, as thorough identification, education, and nonpharmacologic therapies show significant benefit.

IDENTIFICATION OF HEADACHE

Identification of a primary headache in a child is the first step to effective treatment. It has been difficult for both parents and health professionals to accurately identify children with primary headache. It is commonly believed that children do not get migraines, that their headaches are not disabling, or that they are feigning the symptoms. Children get migraines as well as other forms of primary headache syndromes, and migraine variants can present before the first birthday. Most patients with migraine report onset of headaches before the age of 20, and 12% report onset before age 7.[4,5] Among children ultimately diagnosed with a primary headache syndrome, 21% are previously misdiagnosed by a health care professional, including neurologists. The time to correct diagnosis is 1 year on average and increases to 3 years if a child has been previously misdiagnosed.[6]

History and Physical Examination

In children, the ability to describe the headache is limited by their developmental stage. Important clues can include paroxysmal events where the child appears unwell or pale, vomits,

KEY POINTS

- Most patients with migraine report onset of headaches in childhood or adolescence, but often several years pass before the correct diagnosis is made.
- Imaging should be considered if there is an abnormal examination, a change in the nature of the headaches, the recent onset of severe headache, coexistence with seizures or other signs of neurologic dysfunction, a history of neurocutaneous syndrome, or the child is younger than 6 years.

or bangs or holds his or her head. The primary goal of the interview is to eliminate any red flags for secondary headaches (discussed in detail in the article ''Secondary Headaches'' in this issue of CONTINUUM) and to obtain enough information to make the diagnosis of a primary headache. It is important to determine the impact of the condition on school and extracurricular activities, including the number of school days missed in a given time period. Efforts should be made to determine additional stressors at school that contribute to recurrent headache. A thorough review of lifestyle practices, including caffeine intake, regularity of meals, sleep habits, and exercise, is important in identifying possible sources of modification. Lastly, the pediatric Migraine Disability Assessment Scale can be helpful in determining the impact of headaches on the child.

In addition to the standard neurologic examination, a comprehensive headache examination that evaluates for specific headache alterations is useful.[7] Also, it is important to measure head circumference to identify macrocephaly, which could be associated with hydrocephalus, and to look for neurocutaneous stigmata. A thorough ophthalmic examination is necessary to look for papilledema.

Further Testing

The guidelines for imaging in pediatric headache differ from those for adults and were set forth in a practice parameter by the AAN in 2002. In most cases, neuroimaging is not necessary. The recommendation is to consider neuroimaging if there is an abnormality on the neurologic examination, a change in the character or frequency of preexisting headaches, recent onset of severe headache, associated features that suggest neurologic dysfunction, or coexistence of seizures. Imaging is not routine for patients with unchanging recurrent headaches and a normal examination.[8] Head imaging in pediatrics often requires discussion about the radiation exposure with CT or the need for sedation with MRI. In nearly all cases MRI is the preferred methodology. Children are particularly vulnerable to the radiation of CT examinations given their size and longer lifespan. Using data from atomic bomb survivors, the calculated risk of head CT on the lifetime attributable risk of death from cancer for children younger than age 15 is 0.01% to 0.075%.[9] This risk needs to be weighed against the benefits of detecting a lesion that may change the management approach. The rate of abnormalities found on standard imaging for headache is between 14% and 28%, but the headache can be attributed to the abnormality found in only 10% to 30%.[10]

Secondary Headaches

Most secondary headaches in children are similar to those found in adults. Particular concern should be raised in children of a young age (younger than 6 years), those with a history of neurocutaneous syndromes, and those with signs and symptoms suggesting increased intracranial pressure. In up to 90% of cases, the cause of secondary headache is a viral or streptococcal upper respiratory tract infection. Meningitis is the most common cause with serious neurologic implications.[11]

Brain tumors. Brain tumors are the second most common malignancy in childhood and the most common solid tumor in children, with about 2200 new cases per year.[12] Headache is the most common presenting symptom and can occur in isolation, but it is often accompanied by vomiting, unsteadiness, or focal weakness. Because initial

symptoms are nonspecific, either the persistence of the symptoms or additional localizing symptoms will prompt further evaluation; the most sensitive indicator is an abnormal neurologic examination or the development of neurologic symptoms such as seizures.[12] A delay in diagnosis does not appear to change the long-term morbidity or mortality.[13] The prevalence of brain tumor in patients with a normal examination and headache history of greater than 6 months is 0.01% to 0.4%. Patients with headaches for less than 6 months and either sleep-related headache, vomiting, confusion, absence of visual aura, absence of family history of migraine, or an abnormal neurologic examination have a brain tumor prevalence of 4%.[14]

Ophthalmoplegic migraine. Ophthalmoplegic migraine was previously classified as a childhood migraine variant with partial or total paralysis of one of the nerves supplying eye movements. The third nerve is most commonly involved, accompanied by headache. This syndrome is now recognized as a cranial neuralgia. The paralysis is often responsive to a brief course of corticosteroids. Ophthalmoplegic migraine is rare, but as more cases are reported because of the availability of modern imaging methods, the classification has been reconsidered. Several case series demonstrated contrast enhancement of the affected nerve during an attack. The ophthalmoplegia can present or persist days or weeks after the headache resolves. The International Classification of Headache Disorders, Second Edition (ICHD-II) has reclassified ophthalmoplegic migraine as a neuralgia, defined as at least two attacks with migrainelike headache accompanied by or followed within 4 days of onset by paresis of one or more of the third, fourth, or sixth cranial nerves with parasellar, orbital fissure, and posterior fossa lesions excluded.[15] This new classification is controversial; not all cases show nerve enhancement and, when studied, CSF does not suggest inflammation. Ophthalmoplegic migraine is seen in individuals with a personal or family history of migraine, and the headache is felt to be a prominent part of the syndrome.[16] Both primary and secondary forms have been described. The primary form, possibly seen more frequently in adults, is likely a variant of migraine with the ophthalmoplegia as a form of aura. The secondary form is demyelinating and is seen in patients with enhancement of the nerve on MRI and a more protracted course. This form may require the use of corticosteroids.[17]

KEY POINT

- Ophthalmoplegic migraine is currently classified as a neuralgia and can be responsive to corticosteroids.

Primary Headaches

The prevalence of migraine is about 10% for girls and about 5% for boys (7% overall), the prevalence of tension-type headache is 0.9% to 24%,[2,3] and the prevalence of chronic daily headache is 3.5%.[18] Headache can significantly affect a child's quality of life, impacting both education and play. It takes a toll on caregivers for child care and doctor's visits. Up to 8% of children lose 6 school days per year as a result of headache.[2]

A complication of making the diagnosis of primary headache disorders in children is that not all headaches fulfill the criteria for a given subtype and some have features of multiple subtypes. Up to 10% cannot be classified by the ICHD-II criteria, and up to 45% are diagnosed in the *probable* category.[19] Typical features of migraine may not develop until later in life. Photophobia and phonophobia often do not develop until after age 12. Children younger than age 12 have a more difficult time describing pain.[20] Also, the nature of the headache can change over time. In follow-up studies, patients whose headaches were labeled as either probable tension-type or

KEY POINTS

- Headache diagnosis can change over time, with patients diagnosed with migraine later developing tension-type headache and vice versa.
- Pediatric migraine can be bilateral and brief, lasting less than 1 hour. Young children often have more prominent vomiting and abdominal symptoms, whereas photophobia and phonophobia often do not appear until the teenage years.
- A high rate of sexual, physical, and emotional abuse is found in teenagers with chronic daily headaches.

probable migraine could develop either migraine or tension-type headache, and patients fulfilling criteria for either migraine or tension-type headache switched diagnoses at least one-fourth of the time.[21]

The differences in the characteristics of pediatric and adult patients with migraine have been recognized for many years; the 2004 edition of the ICHD-II documents the special considerations in pediatrics in the footnotes. Headaches can be of shorter duration, with a lower limit of 1 hour, are more likely to be bilateral, and photophobia and phonophobia can best be inferred by behavior,[15] as exhibited in **Case 8-1**. More comprehensive criteria for migraine may include headache lasting 72 hours or less with two of the following four features: focal location, pulsatile quality, moderate or severe pain, and worsening or limiting physical activity.[20] Currently there are no differences in the classification of adult and pediatric tension-type headache.

Chronic daily headache is not as prevalent in children compared to adults but still exists in the pediatric population and can be a source of disability, as seen in **Case 8-2**. The most accurate prevalence rate for chronic migraine in 12- to 19-year-olds is 0.79% (1.75% if medication overuse is included).[18] Adolescents generally have fewer days with headache, and less than half have medication-overuse headache, compared to 71% of adults. Although transformed migraine is the headache type of most patients, it accounts for only 69% of headaches in adolescents compared to 87% in adults.[5] Because children and adolescents with chronic migraine may have a history of sexual abuse, inquiry is appropriate.[22] Similar to adults, this population is underserved, with over 60% not visiting a health care provider about their headaches in the past year and less than 20% taking prevention.[18]

Migraine Variants

The term *migraine variants* is used to describe syndromes that appear in children with a family history of migraine and in children who later develop migraine (**Table 8-1**). The reason these variants occur in childhood is unknown. These conditions can be seen in adulthood, and differences from migraine in proposed pathophysiology may exist.

Cyclic vomiting syndrome. Cyclic vomiting syndrome (CVS) is characterized by stereotyped episodes of intense vomiting followed by periods of complete resolution. Triggers of CVS in children include lack of sleep, coexisting illness, and stress. The prevalence of CVS is between 0.04% and 2%. The average age at onset is approximately 5 years, although CVS is seen in children as young as 1 month and is identified even in adults. CVS generally resolves 10 years after onset, and approximately 20% to 75% of affected children will develop migraines. Acute treatment focuses on sleep induction with benzodiazepines. Antiemetics and triptans are used with varying success. Preventive medications, including amitriptyline and propranolol, are used with good result.[23]

Abdominal migraine. Characterized by repeat attacks of severe noncolicky midline abdominal pain, abdominal migraine can be associated with typical migraine prodromes and aura. The estimated prevalence is 2% to 4%.[23] Treatment is based on prevention, including trigger avoidance, and standard migraine preventive medications such as cyproheptadine, propranolol, or divalproex. Acute treatments, such as nonsteroidal anti-inflammatory drugs, triptans, and antiemetics, may be successful.

Paroxysmal vertigo. Paroxysmal vertigo is characterized by discrete episodes that can last from minutes to an hour. The episodes involve sudden

Case 8-1

An 8-year-old boy presented with 1 year of headaches that occurred at a stable frequency of 3 times per month. The patient did not want to talk with the neurologist but when asked, ''Where is your headache?'' pointed to the front of his head and drew a picture (**Figure 8-1**). His mother reported that during a headache he would become pale, stop his activity, and complain of a stomachache. All he wanted to do was lie down, and after a 45-minute nap he would awaken feeling normal. Including the nap, the total length of the headache was about 1 hour. The mother had been instructed by her pediatrician to give him acetaminophen, but it did not seem to help. She had to pick him up from school at least once per month. From age 3 until last year he had an unknown severe gastrointestinal illness characterized by several days of repeated vomiting. A gastroenterologist had evaluated him, but none of the tests, including endoscopy, was revealing. The patient and mother had a history of motion sickness, and his maternal grandmother had headaches. The patient's examination was normal.

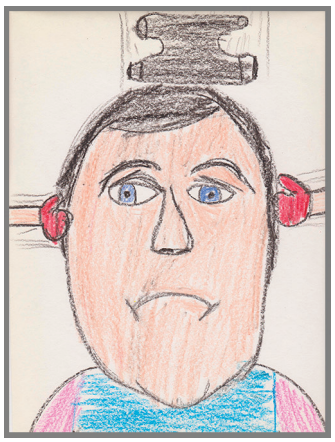

FIGURE 8-1 Drawing from an 8-year-old boy when asked where his headache was.

Courtesy of Kathleen Farmer, PsyD, and Roger Cady, MD, Springfield, Missouri.

Comment. This is a typical description of a child with migraine. Migraines in young children are of shorter duration, often bilateral, and respond well to sleep. Sometimes children are unable or unwilling to describe the headache, so use of drawings may be informative and parental observations are important. A history of migraine comorbidities, such as motion sickness or migraine variant, can help strengthen a diagnosis. In this case, the repeated episodes of gastrointestinal illness with negative workup may be cyclic vomiting syndrome. The examination is normal and the headache frequency is stable so this child does not need imaging. Treatment should begin with a review of triggers and lifestyle practices to determine modifications and a referral to biofeedback. In order to minimize school absences, arrangements should be made with the school staff to allow the patient to nap during a headache and return to class when he recovers. In addition, acute medication should be made available as early as possible, including keeping medication in his desk if deemed appropriate. It is important to review proper dosing with the parents. A triptan may be of value if ibuprofen or acetaminophen is ineffective.

unexplained fright, grasping of someone nearby, refusal to stand, and difficulty with balance. Events can be associated with pallor, nausea, perspiration, light and sound sensitivity, and unusual head positions. Prevalence in the general population is approximately 2%, and onset occurs at approximately 2 to 4 years of age with resolution by age 5.[23] An EEG is usually performed to exclude occipital lobe epilepsy. Treatment is often unnecessary because the events are brief, but in children with frequent or disabling attacks cyproheptadine has been used.

Paroxysmal torticollis. Characterized by episodes of head tilt that resolve completely between events, paroxysmal torticollis attacks can be prolonged, lasting several days. Recently, at least one abnormal gene, the calcium channel, voltage-dependent, P/Q type, α1A subunit gene, *CACNA1A*, has been identified in these individuals. This genetic abnormality is also seen in familial hemiplegic migraine type 1.[23] Treatment success with cyproheptadine has been reported.

Hemiplegic migraine. Hemiplegic migraine is characterized by migraine

KEY POINT

- Migraine variants are often precursors to migraine headaches and should be noted in the history. This strengthens the diagnosis of migraine.

Case 8-2

A 16-year-old girl came for consultation after 2 years of daily headache. The headache was constant throughout the day, moderate, and holocephalic with exacerbations of severe, pounding, bitemporal pain every few days. She took no medication for pain because nothing over-the-counter was efficacious. She had visited a neurologist who prescribed topiramate, which she had discontinued after 1 week because of side effects. An MRI of her head, bloodwork, and lumbar puncture including opening pressure were normal. She had been out of school for 6 months and had just started homeschooling. She did not exercise and her bedtime was variable, but she usually was asleep by midnight and awakened at 8:00 AM. Her neurologic examination was normal.

Comment. This case describes a teenager with chronic daily headache, most likely chronic migraine. Like many teenagers with chronic daily headache, no medication overuse is present. The patient should be interviewed privately to address sensitive topics such as drug use, sexual activity (including birth control), and the possibility of physical and sexual abuse. The patient should be allowed to speak about how the headache is affecting her life, potential contributing factors such as depression or anxiety, and how she thinks the headaches can be treated. Treatment of older children, especially teenagers, requires that they take an active role in headache management. She should be allowed to make decisions about which medications are used and how lifestyle modifications are addressed. She and her family need expectations clarified with regard to medication side effects and how to handle them, overall time course of treatment, and what constitutes improvement. In this case, progressive isolation from school, friends, and regular extracurricular activities has likely contributed to the protracted course. Every effort should be made to return the patient to regular school hours. In collaboration with the school, the patient can start with modified hours and slowly build up to a full day, and clear guidelines should be established for when headaches can cause school absence. The patient should be referred for psychotherapy to learn techniques to manage pain and address other stressors. She needs to adopt a regular, active, and healthy lifestyle. When a patient sets one goal for the next visit and is held accountable, the goals often become more attainable.

headache that has an aura of hemiplegia or even quadriplegia. The paresis or plegia can last for days, at times independent of headache. Hemiplegic migraine can occur in families or sporadically. The sporadic form is more common and typically presents in teenage years, whereas the familial form can present earlier, between ages 11 and 13. Familial hemiplegic migraine has been associated with several genes, resulting in improved understanding of the pathophysiology of migraine (**Table 8-2**). The paralysis is often the most disabling component of the attack, and acute treatment has been difficult. Treatment with an NMDA antagonist, ketamine, shows some promise, but nothing is predictably useful. Prevention of the attacks using agents such as acetazolamide, flunarizine (not available in the United States), and other calcium channel blockers such as verapamil remains

TABLE 8-1 Migraine Variants

Variant	Pathognomonic Symptoms	Differential Diagnosis	Usual Age at Onset	Duration of Episodes
Cyclic vomiting syndrome (CVS)	Attacks of self-limited stereotyped vomiting Vomiting at least 4 times/h for 1 h	Intestinal obstruction Gallbladder disease Pancreatitis Uteropelvic dysfunction Metabolic disorders (fatty acid oxidation, urea cycle, or organic/amino acidopathies) Increased intracranial pressure	3 y to 5 y	1 h to 5 d (usually 2 d)
Abdominal migraine	Attacks of moderate to severe dull midline/ poorly localized pain Vomiting less prominent than in CVS	Urogenital disorders Ulcers Cholecystitis Gastroesophageal reflux disease (GERD) Inflammatory bowel disease Irritable bowel syndrome	7 y to 10 y	1 h to 3 d
Paroxysmal torticollis	Attacks of head tilt to either side	Sandifer syndrome (GERD) Torsional dystonia Complex partial seizures Posterior fossa tumor	2 mo to 8 mo	Minutes to days (usually hours)
Paroxysmal vertigo	Vertigo or sudden episodes of fear or falling to the ground	Benign paroxysmal positional vertigo Episodic ataxia Pontocerebellar angle or posterior fossa tumors Epilepsy Peripheral vestibulopathy	2 y to 4 y	Minutes to hours (usually 5 min)
Alternating hemiplegia of childhood[a]	Attacks of hemiplegia/ dystonia that switch sides, often with eye movement abnormalities Baseline encephalopathy, seizures, and movement disorder	Pyruvate dehydrogenase deficiency Mitochondrial encephalomyopathy, lactic acidosis, and strokelike episodes syndrome (MELAS) Glucose transporter type 1 deficiency	Must start before 18 mo	Days
Hemiplegic migraine	Migraine aura with motor weakness	Stroke Tumor Encephalitis Epilepsy MELAS Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy Alternating hemiplegia of childhood	Familial hemiplegic migraine: 11 y to 13 y Sporadic hemiplegic migraine: adolescence	5 min to 24 h (aura not headache); can be longer

Continued on next page

TABLE 8-1 *Continued*

Variant	Pathognomonic Symptoms	Differential Diagnosis	Usual Age at Onset	Duration of Episodes
Basilar migraine	Migraine aura with at least two of the following symptoms: dysarthria, vertigo, tinnitus, decreased hearing, diplopia, visual symptoms in both visual fields, ataxia, decreased level of consciousness, bilateral paresthesia	TIA Chiari malformation Peripheral vestibulopathy Epilepsy Panic disorder	Adolescence	5 min to 60 min (aura not headache)

[a] Not considered a true migraine variant.

KEY POINTS

- Hemiplegic migraine can be either familial or sporadic. The familial form includes three subtypes based on genetic testing.
- Alternating hemiplegia of childhood (AHC) is characterized by eye movement abnormalities, attacks of hemiparesis or dystonia that can continue for days, baseline cognitive delay, ataxia, chorea, and epilepsy. While AHC can be associated with migraine, it is unlikely to be a migraine variant.

the mainstay of treatment.[24] Triptans and ergots are avoided because of the theoretic risk of vasoconstriction.

Alternating hemiplegia of childhood. Alternating hemiplegia of childhood (AHC) is a rare condition that presents in infancy with eye movement abnormalities, characteristically paroxysmal strabismus, or unilateral nystagmus. Within the next year the child experiences attacks of sudden paralysis of a limb or multiple limbs, often switching from one limb to another during an attack; dystonic posturing; and autonomic changes such as pallor or sweating. Attacks last from hours to days, during which the paralysis or dystonia disappears during sleep but returns upon awakening. AHC has been considered a precursor or variant of migraine, as migraine often accompanies an attack or exists independently in the patient or a family member. In addition, patients with AHC describe premonitory symptoms or sensory auras prior to onset of attacks, and triggers such as emotional stress or fatigue are known. Patients with AHC are rarely asymptomatic between attacks, and they experience cognitive and other developmental delays, persistent paresis of limbs, ongoing chorea, ataxia, and epilepsy. Genetic studies have revealed no linkage to hemiplegic migraine, and while some of the pathophysiology overlaps with migraine, AHC is likely a separate entity.[25] The mainstay of treatment is flunarizine (not available in the United States), and some reports indicate benzodiazepines and verapamil are useful. Other standard antimigraine medications, including antiepileptics, do not seem to be effective. A recently described syndrome called *alternating nocturnal hemiplegia of childhood* is more likely to be a migraine variant. It presents with attacks of hemiparesis with onset during sleep. The child will awaken and appear irritable, with hemiplegia lasting minutes to hours. It has been described in families with migraine or in children with personal history of headache. Unlike AHC, no dystonia, abnormal eye movements, or persisting deficits are associated with the nocturnal syndrome.[26]

Basilar migraine. Basilar migraine is a variant most commonly found in teenaged girls describing an occipital headache and at least two brainstem symptoms. If any focal weakness is part of the syndrome it is considered a form of hemiplegic migraine. There may not

TABLE 8-2 Familial Hemiplegic Migraine

Subtype	Genes With Potential Mutations	Gene Function	Other Conditions Associated With Genetic Mutation	Unique Features
Familial hemiplegic migraine (FHM) 1	Calcium channel, voltage-dependent, P/Q type, α1A subunit, *CACNA1A*	Subunit of neuronal P/Q calcium channel May lead to a reduced threshold for cortical spreading depression	Episodic ataxia type 2 Spinocerebellar ataxia type 6	Cerebellar signs with cerebellar atrophy, attacks triggered by trauma, bilateral and prolonged attacks
FHM 2	ATPase, Na+/K+ transporting, α2 polypeptide, *ATP1A2*	Subunit of glial/neuronal Na/K pump May impair glutamate reuptake in glia and slow recovery from excitation	Familial basilar migraine	Associated with high rates of epilepsy and severe attacks with coma
FHM 3	Sodium channel, voltage-gated, type I, α subunit, *SCN1A*	Subunit of sodium channel May decrease inhibition of interneurons and increase excitability	*SCN1A*-epilepsy syndromes (including febrile seizures and generalized epilepsy with febrile seizures plus)	Repetitive daily blindness

be a distinction between basilar migraine and standard migraine with aura. In a prospective study of patients with typical aura, up to 85% had one brainstem symptom and 74% fit criteria for basilar migraine.[27] Acute treatment with triptans is avoided because these drugs have not been studied in this population and there is a theoretic risk of potentiating brainstem ischemia. Nonsteroidal anti-inflammatory drugs are the medication of choice. Recently, use of topiramate for prevention has been successful.[28]

Confusional migraine. The term *confusional migraine* describes migraine accompanied by disorientation, memory disturbance, and facial recognition problems and is not identified as a separate entity in the ICHD-II. Prevalence has been quoted to be 0.04% of children with migraine.[29] The confusional state often occurs after a typical aura and can be triggered by minor

KEY POINT

■ Sleep is frequently disturbed in children with migraine, and they have a high prevalence of sleep-disordered breathing.

head trauma. Initial presentations should be evaluated for an underlying infectious process as well as seizures, toxic exposure, and metabolic derangement. Confusional states can be seen in patients who eventually develop cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) and in those with familial hemiplegic migraine and headache associated with neurologic deficits and lymphocytic pleocytosis (HaNDL) syndrome.[29]

Other Primary Headaches

Almost all of the headache syndromes, even those previously thought to affect only older adults, such as hypnic headache, are being described in young patients.[30] Primary headaches other than migraine and tension-type headache are unusual, and any child presenting with symptoms similar to or even characteristic of other headache syndromes should be evaluated for secondary causes. Five percent to 10% of patients with cluster headache develop their headaches in adolescence. In children with cluster headache, there is greater equivalence in prevalence between sexes, fewer autonomic features, shorter cluster periods, and longer intervals between clusters. Indomethacin is more frequently effective in children than in adults.[31] New daily persistent headache appears to be relatively more common in children and adolescents than in adults and comprises a larger percentage of adolescents with chronic daily headache.[32]

Comorbidities

Several conditions are comorbid with the primary headache disorders, in particular migraine. It is important to identify them as they may alter management.

Mood disorders. In adults a strong association exists between migraine and many mood disorders, including depression, bipolar disorder, and anxiety. In children, reports show an increased risk of suicidality.[33] A recent large systematic review shows that children with migraine seen in tertiary care centers do not have greater psychological dysfunction or more comorbid psychiatric diagnoses than healthy controls.[34] Screening for mood disorders is recommended, and, if a disorder identified, aggressive treatment should ensue.

Obesity. Obesity in children is a prominent issue, and reports about its effect on headache are mixed. Obesity is most clearly linked to chronic headaches. Higher body mass indexes (BMIs) increase the risk of chronic headaches, particularly chronic tension-type headaches,[35] and are positively correlated with headache frequency and disability. In patients who are at risk for overweight and obesity, a reduction in BMI will lead to a reduction in headache frequency.[36]

Sleep disturbance. The most common trigger for headaches in children is impaired sleep.[37] Children with migraine report poorer sleep quality, more daytime sleepiness, longer sleep latencies, and reduced total sleep duration compared to individuals without migraine. Evidence shows that patients with migraine, particularly those who are overweight, have increased rates of sleep-disordered breathing and a higher rate of parasomnias.[38] Higher headache frequencies are positively associated with poorer sleep quality, and this association does not resolve when preventive migraine medications are used, suggesting that an underlying alteration in normal sleep patterns may be present in patients with migraine.[39]

Other Periodic Syndromes of Childhood

Children with migraine commonly voice other concerns that do not necessarily alter management but

may help strengthen the diagnosis. Motion sickness is reported with high frequency in children with migraine. Recurrent limb pain has been reported in many children with migraine and is described as a deep, localized pain in an arm or leg that can last up to 72 hours and is sometimes associated with anorexia or nausea.[38] One-fourth of children with migraine also experience red ear syndrome,[40] characterized by intermittent unilateral ear pain or burning with redness of that ear that may be associated with headache. Activation of the auriculotemporal nerve, often through touch, can trigger this condition.

EXPECTATIONS/PROGNOSIS

The natural history of recurrent headaches in children shows that approximately one-third will experience remission. Those with tension-type headache, probable migraine/tension-type headache, or unclassifiable headache have higher rates of remission than those with migraine. In long-term follow-up of childhood migraine, one-fourth of patients are headache free by age 25, but more than one-half report migraine relapse between age 30 and 50. Risk factors that predict persistence include female sex, maternal history of headache, and a psychiatric diagnosis.[21] It remains to be seen if early and aggressive treatment is disease modifying. However, more than 93% of patients treated with a multidisciplinary team approach described significant improvement in headaches after 5 years.[41]

TREATMENT OPTIONS

Biobehavioral Management

Biobehavioral therapies are effective for migraine and tension-type headache in children, especially in those younger than age 6. Healthy habits, including regular sleep, avoidance of caffeine overconsumption, and regular exercise, can be effective. The efficacy of biofeedback, relaxation techniques, and cognitive-behavioral therapy has been documented over several years of follow-up.[37] All patients should explore these options, whether as sole therapy or in combination with medication.

Vitamins

Many supplements have been used in children and are often an attractive option for parents, given the minimal risks. No convincing evidence supports their efficacy. Coenzyme Q10 has been shown to be no more effective than placebo.[42] Studies of riboflavin at varying doses show no improvement with migraine but a trend toward improvement in tension-type headache.[43] Magnesium has some demonstrated benefit in tension-type headache.[44] Despite the paucity of evidence, it may be reasonable to try supplements given the large placebo effect and benign side effect profile.

Acute Medication

Possibly the most effective acute treatment for children with migraine is rest and sleep in a quiet, dark room. The mainstays of medication are ibuprofen and acetaminophen. The AAN reports that for children older than 6 years ibuprofen is effective and acetaminophen is probably effective. Both are used for the acute treatment of tension-type headaches. The triptans have been used for children as young as age 6 with tolerable side effects but mixed results in efficacy. Triptans are often no better than placebo, possibly because of the high placebo response and the headache duration being less than the 2-hour efficacy end point of traditional triptan studies. Almotriptan has been US Food and Drug Administration approved for use in children older than age 12, and recently rizatriptan was approved for children older than

KEY POINTS

- Motion sickness, recurrent limb pain, and red ear syndrome occur with higher prevalence in children with migraine.
- About one-third of children with headache will experience remission in the coming years; however, over one-half of those with migraine will go on to have migraines into adulthood.
- Nonmedication treatment such as sleep and biofeedback can be effective in children.

TABLE 8-3 Acute Treatment of Migraine[a,b,c]

Agent	Formulations	Dosing	Lower Age Limit
Acetaminophen	Chewable tablet: 80 mg Oral disintegrating tablet: 80 mg, 160 mg Tablet: 325 mg, 500 mg Liquid: 160 mg/5 mL, 500 mg/5 mL	15 mg/kg/dose	None
Ibuprofen	Chewable tablet: 100 mg Tablet: 100 mg, 200 mg, 400 mg, 600 mg, 800 mg Liquid: 100 mg/mL, 40 mg/mL	10 mg/kg/dose	6 mo
Ketorolac	IV Tablet: 10 mg	IV: 0.5 mg/kg/dose (maximum 15 mg) Oral: 1 mg/kg/dose (maximum 10 mg)	2 y
Naproxen	Tablet: 220 mg, 250 mg, 275 mg, 375 mg, 500 mg, 550 mg Liquid: 125 mg/5 mL	5 mg/kg/dose to 10 mg/kg/dose	2 y
Metoclopramide	IV Orally disintegrating tablet: 5 mg, 10 mg Tablet: 5 mg, 10 mg Liquid: 5 mg/5 mL	0.2 mg/kg/dose (maximum 10 mg)	2 y
Prochlorperazine	IV Tablet: 5 mg, 10 mg Suppository: 25 mg	0.15 mg/kg/dose (maximum 10 mg)	8 y for migraine, 2 y for other indications
Almotriptan	Tablet: 6.25 mg, 12.5 mg	12.5 mg	12 y
Rizatriptan	Orally disintegrating tablet: 5 mg, 10 mg Tablet: 5 mg, 10 mg	Patients <40 kg: 5 mg Patients >40 kg: 10 mg	6 y
Sumatriptan	Tablet: 25 mg, 50 mg, 100 mg Nasal spray: 5 mg, 20 mg Subcutaneous injection: 4 mg, 6 mg	Oral: <12 y: 50 mg, >12 y: 100 mg Intranasal: patients 20 kg to 39 kg: 10 mg; patients >40 kg: 20 mg Subcutaneous: 0.06 mg/kg/dose	Oral: 8 y Intranasal: 5 y Subcutaneous: 6 y
Zolmitriptan	Orally disintegrating tablet: 2.5 mg, 5 mg Tablet: 2.5 mg, 5 mg Nasal spray: 5 mg	<12 y: 2.5 mg >12 y: 5 mg	6 y
Dihydroergotamine	IV Nasal spray: 4 mg/mL (each spray = 0.5 mg) IM injection: 1 mg/mL	IV: Patients <9 y or <25 kg: 0.5 mg/dose; patients >9 y or >25 kg: 1 mg/dose Intranasal: Patients <12 y: 0.5 mg, repeat in 15 min every 8 h for 3 d; patients >12 y: 1 mg, repeat in 15 min every 8 h for 3 d	6 y

IV = intravenous; IM = intramuscular.

[a] Data from Hershey AD, Lancet Neurol.[37] *www.sciencedirect.com/science/article/pii/S1474442209703035.*
[b] Data from O'Brien HL, et al, Curr Treat Options Neurol.[46] *www.springerlink.com/content/c6824k0u0m502v30/?MUD=MP.*
[c] Data from Lexi-Drugs.[47]

TABLE 8-4 Preventive Treatment of Migraine[a,b,c]

Agent	Formulations	Dosing	Lower Age Limit	Additional Comments
Amitriptyline	Tablet: 10 mg, 25 mg, 50 mg, 75 mg, 100 mg, 150 mg	Starting dose: 5 mg Goal dose: 50 mg or 1 mg/kg/d in the evening	3 y	Can be used for bedwetting May be given at dinner time to avoid early-morning sleepiness
Cyproheptadine	Tablet: 4 mg Liquid: 2 mg/5 mL	Starting dose: 2 mg every night at bedtime Goal dose: <6 y: 12 mg/d; >6 y: 16 mg/d or 0.25 mg/kg/d to 1.5 mg/kg/d divided into two or three daily doses	2 y	Good for increasing appetite Avoid over age 10 because of dosing limits and appetite effects
Propranolol	Tablet: 10 mg, 20 mg, 40 mg, 60 mg, 80 mg Tablet (extended/sustained release): 60 mg, 80 mg, 120 mg, 160 mg Liquid: 4 mg/mL, 8 mg/mL	Starting dose: 20 mg/d and increase to 3 times a day for 3 wk Goal dose: <12 y: 120 mg/d; >12 y: 240 mg or 2 mg/kg/d to 4 mg/kg/d once-daily formulation if possible, otherwise 3 times daily	In migraine 3 y (use for other indications in infancy)	Avoid in patients with asthma
Flunarizine	Tablet: 5 mg	Starting dose: 5 mg Goal dose: 5 mg to 10 mg	5 y	Not available in the United States Approved in Europe and Canada for the prevention of migraine
Topiramate	Tablet: 25 mg, 50 mg, 100 mg, 200 mg Sprinkle capsules: 15 mg, 25 mg	Starting dose: 15 mg Goal dose: 100 mg/d or 1 mg/kg/d to 2 mg/kg/d divided into two daily doses	8 y for migraine 2 y for epilepsy Used for other indications in infancy	
Valproate	Tablet: 250 mg Tablet (delayed release): 125 mg, 250 mg, 500 mg Tablet (extended release): 250 mg, 500 mg Sprinkle capsules: 125 mg Liquid: 250 mg/5 mL	Starting dose: 250 mg/d or 10 mg/kg/d Goal dose: 20 mg/kg/d to 40 mg/kg/d or 500 mg/d to 1000 mg/d Once-daily dosing with extended release, otherwise given 2 to 3 times daily	2 y	Increased risk of fatal hepatotoxicity in children younger than 2 y Avoid if any concern of a metabolic disease
Coenzyme Q10	Tablet: 100 mg	100 mg/d	3 y	
Magnesium (chelated)	Tablet: 250 mg, 400 mg	9 mg/kg/d divided into three daily doses (maximum of 500 mg)	3 y	Good if child is constipated
Riboflavin	Tablet: 50 mg, 100 mg	200 mg/d to 400 mg/d divided into two daily doses	8 y	Can turn urine yellow/orange Only 50 mg can be absorbed at a time

[a] Data from Hershey AD, Lancet Neurol.[37] *www.sciencedirect.com/science/article/pii/S1474442209703035.*
[b] Data from O'Brien HL, et al, Curr Treat Options Neurol.[46] *www.springerlink.com/content/c6824k0u0m502v30/?MUD=MP.*
[c] Data from Lexi-Drugs.[47]

KEY POINTS

- Nonsteroidal anti-inflammatory drugs and acetaminophen are the mainstays of acute treatment, although the US Food and Drug Administration has approved almotriptan for use in patients older than 12 years and rizatriptan for patients older than 6 years.
- The standard preventive medications used in adult headache are used in pediatrics, although scant evidence supports their use.

age 6. The AAN practice parameters note that sumatriptan nasal spray is effective and safe in patients older than age 12.[45] Zolmitriptan 2.5 mg to 5.0 mg and oral rizatriptan have shown efficacy in adolescents.[37] If a child requires IV therapy, ketorolac and dopamine antagonists are considered first-line treatments, and both have good effect. Metoclopramide is commonly used because of concern about extrapyramidal symptoms with other dopamine antagonists. It has not been shown that prochlorperazine is less well tolerated, and it has been shown to be more effective than metoclopramide and ketorolac.[46] The IV and intranasal forms of dihydroergotamine have been used successfully in children.[46] **Table 8-3**[37,46,47] shows standard forms and dosing.

Preventive Medication

No preventive medications with level A evidence in the pediatric population are available, and the only medication with level B evidence, flunarizine, is not available in the United States. Evidence is insufficient to provide a recommendation for topiramate, divalproex, cyproheptadine, and amitriptyline. The evidence for propranolol is conflicting.[45] Since the release of the AAN practice parameters in 2004, several studies have had positive results with topiramate, valproate, and propranolol.[37] Studies of prevention for tension-type headache are scarce, and the most commonly used agent is amitriptyline, although some evidence exists for the use of melatonin.[44] Medication should be initiated at the lowest possible dosage form available, taking into consideration whether the child can swallow tablets or requires a liquid formulation, and then titrated weekly until a moderately effective dose has been reached or is limited by side effects (**Table 8-4**).[37,46,47] It should be noted that most of these medications need to be administered twice a day because of the more rapid elimination of medications in children. One study has evaluated the use of onabotulinumtoxinA in teenagers older than age 14 with chronic daily headache with some success.[48]

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