Headaches in Primary Care

Cathy L Bays, PhD, APRN, AGNP-C
Neurology Nurse Practitioner
University of Louisville

Acknowledgments
Michael K. Sowell, MD, FAHS
Professor of Neurology, Associate in Pediatrics
Director, UofL Comprehensive Headache Program

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Objectives

1. Describe common primary headache syndromes seen in primary care.
2. Describe diagnostic criteria for common types of headaches.
3. Identify treatment modalities for treating headaches in the primary care setting. Dosage, treatment and side effects for RX and supplements will be discussed.

Cerebral Pain Sensitive Structures

- Portions of the Meninges
  - Basal Dura Mater
  - Venous Sinuses and tributaries
- Neural Structures
  - Trigeminal Cranial Nerve (CN V)
  - Glossopharyngeal Nerve (CN IX)
  - Vagus Nerve (CN X)
- Scalp and superficial Structures
- Vascular Structures
  - Dural Arteries
  - Carotid / Vertebral Arteries
  - Proximal portions of the cerebral vessels
Evaluation of the Patient with Headache

► Patient’s name
► Date of initial visit
► Headache types:
► Headache onset:
► Location:
► Frequency:
► Severity:
► Exertional aspects to headache:
► Duration:
► Aura:
► Premonitory symptoms:
► Associated symptoms:
► Sleep pattern:
► Family History:

► Menses (if applicable):
► Seasonal:
► Tests:
► Headache medications:
► Other medications:
► Past surgical history:
► Past medical history:
► Alcohol use:
► Tobacco use:
► Allergies:
► Neurological examination:
► Physical examination:

International Classification of Headache Disorders
ICHD-3 Beta Version (2013)

Primary
1. Migraine
2. Tension-type
3. Trigeminal Autonomic Cephalalgias
4. Other primary headache disorders

Secondary
5. HAT trauma or injury to the head and/or neck
6. HAT cranial or cervical vascular disorder
7. HAT non-vascular intracranial disorder
8. HAT a substance or its withdrawal
9. HAT infection
10. HAT disorder of homeostasis
11. Headache of facial pain attributed to disorder of the cranium, neck, eyes, ears, nose, sinuses, teeth, mouth or other facial or cervical structures
12. HAT psychiatric disorder
13. Painful cranial neuropathies and other facial pains
14. Other headache disorders

Secondary Headache
Attention to symptoms of increased intracranial pressure or other ominous neurologic symptoms/signs—“red flags”

► “Worst headache of my life”
► Recent or sudden (thunderclap) onset, increasing in severity & frequency
► Headache awakens the patient at night or always occurs in the am
► Progressive lethargy
► Personality change
► Nausea, vomiting (esp. projectile)
► Visual difficulties
► Change in headache pattern
  ▪ Progressive headache with loss of headache-free periods
  ▪ Change in frequency or severity
► Neurologic symptoms or abnormal physical findings
  ▪ Cognitive changes
  ▪ Asymmetry on examination
► SNOOP4

Chronic Progressive Headache Syndrome: Key Points

► Chronic progressive headache strongly suggestive of organic pathology
► No invariable brain tumor headache profile
► Key symptoms
  ▪ Nocturnal or morning headache
  ▪ Aggravation by Valsalva maneuver or exertion
  ▪ Seizures
► Key signs
  ▪ Papilledema
  ▪ Cranial nerve palsies
  ▪ Ataxia
  ▪ Focal signs, motor or sensory
► Look for neurocutaneous syndromes (phakomatoses)
► Examine the discs!
► Always check the head circumference in children.
7.1 Pseudotumor Cerebri (or IIH): Diagnostic Criteria

A. Any headache fulfilling criterion C
B. Idiopathic intracranial hypertension (IIH) has been diagnosed, with CSF pressure >250mm CSF (measured by lumbar puncture AFTER imaging performed in the lateral decubitus position, without sedative medications, or by epidural or intraventricular monitoring)
C. Evidence of causation demonstrated by at least two of the following:
   1. headache has developed in temporal relation to IIH, or led to its discovery
   2. headache is relieved by reducing intracranial hypertension
   3. headache is aggravated in temporal relation to increase in intracranial pressure
D. Not better accounted for by another ICHD-3 diagnosis.

ICHD-3 beta, Cephalalgia, 33(9) 629–808, International Headache Society 2013

Most common symptoms:
- headache (94%)
- transient visual obscurations or blurring (68%)
- pulse synchronous tinnitus or “wooshing noise” in the ear (58%)
- pain behind the eye (44%)
- double vision (38%)
- visual loss (30%)
- pain with eye movement (22%)

Diagnostic Tests:
- MRI w/o and with, MRV
- Labs: TSH, am cortisol, CBC, CMP, Vitamin D
- LP fluoroscopy guided

Treatment:
- acetazolamide
- Migraine abortive and preventive

Criteria for Neuroimaging in Headache Disorders

►Abnormal neurological examination, or unexplained neurologic findings
►Headache with worrisome symptoms (e.g. awakening from sleep, worsening w/Valsalva maneuver) or signs
►New headache in the older population
►With respect to migraine-atypical headache features or failure to meet full criteria for migraine

Common Clinical Indications for Lumbar Puncture in Headache Disorders

- Unexplained fever (typically AFTER neuroimaging with either CT or MRI w & w/o contrast)
- Suspected Pseudotumor Cerebri (Idiopathic Intracranial Hypertension)
- Suspected subarachnoid hemorrhage (typically in the emergency department)
- Fever of undetermined origin in a child
Direct and Indirect Costs of Migraine Headaches

- Direct Costs (est. $1 billion)
  - Medical care (e.g. ER visits, Meds, Clinical consultations, inpatient stays)
- Indirect Costs (est. $13 billion)
  - Absenteeism, reduced work productivity
  - Disruption of activity in other roles (e.g. child care, family activities)

It is estimated that migraineurs cost employers 14 billion dollars annually in direct and indirect costs.

Migraine is Associated with Other Medical Disorders (Comorbidity)

- Neurologic Disorders
  - Stroke (esp. in women under 45)
  - Epilepsy
  - Positional vertigo
  - Essential tremor
- Medical Disorders
  - Raynaud’s syndrome
  - Irritable bowel syndrome
  - Intestinal cystitis
  - Asthma
  - Hyper- or hypotension
  - Mitral valve prolapse
  - Angina/myocardial infarction
- Psychiatric Disorders
  - Depression
  - Anxiety disorders
  - Panic disorder
  - Bipolar illness
  - Phobias

Understanding of Migraine Pathophysiology has Evolved

- Activation of the trigeminovascular system
- Cortical spreading depression
- Neurogenic inflammation
- Central sensitization

Trigeminovascular Theory of Migraine Pathogenesis

Pathophysiology of Migraines

- Cortical spreading depression of Leao

Nerve storms (Living, 1873)
Serotonin (Sicuteri, 1959)
Neurogenic inflammation (Moskowitz, 1984)
Sensitization and allodynia (Burstein, 1996)
Vasodilation (Willis, 1683; Graham and Wolff, 1938)
CSD (Leão, 1944)
Oligemia (Olson and Lauritzen, 1981-82)
CGRP (Goadsby and Edvinsson, 1990)
PACAP (Schytz, 2009)
Precipitating Psychic and Physical Factors

1. Emotional upset/family or friends
2. Emotional upset/occupation
3. Business/reversal
4. Business/success
5. Vacation days
6. Weekends
7. Strenuous exercise
8. Strenuous labor
9. High-altitude location
10. Anticipation anxiety
11. Crisis/serious
12. Postcrisis period
13. New job/position
14. New move
15. Menstrual days
16. Physical illness
17. Oversleeping
18. Weather
19. Fasting
20. Missing a meal
21. Other

Food and Drink Trigger Factors (In Excess)

A. Ripened cheese (pizza)
B. Herring
C. Chocolate
D. Vinegar
E. Fermented foods (pickled or marinated, sour cream/yogurt)
F. Freshly baked yeast products
G. Nuts (peanut butter)
H. Monosodium glutamate (MSG; asian food)
I. Pods of broad beans
J. Onions
K. Canned figs
L. Citrus food
M. Bananas
N. Pork
O. Caffeinated beverage
P. Avocado
Q. Fermented sausage (cured cold cuts)
R. Chicken liver
S. Wine
T. Alcohol
U. Beer
V. Skipping meals

Evolution of a Migraine Attack

Premonitory and Postdromal Symptoms

Premonitory
- Excitatory: Irritability, Elation, Physical hyperactivity, Yawning, Food craving, Photophobia/phonophobia, Increased bowel and/or bladder activity
- Inhibitory: Poor concentration, Mental/physical slowing, Word finding difficulty, Weakness/fatigue, Chill, anorexia, constipation, abdominal bloating

Postdromal
- Poor concentration
- Mental/physical slowing “fog”
- Weakness/fatigue
- Dizziness
- Photophobia

Migraine classification

1.1 Migraine without aura
1.2 Migraine with aura
1.3 Chronic migraine
1.4 Complications of migraine
1.5 Probable migraine
1.6 Episodic syndromes that may be associated with migraine

Migraine without Aura

Diagnostic Criteria:

A. At least five attacks fulfilling criteria B–D
B. Headache attacks lasting 4-72 hours (untreated or unsuccessfully treated)
C. Headache has at least two of the following four characteristics:
   1. unilateral location
   2. pulsating quality
   3. moderate or severe pain intensity
   4. aggravation by or causing avoidance of routine physical activity (e.g. walking or climbing stairs)
D. During headache at least one of the following:
   1. nausea and/or vomiting
   2. photophobia and phonophobia
E. Not better accounted for by another ICHD-3 diagnosis.
Migraine with Aura

Diagnostic criteria:
A. At least two attacks fulfilling criteria B and C
B. Aura consisting of visual, sensory, and/or speech and/or language
   BUT NO motor, brainstem or retinal
C. At least two of the following four characteristics:
   1. at least one aura symptom spreads gradually over 5 minutes,
      and/or two or more symptoms occur in succession
   2. each individual aura symptom lasts 5-60 minutes
   3. at least one aura symptom is unilateral
   4. the aura is accompanied, or followed within 60 minutes, by headache
D. Not better accounted for by another ICHD-3 diagnosis, and transient ischaemic
   attack has been excluded.

Modified from: Cephalalgia 33(9) 629–808, © International Headache Society 2013

Migraine Treatment

- Acute/Abortive
- Preventive
  - Oral agents
  - Botox
  - CGRP mAbs
  - Neuromodulation

Migraine may intensify or remit

- Risk factors for progression from EM to CM include:
  1.5 - Nonmodifiable factors: age, gender
  - Modifiable: headache frequency, acute medication overuse, stressful life events
  - Certain comorbidities: anxiety, depression, obesity, apnea, head injury

Acute (Abortive) Treatment

Options in Migraine
- Triptans (relatively "migraine-specific")
  - e.g. sumatriptan, zolmitriptan, rizatriptan, almotriptan, eletriptan
  - LA: naratriptan, frovatriptan
  - Contraindications: uncontrolled HTN, chest pain, hemiplegic or basilar
    migraine
- Antiemetics/antinauseants
  - e.g. promethazine, prochlorperazine, ondansetron
- AEDs
  - e.g. levetiracetam
- NSAIDs
  - e.g. naproxen, ibuprofen, aspirin, diclofenac potassium
- Ergot alkaloids
  - e.g. dihydroergotamine, methylergonovine
- Combination analgesics
  - e.g. aspirin, acetaminophen, butalbital and/or caffeine

Factors to consider when deciding on use of Fioricet for acute (abortive) therapy with
migraines:
- FDA approved November 9, 1984 for for
  Tension Type headaches
- Combination of butalbital (Phrenilin), acetaminophen (Tylenol) and caffeine
- Chronic use can lead to rebound headaches
- Consider using: Probably NO place considering the variety of abortives available today
Challenges Remain in the Use of Preventive Therapy

40% of migraine patients could benefit from preventive therapy

80% of patients who initiated a trial of oral migraine preventive medicines were no longer taking preventive treatment

<15% currently use it

12 months later

Onabotulinum A (Botox)

- PREEMPT
- Criteria:
  - ≥ 15 HA days/month, at least 8 being migraines
  - Each lasting ≥ 4 hours
  - ≥ 18 years old
  - Failed at least 2 preventive categories
- Procedure:
  - 31 injections
  - Every 12 weeks

CGRP Plays a Primary Role in Migraine and Is an Important Therapeutic Target

CGRP:
- Is a potent vasodilator, mast cell degranulator, and mediator of inflammation
- Modulates the transmission of pain signals from the meninges to the CNS
- Is released when the trigeminal ganglion is stimulated
- Administration triggers headaches in patients with a history of migraine
- Levels are significantly, persistently elevated in patients with chronic migraine
- Release is suppressed by anti-migraine agents such as triptans

Mechanism of Action of CGRP mAbs

Migraine Preventive (Prophylaxis) Agents

- Anticonvulsants
  - Topiramate, zonisamide, divalproex sodium, gabapentin
- Antidepressants (e.g. specific to sx, in conjunction with psychiatry)
  - amitriptyline, venlafaxine, escitalopram, citalopram, duloxetine, etc...
- Antihypertensives
  - Propranolol, timolol, metoprolol; candesartan, lisinopril; verapamil, nicardipine
- Complementary and alternative medications
  - Coenzyme Q 10, riboflavin, magnesium oxide, melatonin, feverfew, butterbur
The 3 mABs to CGRP for Migraine Prevention

- All data announced to date for Episodic and Chronic Migraines have shown a reduction in mean monthly migraine days (MMDs) with a magnitude of 1-3 days/month drop over placebo, similar to the registration studies for onabotulinumtoxinA.
- All mABs to CGRP approved to date appear to be safe and effective in migraine prevention.
- We are beginning to see longer term data with safety & efficacy evidence.
- Elimination is by the reticuloendothelial system and all appear to have few to no drug interactions and few to no contraindications.
- There are subtle differences between the mABs to CGRP involving dosing interval (monthly vs quarterly), route of administration (SQ vs IV) and site of action (receptor vs ligand).
- There may be logistical differences on a practical basis regarding availability on formularies, cost, support systems, loyalty programs, etc.

Neuromodulation

- Supraorbital stimulation (tSNS, e-TNS) holds promise for migraine prevention and limited evidence suggests benefit for acute relief of migraine
- stMS was safe and effective (now FDA approved) for acute treatment of migraine with aura. stMS (ESPOUSE) may be safe and effective for migraine prevention (not FDA approved)
- rTMS at 10 Hz was found to be safe and effective for prevention of migraine (not FDA approved)
- nVNS may be effective:
  - as acute treatment for HFEM or CM and may help reduce medication overuse or medication associated adverse events
  - for acute treatment of episodic migraine (PRESTO)

Daith Piercing

Tension-Type and Cluster Headaches

2. Tension-type headache (TTH)

2.1 Infrequent episodic tension-type headache
2.2 Frequent episodic tension-type headache
2.3 Chronic tension-type headache
2.4 Probable tension-type headache

Tension-type headache (TTH)

- The most common headache disorder among the general population
- May be episodic or chronic
- Least distinct of the headache disorders
- Least well-studied of the headache disorders
- Bland, dull, bifrontal, pressing, tightening pain
Infrequent episodic TTH

A. At least 10 episodes of headache occurring on <1 d/mo (<12 d/y) and fulfilling criteria B-D
B. Lasting from 30 min to 7 d
C. ≥2 of the following 4 characteristics:
   1. bilateral location
   2. pressing or tightening (non-pulsating) quality
   3. mild or moderate intensity
   4. not aggravated by routine physical activity
D. Both of the following:
   1. no nausea or vomiting
   2. no more than one of photophobia or phonophobia
E. Not better accounted for by another ICHD-3 diagnosis

TTH Treatment

• Medication: TCAs, AEDs, Tizanidine
• Behavioral Therapies: CBT, Relaxation, Biofeedback
• Trigger Point Injections, Acupuncture, PT

3. Trigeminal autonomic cephalgias (TACs)

3.1 Cluster headache

3.2 Paroxysmal hemicrania

3.3 Short-lasting unilateral neuralgiform headache attacks

3.4 Hemicrania continua

3.5 Probable trigeminal autonomic cephalgia

Cluster Headache: Features

• Relatively Uncommon
• More prevalent in men than women (6:1)
• Predominantly afflicts men in their 20s and 30s
• Genetic predisposition?
• Attacks tend to occur at night
• Perhaps association with smoking

Cluster Headache: Treatment

• Acute Treatment
  – 100% O₂ via face mask at 7 liters per min
  – Subcutaneous sumatriptan
  – Intranasal zolmitriptan
• Treatment to induce remission
  – Short burst of prednisone
• Prevention
  – Verapamil
  – Valproic acid
  – Lithium carbonate
• Neuromodulation:
  – Occipital nerve stimulation appears to show benefit in chronic drug-resistant cluster headache. In addition, ONS may have benefit in chronic migraine
  – nVNS is safe and effective for acute treatment of cluster (PREVA), with perhaps greater benefit for episodic cluster patients (ACT2)
Pregnancy

- Regular meals and exercise
- Hydration
- Sleep
- Relaxation-Dawn Buse
  www.dawnbuse.com
- Tylenol, Antiemetic-OB/GYN or Pediatrician

Comprehensive HA Program

- Medications
  - Preventive
  - Abortive
- Lifestyle
  - HA Diary-Migraine Buddy, Headache Lite
  - Caffeine
  - Sleep
- Emotional
  - Stress
  - Depression
  - Counseling
- Education

Choosing Wisely

American Academy of Neurology (2013)
Five Things Physicians and Patients Should Question
1. Don't perform electroencephalography (EEG) for headaches.
2. Don't perform imaging of the carotid arteries for simple syncope without other neurologic symptoms.
3. Don't use opioid or butalbital treatment for migraine except as a last resort.
   Opioids and butalbital treatment for migraine should be avoided because more effective, migraine-specific treatments are available.
   Frequent use of opioid and butalbital treatment can worsen headaches. Opioids should be reserved for those with medical conditions precluding the use of migraine-specific treatments or for those who fail these treatments.
4. Don't prescribe interferon-beta or glatiramer acetate to patients with disability from progressive non-relapsing forms of multiple sclerosis.
5. Don't recommend CEA for asymptomatic carotid stenosis unless the complication rate is low (<3%).

http://www.choosingwisely.org/doctor-patient-lists/american-academy-of-neurology/

Summary Points:
Primary Headache Disorders

- Primary Headache Syndromes are diagnosed by defining the individual’s attacks and applying them to established definitions.
- The majority of headaches seen in primary care will be one of the primary headache disorders.
- If care is taken to identify “red flags”, then the chances of missing a secondary headache are greatly diminished.

References
