Practice Guideline for Diagnosis and Management of Migraine Headaches in Children and Adolescents: Part Two

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This is the second part in a two-part practice guideline for the diagnosis and management of headaches (with emphasis on migraine headaches) in children and adolescents. Part One (Gunner & Smith, 2007) reviewed the epidemiology, International Headache Society headache classification and diagnostic criteria, key points of the history and physical examination, and differential diagnoses of headaches. Part Two focuses on the pathophysiology and management of migraine headaches in children and adolescents.

PATHOPHYSIOLOGY

Newer diagnostic and research tools, such as magnetic resonance imaging, functional brain imaging with positron emission tomography scans, and localization of familial types of migraine to chromosomes 19p13 and 1q23 (among other loci), have led to improved understanding of the pathophysiology of migraine (Borsook, Burstein, Moulton, & Becerra, 2006; Pringsheim & Edmeads, 2004). In general, migraine may be understood as the complex interaction of vasoconstriction and then vasodilatation in response to neurotransmitter release and subsequent effects on ion channels (Dafer & Birbeck, 2006). Occipital vasoconstriction to a variety of reported "triggers" is thought to be the inciting event; platelets aggregate with lymphocytes and leukocytes in an inflammatory "cascade," resulting in a release of serotonin and glutamate, which may increase pain sensitivity of the arterial wall. This response then causes irritation of the cranial nerves that lie in close proximity, especially to the temporal artery structures such as the temporomandibular branch of the

trigeminal nerve. In basilar artery migraine and ophthalmoplegic migraine, anatomic relationships may particularly predispose these areas of the brain to the described phenomena in some patients. Once vasoconstriction in an area of the brain occurs, the sympathetic nervous system responds and compensatory vasodilatation occurs in neighboring areas of the meningeal circulation. This increase in blood flow is what is responsible for the "throbbing" of the migraine headache. Conversely, the initial vasoconstriction may be associated with depression of cortical blood flow and decreased normal neurotransmitter activity, resulting in an aura. This initial vasoconstriction causes complex migraine symptoms such as vision loss in ophthalmoplegic migraine, syncope in basilar artery migraine, and hemiplegia in hemiplegic migraine.

In the pubertal girl and in women, a relative decrease in estrogen levels during menstruation and premenstrual shifts in ion channels are strong triggers for migraine. Young women treated with hormonal contraceptives usually derive relief from migraine headaches, but cerebral ischemia has been reported rarely as a presumed adverse effect of such therapy in those young women with both a family history of migraine and cerebral ischemia (Ashkenazi & Silberstein, 2006).

MANAGEMENT

The management plan for migraine relief in children and adolescents is based on goals (Box 1) established by the American Academy of Neurology (Silberstein, 2000) and several general principles (Box 2). The most significant concept within this framework is that the plan is individualized based on the symptoms, responses to treatment, and patient/family preference for treatment options. Often a variety of treatment options must be tried before the combination that provides optimal relief is found. These treatment options are categorized into four main approaches: nonpharmacologic interventions, pharmacologic interventions, bio-behavioral modalities, and complementary and alternative interventions. Generally, the interventions are initiated in a stepwise fashion in the order listed above.

BOX 1. Goals for management of migraines

1. Reduce number and severity of headaches
2. Reduce reliance on ineffective or undesired medications
3. Improve quality of life
4. Reduce reliance on acute headache medications
5. Educate and empower patients and families to manage the disease
6. Reduce headache-associated anxieties

Data from Silberstein, 2000.

Management: Nonpharmacologic interventions

Nonpharmacologic options are effective in treating children/adolescents and are initiated before pharmacologic therapy is considered (Damen, Bruijn, Koes, et al., 2006; Lewis, Yonker, Winner, & Sowell, 2005; Unger, 2006).

Maintenance of a headache calendar

- Maintenance of a headache calendar can assist with trigger identification and allows for management plan adjustment based on an individual's response to interventions.
- Adjustment of lifestyle habits should include maintenance of routine patterns of sleeping, eating, and exercise.

Sleep: Children with migraines tend to have sleep disturbances

- A child should sleep 8 to 10 hours nightly with scheduled bedtime and awakening. Some adjustment can be made on weekends, but the regular bedtime should be resumed on Sunday night (Powers & Andrasik, 2005).
- Adolescents can sleep later on weekends as well but should plan to awaken briefly at the regular time, get out of bed, drink juice or eat a snack, and go back to sleep (Unger, 2006).
- A quiet routine before bedtime is recommended. Young children should avoid frightening books, movies and television shows. Night lights or white noise might help.

Nutrition and dietary patterns

- The child should eat three meals and one to two snacks a day at routine times. Breakfast should not be skipped.
- In general, avoidance diets are not recommended for children or adolescents unless a trigger has been identified.
- About one third of children report that certain foods trigger headaches. Chocolate, citrus fruits, and cheeses are common triggers; processed meats, yogurt, fried foods, monosodium glutamate, aspartame, and alcoholic beverages are known triggers as well (Lewis et al., 2005).
- Caffeine should be avoided because it is linked to sleep disturbances and mood disruptions, both headache triggers (Lewis et al., 2005).
- Inadequate hydration should be avoided. Adolescents are encouraged to drink 2 liters (L) of noncaffeinated liquids, ideally water, per day, increasing to 3 L a day during the summer and periods of exertion (Powers & Andrasik, 2005).

Physical activity

- Children and adolescences are encouraged to participate with family or friends in at least 30

BOX 2. General principles of management of migraines in children and adolescents

1. Establish a diagnosis
2. Assess the degree of disability and impact on the child's/adolescent's quality of life; evaluate school attendance and school performance, especially in the areas of attention, math, and performance; consider a stress or depression-related etiology if child is often absent from school and the headaches affect other family members' ability to work or participate in outside activities
3. Educate the child and family about the condition and risk/benefit ratios of treatment options
4. Establish realistic expectations
   - Set appropriate goals
   - Discuss the expected benefits of therapy and time course to achieve them
   - Empower the patient and family to be involved in management (such as tracking progress with a headache diary or calendar)
5. Create an individualized, formal management plan
   - Consider the patient's response to and tolerance for specific medications
   - Consider comorbidities and treatment options dictated by these conditions (for example, children with depression may benefit from antidepressants as migraine prophylaxis, and those with asthma should not take β-blockers as migraine prophylaxis)
   - Encourage recognition and avoidance of triggers

Data from Linder (2006), Rosenblum & Fisher (2001), and Silberstein (2000).

minutes of enjoyable, aerobic activity 3 to 7 days a week.

Prioritization of activities and evaluation of performance expectations

- Excessive or unrealistic expectations of performance in school, athletics, and other activities may contribute to migraines. Sport performance and college acceptance are two common stressors. If after-school activities are excessive, consideration should be given to eliminating some of the activities.

Management: Pharmacologic Interventions

Few well-designed trials have evaluated the acute pharmacologic management of migraine in children (Damen et al., 2005; Lewis et al., 2004). For this reason, ibuprofen and naproxen are the only medications approved by the U.S. Food and Drug Administration (FDA) for the acute treatment of migraines in children from 2 to 18 years of age (Lewis et al., 2005), although a variety of agents are commonly utilized (Table 1).

Migraine preventive medications, when given, should decrease the number, intensity, and duration of headaches, improve how patients respond to acute treatment, and improve the quality of life (Lewis et al., 2004). In general, prophylactic medications are considered when patients have more than four headaches per month or the headaches are so severe that they interrupt normal activities (Damen, Bruijn, Verhagen, et al., 2006). To minimize adverse effects, prophylactic medications are started at the lowest dose and titrated upward as needed (Unger, 2006). Unfortunately, because of the lack of evidence, the FDA has not approved any preventive migraine medications in children. Given the available evidence, the medications listed in Table 2 can be considered (Unger, 2006).

Adjustment of lifestyle habits should include maintenance of routine patterns of sleeping, eating, and exercise.

Acute/abortive: Analgesics

- Ibuprofen works better than placebo (Damen et al., 2005; Lewis et al., 2004; Lewis et al., 2005).
- When compared with acetaminophen, ibuprofen offers no statistically significant but some nonstatistically significant benefits in abortive relief (Lewis et al., 2004).
- Intravenous prochlorperazine (Compazine) works better than intravenous ketorolac (Damen et al., 2005).

Acute/abortive: 5-Hydroxytryptamine receptor agonists (5-HT1, triptans)

- 5-Hydroxytryptamine receptor agonists promote cerebral vasoconstriction and block the neuropeptide-mediated inflammatory response resulting from trigeminal stimulation.
- Nasal sumatriptan, studied in children 12 years and older, appears to be safe and efficacious. Subcutaneous sumatriptan is effective, but adverse effects such as chest pressure often are seen. Oral triptans do not appear to be more effective than placebo (Damen et al., 2005; Lewis et al., 2004; Lewis et al., 2005).

TABLE 1. Medications for acute/abortive migraine therapy

Generic name	Brand name	Type of drug	Amount per dose (maximum/dose)
Acetaminophen	Tylenol	Analgesic	15 mg/kg PO (1000 mg)
Ibuprofen	Advil/Motrin	NSAID	10 mg/kg PO (800 mg)
Naproxen	Aleve	NSAID	5-7 mg/kg PO (500 mg)
*Ketorolac	Toradol	NSAID	0.5 mg/kg IM/IV (30 mg)
*Sumatriptan	Imitrex	Triptan	25-100 mg PO 5-20 mg IN; 6 mg SQ
*Rizatriptan	Maxalt	Triptan	5-10 mg PO
*Zolmitriptan	Zomig	Triptan	1.25-2.5 mg PO
*Dihydroergotamine	Migranal	Ergot	0.1 mg IV (6-9 y) 0.2 mg IV (9-12 y) 0.3 mg IV (12-16 y)
*Prochlorperazine	Compazine	Antiemetic	0.1-0.15 mg/kg IM (10 mg)

IM, Intramuscular; IN, intranasal; IV, intravenous; NSAID, nonsteroidal anti-inflammatory drug; PO, by mouth; SQ, subcutaneous.
Data from Lewis, Yonker, Winner, & Sowell (2005); Robertson & Shilkofski (2005); Tarascon Pocket Pharmacopoeia, 2007; and Unger (2006).

**Not approved by the U.S. Food and Drug Administration for use in children and adolescents with migraine headaches.*

TABLE 2. Oral medications for prophylactic migraine therapy

Generic name	Brand name	Type of drug	Amount per day (maximum per day)
*Propranolol	Inderal	β-blocker	1-4 mg/kg/day bid-tid; 40 mg bid max adult dose to start (240 mg max adult dose)
*Amitriptyline	Elavil	Tricylclic	0.1-2 mg/kg/day q HS; 0.25 mg/kg/d max to start; need to titrate; >1 mg/kg/day give bid and monitor EKG (75 mg)
*Valproic acid	Depakote	Anticonvulsant	15-30 mg/kg/day bid; 250 mg bid max to start in adult (1000 mg)
*Topiramate	Topamax	Anticonvulsant	2-3 mg/kg/day bid; 25 mg q HS max to start; need to titrate; >50 mg, give bid (200 mg)
*Cyproheptadine	Periactin	Antihistamine	0.25-0.4 mg/kg/day bid-tid (2-6 yo, 12 mg) (7-14 yo, 16 mg) (adult, 32 mg)

bid, Twice a day; EKG, electrocardiogram; HS, at bedtime; q, every; tid, three times a day; yo, year old.
Data from Lewis, Yonker, Winner, & Sowell (2005); Robertson. & Shilkofski (2005);. Tarascon Pocket Pharmacopoeia (2007); & Unger, J. (2006).

**Not approved by the U.S Food and Drug Administration for use in children and adolescents with migraine headaches.*

- Although not FDA labeled for use in persons younger than 18 years, triptans can be considered for children 12 years and older when there is no response to analgesics (Lewis et al., 2004; Lewis et al., 2005).
- For some children, giving a dose and monitoring for reactions or adverse effects in the office (whether or not they have a migraine) may be indicated (Unger, 2006).
- Contraindications and adverse effects occur in adults.

—Adverse effects: bad taste from the nasal form; nausea; chest discomfort; triptan sensation (i.e., warmth, stinging sensation, or paresthesias) (Damen et al., 2005).

—Contraindications: cardiovascular disease; uncontrolled hypertension; hemiplegic or basilar migraines; use of 5-HT1 agonist in the past 24 hours; and use of a monoamine oxidase inhibitor in the past 2 weeks (Lewis et al., 2005).

Acute/abortive: Ergot alkaloids (dihydroergotamine)

- Ergot alkaloids are available in oral, intranasal, subcutaneous, intramuscular, and intravenous routes. Oral dihydroergotamine appears to be of no benefit (Damen et al., 2005). Intravenous dihydroergotamine can result in nausea necessitating pretreatment with an oral anti-emetic such as promethazine (Lewis et al., 2005).

Acute/abortive: Anti-emetics

- Effective agents include prochlorperazine (Compazine), particularly in those with nausea and vomiting, albeit with the theoretic risk of extra-pyramidal adverse effects (Damen et al., 2005; Lewis et al., 2005).

Prophylaxis/Anti-hypertensives

- Calcium channel blockers selectively inhibit vasoactive substances on cerebrovascular smooth muscle. Nimodipine is

not consistently effective, but flunarizine (not available in the United States) was effective in several trials (Lewis et al., 2004; Lewis et al., 2005).

- β-Blockers (propranolol) have been studied in children and are of questionable effectiveness (Lewis et al., 2004; Lewis et al., 2005); other agents (timolol, atenolol, metoprolol, and nadolol) have not been effective (Damen, Bruijn, Verhagen, et al., 2006). β-Blockers cannot be used in patients with a history of asthma and are used with caution in patients with a history of depression.
- An α-adrenergic agonist (clonidine) was found to be no better than placebo in children (Lewis et al., 2004).

Prophylaxis/antidepressants

- Amitriptyline (Elavil) reduces headache frequency and strength but not duration (Lewis et al., 2004; Lewis et al., 2005).
- Selective serotonin reuptake inhibitors (SSRIs) have not been studied in children or adolescents for the prophylaxis of migraines (Lewis et al., 2005), and the black box warning concerning increased suicidality, but not suicide, in adolescents may limit their use (U.S. FDA, 2007). However, in children with co-morbid anxiety and/or depression, SSRIs may be the best option. Of the SSRIs, only fluoxetine is approved in children and adolescents for major depressive disorders (U.S. FDA, 2007). The American Academy of Child and Adolescent Psychiatry published a Practice Parameter for Assessment and Treatment of Children and Adolescents with Depressive Disorders. It concluded that the risk to benefit ratio for SSRI use in pediatric depression appears to be favorable with careful monitoring for suicidal thoughts and behavior as well as for other adverse effects (Birmaher & Brent, 2007). The FDA further defines specific criteria for monitoring adolescents and young adults initially started on antidepressants (U.S. FDA, 2007).
- The FDA issued an alert stating that there is a possibility of a life-threatening serotonin syndrome (change in mental status, autonomic instability, neuromuscular abnormalities, and gastrointestinal symptoms) when patients are taking both triptans and SSRIs (U.S. FDA, 2006).

Prophylaxis/anticonvulsants

- Valproic acid (Depakote) was effective in open-label trials in children and adolescents, but the adverse effects in adolescent women, including hair loss, weight gain, and possible teratogenic effects, must be considered (Lewis et al., 2004).
- Newer antiepileptic medications (gabapentin, levetiracetam, and topiramate) reduced headache frequency in open-label, retrospective trials (Lewis et al., 2004; Lewis et al., 2005).

Prophylaxis/antihistamines

- Cyproheptadine has antiserotonergic and calcium channel blocker effects; it is used extensively for migraine prophylaxis in young children but has not been well studied and has the adverse effects of sedation and increased appetite (Lewis et al., 2004; Lewis et al., 2005).

Management: Biobehavioral Modalities

Relaxation training and biofeedback programs are aimed at reducing the frequency and severity of migraines. The combination of biofeedback and relaxation treatments provides the child/adolescent with objective data to evaluate their response (Powers & Andrasik, 2005). While all children with migraines may benefit from these therapies, they are reserved primarily for children with disabling headaches.

- Relaxation treatments include progressive muscle relaxation, diaphragmatic or deep breathing, and guided imagery. Generally, children must be at least 7 years old before they can comprehend the concepts involved in these techniques (Powers & Andrasik, 2005).
- Biofeedback frequently is used as an adjunct to relaxation training. Two different techniques can be used with children and adolescents:
  - Electromyographic activity, in which an electrical discharge in the muscle fiber indicates skeletal tension.
  - Peripheral skin temperature monitoring measures vasomotor mechanisms. As the child relaxes, the skin temperature rises.

Management: Complementary and Alternative Interventions

Few studies in adults or children have evaluated the efficacy and safety of various complementary and alternative methods of migraine control. Herbs (feverfew, ginkgo, and valerian root), minerals (magnesium), and vitamins (riboflavin) commonly have been used in the treatment of migraines (Lewis et al., 2005). Of these, only feverfew in one study in adults was found to be an effective preventative medication (Diener, Pfaffenrath, Schnitker, Griede, & Henneike-von Zepelin, 2005). Evidence-based treatment recommendations in children for the use of hypnosis, acupuncture, transcutaneous electrical nerve stimulation, chiropractic or osteopathic cervical manipulation, occlusal adjustment, and hyperbaric oxygen as preventive or acute therapy for migraine are not yet possible (Alecrim-Andrade, Maciel-Junior, Cladelleas, Correa-Filho, & Machado, 2006; Silberstein, 2000). Some persons have recommended that some of these treatment modalities may be considered by the patient who is not interested in pharmacologic options or for patients who prove to be refractory to conventional therapies (Lewis et al., 2005).

BOX 3. Resources

For child/family:

American Academy of Neurology (AAN)
1080 Montreal Ave
St. Paul, MN 55116
The AAN and the Child Neurology Society have developed a fact sheet entitled "AAN guideline summary for patients, parents and caregivers: Treatment of migraine headache in children and adolescents." It is located at the following Web site: http://www.aan.com/professionals/practice/pdfs/Headaches_Peds_Patients.pdf

American Council for Headache Education
19 Mantua Rd
Mt. Royal, NJ 08061
Web site: http://www.achenet.org
The Web site has a section, "Kids and Headaches," that includes several handouts describing types of migraines, triggers, and other information useful for understanding and preventing migraines in children and adolescents.

The Headache Care Center
Web site: www.headachecare.com
A comprehensive site with in-depth coverage of topics ranging from types and treatments of headaches to a page devoted to self-evaluation. "The Migraineur's Guide to Migraine" is a helpful guide to understanding phases of migraines, detailing preventative lifestyle habits, and detailing concerns that are common to individuals with migraines. This site is geared toward adults but would be beneficial to older adolescents and young adults.

Lewis, D. W. (2002 February 15). Migraine headache in children and adolescents. American Family Physician.
This patient handout provides a comprehensive review of description of migraines, causes, treatments, and actions parents can take to prevent migraines. This handout follows the following article: Lewis, D. W. (2002, February 15). Headaches in children and adolescents. *American Family Physician.* Retrieved from www.aafp.org/afp//20020215/625.html

National Institute of Neurological Disorders (NINDS), National Institute of Health.
Web site www.ninds.nih.gov/disorders/headche/detail_headache.htm
This Web site has several publications that address headaches. One publication, *Headache: Hope Through Research*, thoroughly discusses causes, diagnosis, and treatments of all types of headaches with special emphasis on migraine headaches. The Web site also lists other resources.

For health care providers:

Fetrow, C. W. & Avila, J. R. (1999). Complementary and alternative medicines. Springhouse, PA: Springhouse Corp.
This book is written by two pharmacists, and each medicine has the following information: Common trade names, common forms, chemical components, actions, reported uses, dosage, adverse reactions, interactions, contraindications and precautions, special considerations, points of interest, analysis, and references.

Primary Care Network
1230 E. Kingsley
Springfield, MO 65804
Web site: www.primarycarenet.org
This not-for-profit association of health care providers provides CME accredited education by offering free seminars, teleconferences, and online and interactive education. There are several programs on management of patients with migraines primarily for adult patients. This organization also conducts clinical trials and therapy research at several sites in the United States.

PATIENT AND FAMILY EDUCATION

The patient and family need to understand that the medicine prescribed is to be taken as directed. If the patient is prescribed acute/abortive and prophylactic medications, the difference between the two must be explained. Acute/abortive medications are taken at the first sign of the headache; prophylactic medications are taken daily regardless of pain (Powers & Andrasik, 2005).

Fluids are taken with the abortive medication to ensure hydration (Powers & Andrasik, 2005).

A medical authorization document signed by the clinician and guardian should be sent to the school explaining the need for immediate administration of the abortive medication accompanied by fluids. The name and dosage of the medication should be included in the letter (Powers & Andrasik, 2005).

Older children should be taught the names, dosages, and usage of all medications (Powers & Andrasik, 2005).

The patients are told that adherence to lifestyle changes may result in the prophylactic medications being discontinued after 6 to 12 months (Powers & Andrasik, 2005).

The provider should emphasize avoidance of other non-prescribed or non-recommended pain medications (i.e., over the counter). Usage of these medications can lead to "overuse" rebound headaches (Lewis et al., 2005).

Source for handouts for patient teaching and other information for both families and health care professionals are listed in Box 3.

REFERRALS

The treatment of migraine headaches is multifactorial and may require interventions beyond the scope of the nurse practitioner (NP). Children with comorbid depressive disorders or other psychiatric disorders who would benefit from psychotherapy and or pharmacotherapy should be referred to a psychiatrist. Similarly, patients who would benefit from biobehavioral therapies require a referral to a psychologist skilled in these methods.

Another group of children and adolescents who require referral are those who are refractory to prescribed therapy, especially those with chronic daily headaches or migraine variants. This group of patients should be referred to a pediatric neurologist or a pediatric headache clinic.

Lastly, the NP must recognize that the majority of the medications for acute and prophylactic treatment are non-FDA approved for use in children and young adolescents, may not been have studied for use in children and adolescents for prophylaxis of migraines, or carry a black box warning. The decision to use these medications is based on the comfort level of the NP, the relationship with the supervising physician, and/or the appropriate state nurse practice act.

SUMMARY

The diagnosis of migraine headaches in children and adolescents is complex and based on guiding goals and general principles. In all cases a thorough history and physical examination encompasses the numerous and/or potentially life-threatening differential diagnoses. The individualized plan is based on the patient's symptoms, contributing factors, response to tried therapies, and patient and family preference for treatment options. Additionally, a stepwise approach is critical when treating children, primarily because few medications are approved by the FDA for use in children and young adolescents. Children and adolescents who require psychotherapy or biobehavioral therapy or who are refractory to prescribed therapy should be referred to the appropriate specialist. The NP also must weigh the risk and benefits of prescribing medications that are not FDA approved and/or require close monitoring.

If the patient is prescribed acute/abortive and prophylactic medications, the difference between the two must be explained.

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