10:45 – 11:45 am

Migraine Headaches: Tools for Successful Management

SPEAKER
M. Susan Burke, MD, FACP

Presenter Disclosure Information

The following relationships exist related to this presentation:

- M. Susan Burke, MD, FACP: Speakers Bureau for Merck & Co., Inc.

Off-Label/Investigational Discussion

- In accordance with pmiCME policy, faculty have been asked to disclose discussion of unlabeled or unapproved use(s) of drugs or devices during the course of their presentations.

Learning Objectives

- Improve the identification of migraines in the patient with recurring HA and disability
- Apply the latest evidence-based recommendations for preventive and abortive migraine treatment
- Recommend complementary and alternative therapies when indicated

Rita, a 31-year-old mother

- Asks for help with her sinus headaches. She has been getting them for several years but they are occurring almost daily now
- Predominantly frontal and maxillary in location; not throbbing
- Takes acetaminophen almost daily, along with pseudoephedrine preparations and occasional loratadine when she has watery eyes and nasal congestion

What else do you need to know?

Headache Screening: Traditional History Method

Timing/Frequency
– First onset/duration/time of day/ relationship to menses

Exacerbating factors/triggers
– Activity, cough, neck position, foods, alcohol, sleep, etc.

Location
– Variable, fixed site, hemicranial

Intensity
– Severity, disability

Nature
– Pulsatile, “ice pick,” steadily increasing

Associated symptoms
– Visual
– Motor
– Sensory
– GI
– Nasal

Diagnosis and Treatment of Headache. Bloomington, MN: Institute for Clinical Systems Improvement (ICSI); 2009

Headache Screening: Standard Examination

- Observe the patient walking
- Assess symmetry of CN, motor, sensory, coordination, DTRs
- Observe patient's body language (eye contact, mood)
- Palpate head, arteries, trigger points
- Examine neck for stiffness and ROM
- Perform fundoscopic exam
- Examine oral cavity/TMJ

Diagnosis and Treatment of Headache. Bloomington, MN: Institute for Clinical Systems Improvement (ICSI); 2009.

Red Flags and SSNOOP

- Systemic symptoms: fever, weight loss
- Secondary risk factors: HIV, cancer
- Neurologic symptoms or signs
- Onset: new, sudden, abrupt, or split-second
- Older: especially > 40 years
- Pattern change:
  - Progressive HA with loss of HA-free periods
  - HA changes type or is unclassifiable

Diagnostic testing indicated if any red flags are present

Dodick D. *Adv Stud Med*. 2003;3:87-92.

Green Flags and Comfort Signs

- Stable pattern > 6 mo
- Long-standing HA history
- Family history of similar HA
- Normal exams
- Consistently triggered by
  - Hormonal cycle
  - Specific sensory input
  - Weather changes

Diagnostic testing not indicated if only green flags present

Diagnostic Tests

CT or MRI? With or without contrast?

- **Yield minimal without neurologic signs: < 1% identify cause for HA**
- MRI: greater detail, more false positives
- MRI for posterior fossa disease
- MRI + MRA for suspected aneurysm/other vascular lesions
- CT without contrast to R/O subarachnoid hemorrhage

- Weigh radiation exposure with CT, renal contrast concerns with CT and MRI vs. potential yield of study

Ropper A, Brown R, eds. *Adams and Victor's Principles of Neurology*. Eighth ed. New York, NY: McGraw-Hill; 2005:16-21. Avitzur O. *Neurology Today*. 2013;13(4):22–24.

Sinus Headache = Migraine With Sinus Symptoms

Summit[1]
Self-Diagnosis Sinus Study
2971 with self-diagnosed recurrent sinus headache

SAMS[2]
Sinus Allergy & Migraine Study
100 with self-diagnosed recurrent sinus headache

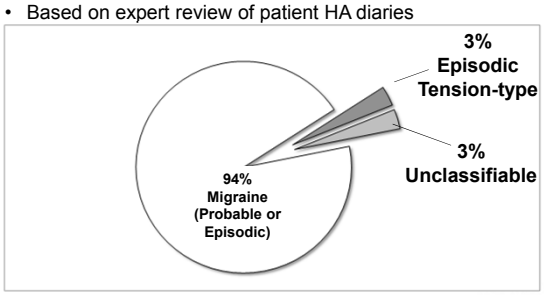
86%-88% with self-diagnosis of sinus headache actually have ICHD* migraine or probable migraine headache

***International Conference Headache Disorders/International Headache Classification from International Headache Society (ICS)[3]**

1. Schreiber CP, et al. *Arch Intern Med*. 2004;164(16):1769-1772.
2. Eross E, et al. *Headache*. 2007;47(2):213-224.
3. International Headache Society. IHS Classification ICHD-II. http://ihs-classification.org/en/02_klassifikation/01_inhalt

HA Prevalence in Primary Care

- Prevalence of all HAs that prompt patients to see their PCP
- Based on expert review of patient HA diaries



Adapted from Tepper SJ, et al. *Headache*. 2004;44(9):856-864.

Recurring moderate to severe headache is migraine until proven otherwise

Migraine Recognition by ICHD Criteria

Migraine without Aura (1.1)

- At least 5 attacks with:
- At least 2 of the following:
  - Unilateral
  - Pulsating
  - Moderate to severe pain
  - Aggravated by or avoidance of routine physical activity
- At least 1 of the following
  - Nausea and/or vomiting
  - Photo and phonophobia
- No organic disease

Migraine with Aura (1.2.1-6)

- At least 2 attacks with:
- At least 1 fully reversible symptom without motor :
  - Visual + and/or -
  - Sensory + and/or -
  - Dysphasic speech
- At least 2 of the following:
  - At least one aura symptom develops gradually over ≥5 min or different symptoms occur in succession over ≥5 min
  - Each symptom lasts ≥5 and ≤60 min
- 1.1 begins with aura or in ≤60 min
- No organic disease

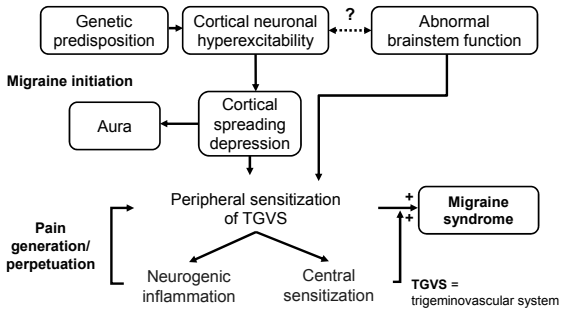
ICHD = International Classification of Headache Disorders.
Cephalalgia. 2004;8(suppl 1):S24-26.

International Headache Society Criteria for Chronic Migraine

A. HA ≥15 days/mo for ≥ 3 months
B. Occurring in those with ≥ five attacks c/w migraine w/o aura
C. On ≥8 days per month for ≥ 3 months HA fulfilled C1 and/or C2:
   1) Has at least two:
      a) unilateral location
      b) pulsating quality
      c) moderate or severe pain intensity
      d) aggravated by/causing to avoid routine physical activities
      And at least one:
      a) nausea and/or vomiting
      b) photophobia and phonophobia
   2) Treated and relieved by triptan(s) or ergot before expected development of C1 above
D. No medication overuse and not attributed to another disorder

http://ihs-classification.org/en/02_klassifikation/05_anhang/01.05.01_anhang.html. Accessed April 22. 2013.

Migraine Pathophysiology: Proposed Mechanisms



Adapted courtesy of Pietrobon D. *Neuroscientist.* 2005;11:373-386.

Understanding the Patient With Migraine

Commonly reported symptoms at various phases of migraine

Prodrome

Fatigue
Cognitive difficulty
Heightened sensory awareness
Muscle pain
Food craving
Fluid retention
Mood changes
Anorexia
Nasal congestion

Aura*

Scotoma
Fortification spectrum
Paresthesias
Weakness
Vertigo
Tinnitus
Dysarthria

*Symptoms utilized by the International Headache Society's diagnostic criteria for migraine

Understanding the Patient With Migraine

Commonly reported symptoms at various phases of migraine (continued)

Mild

Dull headache
Pressure
Mild sensory sensitivity
Sinus congestion/pressure
Muscle pain
Anorexia
Fatigue
Aura

Moderate/Severe

Throbbing headache*
Headache aggravated by activity*
Nausea*
Vomiting*
Photophobia*
Phonophobia*
Osmophobia
Fatigue
Aura
Lacrimation
Rhinorrhea
Cognitive impairment

Postdrome

Fatigue
Anorexia
Poor concentration
Muscle pain

*Symptoms utilized by the International Headache Society's diagnostic criteria for migraine

Migraine-Associated Nausea

- Nausea is the single most important symptom identifier for migraine
- Validated in community-based, college student, neurology clinic and headache clinic
  - Overall sensitivity: 81%
  - Overall specificity: 83%

Martin VT, et al. *Headache*. 2005;45:1102-1112.

Closing the HA Diagnosis Gap
ID Migraine™ – A Validated Screener

Choose Yes or No

- When you have a HA, do you feel nauseated or sick to your stomach?
- When you have a HA, does light bother you (a lot more than when you don't have a HA)?
- During the last 3 months, have your HAs limited your ability to work, study, or do what you needed to do?

2/3 Yes for migraine:
Sensitivity: 0.81
Specificity: 0.75

=

Positive predictive value of 93% in primary care setting

Lipton RB, et al. *Neurology*. 2003;61(3):375-382.

Closing the HA Diagnosis Gap: POUND Mnemonic

POUND mnemonic useful for the diagnosis of migraine:

- Pulsatile
- One-day duration (episodes lasting 4-72 hours if untreated)
- Unilateral
- Nausea/vomiting
- Disabling

The likelihood ratio (LR) for migraine by the number of POUND criteria:

4 of 5 criteria: LR(+) = 24
3 of 5 criteria: LR(+) = 3.5
2 or fewer criteria: LR(–) = 0.41

Detsky ME, et al. *JAMA*. 2006;296:1274-1283.

Rethink Your Approach to Headache Complaints

- Ask open ended questions:
  - "Describe your worst headache"
    - If it's a migraine, then *that's* their diagnosis
      - Don't think they have different HAs like sinus, tension *and* migraine
  - "How do you feel between headaches?"
    - If not normal, they likely have a migraine and may also have transformed or have chronic migraine
- Use a migraine screener, then move forward with treatment plan

Clinical Pearls

- Migraine patients can experience many different types of HAs from the same underlying mechanism
- Prompt treatment may restore normal neurologic function and prevent the evolution of episodic to chronic HA

Principles of Migraine Management

- Establish realistic expectations
  - ≈50% reduction with prevention
  - ≥70% relief with acute treatment
- **THERE IS NO "CURE"!**

Principles of Management for the Patient

- Encourage patients to participate in their care
  - Accept that some Rx side effects are inevitable
  - Optimize behavioral management
  - Acute: Treat early, ≤2 days/week or 9 days/mo.
  - Prevention: follow guidelines for drug/complementary/alternative treatments
  - Regular patient follow-up with dose/drug/combination changes as needed

Roger, a 31-year-old CPA

- Has history of very occasional migraines since his early twenties which he manages with a triptan
- Started new job 6 months ago, requiring him to work long hours
- Headaches have increased and now occur on most weekend days for the last few months

What might be contributing to the increase in his headaches?

Behavioral Strategies

1. **Sleep** – 6 to 8 hours, consistent within 1 hour to bed/rise (even weekends!)
2. **Exercise** – Any better than none; aerobic >> nonaerobic
3. **Stress management**– Biofeedback/relaxation, cognitive-behavioral, time management
4. **↓Substance use** – Taper caffeine to maximum 1-6 oz cup – Eliminate artificial sweeteners, decongestants, smoking
5. **Eat** – Fresh, non-processed, small, frequent healthy meals/snacks

Headache Diary and Calendar

- Have patient note HA characteristics, including intensity, timing, duration, triggers and medications used
- Consider withdrawal of all processed foods for 1-2 weeks; if HAs are better, reintroduce individual additives slowly

Management of Migraine with Behavioral Strategies

Evidence-based Medicine
Specific Treatment Recommendations

- ✓ All types: eg, relaxation, EMG biofeedback, cognitive behavioral therapy - may be considered as treatment options for prevention (Grade A)
- ✓ Behavioral therapy combined with preventive drug therapy achieves additional improvement (Grade B)

Courtesy of Donald Penzien, PhD, US Headache Consortium Guidelines, 2000. www.aan.com/professionals/practice/pdfs/gl0089.pdf. Accessed March 21, 2009.

Abortive Treatments

- Administer early, rapidly, and consistently– ideally within 15 minutes
  - Minimizes use of backup and rescue medication
- Consider formulation (route, onset, duration of action) based on symptoms
- Note: can't "cure" *every* HA with "quick fixes"
  - Takes time, patience, and follow-up
- Avoid both under treatment and overtreatment with acute medications

Cady R, et al. *Headache.* 2004;44:426-435.

Abortive Agents: General Principles

- Treat 2-3 attacks with agent to assess efficacy
  - If little success, consider:
    - Different agent or route in same class
    - Adding co-therapy
    - Switching to different class
- *Use abortive agent no more than*
  - 2-3 days/week
  - 9 days/month
  - 12-15 doses/month *of anything*

Evidence-Based Guidelines for Migraine Headache in the Primary Care Setting: Pharmacological Management of Acute Attacks. http://www.aan.com/professionals/practice/pdfs/gl0087.pdf. Accessed December 17, 2007.

Abortive Agents

Evidence-based guidelines adopted by AAFP, ACP-ASIM, and AAN

- **First line: NSAIDs**
- Triptans (or dihydroergotamine) for NSAID intolerance/unresponsiveness
- No evidence for butalbital compounds in migraine
- Little evidence for isometheptene compounds
- Opioids "reserved for use when others cannot be used"
  - May worsen central sensitization; should be avoided
- Metoclopramide recommended for oral therapies as prokinetic if gastric stasis present*

AAFP = American Academy of Family Physicians. ACP-ASIM = American College of Physicians-American Society of Internal Medicine. ANN = American Academy of Neurology.
* European Headache Federation recommendation

Snow V, et al. *Ann Int Med*. 2002;137 840–849; Jakubowski M, et al. *Headache*. 2005;45:850–861.

Combination Abortive Therapies

- Consider drugs which may complement each other
  - Triptan + NSAID
  - Acetaminophen/ASA/caffeine
  - NSAID + caffeine
  - Metoclopramide + triptan *or* NSAID *or* ASA
- Tailor to coincident symptoms

Silberstein SD, et al. *Postgrad Med*. 2006, Apr., Spec No: 20-6.

Migraine Prevention

Many patients qualify,
few are chosen….

…Offer preventive treatment early

Guidelines for Initiating Migraine Prevention Therapy

- ≥2 attacks/mo with disability totaling >3 d/mo
- Recurring HA significantly interfering with patient's daily routine despite acute Rx
- Acute medications overused >2 d/wk, ineffective, intolerable side effects, or contraindicated
- Presence of uncommon migraine conditions: hemiplegic migraine, prolonged aura
- Patient preference, cost considerations or intolerance to acute agents

Ramadan NM. Evidence-based guidelines. http://www.aan.com. Accessed December 18, 2007; Silberstein SD, et al. Wolff's Headache and Other Head Pain. 2001.

Goals of Prevention

1. Fewer HAs
   - Best expectation: 50% reduction in ~50% of HAs
2. More/better response to acute "quick fix" drugs
   - Reduced HA impact (duration, intensity, symptoms)
3. Restoration of function
   - Less disability related to work/family/home activities

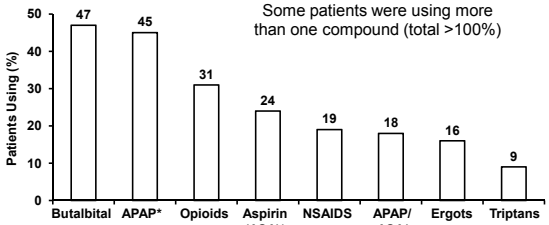
Silberstein SD. *Curr Opin Neurol*. 2005;18:289–292.

Medication-Overuse Headache (Formerly Rebound Headache)

- A pharmacologically maintained HA
- >15 d/mo with HA
- Regular acute drug use >10 d/mo (>15 d for simple analgesics) for >3 mo
- HA worsens over time of overuse
- HA resolves or reverts to previous pattern within 2 mo of overuse elimination

http://www.americanheadachesociety.org/assets/1/7/Stephen_Silberstein_-_Medication_Overuse_Headache.pdf Accessed April 7, 2013.

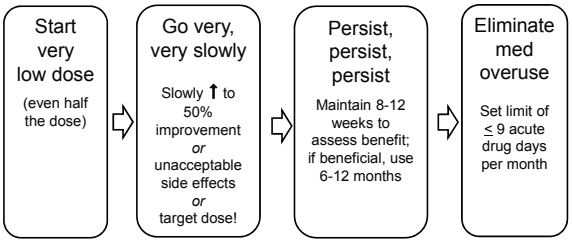
Medication Overuse Headache Hierarchy of Common Culprits



*ASA and APAP alone, or in compounds except for APAP/ASA/caffeine,which was considered separately.

Bigal ME, et al. *Cephalalgia*. 2004;24:483-490.

Prevention: General Concepts



Silberstein, SD et al. *Headache in Clinical Practice*. 2nd ed. 2002.

Migraine Preventive Therapies
US Classification and Level of Evidence

Level A: Medications with *established* efficacy*

- **Antiepileptic drugs**
  - Divalproex sodium
  - Sodium valproate
  - Topiramate
- **Beta blockers**
  - Metoprolol
  - Propranolol
  - Timolol
- **Triptans**
  - Frovatriptan

  (for menstrual-related migraine)

* in ≥ 2 Class I Trials

Not all agents are approved for migraine prevention

Silberstein SD, et al. *Neurology* 2012;78;1337-1345.

Migraine Preventive Therapies
US Classification and Level of Evidence

Level B: Medications which are *probably* effective*

- **Antidepressants/SSRI/SSNRI/TCA**
  - Amitriptyline
  - Venlafaxine
- **Beta blockers**
  - Atenolol
  - Nadolol
- **Triptans**
  - Naratriptan
  - Zolmitriptan

  (for menstrual-related migraine)

* in 1 Class I or 2 Class II studies

Not all agents are approved for migraine prevention

Silberstein SD, et al. *Neurology* 2012;78;1337-1345.

Migraine Preventive Therapies
US Classification and Level of Evidence

Level C: Medications which are *possibly* effective*

- **ACE inhibitors**
  - Lisinopril
- **Angiotensin receptor blockers**
  - Candesartan
- **Alpha agonists**
  - Clonidine
  - Guanfacine
- **Antiepileptic drugs**
  - Carbamazepine
- **Beta blockers**
  - Nebivolol
  - Pindolol
- **Antihistamines**
  - Cyproheptadine

* in 1 Class II Study

Not approved for migraine prevention

Silberstein SD, et al. *Neurology* 2012;78;1337-1345.

Migraine Preventive Therapies
US Classification and Level of Evidence

Agents with *inadequate* data or *probably* ineffective

Inadequate Data	Probably Ineffective
– Verapamil	– Lamotrigine
– Nicardipine	– Oxcarbazepine
– Nifedepine	– Clonazepam
– Fluoxetine	– Nabumatone
– Acetazolamide	– Telemisartan
– Gabapentin	

Not approved for migraine prevention

Silberstein SD, et al. *Neurology* 2012;78;1337-1345.

Selection of Prevention Medication

Consider patient comorbidities

- Beta blockers
  - Hypertension, angina
- Anticonvulsants
  - Seizures, mood disorders (valproate), obesity (topiramate)
- Antidepressants
  - Underweight, trouble sleeping, depression

Migraines and Pregnancy

- 50%–80% of migraineurs note decreased HA frequency after 1st trimester
- New-onset migraines in pregnancy warrant workup to r/o secondary causes
- Optimize trigger management and nonpharmacologic treatments
  - Massage, relaxation
- Acetaminophen, metoclopramide, (NSAIDS before third trimester), triptans
- If prevention is needed, use category C drugs if benefits outweigh risks*
  - propranolol - verapamil - ?magnesium?

Tozer BS, et al. *Mayo Clin Proc*. August 2006;81:1086-1092
http://www.aafp.org/afp/2011/0201/p271.pdf. Accessed April 22, 2013.

NSAIDs/Complementary Treatments for Migraine Prevention: Level of Evidence

Level A: Established efficacy
- Butterbur (*Petasites hybridus)*

Level B: Probable efficacy
- NSAIDs - ibuprofen, naproxen, fenoprofen, ketoprofen
- Herbal, vitamins, minerals, other
  - Magnesium, riboflavin, MIG-99 (feverfew), histamine SC

Level C: Possible efficacy
- NSAIDs – flurbiprofen, mefenamic acid
- Herbal, vitamins, minerals, other
  - Co-enzyme Q10, estrogen

Not approved for migraine prevention

Holland S, et al. *Neurology*. April 24, 2012 ;78 (17):1346-1353.

Commonly Used Alternative Therapies

- Butterbur (petasite): 50-75 mg BID
- Oral magnesium: 400-600 mg/d
- Vitamin B_2 (riboflavin): 400 mg/d
- Feverfew: No standardized preparations
- NSAIDs: naproxen 500 mg BID and others
- Co-enzyme Q-10: 100 mg TID effective in small trial

http://www.neurology.org/content/78/17/1346.full.pdf+html. Accessed March 10, 2013.

Acupuncture

- Appears effective for migraine prophylaxis
  - May be slightly better than pharmacotherapy
  - Sham just as effective as real
  - Strength of Recommendation = A

http://summaries.cochrane.org/CD001218/acupuncture-for-migraine-prophylaxis.
Accessed March 10, 2013.

Osteopathic or Spinal Manual Therapy (OMT or SMT)

- Studies suggest spinal, or osteopathic, manipulation may be beneficial for migraines[1]
  - Studies difficult to standardize and randomize due to varying nature and presentations of migraine headaches
- Head to head trial in 218 patients for prophylaxis of migraines[2]:
  - 8 wks of amitriptyline vs SMT had equivalent efficacy
  - Efficacy not better with combination
  - Efficacy better in SMT group 4 wks after both therapies stopped
  - SMT better tolerated than amitriptyline

1. Bronfort G, et al. J Manipulative Physiol Ther. 2001;24(7):457-66
2. Nelson CF et al. J Manipulative Physiol Ther. 1998;21(8):511-9

Additional Alternative Considerations

- Exercise
- Yoga
- Tai Chi
- Homeopathy
- Hypnotherapy
- Cold therapy
- Massage
- Physical therapy

Chronic Migraine Treatment

- OnabotulinumtoxinA (botox)
  - Approved for prophylaxis of chronic migraine (≥ 15 headache days/month)
  - 8-9 fewer HA compared to 6-7 with placebo
  - 31 injection sites into head/neck Q 3 mo.
  - Boxed warning re: possibility for spread causing weakness in distant area(s)

http://www.accessdata.fda.gov/drugsatfda_docs/label/2013/103000s5251lbl.pdf

Summary

- **Recurring HA with disability is migraine until proven otherwise**
- Both clinician and patient must have realistic expectations
- Use of acute meds > 9 days/month can lead to medication overuse
  - Avoid opiate and barbiturate use
- Chronic migraines can be reduced with prevention strategies, *so*
- Offer preventive treatment early