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Headache in Children and Adolescents

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Abstract

PURPOSE OF REVIEW: This article reviews the approach to a child or adolescent with headache, the criteria for common diagnoses, and the evidence base for treatments.

RECENT FINDINGS: The guidelines for acute and preventive treatment of migraine were updated in 2019. These guidelines summarize the available evidence and outline the questions that should be addressed in future research. The US Food and Drug Administration (FDA) approval of several new classes of drugs and devices to treat adult migraine in the past few years has resulted in ongoing or planned pediatric trials.

SUMMARY: Headache is a common symptom in children, and it is important to take a detailed history and perform a thorough physical examination to make the diagnosis. Nearly 1 in 10 children experience recurrent headaches due to migraine, which cause significant impairment in school performance and quality of life. The acute and preventive treatments that are currently

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UNLABELED USE OF PRODUCTS/INVESTIGATIONAL USE DISCLOSURE:
Dr Szperka discusses several therapies for the treatment of headache disorders in children. Even when these therapies have a labeled use for migraine in adults, the majority of them are unlabeled/investigational in children.

USEFUL WEBSITES

AMERICAN MIGRAINE FOUNDATION: UNDERSTANDING PEDIATRIC MIGRAINE
This website includes information about migraine in children from the American Migraine Foundation, which seeks to mobilize a community for patient support and advocacy as well as drive and support impactful research that translates into advances for patients with migraine and other disabling diseases that cause severe head pain.
americanmigrainefoundation.org/resource-library/pediatric-migraine/

HEADACHE RELIEF GUIDE
This website was created as part of the Headache Action Plan Project for Youth (HAPPY) to help teens and their families to gain better control of headaches, get appropriate medical care, and limit the disability caused by headaches.
headachereliefguide.com

MIGRAINE AT SCHOOL
This website was developed by the Coalition for Headache and Migraine Patients and is a collection of the resources for students, parents, and educators.
migraineatschool.org

THE AMERICAN ACADEMY OF PEDIATRICS PARENTING WEBSITE
This website provides recommendations on lifestyle behaviors from the American Academy of Pediatrics.
healthychildren.org

CENTERS FOR DISEASE CONTROL AND PREVENTION HEADS UP
This website provides concussion resources from the Centers for Disease Control and Prevention.
cdc.gov/headsup

available will help at least two-thirds of children with migraine, and several trials of new therapies offer hope for the future.

INTRODUCTION

Headaches are a very common and disabling problem for children and adolescents. Globally, nearly 60% of children and adolescents experience significant headache, and 7.7% to 9.1% have migraine.[1,2] If the criteria are expanded to include probable migraine, the prevalence is much higher. Children with migraine miss more school than their peers[3] and have impaired school performance[4] and impaired quality of life, similar to that of children with rheumatoid arthritis or cancer.[5] This disability is complicated by the fact that migraine is a silent disease; no outward findings are visible, so the child's report of pain may be doubted, leading to shame and frustration.

In addition to the problems of disability in childhood, up to three-fourths of children with migraine will continue to have symptoms into adulthood.[6] Migraine is the leading cause of disability worldwide for older adolescents and young adults.[7] However, there is reason to hope: at least two-thirds of children will respond to currently available therapies,[8,9] and children who benefit from preventive therapy are likely to maintain better headache control into adulthood.

This article is organized to mirror the clinical encounter: history and physical examination, differential diagnosis, and treatment of migraine. Treatment includes both a summary of guideline-recommended acute and preventive therapies and practical recommendations to cover areas where evidence is insufficient.

HISTORY TAKING

With a young child, the history will come from both the child and the parent(s)/guardian(s), so it is important to make both child and parent(s)/guardian(s) comfortable. The child should be kept as calm as possible, so the clinician's actions may need to vary a bit based on the child's temperament. The child should be approached in a nonthreatening way; the clinician may crouch down to the child's eye level, wave hello, and introduce themselves to the child. If the child looks frightened or recoils into their parent/guardian, the clinician may need to physically back away and give the child space. If the child is comfortable, they may be asked if they know why they have come for the visit. The child should be given an overview of what to expect, with an explanation that they will begin by talking for a while. The child can keep playing initially while the parent/guardian is asked many questions, but the child should be asked a few questions also, since they are the expert on how their head feels. The clinician may explain that the examination is just like the one that the pediatrician does and that then the clinician and child will decide together how to help the child feel better. Young children often associate the doctor's office with painful procedures, so once enough of a history has been taken to clarify, the child can be reassured that no shots are planned that day. It is often helpful to have paper and crayons available so the child can color whatever they want in the beginning. Once the child is comfortable, they can be asked to draw a

picture of how they feel when they get a headache, as drawings with migraine features have high concordance with migraine diagnosis.[10]

The style for older children and teenagers is different. Teenagers can be directly questioned, then the parent/guardian later given the opportunity to relay perceived differences or additional details. To prepare teenagers to transition to adult care, it is important to coach them to take increasing independence with medical care.

The author recommends starting the history taking with an open-ended question, such as, "What brings you here today?" Parents/guardians usually state their worries and ideas about etiology right away, but if they do not offer that information up front, they should be asked more explicitly at the end of the history. After starting with a few open-ended questions, the author explains that she is going to ask a lot of detailed questions to make sure that she understands what is happening, keeping a paper and pen nearby to scribble a note if the parent/guardian mentions something that is out of the usual order to remember to return to it to clarify later. A headache questionnaire can be integrated into the electronic health record, so that the parent(s)/guardian(s) may have answered a lot of questions about the child's headaches before the visit. This increases the efficiency of history taking because it has asked the patient and parent(s)/guardian(s) to think about the pattern of headache, recent changes, and current frequency before the conversation starts. Those answers should be reviewed in a semistructured interview, making sure that all the questions were understood, paying particular attention to the following:

- Headache frequency: Ask about both bad and mild headaches. Many parents/guardians are surprised to realize that the child has unreported frequent mild headaches or even constant pain.
- Headache pattern: Ask if the headaches have been intermittent for several months or if this is a new or escalating problem.
- Headache location: Ask the child to point to the places on the head that hurt with headache.
- Headache quality: Ask about the quality of the pain. For young children, ask if the pain feels like someone squeezing their head (while squeezing the hands together), like someone knocking on their head (while pounding one fist gently into the other), or like their head is exploding (moving the hands outward).
- Headache severity: Ask about headache severity using the Faces Pain Scale,[11] or clarify whether the pain is little, medium-sized, or really bad. Teenagers can be asked to rate their headache on a numeric 0 to 10 scale. Children may report a severity number larger than expected by the observer. Remember that pain is subjective and relative to the child's own history of pain.
- Associated features: Ask the parent/guardian whether the child's behavior or appearance changes before or during a headache. The author explicitly reviews the following:
  - Premonitory symptoms: Before pain onset, about one-third of young children and two-thirds of older children and adolescents with migraine

experience premonitory symptoms such as facial pallor, fatigue, irritability, mood changes, and yawning.12

- Migraine aura: Visual aura is most common in children, sometimes accompanied by sensory, speech, or motor symptoms.[13] Children may not volunteer other symptoms that come with headache, so they should be explicitly and concretely asked. Ask the child if they see any extra spots, lights, or lines; if anything is missing from their vision before or during a headache; and whether they have associated numbness or tingling. The time course should be clarified, as sometimes children will report that they see spots in their vision upon standing during migraine from orthostasis, which does not fit the criteria for aura. If a child reports weakness, clarify whether it is a feeling of all-over muscle fatigue, numbness resulting in clumsy movements, or focal weakness. The latter is uncommon but raises the possibility of familial hemiplegic migraine, which can be caused by mutations in *CACNA1A, ATP1A2, or SCN1A*.
- Migraine symptoms: Sensitivity to light and sound and nausea and vomiting are diagnostic criteria for migraine. Pallor and anorexia are also common in young children,[14] as are difficulty thinking, lightheadedness, fatigue,[15] and osmophobia in older children. These symptoms may be observed by parent(s)/guardian(s) rather than reported by the child (CASE 9–1).
- Cranial autonomic symptoms:These symptoms include conjunctival injection, lacrimation, nasal congestion, rhinorrhea, ptosis, ear pressure, and facial flushing and are common in children with migraine and usually bilateral.[16] Unilateral autonomic symptoms can be present with migraine but may suggest a trigeminal autonomic cephalalgia.
- Postdromal symptoms: Nonpain symptoms such as fatigue, cognitive difficulties, and nausea often persist for hours after the pain has resolved. More than 80% of children develop new symptoms, including thirst, somnolence, visual disturbances, and food cravings, after the pain has resolved.17

- Red flags for secondary headache: Screening for secondary headache is discussed below in the section on diagnostic considerations.
- Headache-related disability: Ask both the child and the parent/guardian how headaches affect their lives, both at home and at school, using the Pediatric Migraine Disability Assessment (PedMIDAS) (cincinnatichildrens.org/service/h/headache-center/pedmidas).[18,19]
- Medical and psychological history: Pay particular attention to comorbidities, which may include the following
  - Related syndromes: Ask whether the child currently has or previously had episodes of recurrent vomiting (cyclic vomiting), disabling

abdominal pain (abdominal migraine), head tilt (benign paroxysmal torticollis), “drunk” gait or inability to stand upright sometimes with nystagmus (benign paroxysmal vertigo), or persistent crying as a baby (colic). These childhood periodic syndromes often occur at a younger age and may be migraine precursors in the developing brain, although cyclic vomiting and abdominal migraine often persist into teenage years.[20]

- Obesity: A high body mass index has been correlated with migraine frequency and disability in children and adolescents.21
- Epilepsy: Patients with epilepsy have an increased rate of migraine and vice versa.22
- Atopic disorders: Children with allergic rhinitis or conjunctivitis have a higher incidence of migraine,[23] and those with migraine, especially migraine with aura, have higher rates of atopic disorders.24
- Anxiety/depression: Adolescents with depression and migraine experience higher rates of disability than those without depression, even after controlling for frequency and severity of migraine attacks.25
- Attention problems and cognitive differences: Studies have demonstrated an association between migraine and attention deficit hyperactivity disorder[26] as well as both within-attack[27] and between-attack[28] cognitive differences. Attention and learning difficulties can cause stress in school, which can, in turn, trigger migraine. Simultaneously, stimulant medications can cause headache as a side effect.
- Sleep disorders: Migraine is associated with narcolepsy[29] and restless legs syndrome[30] in children.

- Social history: Ask about sources of emotional stress on both the child and the family. Studies have demonstrated that adverse experiences in childhood (eg, financial stress; physical, emotional, or sexual abuse; parental divorce; death; mental illness; or addiction) predispose to headache in childhood as well as later in life.[31] Give teenagers a moment away from parent(s)/guardian(s) to discuss safety, sexuality, and substance use.

KEY POINTS

- Headaches are a very common and disabling problem for children and adolescents. Globally, nearly 60% of children and adolescents experience significant headache, and 7.7% to 9.1% have migraine.
- Children with migraine miss more school than their peers and have impaired school performance and impaired quality of life, similar to that of children with rheumatoid arthritis or cancer. This disability is complicated by the fact

that migraine is a silent disease; no outward findings are visible, so the child's report of pain may be doubted, leading to shame and frustration.

- Migraine is the leading cause of disability worldwide for older adolescents and young adults.
- Children may not volunteer other symptoms that come with headache, so they should be explicitly and concretely asked.

PHYSICAL EXAMINATION

For all new patients with headache, a detailed general and neurologic examination should be performed, specifically looking for any facial asymmetry, visual or eye movement abnormalities, papilledema, or motor asymmetry. Vital signs should be noted, looking for hypertension or tachycardia; growth parameters should also be noted, especially changes in or disproportionate head circumference (which should be measured in all pediatric patients with headache). As part of the neurologic examination, eye alignment and convergence and saccadic eye movements should be checked; these are often abnormal after concussion, but in the author's experience, saccadic eye movements can also be abnormal when headache is present. In addition, thinking about specific causes for headache, a "headache examination" should be performed[32]:

- Examine the neck (looking for limitations in range or pain with motion) and the spine (looking for scoliosis).
- Palpate over the sinuses to assess for focal tenderness.
- Examine the jaw for tenderness or clicking to suggest temporomandibular joint dysfunction, which can be comorbid with migraine.
- Listen over the eyes and temples for bruits, which can signal vascular abnormalities.
- Rub lightly over the forehead and scalp to test for significant allodynia and palpate over the bilateral greater and lesser occipital nerves and supraorbital and supratrochlear nerves to assess for tenderness. The presence of allodynia or nerve tenderness do not guide the differential diagnosis but demonstrate the presence of sensitization as part of underlying pathophysiology.
- For patients with continuous or positional headache, assess for an orthostatic change in pulse rate. A significant pulse change (usually defined as ≥40 beats/min) when going from lying to standing and persisting over several minutes is consistent with postural tachycardia syndrome.[33] In addition, the Beighton scale for hypermobility can be used, which can signify Ehlers-Danlos syndrome, associated with both postural tachycardia syndrome and spontaneous intracranial hypotension.[34]

KEY POINTS

- Studies have demonstrated that adverse experiences in childhood (financial stress; physical, emotional, or sexual abuse; parental divorce; death; mental illness; or addiction) predispose to headache in childhood as well as later in life.
- It is important to know what the child does not have as well as what the child does have. Life-threatening causes such as brain tumors occur in approximately 2% to 3% of children who present to the emergency department for headache and in about 1% of children with headache seen in primary care.

DIAGNOSTIC CONSIDERATIONS

When approaching a child or teenager with headache, it is important to consider the full differential diagnosis of secondary and primary headache disorders.

Step 1: Screening for Secondary Headache

It is important to know what the child does not have as well as what the child does have. Life-threatening causes, such as brain tumors, occur in approximately 2% to 3%[35] of children who present to the emergency department for headache and in about 1% of children with headache seen in primary care.[36] Potential concerning features indicating a serious cause for headache are described in TABLE 9–1,[37–46] organized by the mnemonic SNOOP4Y (systemic signs/symptoms, neurologic signs/symptoms; onset sudden; onset in sleep/early morning; positional exacerbation, precipitated by Valsalva, parents [lack of family history], progressive or new; young age), adapted from the SNOOP4 mnemonic for signs and symptoms of secondary headache in adults.[37]

Studies that have tried to identify signs and symptoms to predict a serious cause for headache have been limited by the very low rate of cases. For example, an occipital location or inability to describe the location of headache were previously thought to be risk factors for serious secondary headache,[45] but all of the children with concerning lesions also had objective neurologic signs. More recent work has questioned the idea that location alone is concerning.[47] The most worrisome features are an abnormal neurologic examination, significant systemic illness, and new or worsening pattern of headaches.

Several studies support that neuroimaging is unnecessary for children with stable frequency of headaches, the absence of concerning features, and normal neurologic examination, such as the child in CASE 9–1.[48] From a health economics perspective, unnecessary imaging results in significant cost.[49] If red flags are present, brain imaging is indicated.[48] The specific study will be dictated by the urgency of the situation, the need for/availability of sedation, and the differential diagnosis suggested by the headache features.[49] If the child has fever and nuchal rigidity or papilledema without evidence of tumor or thrombosis, lumbar puncture should be performed. Laboratory studies also depend on clinical symptoms, and infectious testing will vary by geographic location and season.[48]

KEY POINTS

- Several studies support that neuroimaging is unnecessary for children with stable frequency of headaches, the absence of concerning features, and a normal neurologic examination.
- Migraine is a primary headache disorder characterized by recurrent (at least five) episodes of moderate to severe pulsating head pain lasting hours and accompanied by nausea/vomiting and sensitivity to light and sound.
- Migraine prevalence and features vary from childhood to adolescence and from boys to girls. Migraine affects approximately 5% of boys and girls by the age of 10, 7% of girls and 5% of boys up to age 15, and 10% of girls and 6% of boys by the age of 20.

Step 2: Identifying the Primary Headache Diagnosis

The majority of children who present to the neurologist will have a primary headache disorder, the features of which are described in this section.

MIGRAINE.—Migraine is a primary headache disorder characterized by recurrent (at least five) episodes of moderate to severe pulsating head pain lasting hours and accompanied by nausea/vomiting and sensitivity to light and sound.[38] In children, migraine attacks can be brief; the *International Classification of Headache Disorders, Third Edition* (*ICHD-3*) criteria define a minimum of 2 hours for children,[38] although experts have proposed that this should be lowered to a minimum of 30 minutes in children 5 and younger[20] or to a minimum of 1 hour for all children.[15] The sensitivity to light and sound can be inferred through behavior.[38] Unilateral pain is part of the diagnostic criteria of migraine in adults, but more than 80% of children report bilateral pain,[15] so the diagnostic criteria allow for this difference.

Migraine prevalence and features vary from childhood to adolescence and from boys to girls. Migraine affects approximately 5% of boys and girls by the age of 10,[50] 7% of girls and 5% of boys up to age 15, and 10% of girls and 6% of boys by the age of 20.[1] Evidence indicates that the prevalence of migraine is rising, at least in some populations.[2] Migraine frequency is lower in children younger than 7 years of age,[51] although they tend to vomit more compared to older children. Headaches in very young children may also have more symptomatic overlap between migraine and tension-type headache.[52] The presence of aura and associated dizziness increases with age.[53]

Genetic and epigenetic factors likely play a role in the age of onset. Children with a parental history of migraine develop the condition an average of 11 to 12 years earlier than their affected parents[54] and 2 to 3 years earlier than children who do not have a migraine family history.[55] Younger age of onset may portend worse prognosis: children seen in pediatric neurology clinics whose headaches begin before age 6 are more likely than those whose headaches begin at age 6 to 10 years to need preventive therapy in the next 2 years.[56] Migraine peak incidence occurs at least 4 years earlier in boys than girls. Those who

develop migraine with visual aura report onset of migraine 3 to 5 years before those who have migraine without aura.[57] Among children without a family history of migraine, lower household income is associated with higher odds of migraine.[58]

Hormones also play a role. Early menarche (≤12 years of age) is associated with increased odds of migraine and other headaches in adolescent girls.[59] A large population-based study found that girls who have reached menarche within the past 2 years are more likely to report recurrent headaches compared to girls who have not reached menarche, but longitudinal analysis of individuals did not demonstrate an increased frequency of migraine after menarche.[60]

TENSION-TYPE HEADACHE.—Tension-type headache describes headaches that are mild to moderate, nondisabling, and without notable associated symptoms such as vomiting. Tension-type headache occurs in 10% to 24% of children and adolescents[52] but does not usually bring the child to medical attention because the attacks are mild and cause little disability.

TRIGEMINAL AUTONOMIC CEPHALGIAS.—Trigeminal autonomic cephalgias, including cluster headache, paroxysmal hemicrania, and short-lasting unilateral neuralgiform headache attacks (SUNHA), have been reported very rarely in young children. Typical adult criteria are used for diagnosis, largely because pediatric cases are so rare. Cluster headache prevalence is believed to be low at 0.1% in adolescents,[61] but many adult patients with cluster headache retrospectively report that their headaches began during adolescence or even childhood. Cluster episodes may increase in frequency and duration from adolescence to adulthood,[62] and restlessness may be less pronounced at younger ages.[20] Substantial clinical overlap exists between paroxysmal hemicrania and cluster headache, and children with paroxysmal hemicrania may not fulfill all *ICHD-3* criteria.[20]

PRIMARY STABBING HEADACHE.—Primary stabbing headache describes very brief episodes of stabbing pain without associated autonomic features. These are often severe and scary to the child and parent(s)/guardian(s) but do not usually require treatment unless they are frequent.[14] They tend to occur in children with other primary headache disorders such as migraine.

KEY POINTS

- Tension-type headache occurs in 10% to 24% of children and adolescents but does not usually bring the child to medical attention because the attacks are mild and cause little disability.
- In population-based self-report studies, at least 1.5% of children report headaches several times per week or daily.

FREQUENT OR DAILY HEADACHES.—In population-based self-report studies, at least 1.5% of children report headaches several times per week or daily. Girls are more likely to report daily headache than boys.[63,64] Overuse of acute medications is less common than in

adults with daily headache.[65] In the past the umbrella term *chronic daily headache* was used, but it is preferable to use the more specific term (chronic migraine, chronic tension-type headache, new daily persistent headache, or hemicrania continua) as some differences exist in treatment and prognosis.

Chronic migraine, defined in *ICHD-3* as headache on at least 15 days per month for at least 3 months with at least 8 days of migraine per month,[38] is more common in girls than boys,[63] and the prevalence increases through the adolescent years.[64] The proportion of children with daily headache who meet the criteria for chronic migraine has changed as the definitions have evolved, but most have some headaches that meet the criteria for migraine.[63] Adolescents may progress from a relatively low to a high frequency of headache attacks, sometimes having features of migraine, over weeks to months (CASE 9–2), whereas adults typically progress over years. Migraine features may remain prominent in adolescents even when the headaches are daily or nearly daily.[66] Not surprisingly, adolescents with chronic migraine have high rates of disability.[64]

Children who did not previously have significant headaches but develop a new-onset headache that persists for 3 months or longer may be diagnosed with new daily persistent headache after an appropriate workup has ruled out sinister causes (CASE 9–3). Clinic-based cohort studies of adolescents with the umbrella term *chronic daily headache* have found that at least one in five have new daily persistent headache.[65] Population-based studies have found a very low prevalence of new daily persistent headache.[63]

Hemicrania continua is rare in the population,[65] but much less rare when considering the population of patients with refractory continuous headache. Hemicrania continua classically causes side-locked continuous headache with ipsilateral autonomic features. Sometimes patients report pain on both sides with words but point to only one side. In these cases, they often clarify that one side always hurts, but the pain spreads bilaterally when severity increases. Similarly, autonomic features are not universal, so a trial of indomethacin is appropriate for any patient with continuous side-locked headache.[67]

It is particularly important to consider comorbidities in children with frequent headaches. Abuse is more common in children with daily headache than in the general population.[68] Studies have found that the majority of children with chronic daily headache have anxiety related to academics,[69] and a subset have significant psychiatric disease and school phobia,[70] which may contribute to the seasonal pattern of new daily persistent headache onset. Similarly, acute family financial distress was found to be a risk for incident chronic daily headache.[71] Depression and anxiety are associated with higher disability,[72] and poor sleep may be a risk factor for poor response to therapy.[73]

TREATMENT

The majority of children and adolescents who seek care in outpatient neurology and headache clinics have migraine.[46] New daily persistent headache or posttraumatic headache with a migrainous phenotype may be treated similarly. Treatment specifics for other headache conditions are discussed elsewhere in this issue.

First-line Acute Treatment

All children with migraine should receive an acute treatment plan to be used at the start of an episode (CASE 9–1)[8] that includes a school note permitting the child to be excused from class at symptom onset to hydrate, take an acute medication, and rest before returning to class. A Pediatric Migraine Action Plan, modeled after the commonly used Asthma Action Plan, organizes treatment recommendations in a format familiar to school nurses (available directly at headachejournal.onlinelibrary.wiley.com/doi/epdf/10.1111/head.13681).[74] Updated guidelines for acute pharmacologic treatment for children were released in 2019 (TABLE 9–2).

NONSTEROIDAL ANTI-INFLAMMATORY DRUGS.—The guidelines recommend ibuprofen 7.5 mg/kg to 10 mg/kg be used as first-line treatment for all children and adolescents.[8] Sometimes other nonsteroidal anti-inflammatory drugs (NSAIDs) that have evidence of efficacy in adults, including naproxen, diclofenac, ketoprofen, and flurbiprofen,[75] may be used.

TRIPTANS.—If ibuprofen is insufficient, a triptan can be considered. Guideline-recommended triptans for adolescents include sumatriptan/naproxen, rizatriptan, and almotriptan oral and zolmitriptan and sumatriptan nasal.[8] This list mostly reflects the triptans that were studied later with novel trial designs to lower placebo response, which enabled the demonstration of both efficacy and safety. Triptans that were tested in parallel-design studies (straight randomization into active versus placebo) were affected by high rates of placebo response. As a result, those trials demonstrated safety but not efficacy for sumatriptan, zolmitriptan, and eletriptan oral.[76] Pharmacokinetic data are also available for frovatriptan[77] and naratriptan[78] in adolescents. Although the guidelines did not specifically recommend triptans for younger children, rizatriptan is US Food and Drug Administration (FDA)–approved for children 6 years of age and older, and many triptans have been studied in this age group with evidence of safety. In practice, the choice of triptan for adolescents is guided substantially by insurance coverage, formulation, and onset and duration of specific medications. For example, adolescents with rapid escalation of pain or with significant nausea may benefit from nasal triptans.[8] If a child is unable to swallow pills, dissolvable tablets or nasal formulations can be considered, with the latter being particularly helpful if the child has significant nausea or rapid rise in headache severity.

KEY POINTS

- All children with migraine should receive an acute treatment plan to be used at the start of an episode that includes a school note permitting the child to be excused from class at symptom onset to hydrate, take an acute medication, and rest before returning to class.
- Menstrual migraine can be particularly disabling and difficult to treat, with the added difficulty of irregular menstrual cycles making prediction more difficult for adolescents.

ANTINAUSEA MEDICATIONS.—If the child has significant nausea/vomiting, adding an antiemetic medication should be considered. Medications that block dopamine, including metoclopramide, promethazine, and prochlorperazine, may help both the nausea and the migraine pain, but specific antiemetics (including ondansetron) may also be used.

LIMITATION OF ACUTE MEDICATIONS.—Concern exists that very frequent use of acute medications could predispose patients to more frequent headaches, termed *medication-overuse headache*.[38] The guidelines recommend counseling families to limit simple analgesics (eg, NSAIDs, acetaminophen) to 14 or fewer days per month and triptans or combination analgesics (containing caffeine) to 9 or fewer days per month.[8]

OPIOIDS.—Opioids are not recommended for acute treatment of migraine in children.

DEVICES.—All four of the devices with FDA clearance for treatment of migraine in adults (external trigeminal nerve stimulation, external vagus nerve stimulation, single-pulse transcranial magnetic stimulation, and remote electrical neuromodulation) can be used acutely. The latter two devices have been beneficial in case series of youth.[79,80]

Acute Treatment of Menstrual Migraine

Treatment of menstrual migraine deserves special attention. If migraine with menses is infrequent and short in duration, then the usual acute medications may be used. However, menstrual migraine can be particularly disabling and difficult to treat,[81] with the added difficulty of irregular menstrual cycles making prediction more difficult for adolescents. Borrowing evidence from adult studies, adolescents with status migrainosus around menses may benefit from short-term prophylaxis. Several medications and supplements have been studied for relatively long durations of time (TABLE 9–3[82–84]), but in reality these therapies are often prescribed for 3 days to avoid concerns about medication overuse and dispensed quantity limitations.

If these strategies are insufficient, hormonal contraceptives may be considered. Progesterone-only and combined progesterone-estrogen oral contraceptives, especially with continuous formulation, have both demonstrated benefit for the prevention of menstrual migraine.[83] Use of high-dose estrogen increases the relative risk of thrombosis, including stroke, in women with migraine with aura. Therefore, the progesterone-only contraceptives may be a safer option. Low-dose and ultra-low-dose combined oral contraceptives may reduce aura frequency but still should be avoided in women who have migraine with aura unless no other options are available and after a discussion of potential risks.[85]

Acute Treatment of Status Migrainosus

An intractable migraine attack is a common clinical scenario (CASE 9–2), yet a paucity of evidence is available to guide treatment. Home strategies may be used to treat a severe or continuous headache cycle, especially when IV or procedural treatments are not feasible. Borrowing from menstrual migraine, treatment options include scheduled NSAIDs and/or triptans 2 to 3 times daily (depending on the specific medication), usually for 3 to 5 days. Neuroleptics may also be used to treat pain, nausea, and related insomnia. Short-term oral

valproic acid is important to avoid in female adolescents given its teratogenicity. Similarly, short-term oral steroids, including dexamethasone, prednisone, and methylprednisolone, may be used. Alternative formulations of medications with demonstrated effectiveness in IV form, such as prochlorperazine given rectally, intramuscular injection of ketorolac, or intranasal dihydroergotamine, can be tried. These anecdotal recommendations are included given that status migrainosus is a common clinical scenario and situational barriers to the use of IV and procedural treatments may be present.

If treatments at home are insufficient to treat an acute migraine attack, more aggressive therapeutic options, such as IV medications or procedures, can be considered. A crossover trial of IV ketorolac and prochlorperazine in the emergency department demonstrated 50% pain reduction in 55% of those who received ketorolac and 85% of those who received prochlorperazine. After nonresponders received the other medication, the overall success rate was 93%.[86] As a result, many institutions use IV fluids, ketorolac, and prochlorperazine or another neuroleptic as their first-line IV therapies. Although not yet widely used, a 2018 trial demonstrated that low-dose propofol was equivalent to standard-of-care therapy with decreased rate of return to the emergency department.[87] If initial IV treatment is not sufficient, open-label case series have described benefit for status migrainosus with repeated doses of dihydroergotamine or magnesium[88] as well as with continuous infusions of valproic acid.[89] Similarly, case series have reported improvement with peripheral nerve blocks as both acute and preventive treatments for migraine in adolescents.[88] Several trials of therapies for severe headache flares are listed at clinicaltrials.gov, including occipital nerve block,[90] intranasal ketorolac,[91] intranasal lidocaine,[92] sphenopalatine ganglion block,[93] and auricular acupuncture.[94]

Preventive Healthy Habits

Consistent lifestyle habits may help to minimize migraine triggers and should be discussed with all patients. Some evidence indicates that poor sleep, inactivity, and skipping breakfast are associated with increased likelihood of headache in adolescents.[95] Changing these behaviors is practical, and consistent education about lifestyle habits may have acted as an effective cointervention in at least one migraine preventive trial.[96] However, factors outside the child's control may preclude change, including school start time,[97] homework, and work schedules of parent(s)/guardian(s). Even when children intend to follow the advice, adherence is difficult.[98] Furthermore, little evidence is available to guide which specific changes actually impact headache frequency. A way to begin is by gathering information organized by the mnemonic SMART (sleep, meals, activity, relaxation, triggers) (TABLE 9–4[99–107]).[40]

KEY POINTS

- Consistent lifestyle habits may help to minimize migraine triggers and should be discussed with all patients.
- Factors outside the child's control may preclude the development of healthy lifestyle habits, including school start time, homework, and work schedules of parent(s)/guardian(s). Even when children intend to follow the advice,

adherence is difficult. Furthermore, little evidence is available to guide which specific changes actually impact headache frequency.

- Preventive treatment should be considered in all children who have frequent headaches or significant headache-related disability, or both.
- High placebo response in trials limits the ability to demonstrate efficacy of a medication. However, in clinical practice, placebo response can be beneficial, as the goal is patient improvement without harm. The guidelines recommend consideration of topiramate, propranolol, and amitriptyline combined with cognitive-behavioral therapy, which was demonstrated to be superior to amitriptyline plus headache education.

While reviewing these lifestyle details, areas of concern and possible remedies can be discussed with the patient and parent/guardian. These may need to be addressed in a letter to the school to ensure access to water and permission to use the bathroom as needed, access to a snack if lunch is unusually early or late in the day, and flexibility with homework when possible to avoid inconsistency of sleep. However, it should be emphasized to the child and parent(s)/guardian(s) that the goal is a healthy lifestyle, not an overly regimented or headache-focused one. It is helpful to know whether staying up late brings on a headache, but it is not helpful if occasionally staying up late brings on significant anxiety (for child or parent[s]/guardian[s]) about the expected headache. These strategies are ways to help the child “be the boss of migraine.”

Preventive Treatment

Preventive treatment should be considered in all children who have frequent headaches or significant headache-related disability, or both (CASE 9–2). In adults, headache on 6 or more days per month is a risk factor for progression to chronic migraine.[108] Most studies of preventive treatment in pediatrics have used a minimum of 4 headache days per month and/or three to four migraine attacks per month.[9] Children with continuous headaches and very high levels of disability have been excluded from these treatment trials, but in clinical practice the treatment approach is the same.

The 2019 American Academy of Neurology/American Headache Society guideline for pharmacologic treatment for pediatric migraine prevention (TABLE 9–5) recommends shared decision making between providers and families, with an open discussion about the fact that many children/adolescents with migraine who received placebo in trials improved and that most preventive medications have not been proven superior to placebo.[9] High placebo response in trials limits the ability to demonstrate efficacy of a medication, and this must be addressed in future trials (perhaps with novel trial designs, change in patient selection, and timing of trials) to increase the number of evidence-based insurance-approved therapies. However, in clinical practice, placebo response can be beneficial, as the goal is patient improvement without harm. The guidelines do recommend consideration of topiramate, propranolol, and amitriptyline combined with cognitive-behavioral therapy, which was demonstrated to be superior to amitriptyline plus headache education. The guidelines also recommend warning patients and parent(s)/guardian(s) about the risk of

suicidality with amitriptyline and of teratogenicity and risk of decreased effectiveness of hormonal contraception with topiramate (and advise supplementation with folic acid).[9]

Acknowledging that trial design may have affected the outcome of several pediatric preventive studies, in clinical practice headache specialists often use medications not included in the guideline recommendations (TABLE 9–6[109–116]). Other pharmacologic treatments without pediatric data but with evidence of benefit in adults, such as candesartan and lisinopril, may be tried. Knowing that full evidence is several years away, the Pediatric-Adolescent Headache Section of the American Headache Society put together recommendations for off-label use of the monoclonal antibodies against calcitonin gene-related peptide.[117]

KEY POINTS

- Nutraceuticals were not reviewed in the current guidelines for pediatric migraine prevention, but some have evidence of benefit and safety and are commonly used by patients even before they are recommended by clinicians.
- Children with recurrent headaches have approximately double the likelihood of recurrent headaches in adulthood and also have increased likelihood of having other physical symptoms and psychiatric comorbidities.

Alternatively, if one interprets that the trials demonstrated the benefit of pill-taking behavior regardless of the content of the pill, it seems prudent to consider other treatments that may have fewer side effects (TABLE 9–6). Nutraceuticals were not reviewed in the guidelines, but some have evidence of benefit and safety and are commonly used by patients even before they are recommended by clinicians. Preliminary data support the use of magnesium and coenzyme Q10 for headache prevention in children. Vitamin D_3 and riboflavin also have evidence of safety in children but mixed or inconclusive data on efficacy.[114] *Petasites* (butterbur) also has evidence of benefit[118,119] but is not recommended because of concerns about liver toxicity.[120] This illustrates that supplements are not always benign, and the lack of regulation and out-of-pocket cost are significant disadvantages.

No current evidence guides the decision of which therapy is first line. For any pill-based therapy, adherence data favor once-daily over twice-daily dosing when appropriate.[98] Response to medication should be monitored, and preventive therapy should be withdrawn once the headaches are infrequent and no longer disabling. Cognitive-behavioral therapy is an appropriate second-line therapy, as it demonstrated added benefit with amitriptyline.[105]

If patients have tried multiple therapies without benefit, it is prudent to reexamine diagnosis and consider comorbidities (CASE 9–3). Sometimes at this juncture patients prefer to try an alternative therapy such as intensive exercise or dietary changes. Given that so many unknowns exist about migraine treatment in youth, clinicians should discuss these ideas openly with patients, encouraging self-efficacy but discouraging therapies with large risk of harm.

PROGNOSIS

How do headaches change in the short-term? A large population-based study with 1-year follow-up found that headache frequency in those 8 to 15 years of age remained the same for about half of respondents, increased in about one-fourth, and decreased in about one-fourth.[121] Over 6-year follow-up, approximately half of children with migraine have persistent migraine, one-fourth have headaches most consistent with the diagnosis of tension-type headache, and headaches have resolved in one-fourth.[122] Girls were more likely than boys to have persistent headache. Among those with continued headaches, many experience a decrease in frequency over the years. Migrainous headaches, parental history of migraine, depression/anxiety, and poor stress coping skills were associated with higher headache frequency over 4- and 5-year follow-up.[123]

What happens to headaches as children grow into adults? Children with recurrent headaches have approximately double the likelihood of recurrent headaches in adulthood and also have increased likelihood of having other physical symptoms and psychiatric comorbidities.[124] These likely compound each other. Long-term follow-up data from a population-based study in Sweden found that among the adolescents who had reported frequent headache at the start of the study, approximately one-fifth still had frequent headaches at 14-year follow-up.[125] Children with higher headache frequency, higher levels of disability, comorbid depression, and female sex were more likely to report headaches at least once per week at long-term follow-up.[125] Children with migraine are more likely to report continued headaches into adulthood compared to children with tension-type headache, and, similarly, higher pain severity increases the odds of continued headache into adulthood.[6] A long-term study of Swedish schoolchildren with migraine found that 60% had a migraine-free period of at least 2 years (average 6 years) by their twenties, although one-third relapsed by their thirties. Boys were much more likely than girls to experience a sustained migraine remission. At the 40-year follow-up, approximately half reported migraine freedom, about one-fourth had migraine at least yearly, and one-fourth had migraine less than once per year. About 34% of male participants but only 15% of female participants had become migraine-free by their early twenties and continued without migraine throughout the 40-year follow-up.[126]

What is the prognosis for children who have very frequent headaches? A follow-up of a school-based study in Taiwan demonstrated that among children who had chronic daily headache at the time of initial interview, one-fourth had significant disability from headaches 8 years later and about one-eighth still had chronic daily headache. The presence of migraine features, onset of chronic daily headache before age 13, duration of chronic daily headache for 2 or more years at the time of the initial interview, and medication overuse predicted higher headache frequency at follow-up.[127] However, this was a population-based sample in which the rate of consultation and treatment was very low, so the chances of continued disability and high headache frequency are likely higher for patients who present to clinic like the patient in CASE 9–3.

ADDRESSING BARRIERS TO CARE

Children with migraine who seek care, receive a diagnosis, and take appropriate treatments have at least a two-thirds chance of significant and sustained improvement. However, three major challenges must be overcome for the delivery of appropriate care.[128]

The first challenge is consulting a health care provider. Population-based studies have demonstrated that despite reporting significant disability from their headaches, only 5% to 40% of adolescents with chronic migraine had visited a health care provider for their headaches within the preceding year.[63,64] Approximately three-fourths of outpatient care for migraine in children is delivered by pediatricians or family physicians and one-fourth by neurologists.[129] For children whose migraine is not helped by the intervention of their primary care provider, prompt referral to a specialist is advised. Delay between the onset of migraine and the first visit to a multidisciplinary pediatric headache clinic predicts higher risk of chronic migraine at 10-year follow-up.[130]

How could consultation rates for children with migraine be increased so that they receive the appropriate care? Given that children must attend school and school-related disability is a major effect of migraine, school is the logical place to intervene. School-based interventions have demonstrated improvements in consultation rates in asthma, a condition with similar prevalence and effect on school attendance.[131] The Headache Action Plan Project for Youth (HAPPY) was a large multipronged educational intervention that asked school nurses to identify children with frequent headaches and explicitly recommend that they seek evaluation for the headaches from their primary care provider.[132] The effect of the intervention on consultation rates in that study was not able to be measured, but additional work is planned.

The next challenge to care is receiving a migraine diagnosis.[128] A large database study from the United Kingdom found that only one in five children who present to their general practitioner for headache were given a diagnosis of migraine.[36] One percent were given a diagnosis of secondary headache, whereas almost four-fifths were not given a specific diagnosis. A study using electronic health record data from a health system in the midwestern United States similarly found that among children who either had a chief complaint of headache/migraine or were given an *International Classification of Diseases* diagnostic code for headache/migraine, only 17.7% were diagnosed with migraine. The nonspecific diagnosis “headache” was made for 36.6%, and 45.7% reported headache or migraine as the reason for the visit but received no diagnosis related to headache.[133] A large portion of those diagnosed with headache likely have migraine. The odds of prescribing evidence-based treatment increased when migraine was diagnosed compared to either headache or no diagnosis.[133]

KEY POINTS

- Children with migraine who seek care, receive a diagnosis, and take appropriate treatments have at least a two-thirds chance of significant and sustained improvement.

- Recurrent headaches are common in children and adolescents. The most common cause, migraine, is underdiagnosed and undertreated. Many unanswered questions about the “correct” approach to migraine treatment for children and adolescents remain.

The third major challenge is prescription use of the appropriate treatment.[128] Even when a diagnosis of migraine has been made, prescription of appropriate therapies by primary care providers is low.[36] A 2019 neurology clinic–based study demonstrated that only 5% of children with migraine who met criteria for use of preventive medication were started on one while awaiting referral to neurology, and no children were prescribed a triptan by their primary care provider.[134] Population-based studies have similarly reported low rates (varying from 1% to 20%) of preventive medication use among adolescents with chronic migraine.[63,64] Prescription of acute treatments is also imperfect. In a study of prescribing practices by primary care providers in a large health system, White youth were more likely than youth of color to receive any acute medication to treat their headaches, but White youth were also more likely to receive a prescription for an opioid or butalbital than youth of color.[133]

Evidence-based solutions are available to improve the rate of appropriate prescriptions. One center demonstrated that headache specialists were more than twice as likely to prescribe triptans as child neurologists who were not headache specialists, indicating that education and awareness will help.[134] Use of a headache questionnaire integrated into the electronic health record at a large academic pediatric neurology practice increased the likelihood of making a specific diagnosis, which, in turn, substantially increased the odds of appropriate treatment.[135] The HAPPY school-based intervention paired with online clinician decision support led to a modest improvement in the rate of prescription of evidence-based acute and preventive headache therapies by primary care providers.[132]

CONCLUSION

Recurrent headaches are common in children and adolescents. The most common cause, migraine, is underdiagnosed and undertreated. Many unanswered questions about the “correct” approach to migraine treatment for children and adolescents remain. Clarifying the best algorithm of first-, second-, and third-line therapies and whether these should vary depending on the particular headache characteristics would make establishing a treatment strategy more efficient and decrease patient disability. In the future, it would be ideal if there were markers to predict individual treatment responsiveness to avoid the current trial-and-error approach. In addition, the appropriate treatment for children with continuous headache and very high levels of disability, who have been excluded from most treatment trials, must be clarified. We must reach the children who are not reaching us, either because their parent(s)/guardian(s) and teachers do not recognize that headache is a treatable problem or because they lack insurance or have not traversed the sometimes-insurmountable barriers to care. Care must not only be evidence-based but must also truly meet the needs of patients and be culturally sensitive.[136]

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CASE 9-1

A 6-year-old boy with a history of mild intermittent asthma presented with headaches. Upon questioning, his mother reported that the headaches had started a couple of years earlier but had increased in frequency to every other week. With each episode he became quiet, withdrew from play, and asked to lie down with the lights off. His parents had tried treating with acetaminophen, but they were not sure it was helping. Sometimes he vomited the medicine back up and then fell asleep. The entire episode seemed to resolve within a couple of hours. They came to clinic because he had an episode at school the previous week. The school nurse mentioned that he might have migraine and needed a better plan, but the boy's mother asked whether he could have a brain tumor. His general and neurologic examinations were normal.

After assessment, he was diagnosed with migraine, and his mother was reassured that imaging was not indicated. A migraine action plan was written, which included an appropriate dose of ibuprofen at onset, noting that an antiemetic or triptan could be used if needed.

COMMENT

This case demonstrates that primary headache disorders including migraine are more common than serious secondary headaches and that a thorough history and examination are usually sufficient for diagnosis.

CASE 9-2

A 13-year-old girl presented for a neurologic consultation reporting a history of headache attacks, some with nausea, since the age of 9. The headaches had slowly increased in frequency over the past 2 years. She recalled that she had about 4 days of headache each week the previous spring. Headaches were a bit better over the summer. One week after the start of the school year and around her menses, she developed a migraine attack, and the pain and associated symptoms had waxed and waned for 2 weeks since then without going away completely despite twice-daily ibuprofen. She had missed 4 days of school. Physical and neurologic examination were normal.

Based on the history and normal physical examination, chronic migraine with status migrainosus was diagnosed. She was sent to the emergency department for IV prochlorperazine and ketorolac to break the current attack, and she was given a note requesting flexibility so that she could return to school even before she had caught up on the work. She returned for a follow-up visit the next week to discuss options for preventive therapies to decrease the frequency and severity of attacks over time.

COMMENT

This case demonstrates that escalating frequency of migraine attacks can be insidious but often comes to attention when the severity or persistence of headache causes more disability. It is important to consider both acute and preventive treatments and to set realistic expectations that improvement may take time and multiple therapeutic trials.

CASE 9-3

A 17-year-old girl presented for a follow-up visit for treatment-refractory new daily persistent headache that had started in the setting of an upper respiratory illness at age 15. After appropriate trials of three oral preventive medications and cognitive-behavioral therapy, she still had continuous headache. She reported attending school consistently, with positive mood overall, but expressed frustration about her pain. Her history, normal physical examination, and past workup were reviewed to consider diagnoses such as spontaneous intracranial hypotension or postural tachycardia syndrome.

The diagnosis of new daily persistent headache was confirmed, and no additional testing was ordered. The risks and benefits of different treatment options were discussed, and she ultimately decided to try an off-label injectable anti–calcitonin gene-related peptide monoclonal antibody.

COMMENT

New daily persistent headache, as the name suggests, can cause persistent, difficult-to-treat headaches, but it is also important to ensure that relevant secondary headaches have been ruled out. New daily persistent headache often has a migrainous phenotype, so treatments for migraine can be used.

TABLE 9–1

Potential Red Flags for Serious Causes of Headache Organized by the Mnemonic SNOOP4Y[a]

Red Flag	Significance
Systemic signs/symptoms	
Fever, acute symptoms	Infections ranging from minor to serious[35] are the most common cause of headache in children in the emergency department
Head trauma	Relatively common cause for headache in the emergency department
Vomiting	Consistent with migraine[38] but also a risk factor for brain tumors[39]
Weight loss	Can be a symptom of malignancy
Comorbidities	Many systemic illnesses, including rheumatologic, oncologic, vascular, and hematologic conditions; genetic syndromes; and abnormalities of the immune system predispose to other serious causes for headache
Medications	Headache can be a medication side effect[40]
Neurologic signs/ symptoms	Abnormal gait, ataxia, papilledema, changes in personality/behavior/cognition, visual disturbances/eye movement abnormalities, and seizure[39] are red flags for serious secondary headache
Onset sudden	Thunderclap onset of headache in which pain peaks instantly is rare in children but can signal serious causes such as cerebral hemorrhage or reversible cerebral vasoconstriction syndrome; the full range of differential diagnosis from adults with thunderclap headache should be considered, and imaging should be pursued
Onset in sleep/early morning	Headache causing a child to awaken from sleep or occurring early in the morning has been associated with intracranial lesions[41] and can be suggestive of sleep apnea and other sleep disorders[42]; however, this diurnal pattern is also common in primary headache disorders[43]
Positional exacerbation	
Worse upright	Headache that resolves when supine and worsens immediately upon standing or slowly throughout the day can suggest spontaneous intracranial hypotension or postural tachycardia syndrome[33]
Worse supine	Consider increased intracranial pressure from tumor or idiopathic intracranial hypertension
Precipitated by Valsalva	Brief headaches triggered by Valsalva maneuvers can signal intracranial abnormalities; headache triggered by cough along with signs/symptoms of brainstem/cerebellum/cervical spinal cord dysfunction[38] may suggest Chiari malformation (although Chiari malformation may be found incidentally with other headaches and is of varying significance)
Parents (lack of family history)	Several studies have found that lack of family history of headaches is associated with higher odds of having a serious cause of headache in children[39]; most children with migraine have a family history of migraine, although the parent(s)/guardian(s) may not be aware of the diagnosis
Progressive or new	Significant change in the headache pattern, new headache, or progressively escalating headache raises the level of concern for secondary cause[44]; however, many new-onset headaches are not caused by structural brain abnormalities[44] and may be attributed to relatively benign causes such as viral infections; furthermore, studies have used different cutoff points from days to months[45] when trying to determine when a "recent-onset" headache is worrisome, so the newness of the headache must be interpreted with the presence or absence of other headache features
Young age	Some studies have found that children of younger age (defined as either ≤5 years[45,46] or <7 years[39]) were more likely to be diagnosed with a life-threatening headache, whereas other studies have refuted that concern[44]

[a]The mnemonic SNOOP4Y is adapted from the SNOOP4 used in adults.[37]

TABLE 9–2

Recommendations of the AAN and AHS 2019 Practice Guideline Update: Acute Treatment of Migraine in Children and Adolescents[a]

Establish a specific headache diagnosis

◆ When evaluating children and adolescents with headache, clinicians should diagnose a specific headache type (primary, secondary, or other headache syndrome).

◆ When evaluating children and adolescents with headache, clinicians should ask about premonitory and aura symptoms, headache semiology (onset, location, quality, severity, frequency, duration, and aggravating and alleviating factors), associated symptoms (nausea, vomiting, phonophobia, and photophobia), and pain-related disability in order to improve diagnostic accuracy for migraine and appropriately counsel the patient.

Acute headache treatment

◆ Clinicians should counsel that acute migraine treatments are more likely to be effective when used earlier in the migraine attack, when pain is still mild.

◆ Clinicians should prescribe ibuprofen oral suspension (10 mg/kg) as an initial treatment option to reduce pain in children and adolescents with migraine.

◆ For adolescents with migraine, clinicians should prescribe sumatriptan/naproxen oral tablets (10/60 mg, 30/180 mg, 85/500 mg), zolmitriptan nasal spray (5 mg), sumatriptan nasal spray (20 mg), rizatriptan orally disintegrating tablets (5 mg or 10 mg), or almotriptan oral tablet (6.25 mg or 12.5 mg) to reduce headache pain.

◆ Clinicians should counsel patients and families that a series of medications may need to be used to find treatments that most benefit the patient.

◆ Clinicians should instruct patients and families to use the medication that best treats the characteristics of each migraine to provide the best balance of efficacy, side effects, and patient preference.

◆ Clinicians should offer an alternate triptan, if one triptan fails to provide pain relief, to find the most effective agent to reduce migraine symptoms.

◆ Clinicians may prescribe a nonoral route when headache peaks in severity quickly, is accompanied by nausea or vomiting, or oral formulations fail to provide pain relief.

◆ Clinicians should counsel patients and families that if their headache is successfully treated by their acute migraine medication but headache recurs within 24 hours of the initial treatment, taking a second dose of acute migraine medication can treat the recurrent headache.

◆ In adolescents whose migraine is incompletely responsive to a triptan, clinicians should offer ibuprofen or naproxen in addition to a triptan to improve migraine relief.

Treatment of associated symptoms

◆ For children and adolescents with migraine who experience prominent nausea or vomiting, clinicians should offer additional antiemetic treatments.

Counseling

◆ Clinicians should counsel children and adolescents with migraine and their families about migraine-healthy habits, including lifestyle modification, identification/disproof/resolution of migraine triggers/aggravating factors, and avoidance of medication overuse.

◆ Clinicians should make collaborative agreements with children and adolescents with migraine and their families on treatment goals that are individualized to the patient.

◆ Clinicians may counsel children and adolescents with migraine and their families to maintain a headache diary to monitor their response to treatments.

◆ Clinicians should counsel patients and families to use no more than 14 days of ibuprofen or acetaminophen per month, no more than 9 days of triptans per month, and no more than 9 days per month of any combination of triptans, analgesics, or opioids for more than 3 months to avoid medication-overuse headache. (No evidence supports the use of opioids in children with migraine.)

Contraindications and precautions to triptan use

◆ Clinicians must not prescribe triptans to those with a history of ischemic vascular disease or accessory conduction pathway disorders to avoid the morbidity and mortality associated with aggravating these conditions.

◆ Clinicians should counsel adolescent patients with migraine with aura that taking their triptan during a typical aura is safe, but that the triptan may be more effective if taken at the onset of head pain.

◆ Clinicians may consider referral of children and adolescents with hemiplegic migraine or migraine with brainstem aura who do not respond to other treatments to a headache specialist to find effective treatment.

AAN = American Academy of Neurology; AHS = American Headache Society.

[a]Data from Oskoui M, et al, Neurology.[8]

TABLE 9–3

Strategies for Perimenstrual Migraine Prophylaxis

Class	Specifics
Nonsteroidal anti-inflammatory drugs	Naproxen 550 mg 2 times a day for 5–6 days, ideally starting 1 day before expected headache onset[81]
	Mefenamic acid up to 500 mg 3 times a day from the start of headache through menses[82]
	The cyclooxygenase-2 (COX-2) inhibitor celecoxib has shown promise[83] in pilot studies
Triptans [81]	Frovatriptan 2.5 mg 2 times a day for up to 6 days, ideally beginning 1 day before expected headache onset
	Naratriptan 1 mg 2 times a day for 5–6 days, ideally beginning 1 day before expected headache onset
	Zolmitriptan 2.5 mg 2 to 3 times a day for up to 7 days, ideally beginning 1 day before expected headache onset
Magnesium [81]	Specific formulation studied is not available in the United States, but it is reasonable to use available forms perimenstrually; can also help with perimenstrual syndrome
Vitamin E	400 IU/d for 5 days beginning 2 days before menses[84]
Estrogen	Supplementation (“add back”) via patch or gel in teenagers who have migraine without aura[83]

TABLE 9–4

SMART (Sleep, Meals, Activity, Relaxation, Triggers) Lifestyle Considerations3

Factor	Advice
Sleep: consistent and sufficient	
Bedtime and wake-up time	Maintain a consistent bedtime routine and avoid daytime napping to prevent disruptions to the sleep-wake cycle[99]; children 3–5 years of age should sleep 10–13 hours per day (including naps), children 6–12 years of age should sleep 9–12 hours per day, and teenagers should sleep 8–10 hours per day[100]
Problems falling asleep	Use bed only for sleep, turn off screens at least 1–2 hours before bed to limit blue light exposure[101]
Problems staying asleep	Consider causes such as sleep apnea, depression
Daytime somnolence	Consider causes such as sleep apnea, depression
Meals and hydration: consistent and sufficient	
Missed meals	Recognize that fasting can be a trigger
Well-balanced diet	Eat a variety of fruits and vegetables, protein, and dairy (or another source of vitamin D)
Access problems or limited time	Address time limitations and food insecurity with individualized solutions; consider social work consult
Water consumption	≥8 cups per day for children older than 9 years of age (more for teenage boys and extra at times of high exertion)[102]
Other beverage consumption	Limit to avoid weight gain as obesity is associated with worsened migraine frequency and disability[21]
Caffeine consumption	High caffeine consumption is associated with increased odds of headache in adolescents,[95] probably because of caffeine withdrawal[103]
Activity: consistent and sufficient	
Address inactivity	Inactivity in adolescents is associated with higher odds of migraine[95]; weight loss in overweight teenagers can contribute to headache improvement[21]
Exercise	Meta-analyses in adults have concluded that exercise may be a beneficial and safe treatment for migraine[104]
Relaxation: cope with stress and prevent migraines	
Sources of stress	Home-related stressors (eg, arguments with siblings, observing parental disagreements) or school-related stressors (eg, difficulty in school, fear of doing poorly) can be triggers for headache
Help cope with stressors	Validate the normalcy and commonality of stressors and discuss coping strategies
Relaxation strategies	Cognitive-behavioral therapy can help migraine in children[105]; mindfulness-based stress reduction looks promising[106]
Triggers: avoidance/management	
Weather	Changes in weather patterns are commonly reported as headache triggers; use of long-acting triptans may help to prevent migraine attacks around storms[107]
Specific foods	Little evidence shows that foods other than alcohol and caffeine are consistent headache triggers, although many patients report avoiding specific foods
Menses	Refer to the section on menstrual migraine

[a]Modified with permission from Blume HK, Szperka CL, Pediatr Ann.[40]

TABLE 9–5

Recommendations of the AAN and AHS 2019 Practice Guideline Update: Pharmacologic Treatment for Pediatric Migraine Prevention[a]

Counseling and education for children and adolescents with migraine and their families
◆ Clinicians should counsel patients and families that lifestyle and behavioral factors influence headache frequency
◆ Clinicians should educate patients and families to identify and modify migraine contributors that are potentially modifiable (ie, being overweight, caffeine and alcohol use, lack of physical activity, poor sleep habits, tobacco exposure, depression)
◆ Clinicians should discuss the potential role of preventive treatments in children and adolescents with frequent headache (defined in trials as a minimum of 4 headache days per month and three to four migraine attacks per month for at least 3 months) or migraine-related disability (PedMIDAS score >30) or both
◆ Clinicians should discuss the potential role of preventive treatments in children and adolescents in medication overuse (taking triptans, ergotamines, opioids, and combination analgesics >9 days in a month or taking over-the-counter analgesics on >14 days in a month)
Starting preventive treatment
◆ Clinicians should inform patients and caregivers that in clinical trials of preventive treatments for pediatric migraine, placebo was effective and the majority of preventive medications were not superior to placebo
◆ Acknowledging the limitations of currently available evidence, clinicians should engage in shared decision making regarding the use of short-term trials (a minimum of 2 months) for those who could benefit from preventive treatment
◆ Clinicians should discuss the evidence for amitriptyline combined with cognitive-behavioral therapy for migraine prevention, inform them of the potential side effects of amitriptyline including risk of suicide, and work with families to identify providers who can offer this type of treatment
◆ Clinicians should discuss the evidence for topiramate for pediatric migraine prevention and its side effects
◆ Clinicians should discuss the evidence for propranolol for pediatric migraine prevention and its side effects
Counseling for patients of childbearing potential
◆ Clinicians must consider the teratogenic effect of topiramate and valproate in their choice of migraine prevention therapy recommendations to patients of childbearing potential
◆ Clinicians who offer topiramate or valproate for migraine prevention to patients of childbearing potential must counsel these patients about potential effects on fetal/childhood development
◆ Clinicians who prescribe topiramate for migraine prevention to patients of childbearing potential must counsel these patients about the potential of this medication to decrease the efficacy of oral combined hormonal contraceptives, particularly at doses over 200 mg daily
◆ Clinicians who prescribe topiramate or valproate for migraine prevention to patients of childbearing potential should counsel patients to discuss optimal contraception methods with their health care provider during treatment
◆ Clinicians must recommend daily folic acid supplementation to patients of childbearing potential who take topiramate or valproate
Monitoring and stopping medication
◆ Clinicians must periodically monitor medication effectiveness and adverse events when prescribing migraine preventive treatment
◆ Clinicians should counsel patients and families about the risks and benefits of stopping preventive medication once good migraine control is established[b]
Mental illness in children and adolescents with migraine
◆ Children and adolescents with migraine should be screened for mood and anxiety disorders because of the increased risk of headache persistence
◆ In children and adolescents with migraine who have comorbid mood and anxiety disorders, clinicians should discuss management options for these disorders

AAN = American Academy of Neurology; AHS = American Headache Society; PedMIDAS = Pediatric Migraine Disability Assessment.

[a]Data from Oskoui M, et al, Neurology.[9]

[b]"Good migraine control" is not well defined.

TABLE 9–6

Preventive Treatments Studied for Pediatric Migraine Prevention

Treatment	Dose	Side effects	Comments	2019 AAN-AHS Guideline Comment[9]
Antiepileptics [9]				
Topiramate	2–3 mg/kg/d; typical dose 100 mg/d; maximum dose 200 mg/d	Paresthesia, anorexia, weight loss, fatigue, cognitive impairment, decreased perspiration Serious side effects: renal stones, depression, teratogenicity, angle closure glaucoma	Lowers potency of oral contraceptive pill, especially when more than 200 mg/d; recommend folic acid supplementation	Probably more likely than placebo to decrease frequency of headache days
Divalproex sodium	15–30 mg/kg/d up to 1000 mg/d	Nausea, weight gain, dizziness, somnolence, tremor, alopecia; monitor for thrombocytopenia, lymphopenia, elevated liver enzymes Serious side effects: pancreatitis, hyperammonemia, hepatotoxicity, teratogenicity	Recommend folic acid supplementation Not recommended for females of child-bearing age due to teratogenicity	Insufficient evidence
Zonisamide[109]	4–10 mg/kg/d, usual maximum 200 mg/d	Somnolence, anorexia, weight loss, paresthesia, dizziness, fatigue	Sometimes used if topiramate side effects intolerable	Not reviewed (no pediatric trials)
Levetiracetam[110]	20–40 mg/kg/d divided into twice daily dosing (usual maximum 3000 mg/d)	Somnolence, fatigue, irritability, behavior/mood change		Not reviewed (no pediatric trials)
Antidepressants [9]				
Amitriptyline	0.25–1 mg/kg/d (at bedtime)	Sedation, dizziness, dry mouth, weight gain; may cause prolonged QTc		Insufficient evidence when used alone; refer to entry for cognitive-behavioral therapy
Antihypertensives [9]				
Propranolol	20–40 mg 3 times a day	Sedation, hypotension, bradycardia, weight gain; may worsen depression and exercise-induced asthma		Possibly more likely than placebo to cause 50% reduction in headache frequency
Flunarizine[111]	5–10 mg at bedtime	Sedation, weight gain	Not available in the United States	Insufficient evidence
Cinnarizine	1.5 mg/kg/d for <30 kg; 50 mg/d for >30 kg	Sedation, weight gain	Not available in the United States	Probably more likely than placebo to decrease headache frequency
Nimodipine	10–20 mg 3 times a day	Abdominal discomfort		Insufficient evidence
Antihistamine [9]				

Treatment	Dose	Side effects	Comments	2019 AAN-AHS Guideline Comment[9]
Cyproheptadine[112]	0.25–0.5 mg/kg/d, maximum 16 mg given either at bedtime or divided 2 times a day	Sedation, increased appetite, weight gain	Liquid dosing option, can also treat cyclic vomiting and gastrointestinal pain	Not reviewed (no pediatric migraine trials)
Toxin [9]				
OnabotulinumtoxinA	74 units or 155 units injected per PREEMPT protocol113 every 12 weeks	Injection site pain, weakness, worsened headache		Insufficient evidence
Nutraceuticals [114]				
Riboflavin	50–400 mg/d either once daily or divided into two doses	Urine discoloration	Limited studies	Not included
Magnesium	Elemental magnesium 9 mg/kg/d with food (magnesium oxide divided 3 times a day; others used)	Diarrhea	Limited studies, some positive	Not included
Coenzyme Q10	1–3 mg/kg/d in the morning with food	Insomnia, gastrointestinal upset	Limited studies, some positive	Not included
Vitamin D	Studies have used 400 IU/d for children with normal blood level of Vitamin D; 800 IU/d for mild and 5000 IU/d for moderate Vitamin D deficiency	Well tolerated	Limited studies	Not included
Melatonin[115]	2–3 mg every day at bedtime	Sedation	Limited studies, some positive	Not included
Polyunsaturated fatty acids	Fish oil compound	Nausea	Limited studies	Not included
Devices				
Single-pulse transcranial magnetic stimulation[80]	Twice daily as preventive therapy with additional pulses for headache attacks plus as needed	Mild discomfort	Open-label pilot study led to US Food and Drug Administration (FDA) clearance in adolescents	Not included
Other				
Cognitive-behavioral therapy	10 sessions		Multiple barriers to implementation; biofeedback can be integrated with cognitive-behavioral therapy or is sometimes done separately	Cognitive-behavioral therapy plus amitriptyline more likely than headache education plus amitriptyline to decrease frequency
Acupuncture[116]	Variable	Discomfort, needle phobia	Safe and effective	Not included

AAN = American Academy of Neurology; AHS = American Headache Society.