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Management Strategies For Acute Headache In The Emergency Department

June 2012
Volume 14, Number 6

Abstract

Approximately 2.1 million patients per year present to United States emergency departments with a primary headache disorder. For emergency clinicians, the responsibility is twofold: First, exclude causes of headaches that pose immediate threats to the life and welfare of patients. Second, provide safe, effective, and rapid treatment of symptoms, while facilitating discharge from the emergency department with appropriate follow-up. While emergency management focuses on identification and treatment of life-threatening causes of headache, such as subarachnoid hemorrhage or bacterial meningitis, there is a tendency to misdiagnose specific primary headache disorders and fail to provide consistent, effective treatments in accordance with published guidelines. These mistakes can be avoided by resisting the temptation to label patients with specific primary headache diagnoses and by adopting a consistent, reproducible strategy for treatment of primary headache disorders in the emergency department that is evidence-based and effective.

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CME Objectives

Upon completion of the article, you should be able to:

1. Classify primary and secondary headache disorders.
2. Describe common pathophysiology and classification of primary headache disorders.
3. Identify multiple treatment options for patients with primary headaches.
4. Discuss discharge planning, including understanding which patients are at higher risk of headache relapse.

Date of original release: June 1, 2012
Date of most recent review: May 10, 2012
Termination date: June 1, 2015
Medium: Print and Online
Method of participation: Print or online answer form and evaluation
Prior to beginning this activity, see "Physician CME Information" on the back page.

Accreditation: EB Medicine is accredited by the ACCME to provide continuing medical education for physicians. **Faculty Disclosure:** Dr. Singh, Dr. Soares, Dr. Edlow, Dr. Huff, Dr. Jagoda, and their related parties report no significant financial interest or other relationship with the manufacturer(s) of any commercial product(s) discussed in this educational presentation.
Commercial Support: This issue of *Emergency Medicine Practice* did not receive any commercial support.

Case Presentations

You arrive for your shift in the ED and are greeted by a trio of patients with a chief concern of headache. The first is a 10-year-old boy brought by his parents for the evaluation of moderate-intensity frontal headaches that have been going on for several months. The headaches occur in the morning, resolve by the afternoon, and are not changing in character or frequency. He has no other symptoms and appears very well on your exam. The parents are concerned that their child has a brain tumor and are requesting a head CT.

The second patient is a 46-year-old female with a history of migraine headaches who presents with a severe, constant pain that started suddenly while running. She admits this "feels different than my normal headaches." On examination, she appears ill and is vomiting. Her neurologic examination demonstrates mild neck stiffness. She asks for a refill of her sumatriptan, which "always works for my headaches."

The third patient arrives by ambulance. She is a 27-year-old "frequent flyer." She describes her typical migraine headache, not controlled with home medications. Her vital signs and examination are unremarkable. You would like to treat her quickly and effectively, knowing that, if you do not, she will make the rest of your day difficult.

Feeling your own head starting to pound, you take a deep breath, grab the charts, and start your day, hoping that you don't become the fourth patient with a headache.

Introduction

The prevalence of headaches is staggering. It is estimated that almost one-half of the world's adult population suffers from a headache disorder. While the vast majority of headache patients do not visit the emergency department (ED) for care, headache remains the fifth most common chief complaint, comprising approximately 2% of all ED visits in the United States.[1-5] Given an average cost of $1800 per patient visit, this translates to billions of dollars per year in healthcare costs.[6] While emergency management focuses on identification and treatment of life-threatening causes of headache, such as subarachnoid hemorrhage (SAH) or bacterial meningitis, there is a tendency to misdiagnose specific primary headache disorders and fail to provide consistent, effective treatments in accordance with published guidelines.[7,8]

Headaches are commonly classified into 2 groups: (1) primary headache disorders, where the etiology is unknown, and (2) secondary headache disorders, where the headache is attributed to a specific underlying cause.[9] **(See Table 1.)** While emergency medicine training focuses on the identification and management of dangerous secondary causes of headache, the vast majority of patients who present to the ED suffer from a primary headache disorder. As such, it is helpful to use evidence-based strategies to diagnose, manage, and treat these patients. This issue of *Emergency Medicine Practice* discusses the initial workup and management of patients with primary headache disorders, with special detail to classification and medication options. Common pitfalls associated with the care of the headache patient are also discussed. Finally, basic algorithms will be presented to aid the emergency clinician in the treatment and disposition of the next headache patient.

For more information on diagnosis and treatment of headache in the ED, see the September 2010 issue of *EM Practice Guidelines Update*, "Current Guidelines For Management Of Headache In the Emergency Department," and the February 2010 issue of *Pediatric Emergency Medicine Practice*, "Pediatric Migraine Headache: An Evidence-Based Approach."

Critical Appraisal Of The Literature

The available literature on headache disorders is sizeable. A literature search was performed using PubMed online with the following search terms: *emergency headache, emergency migraine, emergency tension headache,* and *migraine treatment.* Approximately 2400 articles from 1960 to present were reviewed. The National Guideline Clearinghouse (www.guideline.gov) and the Cochrane Database of Systematic Reviews were searched with the term *headache* and included 7 and 15 review articles, respectively. Guidelines released by the American College of Emergency Physicians (ACEP) and the American Academy of Neurology (AAN) were also searched. The Canadian, French, and European neurology guidelines were also reviewed. To find additional primary literature, a search for headache and migraine was performed in the following emergency medicine journals: *Annals of Emergency Medicine, the American Journal of Emergency Medicine, Academic Emergency Medicine, BMC Emergency Medicine, Canadian Journal of Emergency Medicine, Emergency Medicine Clinics of North America, European Journal of Emergency Medicine, Journal of Emergency Medicine,* and *Western Journal of Emergency Medicine.* The bibliographies from these articles were examined to verify accurate representation from the literature.

Relevant Practice Guidelines

- ACEP: Clinical Policy for the Initial Approach to Adolescents and Adults Presenting to the Emergency Department with a Chief Complaint of Headache, 1996,[10] 2002,[11] 2008.[12]
- AAN, US Headache Consortium: Practice Parameter: Evidence-based Guidelines for Migraine Headache (An Evidence-Based Review), 2000.[13]
- Canadian Headache Society: Guidelines for the Diagnosis and Management of Migraine in Clinical Practice,1997.[14,15]

- European Federation of Neurological Societies (EFNS): EFNS Guideline on the Drug Treatment of Migraine – Revised Report of an EFNS Task Force, 2009.[16]
- French Guidelines for the Diagnosis and Management of Migraine in Adults and Children, 2004.[17]

Classification Of Headaches

Prior to 1988, there were no formally recognized headache classification systems; "headache was largely regulated to the domain of psychiatric and social maladies."[18] In response, the International Headache Society (IHS) was formed and created a comprehensive, objective classification system for headache disorders, known as the International Classification of Headache Disorders (ICHD), with a subsequent revision to this guide occurring in 2004, the ICHD-2.[9] The ICHD-2 is currently the accepted standard diagnostic criteria for headaches as well as the benchmark for classification in headache research.

The ICHD-2 is a tiered classification system. It initially divides headaches into 2 parts: (1) primary headache disorders where the headache itself is the disease entity, and (2) secondary headache disorders where the headache is a symptom attributed to another underlying disorder (for example, secondary to bleeding, infection, or tumor). Primary headache disorders are further subdivided into 4 categories: (1) tension-type, (2) migraine, (3) cluster, and (4) other. **(See Table 1.)**

Tension-Type Headaches

Tension-type headaches are the most common type of primary headache, with an estimated prevalence approaching 40%. Patients who are Caucasian, female, and ages between 30 and 40 years display a higher prevalence of tension headaches.[19] Tension-type headaches are defined as having 2 of the following characteristics: bilateral location, nonpulsating quality of pain, mild to moderate intensity, and not aggravated by physical activity.

Migraine Headaches

Migraine headaches are the next most common headache disorder, affecting 12% of the United States population. The prevalence of migraine has remained stable both in the United States and throughout the world over the past 20 years. Adult women suffer migraines more frequently than men (3:1), with the highest rates in Caucasian and African American women.[20-22] According to the ICHD-2, migraines are typically unilateral, pounding, moderate to severe pain, worse with exercise, and often associated with nausea, vomiting, photophobia, or phonophobia. Migraines are generally subdivided into aura types and non-aura types, although the ICHD-2 lists over 20 specific subtypes of migraine.

Cluster Headaches

Cluster headaches and other trigeminal autonomic cephalalgias are rare when compared with tension or migraine headaches. The prevalence is estimated to be 0.1% of the population or 124 per 100,000 persons.[23] Cluster headaches are defined as severe, frequent headaches with parasympathetic autonomic features including injected sclera, lacrimation, rhi-

Table 1. ICHD-2 Primary Headache Diagnostic Criteria[9]

Tension-Type Headache

1. At least 10 episodes of headache attacks lasting from 30 minutes to 7 days
2. At least 2 of the following criteria:
   - Pressing/tightening (nonpulsatile) quality
   - Mild or moderate intensity (may inhibit but does not prohibit activity)
   - Bilateral location
   - No aggravation by walking, stairs, or similar routine physical activity
3. Both of the following:
   - No nausea or vomiting (anorexia may occur)
   - Photophobia and phonophobia are absent, or one but not both are present

Migraine Without Aura

1. At least 5 headache attacks lasting 4 to 72 hours (untreated or unsuccessfully treated), which have at least 2 of the 4 following characteristics:
   - Unilateral location
   - Pulsating quality
   - Moderate or severe intensity (inhibits or prohibits daily activities)
   - Aggravated by walking, stairs, or similar routine physical activity
2. During headache, at least 1 of the 2 following symptoms occur:
   - Phonophobia and photophobia
   - Nausea and/or vomiting

Cluster Headache

1. At least 5 attacks of severe unilateral orbital, supraorbital, and/or temporal pain lasting 15 to 180 minutes untreated, with 1 or more of the following signs occurring on the same side as the pain:
   - Conjunctival injection
   - Lacrimation
   - Nasal congestion
   - Rhinorrhea
   - Forehead and facial sweating
   - Miosis
   - Ptosis
   - Eyelid edema
2. Frequency of attacks is from 1 every other day to 8 per day

Other Primary Headaches

Includes:

Primary exertional headache

- Hypnic headache
- Primary thunderclap headache
- Primary headache associated with sexual activity

Abbreviation: ICHD, International Classification of Headache Disorders.

norrhea, facial sweating, and eyelid swelling. Pain is often so severe that patients "are usually unable to lie down and characteristically pace the floor."[18]

Other Primary Headaches

The fourth category of primary headaches encompasses a wide range of diagnoses including primary cough headache, exertional headache, headache associated with sexual activity, and thunderclap headache. These other primary headaches can be difficult to distinguish from dangerous secondary causes, and the diagnosis is reserved for neurologists or other headache specialists.

Pathophysiology

It is important to review basic pathophysiology to help illuminate the mechanisms and limitations of medications used to treat headaches.

Pain sensed in headaches does not originate from the brain parenchyma, as it has no pain receptors. Rather, the sensation is referred from cranial vessels, which are the only known innervated central nervous system (CNS) structures. It is hypothesized that cortical depression—a wave of depolarization of unclear etiology—stimulates cerebral vessel neurons, activating multiple nerve complexes, including the trigeminal ganglion nerve complex. It is the activation of these specific nerve ganglion complexes by neuropeptides, including substance P and calcitonin gene-related peptide (CGRP), that promotes neurogenic inflammation that contributes to the pain associated with headache.[24,25]

This so-called "neurovascular" theory of headaches represents a change from the prior hypothesis of cerebral vascular dilation and constriction as the etiology of headache. Historically, it was thought that vasoconstriction led to transient hypoxia, with subsequent rebound vasodilation causing headache. It is now thought that vasodilation is a secondary effect of cortical depression and neuropeptide release. Current literature suggests that neuropeptide release and subsequent neurogenic inflammation contribute to pain in headaches, specifically migraines.[26]

Although best studied in migraines, the neurovascular theory of pain is thought to be a common pain pathway for many headaches. Medications used for primary headaches appear to modulate the neurogenic inflammatory process. Nonsteroidal anti-inflammatory drugs (NSAIDs) act as direct anti-inflammatory medications. Triptans, ergots, and serotonin receptor agonists appear to modulate neurotransmitters, including CGRP, to reduce neurogenic signal and inflammation. Neuroleptics, including metoclopramide and prochlorperazine, have strong antiserotonin, anticholinergic, antidopaminergic, and antihistamine effects on neuroreceptors.

While NSAIDs, triptans, and neuroleptics act to reduce acute inflammation, preventing chronic migraine states involves preventing sensitization of neural pathways and chronic inflammatory states. Medications like tricyclic antidepressants and beta-blockers are postulated to decrease neuronal hyperexcitability caused by multiple episodes of acute headaches. Although prescribing preventative migraine medications is not in the emergency clinician's scope of practice, referral of frequent headache patients to appropriate specialists can help decrease chronic headache states.

Because both primary and secondary headaches appear to have a common pain pathway, the authors advise against using a patient's response to medication to exclude dangerous secondary etiologies of headache. Multiple case reports and case series document pain relief from triptans, neuroleptics, and NSAIDs in patients with brain tumors and SAH.[27-30] Therefore, in accordance with ACEP guidelines, excluding dangerous secondary causes of headache should not be based on response to medication. (ACEP Level C recommendation.[12])

Differential Diagnosis

The priority of emergency clinicians is not to diagnose primary headache disorders, but rather to rule out or treat secondary causes of headaches that pose an immediate threat to the lives and welfare of patients. **Table 2** lists the important secondary causes of headaches that are considered when evaluating a patient with an undifferentiated headache.

Prehospital Care

There are little prospective data on evaluation and management of the headache patient in the prehospital care setting. As with all patients, local and national emergency medical services (EMS) guidelines should be followed, including a primary survey, vital signs, stabilization, and transport to an appropriate facility.

Generalized recommendations include the following: (1) eliciting a basic history, (2) evaluating mental status, and (3) performing a brief neurologic examination (eg, Cincinnati Prehospital Stroke Scale).[31] **(See Table 3.)** If there is any abnormality in the neurologic or mental status examination or if the patient appears unwell, emergent transport should be activated. While most headaches remain undifferentiated, conditions such as stroke and traumatic brain injury must be considered, and patients must be transported to an appropriate specialty care center, when indicated.

In the field, the initial approach includes making the patient comfortable prior to giving medications (adjusting temperature, minimizing unnecessary light or noise, placement into a comfortable posi-

tion). Acetaminophen can often be used as a first-line medication. We recommend against the routine use of opioids unless patients are in such severe pain that they cannot be safely transported.

Emergency Department Evaluation

The foundation of evaluating a patient with headache is to rule out dangerous secondary etiologies underlying the presentation. As such, the history and physical examination are paramount and will guide decisions for further tests and imaging studies.

History

The history includes a detailed account of the current headache, with special attention to "red flag" symptoms that may suggest a dangerous secondary etiology. **(See Table 4.)** In addition, the provider should elicit the onset, location, and quality of the headache as well as associated symptoms. **(See Table 5, page 6.)** If the patient has a history of prior headaches, it is important to explore differences between the current headache and prior headaches. While the majority of patients with prior primary headaches present with exacerbations of past headache disorders, subtle differences in onset, location, and severity may provide clues to new and dangerous secondary headache etiologies.

The description of a patient's "worst headache" is neither sensitive nor specific to alone guide treatment decisions. A recent prospective cohort study evaluating high-risk clinical characteristics for SAH found that 93% of patients with SAH had the "worst headache of their life;" however, 77% of patients without SAH also described the "worst headache of their life."[32] As such, the descriptive "worst headache" must be taken in the context of other signs and symptoms.[33] When a patient states he or she has an unusually severe headache, it should concern the provider and raise pretest probability of a secondary etiology, but it does not automatically signal the need for an extensive workup. Conversely, patients with less-severe headaches may still harbor a dangerous secondary diagnosis.

Physical Examination

Physical examination is essential to exclude dan-

Table 2. Important Secondary Causes Of Headache

Secondary Headache Causes	Red-Flag Findings
Subarachnoid hemorrhage	Thunderclap (sudden, severe onset) headache
Meningitis	Fever, neck stiffness, immunosuppression
Temporal arteritis	Jaw claudication, vision changes, polymyalgia rheumatica
Carbon monoxide poisoning	Waxing and waning headache, cluster of cases
Acute glaucoma	Unilateral vision change, eye pain, and redness
Cervical artery dissection	Neck pain, trauma, stroke symptoms, Horner syndrome
Venous sinus thrombosis	Pregnancy, postpartum, hypercoagulable, oral contraceptive use
Intracerebral tumor	Chronic progressive headaches, papilledema, history of malignancy
Cerebellar infarction	Ataxia, dysmetria, vertigo, vomiting
Idiopathic intracranial hypertension	Papilledema, worse when lying flat, obesity
Pituitary apoplexy	Hypotension, hypoglycemia, hyponatremia, visual field deficit, history of pituitary tumor
Pre-eclampsia	Hypertension, proteinuria, nondependent edema, pregnancy
Hypertensive encephalopathy	Altered mental status, hypertensive, neurologic signs in nonanatomic distribution
Subdural hematoma	Trauma, coagulopathy
Intracerebral hemorrhage	Hypertension, cerebral aneurysm, arteriovenous malformation

Table 3. Cincinnati Prehospital Stroke Scale[31]

Facial Droop (Ask patient to smile)
- Normal: No facial droop
- Abnormal: One side of face does not move as well as the other

Arm Drift (Ask patient to extend both arms for 10 seconds)
- Normal: Both arms move the same or not at all
- Abnormal: One arm drifts down

Speech (Ask patient to repeat, "The sky is blue in Cincinnati")
- Normal: Correct speech
- Abnormal: Slurred speech, wrong words, no words

Table 4. Red-Flag Signs And Symptoms Of Dangerous Secondary Headaches

- New headache in patient older than 50 years of age
- Maximal intensity within minutes of onset (thunderclap headache)
- Posterior headache with neck pain or stiffness
- Change in vision
- Change in consciousness
- Syncope
- History of HIV or immunocompromise
- History of malignancy
- Pregnancy or postpartum
- History of neurosurgery or cerebral shunt
- Headache with seizure

gerous secondary headaches. A general examination with particular emphasis on the neurologic, ophthalmologic, and head and neck examinations is recommended.

Neurologic Examination

A focal neurologic abnormality in the setting of headache has consistently been shown to have the highest likelihood ratio for detecting abnormalities on imaging.[34] As such, a thorough neurologic examination on patients with headaches is indicated. Cranial nerve abnormalities suggest intracranial or carotid pathology. Focal weakness may help to localize intracranial hemorrhage or elucidate carotid dissection, or if symptoms do not localize to a defined neurologic distribution, may suggest venous infarct or venous sinus thrombosis. Tests of neurologic function related to the posterior circulation, including dysarthria, dysphagia, double vision, ataxia, and dizziness may indicate pathology in the brainstem or cerebellum. Finally, altered mental status suggests a malignant secondary etiology such as SAH, meningitis, dissection, carbon monoxide poisoning, or stroke. **(See Table 6.)**

Ophthalmologic Examination

The eye examination provides information about intracranial pressure, visual acuity, and visual field deficits. Defects in visual acuity and pupillary response may suggest temporal arteritis, glaucoma, third nerve palsy, or Horner syndrome (associated with carotid dissection). Increased monocular pressures with headache and fixed midrange pupil are diagnostic of acute closed angle glaucoma. If intraocular pressures are normal, providers can consider dilated fundoscopy to evaluate for papilledema.

Head And Neck Examination

Unilateral tenderness or nodularity over a temporal artery suggests temporal arteritis. Sinusitis and nasal congestion can exacerbate headache disorders, although many cases of migraine are misdiagnosed as sinusitis. Periapical dental infections can cause

Table 5. General History Questions For Evaluation Of Headache

History Questions	Concerning Responses
Onset: • When did the headache start? • What were you doing when it started?	Sudden headache with exercise, coughing, straining, or orgasm is concerning for SAH.
Provocation: • What makes the pain better or worse? Position? Exercise? Straining?	Pain exacerbated by supine position or cough is concerning for increased ICP.
Quality: • Describe the pain. • Where is the pain located?	Occipital headache with neurologic signs of dysarthria, dysphagia, double vision, or ataxia are concerning for posterior bleed, tumor, or stroke.
Radiation: • Does the pain move or radiate?	Pain with radiation down the neck or neck stiffness is concerning for SAH, meningitis, or carotid or vertebral artery dissection.
Severity: • How long until your headache reached its maximum?	Thunderclap headache (maximal pain within minutes of onset) is concerning for secondary pathology including SAH, venous sinus thrombosis, or intracranial hemorrhage.
Temporal: • Has the pain changed over time?	Chronic, progressively worsening headaches are concerning for possible structural mass or lesion.
Associated: • Are there any other symptoms you have had?	Associated neurologic deficits, vision changes, or fever are concerning for dangerous secondary etiology.

Abbreviations: ICP, intracranial pressure; SAH, subarachnoid hemorrhage.

Table 6. Selected Concerning Neurologic Examination Findings For The Headache Patient

Cranial Nerve/Examination Finding	Possible Cause
CN II – Optic nerve or its central connections • Vision loss / visual field deficit	• Unilateral vision loss can be the result of ischemia, temporal arteritis, glaucoma, or optic neuritis. • Bilateral visual field loss suggests CNS involvement posterior to the optic chiasm.
CN III – Oculomotor nerve • Defect in pupillary constriction, eyelid raise, extraocular movements (down and out eye)	• May indicate posterior communicating artery aneurysm, uncal herniation, SAH, or mass lesion. • Consider cavernous sinus thrombosis.
CN VI – Abducens nerve • Defect in lateral movement of eye	• Consider increased or decreased ICP, brain herniation.
Ataxia, coordination deficit • Unsteady gait, unable to perform finger-to-nose, heel-to-shin	• Consider cerebellar infarct or bleed. • Consider posterior/vertebral injury.
Altered mental status	Concern for mass or vascular lesion, SAH, hypertensive encephalopathy, meningitis, venous sinus thrombosis, carbon monoxide poisoning, or dissection.

Abbreviations: CN, cranial nerve; CNS, central nervous system; ICP, intracranial pressure; SAH, subarachnoid hemorrhage.

referred headache. With regards to the neck examination, neck rigidity raises concern for meningitis and SAH. While Kernig sign and Brudzinski sign are neither sensitive nor specific, jolt accentuation of the headache (rapid rotation of head 2-3 times per second, examining for worsening headache) appears to be the most specific sign for meningeal irritation.[35]

Other Examinations

ACEP guidelines recommend basic cardiopulmonary and abdominal examinations to fully evaluate and exclude the dangerous etiologies of headache.[10] An ED headache physical examination format is presented in **Table 7**.

Diagnostic Studies

No diagnostic studies are indicated if history and physical examination have excluded dangerous secondary causes of headache.[36] Individual diagnostic studies for secondary headaches are indicated if the emergency clinician is not able to exclude secondary headache etiologies. **(See Table 8.)** The most common studies include noncontrast head computed tomography (CT), magnetic resonance imaging (MRI)/magnetic resonance venography (MRV) brain, lumbar puncture with cerebrospinal fluid analysis, visual acuity and intraocular pressure, erythrocyte sedimentation rate, and carboxyhemoglobin. These tests should be used in a selective fashion to rule out specific secondary causes suspected by history and examination.

Making The Diagnosis

Once secondary headaches have been excluded, there is often pressure to diagnose the specific primary headache disorder. Though of questionable importance, emergency physicians' ability to correctly classify primary headache disorders has been reported to be poor when compared to neurologists.[37] In response, criteria and mnemonics have been formulated to aid in making the correct diagnosis, with limited utility.[38]

Given the difficulty of accurately diagnosing specific primary headache disorders in the ED, combined with the danger of mislabeling a patient with a chronic headache condition and thereby facilitating future anchoring bias, we argue that emergency clinicians do not need to classify patients with specific primary headache disorders; it is enough to say that a patient does not have a dangerous secondary headache etiology and to diagnose simply as primary headache. This avoids mislabeling and accepts that true diagnosis of primary headache disorders occurs over multiple occasions, as ICHD-2 recommends.

Treatment

The literature on acute treatment of primary headache disorders is vast, spanning multiple decades. In general, recent research has focused more on treatment of migraines than other primary headache disorders. Nonetheless, because of inherent misclassification of headaches in research, the common pain pathway, and our underdiagnosis of migraines in the ED, we believe much of the migraine treatment literature can be generalized to all primary headache disorders.[39-41]

Following is a brief summary of evidence for specific therapies for primary headaches. Evidence is organized by meta-analysis and large randomized clinical trials. The grades of evidence, as assigned by the AAN/US Headache Consortium guidelines, along with doses, are described in **Table 9 (page 8).** It is important to note that evidence from these guidelines includes studies of ambula-

Table 7. Example Physical Examination For Emergency Patient With Headache

Neurologic	• Visual fields, extraocular movements, facial symmetry, tongue position • Strength and sensation in all 4 extremities • Gait, tandem gait, finger-to-nose, heel-to-shin performance • Mental status
Ophthalmologic	• Visual acuity, pupillary response, intraocular pressure, fundoscopy, swinging flashlight test (to assess afferent nerve function)
Head and neck	• Tenderness over temporal artery, temporomandibular joint, mouth/dentition • Nuchal rigidity, jolt accentuation of headache, tenderness/bruits over carotid
Chest and abdomen	• Heart rate and rhythm, murmur, equal pulses, focal abdominal tenderness

Table 8. Excluding Secondary Causes Of Headache, By Study

Test	Secondary Cause
Noncontrast CT head	Trauma, SAH, CNS tumor/mass
MRI/MRV brain	Cerebral/dural venous thrombosis, pituitary apoplexy, hypertensive encephalopathy
Lumbar puncture with cerebrospinal fluid analysis and OP	Meningitis, SAH, idiopathic intracranial hypertension
Visual acuity with IOP	Acute glaucoma
Erythrocyte sedimentation rate	Temporal arteritis
Carboxyhemoglobin	Carbon monoxide

Abbreviations: CNS, central nervous system; CT, computed tomography; IOP, intraocular pressure; MRI, magnetic resonance imaging; MRV, magnetic resonance venography; OP, opening pressure; SAH, subarachnoid hemorrhage.

tory and outpatient subjects, and it may represent a slightly different population than encountered by emergency clinicians.

NSAIDs

NSAIDs are considered first-line therapy for migraine headaches. They are safe, have minimal side effects, and are effective at reducing and alleviating pain. All NSAIDs decrease inflammation by suppressing prostaglandin synthesis through the COX-1 and COX-2 pathways. Common side effects include nausea and mild abdominal pain.[42] Caution should be used in patients with history of upper gastrointestinal bleed, renal dysfunction, and labile hypertension.

Ibuprofen

A 2010 Cochrane review evaluating 9 randomized controlled trials (RCTs) (totaling 4373 patients, 5223 attacks) found that ibuprofen was associated with significant improvement in acute migraine headache. For ibuprofen 400 mg versus placebo, the number needed to treat (NNT) for 2 hours pain-free (26% vs 12% with placebo), 2-hour headache relief (57% vs 25%), and 24 hours sustained headache relief (45% vs 19%) were 7.2, 3.2, and 4.0, respectively. Associated symptoms of nausea, vomiting, photophobia, phonophobia, and functional disability were reduced within 2 hours, and fewer participants used rescue medication with ibuprofen compared with placebo. Similar numbers of participants experienced adverse events, which were mostly mild and transient.[43] Two large RCTs found similar results.[44,45]

Table 9. Medications For Primary Headache, Dosing, And American Academy Of Neurology Quality Of Evidence[13]

Medication	Dose	AAN Quality of Evidence
Ibuprofen	400-600 mg PO	A
Aspirin	1000 mg PO	A
Naproxen	500-825 mg PO	B
Ketorolac	15-30 mg IV	B
Acetaminophen	900-1000 mg PO	B
Aspirin / acetaminophen / caffeine	500 mg / 500 mg / 130 mg PO	A
Dihydroergotamine IV	0.5-1 mg IV	B
Chlorpromazine	0.1 mg/kg IV	B/C
Metoclopramide	20 mg IV	B
Prochlorperazine	10 mg IV	B
Sumatriptan SQ	6 mg SQ	A
Sumatriptan PO	100 mg PO	A
Opioids	Varies	B
Dexamethasone	6-10 mg PO/IV	C

Abbreviations: AAN, American Academy of Neurology; IV, intravenous; PO, by mouth; SQ, subcutaneous.

Recently, an injectable form of ibuprofen has been released in the United States; however, there are no trials evaluating its use in patients with headache.

Aspirin

A 2010 Cochrane review evaluating 13 trials (4222 patients) for aspirin compared to placebo in the treatment of acute migraine headache had similar results as seen with ibuprofen. For aspirin 900-1000 mg, NNT for 2 hours pain-free (24% vs 11% with placebo), 2-hour headache relief (52% vs 32%), and 24 hours sustained headache relief (39% vs 24%) were 8.1, 4.9, and 6.6 respectively. As with ibuprofen, associated symptoms of nausea, vomiting, photophobia, and phonophobia were reduced with aspirin compared with placebo.[46]

Naproxen

A 2010 meta-analysis of naproxen sodium in the acute treatment of migraine included 4 trials (2168 patients). For naproxen sodium 500 to 825 mg PO versus placebo, the NNT for 2 hours pain-free, 2-hour headache relief, and 24 hours sustained relief were 10, 7, and 9, respectively. Associated symptoms of nausea, vomiting, photophobia, and phonophobia were reduced in the naproxen sodium group.[47]

Diclofenac

A 2012 Cochrane review evaluated 5 trials (1356 patients) for diclofenac 50 mg compared to placebo in the treatment of acute migraine headache. For diclofenac versus placebo, the NNT for 2 hours pain-free, 2-hour headache relief, and 24 hours sustained relief were 6.2, 8.9, and 9.5 respectively. Associated symptoms of nausea, photophobia, phonophobia, and functional disability were reduced within 2 hours. Similar numbers of participants experienced adverse events, which were mostly mild and transient.[48]

Ketorolac

For those patients with headache and significant nausea or vomiting, ketorolac offers the benefit of parenteral administration of an NSAID. Unfortunately, there are no trials comparing oral NSAIDs with IV ketorolac for headache. Well-done RCTs involving 119 and 82 ED patients with acute musculoskeletal pain found equivalency between intramuscular (IM) ketorolac 60 mg and oral ibuprofen 800 mg.[49,50] IM ketorolac has been compared to chlorpromazine[51] and meperidine[52-54] in the treatment of headache, with comparable efficacy. IV ketorolac and its effect on migraines has been examined in 3 studies. The first found increased efficacy when compared to nasal sumatriptan[55]; the second found decreased efficacy when compared to IV prochlorperazine[56]; and the third found decreased efficacy compared to subcutaneous (SQ) sumatriptan, but to a specialized group of migraine patients with allodynia.[57]

Given the available data, oral NSAIDs (preferably oral ibuprofen) are part of first-line therapy in patients who are able to tolerate oral medications and who do not have a contraindication or allergy to these medications. In patients with nausea or vomiting, the authors routinely give IM/IV ketorolac 15 to 60 mg as part of a cocktail of medications to relieve headache pain and associated symptoms.

Acetaminophen

Although considered safe when taken appropriately, acetaminophen (also known as paracetamol) is less effective than other medications for alleviating migraine headaches. The mechanism of acetaminophen in migraine pain relief is unknown, but it is postulated to have some effects on COX-2 receptors controlling inflammation. A 2011 Cochrane review pooled data from 9 RCTs and found that acetaminophen 1000 mg was reasonably effective in treating migraine headache. For all efficacy outcomes, acetaminophen was superior to placebo, with NNT = 12, 5.2, and 5.0 for 2 hours pain-free and 1- and 2-hour headache relief, respectively, when medication was taken for moderate to severe pain. Nausea, photophobia, and phonophobia were reduced more with acetaminophen than with placebo at 2 hours (NNT = 7-11), more individuals were free of any functional disability at 2 hours with acetaminophen (NNT = 10), and fewer participants needed rescue medication over 6 hours (NNT = 6).[58] While side effects are minimal, overuse is a major contributor to liver failure in the United States. In addition, new epidemiological information suggests a correlation between childhood acetaminophen use and asthma.[59] As with ibuprofen, an injectable formulation of acetaminophen has recently been made available in the United States.

Acetaminophen has been evaluated as part of a combination pill and as complimentary therapy to metoclopramide in the treatment of acute migraine headache. A large RCT of 1555 migraine patients demonstrated significant pain relief and rapidity of onset with the combination of acetaminophen 500 mg, aspirin 500 mg, and caffeine 130 mg when compared with ibuprofen 400 mg and placebo.[60] Two studies with a total of 721 participants evaluated acetaminophen 1000 mg plus metoclopramide 10 mg with sumatriptan 400 mg. Acetaminophen plus metoclopramide was not significantly different from oral sumatriptan for 2-hour headache relief or relief of "light/noise sensitivity" at 2 hours. Slightly more individuals needed rescue medication over 24 hours with the combination therapy (NNT = 17).[58]

Ergot

Ergots were the first migraine-specific medications; in fact, their discovery helped shape early theories of migraine pathophysiology. Unlike triptans, which are selective 5-HT_1 agonists, ergots interact with more serotonin receptors. The most common ergot is dihydroergotamine (DHE), a formulation with fewer side effects than other ergots. A systematic review of 11 studies that evaluated the use of DHE in acute migraine headache failed to demonstrate a significant benefit when compared to sumatriptan and phenothiazines; however, when DHE was administered with an antiemetic, the combination was as effective or more effective than meperidine, valproate, or ketorolac across all pain, nausea, and relapse outcomes.[61] In addition, because of its extended spectrum of activity antagonizing multiple serotonin receptors, DHE is associated with a lower incidence of recurrent headaches and is favored among headache specialists for refractory migraine headaches. Nausea, drowsiness, and dizziness were as common or less common in patients treated with DHE and an antiemetic. When combined with an antiemetic, DHE is an effective abortive agent for migraine headache and is a viable nonnarcotic agent in the treatment of this condition; however, given increased side effects and the relative ease of use of triptans, DHE is used less commonly in the emergency setting.

Neuroleptics

The neuroleptics—or dopamine antagonists—are thought to act on the limbic system and basal ganglia to modulate headache pain. They also have antiserotonergic, antihistamine, and anticholinergic effects. The neuroleptics are effective adjunctive therapy for headache patients in the ED.[62] The most common neuroleptics used for headache in the ED are chlorpromazine, metoclopramide, and prochlorperazine.

Chlorpromazine (Thorazine®)

Chlorpromazine has been studied in 2 randomized, double-blind, placebo-controlled trials in the ED.[63,64] In a randomized double-blind placebo-controlled study involving 36 patients, a higher proportion of patients receiving chlorpromazine 1 mg/kg IM had sufficient headache relief to allow resumption of normal activities at 1 hour compared to placebo (47.4% vs 23.5%, P = not significant [NS]). Although this outcome did not reach statistical significance, given the small sample size, a significantly higher number of patients experienced some relief in headache and improvement in nausea compared to placebo.[63] A second well-done study involving 128 patients showed significant improvements in headache pain as well as nausea, photophobia, phonophobia, and need for rescue medication at 1 hour with chlorpromazine 0.1 mg/kg IV compared to placebo (82% vs 15%, $P < 0.01$; NNT = 2).[64] Head-to-head comparisons of chlorpromazine demonstrated greater efficacy when compared to lidocaine, DHE, and meperidine, with efficacy equal to SQ sumatriptan 6 mg.[65-67] Chlorpromazine does have significant side effects, including anticholinergic side effects

(sedation, urinary retention) as well as hypotension. Given the availability of alternative neuroleptics with fewer side effects, chlorpromazine has largely fallen out of favor as first-line therapy.

Metoclopramide (Maxolon®, Metozolv®, Reglan®)

Metoclopramide has been shown to be more effective than placebo in the treatment of migraine.[68-70] Colman et al pooled data from 3 placebo-controlled studies (185 total patients) and showed a significant reduction in pain in 47 of 88 patients who received metoclopramide compared to 30 of 97 in the placebo group (53.4% vs 30.9%, $P < 0.05$).[71] When compared to sumatriptan[72] and ibuprofen,[73] metoclopramide appears to have similar efficacy.

Prochlorperazine (Compazine®, Compro®)

Prochlorperazine has also been shown to be more effective than placebo in the treatment of acute headache.[74,75] In a prospective randomized double-blind clinical trial of 82 adult patients with headache, prochlorperazine 10 mg IV resulted in complete or partial relief in 37 of 42 patients compared to 18 of 40 in the placebo group (88% vs 45%, $P < 0.05$).[74] Three trials have evaluated prochlorperazine versus metoclopramide for relief of acute migraine headache in the ED.[75-77] Jones et al compared the efficacy of prochlorperazine 10 mg IM, metoclopramide 10 mg IM, and matching placebo in 86 patients and found median headache scores were significantly better with prochlorperazine (67% reduction in median headache score with prochlorperazine vs 34% reduction with metoclopramide vs 16% with placebo, $P < 0.05$).[77] Coppola et al compared prochlorperazine 10 mg IV, metoclopramide 10 mg IV, and matching placebo in 70 patients and found improved pain control with the administration of prochlorperazine (82% of patients achieved a decrease of 50% of more in the 30-minute pain score compared to the initial score or an absolute pain score of 2.5 cm or less with prochlorperazine vs 46% with metoclopramide vs 29% with placebo, $P = 0.03$).[75] Lastly, Friedman et al compared prochlorperazine 10 mg IV plus diphenhydramine 25 mg IV to metoclopramide 20 mg IV plus diphenhydramine 25 mg IV in 77 patients with acute migraine headache. Both strategies resulted in a similar amount of pain relief at 1 hour, 2 hours, and 24 hours; however, more side effects were reported in the prochlorperazine group.[76] When compared with other headache agents, prochlorperazine performed better than most other medications. Comparisons with sumatriptan 6 mg SQ,[78] valproic acid 500 mg IV,[79] octreotide 100 micrograms IV,[80] and promethazine 25 mg IV[81] all favor the use of prochlorperazine.

Common side effects encountered in studies involving neuroleptics included akathisia (the uncomfortable, restless feeling most associated with prochlorperazine[82] and metoclopramide). Slow infusion (over 15 minutes) of metoclopramide appears to lower rates of akathisia[83]; however, this does not hold true for prochlorperazine.[84] Pretreatment with diphenhydramine may decrease rates of akathisia associated with prochlorperazine[85] but not metoclopramide.[86]

Butyrophenones

Butyrophenones, such as haloperidol and droperidol, act as dopamine receptor antagonists, and have been postulated to have a similar effect as the neuroleptics on headaches. In a randomized double-blind placebo-controlled trial involving 40 patients with acute migraine headache who were admitted to the hospital, a greater number of patients who received 5 mg of IV haloperidol achieved significant pain relief compared to placebo (80% vs 15%, $P < 0.0001$). However, in the study, 16% of patients stated that, given the side effects of sedation and akathisia, they would not want haloperidol again.[87] Given the few studies, significant side effects, and availability of other effective medications, haloperidol is not recommended by current guidelines as primary treatment.[13]

Droperidol was used in the ED treatment of headache for years prior to the United States Food and Drug Administration (FDA) black box warning in 2001 regarding QT prolongation. Silberstein et al evaluated the use of droperidol at several different doses in 331 patients with acute headaches in a randomized double-blind placebo-controlled trial. Pain relief was significantly better in the treatment groups receiving droperidol IM at doses of 2.75 mg (87%), 5.5 mg (81%), and 8.25 mg (85%) compared to placebo (57%, $P < 0.002$).[88] A randomized double-blind clinical trial by Richman et al found 2.5 mg of IM droperidol was similar in efficacy to 1.5 mg/kg of IM meperidine for the relief of headache.[89] Additional trials comparing IV formulations of droperidol to prochlorperazine have found droperidol to be equivalent to or superior to prochlorperazine for the treatment of acute headache.[90,91] In summary, droperidol is a highly effective agent for the treatment of headache. Practitioners should follow hospital policy, regulations, and recommendations regarding cardiac QT monitoring if this agent is to be used.

Neuroleptics Summary

In summary, neuroleptics—most commonly chlorpromazine, metoclopramide, and prochlorperazine—have all been shown to be more effective than placebo in controlling migraine headaches. Head-to-head comparisons are more difficult, given limited patient group size, different dosing, routes of administration, and outcomes. Standardized trials are needed to further clarify relative efficacy and the relationship from placebo. Nonetheless, given the current research, we recommend, as part of a "headache cocktail," prochlorperazine 10 mg IV with diphenhydramine 25 mg IV (to prevent akathisia) or, as second-line, metoclopramide 10 mg to 20 mg IV.

Triptans

Triptans are agonists of the serotonin 5-HT_1 receptor and a first-line therapy for acute migraine. Originally thought to alleviate migraine pain by vasoconstriction of cerebral vessels, it is now thought that triptans mediate vasoactive peptides in the trigeminal nucleus.[92,93] Although there are many different triptans, this review focuses on sumatriptan, given that it is effective, has the most varied formulations, and is the least expensive.

Sumatriptan comes in forms for oral, rectal, and intranasal routes as well as a subcutaneous injection form. A recent set of Cochrane Review meta-analyses reviewed all formulations.[94-97] **(See Table 10.)** Briefly, sumatriptan 6 mg SQ appears to be the most effective at both reducing and alleviating pain as well as having the fastest onset. Drawbacks include increased risk of headache relapse, slightly increased rate of side effects, as well as need for injection. Rectal sumatriptan appears to be the second most effective; however, drawbacks include discomfort with administration, availability, and (due to lack of studies) fewer data on rates of adverse effects. Oral sumatriptan 100 mg is the third most effective formulation, with the benefit of ease of use and decreased incidence of headache relapse; however, the oral formulation necessitates the patient not be vomiting. Finally, the intranasal formulation has a bitter taste and appears to be the least effective, but it offers an alternative for patients who are nauseated and vomiting without having an injection or rectal suppository.

The problem of headache relapse spans all medical therapies, but it is postulated that the relatively short half-life of sumatriptan makes it especially prone to result in headache relapse. Headache relapse with sumatriptan is high, occurring in 40% to 75% of all subjects.[98] Multiple studies have evaluated redosing sumatriptan, both oral and SQ, but to date, there has been no proven benefit that subsequent doses prevent relapse.[99-101]

With all sumatriptan formulations, side effects occur in 1% to 10% of patients and include chest pain, chest tightness, sweating, and dizziness. These symptoms are usually benign and self-limited. Patients should be warned of common side effects to avoid anxiety and further exacerbation of headache. Case reports exist of myocardial ischemia and even death from coronary vasoconstriction thought to be secondary to the presence of occasional 5-HT_1 receptors in coronary arteries. These events are rare, estimated at 1 event per 4 million uses.[102] Another serious potential side effect is drug interactions, particularly serotonin syndrome.[103] As such, there are relative and absolute contraindications to use of triptans. **(See Table 11.)**

Opioids

Many headache guidelines discourage the use of opioids for treatment of migraine headaches, although there are few prospective studies showing the harm of opioid administration. For the emergency clinician, opioids are fast, work on a variety of painful conditions, and are relatively safe. Nonetheless, headache specialists concerned about creating a chronic migraine state (ie, status migrainosus) advise against opioids for migraine. These physicians cite evidence from clinic-based, case-control, and longitudinal studies as well as structural, physiologic, and biochemical alterations in the brains of patients with chronic migraine.[105] While this evidence may be persuasive, there are no data to suggest that the acute treatment of a severe headache with opiates in the ED will lead to the development of a refractory headache.

There are relatively few good trials that have evaluated the use of parenteral opiates in the treatment of acute headache. The most well-studied opiate has been meperidine (typically 75-100 mg IM), which was also the topic of a recent meta-analysis.[106] In this review, 11 trials were identified that evaluated meperidine versus DHE (4 trials, 254 patients), meperidine versus an antiemetic (4 trials, 248 patients), and meperidine versus ketorolac (3 trials, 123 patients). Although more patients who received meperidine (40 of 63) compared to ketoro-

Table 10. Cochrane Review Summary Of Percentage Of Patients With Pain Relief Or Pain-Free Using Various Formulations Of Sumatriptan[94-97]

Sumatriptan Formulation	2-hour relief (%)	2-hour relief (placebo) (%)	2 hours pain-free (%)	2 hours pain-free (placebo) (%)
6 mg SQ	79	31	59	15
100 mg PO	61	32	32	11
20 mg IN	50	32	24	10
25 mg rectal	71	30	41	17

Abbreviations: IN, intranasal; PO, by mouth; SQ, subcutaneous.

Table 11. Contraindications For Triptan Use

- Uncontrolled hypertension
- Ischemic heart disease
- Prinzmetal angina
- Cardiac arrhythmias
- Multiple risk factors for atherosclerotic vascular disease
- Primary vasculopathies
- Basilar and hemiplegic migraine
- Use of ergot in past 24 hours
- Use of MAOI or SSRI
- Use of triptan in past 24 hours

Abbreviations: MAOI, monoamine oxidase inhibitor; SSRI, selective serotonin reuptake inhibitor.

lac (30 of 60) reported headache relief, this did not achieve statistical significance (63% vs 50%, P = NS). Meperidine was less effective than DHE or antiemetics at providing headache relief. In addition, due to increased side effects and potential for abuse, many hospitals no longer carry meperidine.

A second issue that sometimes arises has to do with opiate administration and length of ED stay. The handful of studies that examined this issue found that opiate administration, in general, is associated with a longer stay in the ED.[107-109] Whether this is due to higher baseline severity of the headache, necessitating opiate administration, sedation resulting from the opiate, or ED policy preventing the early discharge of patients who receive opiates is unknown.

Current guidelines recommend opioids only for severe, refractory headaches. However, ***it is our opinion*** that patients presenting to the ED often present with headaches refractory to home therapy and require multiple medications. Further, we are not convinced that limited use of opioids in the ED leads to the development of chronic migraine states. As such, we will often use opioids early in the treatment of severe primary headaches in the ED. We are selective in using opiates for patients who have multiple visits, have unconfirmed drug allergies to nonopiate medications, or exhibit suspicious, narcotic-seeking behavior.

Steroids

Corticosteroids are thought to prevent recurrence of headache in patients with acute migraine, a phenomenon thought to occur in up to two-thirds of patients within the first 48 hours. It is believed that corticosteroids work by suppressing the inflammatory response that occurs with neurogenic inflammation from prolonged migraine headache. The corticosteroid, dexamethasone, has been used with several CNS ailments due to its superior potency, prolonged duration of action, and better CNS penetration compared to other corticosteroids. Several uncontrolled clinical trials have shown that in both the inpatient setting and outpatient clinic setting, dexamethasone is highly effective in reducing the severity of migraine headache and the rate of headache recurrence. Although initial controlled clinical trials demonstrated the same high level of efficacy, several RCTs evaluating the role of corticosteroids in acute headache have concluded that there is no benefit to their administration. These trials all showed a consistent, approximately 10% clinical benefit with dexamethasone but were inadequately powered to show a true difference.[110-117] Two recent meta-analyses pooling these trials suggest a modest and significant therapeutic benefit in reducing the risk of recurrent headache (NNT = 10).[118,119]

Treatment For Cluster Headache

Cluster headaches are often the exception in primary headache management. Acute in nature, they usually involve autonomic symptoms that make their recognition and diagnosis easier for the emergency clinician. As such, the recommendations for treatment of cluster headache are different than for other primary headache disorders.

Acute abortive therapy for cluster headaches falls into 2 groups: (1) triptans, and (2) high-flow oxygen. With regard to triptans, a recent Cochrane review examined the effect of triptans on cluster headaches. Six RCTs examining sumatriptan and zolmitriptan were analyzed. In total, 231 participants received zolmitriptan 5 mg, 223 received zolmitriptan 10 mg, 131 received sumatriptan 6 mg, 88 received sumatriptan 12 mg, and 326 received placebo. Overall, the triptans studied were better than placebo for headache relief and pain-free responses, with a NNT = 2.4 for 15-minute pain relief with sumatriptan 6 mg SQ (75% with sumatriptan and 32% with placebo), and 2.8 for 30-minute pain relief with zolmitriptan 10 mg intranasal (62% with zolmitriptan and 26% with placebo). Fewer participants needed rescue medication with triptans than with placebo, but more experienced adverse events.[120]

Oxygen therapy has been examined in 2 Class I crossover studies comparing high-flow oxygen to compressed air. In the first trial, 19 male patients aged 20 to 50 years were treated in a double-blind crossover study comparing oxygen versus air inhalation at 6 L/min via face mask for 15 minutes or less. Patients receiving oxygen experienced substantial relief compared to those receiving air.[121] In the second trial, 109 adults with cluster headache were treated with a similar protocol but using 12 L/min of oxygen via face mask for 15 minutes. Within 15 minutes of treatment, 78% of patients receiving oxygen were pain-free compared to 20% in the group receiving air ($P < 0.05$). Over 50% of patients in the air group required a rescue medication for relief, and only a quarter of patients in the oxygen group needed the same.[122] The AAN gives both oxygen and triptans Level A recommendations and recommend them as first-line therapy for cluster headaches.

Treatment Summary

With hundreds of studies comparing various medications and doses as well as different definitions, formulations, and pain scales, it can be challenging for the emergency clinician to formulate evidence-based treatment plans for the acute primary headache. While society guidelines help, they are often written from the vantage point of the specialist in clinic and may not reflect the practical nature of emergency treatment.

Studies have demonstrated that emergency clinicians underdiagnose migraines, that they underuse triptans, and that they rely too frequently on opioid

medications as primary therapy for headaches in the ED.[8,123] Keeping these factors in mind, we have devised a simple treatment algorithm for primary headaches that is evidence-based, in line with guidelines, and is easy to administer. **(See the Clinical Pathway For Treatment Of Primary Headache, page 14.)**

Patients with mild pain from their primary headache, as judged by the provider, should be treated with oral medications (NSAIDs or aspirin or aspirin/acetaminophen/caffeine). For those who have no contraindications or who have used triptans before, sumatriptan 6 mg SQ or 100 mg PO can be considered. Alternatively, IM medications such as ketorolac, phenothiazines, diphenhydramine, and opiates can be used if significant nausea or vomiting is present and IV access is difficult.

Patients who have severe pain are treated with either sumatriptan 6 mg SQ and an NSAID (for those without contraindications and who have responded in the past), or, more commonly, an IV is started and the patient is given a neuroleptic (normally prochlorperazine 10 mg with diphenhydramine 25 mg or metoclopramide 20 mg IV) along with ketorolac 15 to 30 mg IV. If that does not alleviate pain, the provider can try sumatriptan, redose the prior neuroleptic, and add an opioid. Patients in the authors' ED will receive up to 5 medications (all IV) in addition to IV fluid hydration when they present with severe pain: hydromorphone 1 mg, ketorolac 15 to 30 mg, prochlorperazine 10 mg with diphenhydramine 25 mg, and dexamethasone 10 mg. If, after 2 rounds of aggressive pain management, the patient's headache has not improved, the provider should consider alternative diagnoses and specialty consultation/hospital admission.

The following treatment algorithm is based on the theory of stratified care. Rather than administer the same medications for all primary headache patients and escalate as needed, we choose therapy based on pain severity. Those patients judged by providers to be in severe pain start with multiple IV therapies, bypassing PO and IM medications. The goal of stratified care is to quickly and safely treat pain and discharge the patient.

The Disabilities in Strategies of Care study (DISC) compared stratified versus stepwise care, randomly assigning 835 adult migraine patients.[123] Participants were divided into 3 groups: 1 group with stratified care, in which the degree of headache disability dictated the treatment strategy; and 2 groups of step care, where patients of all headache severity were treated with a single approach, with rescue medication reserved for nonresponders. The authors of this trial found that headache response at 2 hours was significantly higher and disability time lower in the stratified group compared to the step care groups.[124] These results suggest that patients have faster alleviation of pain and discharge from the ED with a stratified treatment strategy based on headache severity. While the study primarily examined aspirin, metoclopramide, and zolmitriptan, we believe the DISC trial approach can be applied to other medications, and we use this theory in our own ED.

Special Circumstances

Pediatric Patients

Evaluation of the pediatric patient with headache presents a unique set of challenges in both diagnosis and treatment. The prevalence of children with headache reaches almost 60%, with approximately 7% migraine. Before puberty, boys tend to suffer migraines more frequently than girls; however, that ratio reverses during puberty.[125,126] While the ICHD-2 classification is still valid, it can be difficult to apply in the pediatric population. Some authors have suggested classifying pediatric headaches into 1 of 4 general patterns to help clinicians distinguish primary from secondary causes of headache.[127] **(See Table 12.)**

Category 1: The new, acute headache in the pediatric patient. This is the most concerning pattern for an emergency clinician, as secondary causes must be excluded. Specific pediatric causes of headache include otitis, sinusitis, diabetes, SAH, meningitis, and encephalitis.

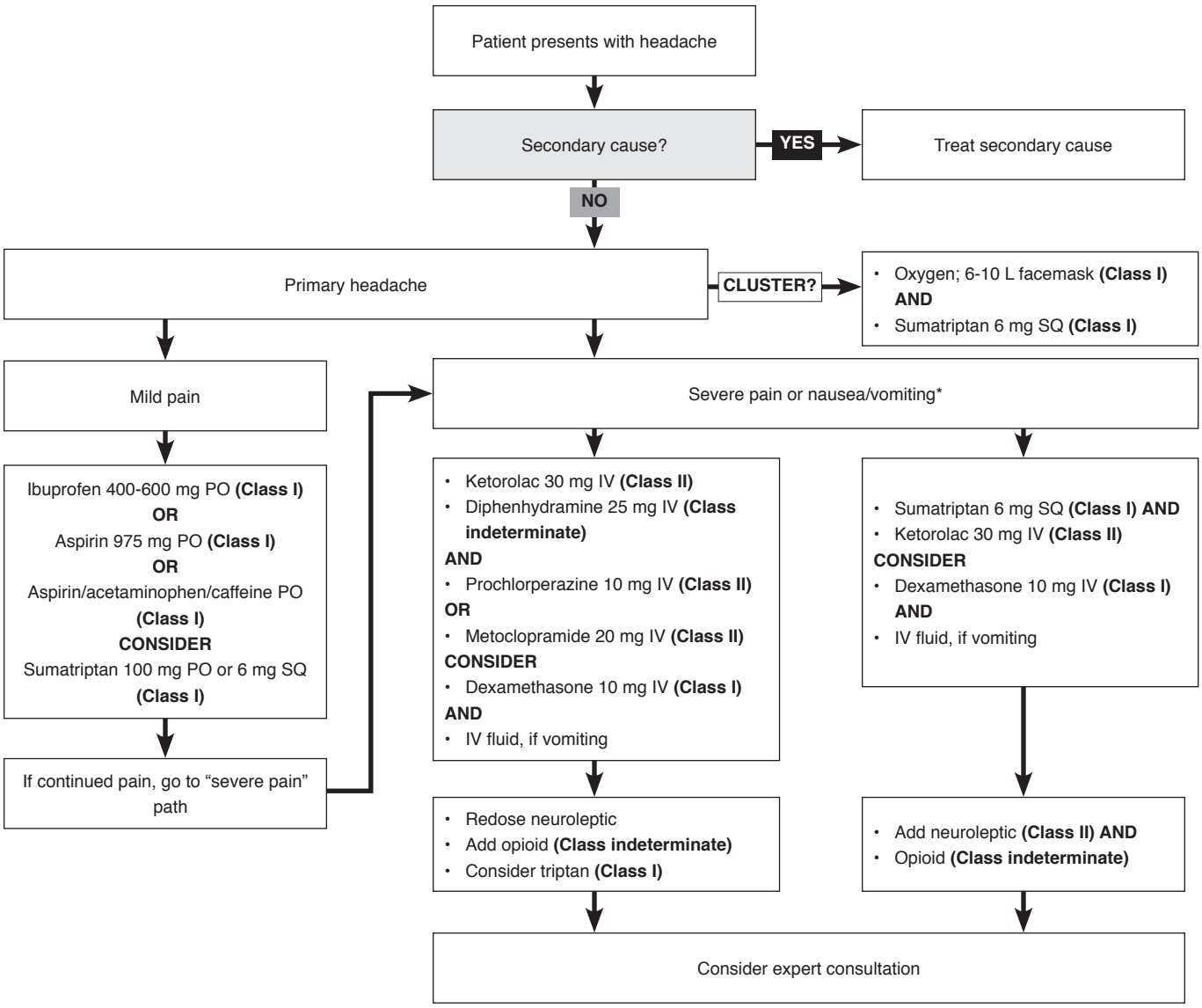
Category 2: The acute headache that has occurred many times before. A recurring headache with pain-free periods between attacks is most often a primary headache disorder, including migraine or tension headache.

Table 12. Patterns Of Childhood Headaches

Child Headache Pattern	Type	Diagnosis
Acute new headache	Concern for secondary	Meningitis, tumor AVM, SAH, CVST
Acute headache; had many times before	Usually primary	Tension or migraine
Chronic progressive daily headache, worsening symptoms	Concern for secondary	Mass, lesion, pseudotumor
Chronic daily headache, stable symptoms	Usually primary	Tension or migraine, also consider social factors

Abbreviations: AVM, arteriovenous malformation; CVST, cerebral venous sinus thrombosis; SAH, subarachnoid hemorrhage.

Clinical Pathway For Treatment Of Primary Headache



*Parallel strategies with evidence supporting either as acceptable.

Abbreviations: IV, intravenous; PO, by mouth; SQ, subcutaneous.

Class Of Evidence Definitions

Each action in the clinical pathways section of *Emergency Medicine Practice* receives a score based on the following definitions.

Class I
- Always acceptable, safe
- Definitely useful
- Proven in both efficacy and effectiveness

Level of Evidence:
- One or more large prospective studies are present (with rare exceptions)
- High-quality meta-analyses
- Study results consistently positive and compelling

Class II
- Safe, acceptable
- Probably useful

Level of Evidence:
- Generally higher levels of evidence
- Non-randomized or retrospective studies: historic, cohort, or case control studies
- Less robust RCTs
- Results consistently positive

Class III
- May be acceptable
- Possibly useful
- Considered optional or alternative treatments

Level of Evidence:
- Generally lower or intermediate levels of evidence
- Case series, animal studies, consensus panels
- Occasionally positive results

Indeterminate
- Continuing area of research
- No recommendations until further research

Level of Evidence:
- Evidence not available
- Higher studies in progress
- Results inconsistent, contradictory
- Results not compelling

Significantly modified from: The Emergency Cardiovascular Care Committees of the American Heart Association and representatives from the resuscitation councils of ILCOR: How to Develop Evidence-Based Guidelines for Emergency Cardiac Care: Quality of Evidence and Classes of Recommendations; also: Anonymous. Guidelines for cardiopulmonary resuscitation and emergency cardiac care. Emergency Cardiac Care Committee and Subcommittees, American Heart Association. Part IX. Ensuring effectiveness of community-wide emergency cardiac care. *JAMA*. 1992;268(16):2289-2295.

This clinical pathway is intended to supplement, rather than substitute for, professional judgment and may be changed depending upon a patient's individual needs. Failure to comply with this pathway does not represent a breach of the standard of care.

Category 3: The chronic daily headache, with a worsening pattern. These headaches may be worse in the morning, when lying flat, and with movement. They are often resistant to over-the-counter medications and have a worsening pattern. When confronted with progressive, worsening headaches, the emergency clinician must consider structural causes, including brain tumors and idiopathic intracranial hypertension. Although there may not be an indication for emergent CT, these patients normally need urgent follow-up with MRI or other diagnostic testing.

Category 4: The chronic daily headaches, without worsening pattern. Often, chronic daily headaches include migraines and tension-type headaches. The emergency clinician should be careful to also ask about stress at home or school, bullying, and abuse, as all can lead to frequent headaches. Often, these headaches require referral for outpatient follow-up.

As in adults, ED treatment of pediatric primary headaches can be stratified into mild headache and severe headache. For mild headache, acetaminophen and ibuprofen can be used alone or in combination and are considered safe and effective initial medications.[128-130] For the child with severe primary headache (with or without vomiting), second-line medications include IV metoclopramide and prochlorperazine.[131]

In the child over age 12 with symptoms suggestive of migraine, triptan therapy can be considered.[132-135] As with adults, opioids are considered third-line therapy, accounting for the risk of side effects and sensitization. **(See Table 13.)**

Pregnant And Postpartum Patients

For many women with primary headache disorders, pregnancy decreases the frequency and intensity of headaches. Nonetheless, for those women who present with a headache and are pregnant, special consideration must be given to specific secondary causes of headache as well as safe and effective treatment options. It is hypothesized that elevations of estrogen and progesterone have a protective effect against migraine and tension-type headaches. Ovarian hormones appear to modulate neurotransmitters in the common headache pain pathway of the trigeminal nerve. Multiple prospective and retrospective studies of migraine headaches demonstrate an improvement rate between 18% and 86%.[136-139]

Despite the theorized protective effect of pregnancy, headaches still occur. When a pregnant patient presents with a headache, she needs to be evaluated for a history of similar prior headaches. If a patient has a new severe headache or a change in the frequency, intensity, or quality of an existing headache disorder, then the provider must exclude dangerous secondary causes of headache including pre-eclampsia, venous sinus thrombus, posterior reversible encephalopathy syndrome, reversible cerebral vasoconstriction syndrome, arteriovenous malformation, ischemic or hemorrhagic stroke, and pituitary apoplexy.

Once diagnosed with a primary headache, the provider must decide on safe and effective treatment. **Table 14** lists recommended medications for primary headaches in pregnant patients with associated FDA safety categories.[140] Acetaminophen is considered safe in pregnancy and the postpartum period and is often a mainstay of treatment. NSAIDs such as ibuprofen and naproxen are safe in the first and second trimester as well as during the postpartum period; however, due to the risk of premature closure of the ductus arteriosus, NSAIDs are contraindicated in the third trimester and should be used with caution.

Table 13. Medications For Childhood Headaches

Medication	Dose	Contraindication
Mild Headache		
Ibuprofen	10 mg/kg PO	Not for less than 3 months
Acetaminophen	15 mg/kg PO	
Severe Headache		
Prochlorperazine	0.15 mg/kg IV (max 10 mg)	
Metoclopramide	0.1-0.15 mg/kg IV (max 10 mg)	
Almotriptan (FDA approved)	6.25-12.5 mg PO	Not for under 12 years
Morphine	0.1 mg/kg IV	

Abbreviations: FDA, Food and Drug Administration; IV, intravenous; PO, by mouth.

Table 14. Medications For Headache In Pregnancy, With FDA Safety Guidelines

Medication	FDA Pregnancy Category	Comments
Acetaminophen	B	Considered safe
Ibuprofen	B/D	Do not use third trimester
Metoclopramide	B	Neuroleptic of choice
Prochlorperazine	C	Not used in pregnancy
Opioids	C	
Triptans	C	Unknown risk. Avoid in pregnancy
Ergot/dihydroergotamine	X	Contraindicated
Dexamethasone, prednisone	C	

Abbreviation: FDA, Food and Drug Administration.

Opioids are another common treatment modality for headaches in pregnant patients. Hydromorphone and other opioids have a Category C rating. Short-term use can be effective in refractory headaches, but long-term use should be avoided, as it is can both precipitate rebound headaches and cause premature labor and fetal opioid withdrawal. Antiemetics, in general, are considered Category C medications during pregnancy except for metoclopramide, which is Category B, and is the antiemetic of choice for pregnant migraine patients with vomiting. Triptans are also a Category C medication. Despite registry data noting no difference in the rate of preterm labor or birth defects in women exposed to sumatriptan during pregnancy, these agents are generally avoided during pregnancy.[141-145] Ergot alkaloids are considered Category X and should never be used in pregnant patients. Ergotamine and DHE are known to cause decreased placental blood flow and are thought to affect cerebral development.

In summary, patients with primary headache disorders will commonly have improvement in headaches while pregnant. If a pregnant headache patient presents, the emergency clinician must be vigilant for new or changing symptoms that could indicate a dangerous secondary headache etiology. Once the diagnosis of primary headache has been established, common treatment includes acetaminophen, NSAIDs (if not third trimester), metoclopramide for nausea and vomiting, and opioids for refractory headaches. Triptans should generally be avoided, and ergots are contraindicated.

Controversies And Cutting Edge

Over the past 10 years, the use of CT in the ED has increased exponentially.[146] When used appropriately, CT is a valuable tool to identify dangerous causes of secondary headache; however, the indiscriminate use of CT for headache leads to both increased costs and unnecessary exposure to radiation. As a result, regulatory and payment agencies have begun to focus on evaluating appropriate CT use in the ED.

In 2011, the Centers for Medicare & Medicaid Services (CMS) proposed collecting retrospective data on the use of emergency CT imaging for patients with headaches and created criteria to determine the appropriateness of the scan, known as Outpatient Measures 15 or OP-15.[147] OP-15 uses primary diagnosis codes to determine the appropriateness of CT head, CT use for primary headache disorders largely labeled as "inappropriate." Patients with specific criteria, determined by diagnostic code **(see Table 15),** are excluded from CMS analysis. Hospital data on rates of appropriate usage of CT scan for headache would then be made available to the public. (www.hospitalcompare.hhs.gov). Further, it has been suggested that OP-15 measures could be used in the future to determine hospital reimbursement.

While the CMS proposal attempts to highlight the inappropriate use of CT in the evaluation of patients with headache, it remains unclear whether exclusion criteria for "appropriate imaging" are valid for the ED population. In addition, academic societies have expressed concern that using only diagnostic coding as inclusion/exclusion criteria does not represent the actual ED workup. A retrospective chart review by Schurr et al evaluating 769 ED patients who met guidelines by CMS for "inappropriate use of CT scan" found low reliability, validity, and accuracy when compared with the clinical chart. The study highlighted specific high-risk cases (ie, an elderly woman on anticoagulation and a man with a history of brain aneurysm) where the CT was viewed as "appropriate" given the clinical scenario; however, because of final diagnostic coding after negative imaging, they were marked as "inappropriate" by CMS standards.[148]

As previously discussed, CT is not indicated in the evaluation and diagnosis of primary headache disorders. While the CMS guidelines attempt to expose and thereby limit inappropriate imaging, concerns have been raised that, by using final diagnostic codes only, CMS criteria risk mislabeling imaging as inappropriate. If published, these data could negatively influence the management of otherwise high-risk headache patients.

Disposition

For patients suffering from primary headache disorders, disposition can be difficult. Headache relapse rates approach 30% and are higher in groups with depression, nausea and vomiting as well as among those who present in severe pain.[149] Successful discharge home depends on many factors.

The first factor for successful discharge is to set expectations. Patients should realize that they will

Table 15. CMS OP-15 Exclusion Criteria

- Lumbar puncture
- Dizziness, paresthesia
- Lack of coordination
- Subarachnoid hemorrhage
- Complicated or thunderclap headache
- Focal neurologic deficit
- Pregnancy
- Trauma
- HIV
- Tumor/mass
- Imaging studies for ED patients admitted to the hospital

Abbreviations: CMS, Centers for Medicare & Medicaid Services; ED, emergency department; OP, Outpatient Measures.

likely not be completely pain-free when they leave the ED and that their headache should continue to resolve over time. Patients should have a plan of what to do if they are at home and their headache returns. Although it remains unclear if redosing of medications prior to discharge prevents headache relapse, giving either sumatriptan PO to those who responded or naproxen as discharge medications may help alleviate recurrent headache.[150]

The second factor is to set return precautions. Patients should expect some waxing and waning in their pain, but in case the initial diagnosis of primary headache was incorrect, patients should be given return precautions for red-flag signs and symptoms as discussed earlier. **(See Table 16.)**

Finally, the emergency clinician should work to establish firm follow-up with a primary doctor. For "frequent flyer" patients, an appointment with a specialist may help initiate prophylactic therapy to manage pain and keep them from the ED.

Summary

Patients with headaches are common in the ED. The most important job as emergency clinicians is to rule out dangerous secondary causes of headache. While criteria exist to diagnose specific primary headache disorders, they do not perform well in the emergency setting and carry the risk of mislabeling a patient with a chronic headache disorder. Once the diagnosis of primary headache has been established, the goal of the emergency clinician is to provide safe and effective medication for pain. While the literature focuses on specific migraine therapy, much of the research applies to all types of primary headache.

We recommend a stratified treatment plan for primary headaches, with mild headaches receiving oral therapy and severe headaches either a combination of IV medications or sumatriptan SQ with other medications. Opioids should be reserved for combination or second-line therapy. Steroids may help prevent headache recurrence in 1 in 10 people. With regards to disposition, patients must be given reasonable expectations for pain management, strict return precautions, and appropriate follow-up. Headaches recur in one-third of patients, and patients must feel empowered to control their headaches or risk return to the ED. Naproxen or sumatriptan may help control relapses.

Table 16. Sample Discharge Instructions

You were seen in the Emergency Department for a HEADACHE.

The cause of your headache is not known. Our evaluation has not revealed a dangerous cause of your headache; however, you should schedule a follow-up appointment with your doctor as soon as possible.

Additionally, you should return to the Emergency Department or seek further care if you have any of the following:

- Worsening or changing headache
- Fever
- Vomiting and unable to drink fluids
- Trouble walking
- Change in vision, speech, weakness
- Anything else that concerns you

Cost-Effective Strategies For Primary Headache

1. Patients suffering from a primary headache disorder require neither laboratory tests nor imaging. The diagnosis of primary headache is a clinical diagnosis based on history and physical examination.
2. For patients with mild to moderate primary headache pain, the physician can use sumatriptan 6 mg SQ with an oral NSAID to provide rapid and effective pain relief without placing an IV.
   Risk management caveat: Be aware of contraindications to triptan use. Patients should be told of common side effects of triptans, including chest pressure.
3. Dexamethasone may help prevent relapse in 1 of every 10 headache patients. For patients who have a headache relapse, providing a prescription for naproxen or sumatriptan (when indicated) may help manage recurrent headaches.
   Risk management caveat: Patients should be given strict return precautions. As emergency clinicians, we may occasionally misdiagnose patients with primary headache disorders; therefore, if headaches are worsening, changing, or involve other symptoms, patients should return for further evaluation.
4. Use a multimodal, stratified treatment approach for patients with primary headache. It is likely that giving a combination of medications to treat pain will decrease length of stay compared to giving these agents in a stepwise fashion.
   Risk management caveat: Confirm in your mind that this is a primary headache before embarking on this approach.
5. High-flow oxygen and sumatriptan SQ are highly effective for cluster headaches. Rather than placing an IV and attempting to treat the patient with multiple medications, first try high-flow oxygen and sumatriptan 6 mg SQ.
6. Set a time limit in your mind on when to re-evaluate your patient. Often, patients are significantly better and can be discharged within the first hour following treatment.

Risk Management Pitfalls For Primary Headache

1. **"She has a history of migraines; I assumed this headache was a migraine as well."**
   Emergency clinicians must be careful not to anchor on prior headache diagnoses. The primary goal is to rule out dangerous causes of headaches, even in those who have a history of benign headaches. Patients with migraines or tension headaches can still suffer from meningitis, SAH, or other causes of serious or secondary headaches.

2. **"I gave him migraine-specific medicine, and his headache got better. I thought that meant his headache had to be a migraine."**
   Given the common pain pathway of headaches, a patient's response to medication should not be used to aid in diagnosis of the headache disorder. Many case reports and case series have demonstrated that SAH and pain from structural brain lesions respond to triptans, neuroleptics, and ergots.[27-30]

3. **"I thought the patient had a new tension-type headache. I forgot to ask about HIV status."**
   While some red flags—such as fever and focal neurological deficits—are apparent on examination, it is the emergency clinician's job to evaluate all red-flag signs and symptoms. Specifically, history of HIV or cancer should lower the threshold for diagnostic imaging, given that secondary headaches can present with apparently benign symptoms.

4. **"I try to provide a specific diagnosis for every primary headache patient according to ICHD-2 guidelines."**
   Studies have demonstrated that it is difficult to assign a specific headache diagnosis in the emergency setting. Primary headache disorders have variable presentations and often require multiple similar headaches for diagnosis by ICHD-2 guidelines. Further, an incorrect diagnosis can mislabel a patient with a chronic headache disorder, leading to anchoring bias by future physicians.[151]

5. **"I only use opioids to treat primary headaches."**
   Repeated opioid use may precipitate chronic migraines and the phenomenon of the "frequent flyer" patient, who becomes dependent on increasing doses of opioids for headache treatment. With many other appropriate drug choices, we do not recommend opioids as monotherapy.[152] If opioids are needed, we recommend them in combination with other medications and only in the acute setting.

6. **"I never refer my primary headache patients for specific outpatient follow-up."**
   Specialist consultants, whether inhospital or outpatient, can develop specific plans for the prevention of primary headaches as well as home treatment strategies to avoid ED visits. Primary headache patients with multiple visits to the ED should have specific and appropriate outpatient follow-up.

7. **"I try to make the patient pain-free prior to discharge."**
   It is difficult to alleviate all pain in many patients suffering from primary headache disorders.[153] We recommend talking with patients and setting appropriate expectations for controlling and managing pain, and working to provide appropriate follow-up and specific return precautions.

8. **"I forgot to tell the patient the side effect of the medication I gave."**
   Many primary headache medications, although benign, can have uncomfortable side effects, including chest tightness and tingling for triptans and akathisia for neuroleptics. It is important to inform patients of these common side effects before giving medications. If not, the experience of the side effect may only serve to worsen their primary headache.

9. **"I screen with neuroimaging all first-time patients that I believe have a primary headache disorder."**
   Neuroimaging is not indicated for patients with primary headache disorders. It is costly, is time-consuming, and carries risks of radiation. Once dangerous secondary causes of headache are excluded by history and physical examination, laboratory tests and neuroimaging are not indicated.[34]

10. **"If my patient bounces back to the ED with recurrent pain, then I have done something wrong."**
    Patients with primary headaches often have recurrence of their pain. In fact, studies have been unable to discover factors that reliably predict which ED headache patients will have recurrence of pain. This should not be seen as a medical error, but rather, a natural progression of the disease. It does, however, emphasize the importance of appropriate discharge instructions to prepare patients if their headache returns.[149]

Children and pregnant women are specialized groups that require additional considerations. Treatments depend on the severity of the headache as well as the safety of the drug used; specialty consult is advised to help facilitate diagnosis, follow-up, and management for children or pregnant women with severe headaches.

Case Conclusions

Given the history provided by the parents, your 10-year-old patient appeared to have a constant, unchanging, daily headache. You recalled that these headaches are often tension-type or migraine and may involve social factors. You asked more about the headaches and found that they only occur on school days. The child admitted to being teased at school, and he said he did not want to go back. After a normal physical exam, you reassured his parents, asked social work to discuss resources, and referred the child back to his pediatrician without invasive testing.

Your second patient was more concerning. Although she had a known primary headache disorder, she described several red-flag features, including nuchal rigidity and pain worst at onset. You recalled a popular headache review paper that highlighted the danger of assuming all headaches in patients with known migraines are benign. You decided to order neuroimaging and, while waiting, moved on to your third patient.

Your third patient – the "frequent flyer" – described her headache exactly the same as the last 7 ED visits. Her examination was otherwise benign. Knowing her history of migraines, you decided to treat with ibuprofen and sumatriptan SQ, which, after 20 minutes, controlled her headache. You added dexamethasone, gave specific follow-up instructions, and gave a referral to a specialist to manage prophylactic medication. You retired back to the charting room.

As you were printing out the discharge paperwork for your first and third patients, you examined the CT head from your second patient and were surprised to find blood in the basal cisterns. You took a deep breath – thankfully, you did not just refill her prescription.

References

Evidence-based medicine requires a critical appraisal of the literature based upon study methodology and number of subjects. Not all references are equally robust. The findings of a large, prospective, randomized, and blinded trial should carry more weight than a case report.

To help the reader judge the strength of each reference, pertinent information about the study will be included in bold type following the reference, where available. In addition, the most informative references cited in this paper, as determined by the authors, are noted by an asterisk (*) next to the number of the reference.

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CME Questions

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1. What is the definition of a secondary headache disorder?
   a. A disorder in which the headache itself is the disease entity
   b. A disorder in which the headache is a symptom attributed to another underlying disorder
   c. Tension-type
   d. Migraine

2. What is the most common type of primary headache disorder?
   a. Tension-type
   b. Migraines
   c. Cluster
   d. Trigeminal autonomic cephalalgias

3. All of the following are characteristic of tension-type headaches EXCEPT:
   a. Bilateral location
   b. Nonpulsating quality of pain
   c. Not aggravated by physical activity
   d. Parasympathetic autonomic features

4. In the United States population, migraine headaches have a prevalence of approximately:
   a. 40%
   b. 30%
   c. 12%
   d. 0.1%

5. **What type of headache typically presents with the symptoms of severe, frequent headaches, injected sclera, lacrimation, and rhinorrhea?**
   a. Tension-type
   b. Migraines
   c. Cluster
   d. Secondary headache disorder

6. **Pain sensed in headaches originates from the brain parenchyma.**
   a. True
   b. False

7. **Patients' description of their headache as the "worst headache" of their life:**
   a. Is neither sensitive nor specific to guide treatment decisions alone
   b. Should automatically initiate a thorough workup including a head CT and lumbar puncture
   c. Is not helpful historical information to the emergency clinician
   d. B and C

8. **Which of the following medications is most effective to treat cluster headaches?**
   a. NSAIDs
   b. Ergots
   c. Neuroleptics
   d. Oxygen

9. **Which of the following statements regarding pregnant patients and headaches is TRUE:**
   a. For primary headache disorders, pregnancy increases the frequency and intensity of headaches.
   b. It is hypothesized that elevations of estrogen and progesterone have a protective effect against migraine and tension-type headaches.
   c. Due to the theorized protective effect of pregnancy, headaches never occur.
   d. Metoclopramide is contraindicated in pregnancy.

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