Headaches: Assessing and Management

H. James Brownlee, Jr. M.D.
Headaches: Objectives

- To explain the similarities and differences between migraine, tension, cluster and sinus headaches in adults.

- To discuss the more frequent incidence of cardiovascular and cerebrovascular disease in individuals with migraine with aura.

- To review the pharmacologic therapies for migraine including “abortive” and “preventative” therapy.
Conflict of Interests

• None
  – I have no relationships with commercial interests in regards to the subject of this lecture
Diagnosing headaches can be a challenge!

HA is the 5th most common symptom at outpatient medical visits.

There are over 300 medical conditions that include headache as a component.
Should this patient be given an OC?

- 23 yr old nulliparous women:
  - desires contraception
  - severe dysmenorrhea, unresponsive to NSAIDs
- prior provider recommended combo OC but pt heard from friends not to use OCs because she has a history of migraine HAs
- describes her HA as bilateral, “tightening sensation”,
  - associated with phonophobia but no visual or other non-visual symptoms

(cont)
• not aggravated by:
  – routine physical activity
  – responds to NSAIDs,
• reports that her mother and sister have been on episodic medications for headaches for many years,

• Should this patient be given an OC?

Yes ok to give OC – not a migraine!
Migraine Diagnosis: Clinical Challenge

• no biological markers/diagnostic tests
• concern of “missing” a serious secondary HA
• comorbidities may obscure symptoms
• migraine patients often suffer from other types of HA
  – 40%: in American Migraine Survey II study

Lipton et al, Headache 41:638-45, 2001
# Migraine Diagnosis By Specialty

<table>
<thead>
<tr>
<th>Specialty</th>
<th>Initially</th>
<th>Most often</th>
</tr>
</thead>
<tbody>
<tr>
<td>Family physician</td>
<td>47%</td>
<td>41%</td>
</tr>
<tr>
<td>Neurologist</td>
<td>12%</td>
<td>11%</td>
</tr>
<tr>
<td>Internist/Pediatrician</td>
<td>13%</td>
<td>15%</td>
</tr>
<tr>
<td>Ob/gyn</td>
<td>4%</td>
<td>3%</td>
</tr>
<tr>
<td>Ophthalmologist</td>
<td>3%</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>Emergency doc</td>
<td>3%</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>Pain/HA specialist</td>
<td>3%</td>
<td>1%</td>
</tr>
<tr>
<td>Other</td>
<td>17%</td>
<td>24%</td>
</tr>
</tbody>
</table>

# Headache Differentiation

<table>
<thead>
<tr>
<th>Character</th>
<th>Migraine</th>
<th>Tension-Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>location</td>
<td>unilateral</td>
<td>bilateral</td>
</tr>
<tr>
<td>frequency</td>
<td>intermittent</td>
<td>intermittent</td>
</tr>
<tr>
<td>duration</td>
<td>variable</td>
<td>variable</td>
</tr>
<tr>
<td>family hx</td>
<td>present</td>
<td>present</td>
</tr>
<tr>
<td>pain</td>
<td>throbbing</td>
<td>band-like</td>
</tr>
<tr>
<td>severity</td>
<td>mod-severe</td>
<td>mild-mod</td>
</tr>
<tr>
<td>associations</td>
<td>N, V, phonophotophobia</td>
<td>uncommon</td>
</tr>
</tbody>
</table>

**MIGRAINE IS A SYNDROME**

*Neurology 42(suppl 2):10, March 1992*
Reported Migraine HA Symptoms

- Moderate-Severe Pain: 97%
- Photophobia: 67%
- Worsened by Activity: 63%
- Unilateral: 63%
- Nausea: 63%
- Pulsating: 53%
- Phonophobia: 40%
- Vomiting: 20%

n=30, (subjects may report more than one symptom)

Schreiber CP, Cady RK Poster presentation at 10th IHC; June 2001 NYC
<table>
<thead>
<tr>
<th>Symptom</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderate-Severe Pain</td>
<td>97%</td>
</tr>
<tr>
<td>Nasal Stuffiness</td>
<td>73%</td>
</tr>
<tr>
<td>Photophobia</td>
<td>67%</td>
</tr>
<tr>
<td>Nasal Drainage</td>
<td>67%</td>
</tr>
<tr>
<td>Worsened by Activity</td>
<td>63%</td>
</tr>
<tr>
<td>Unilateral</td>
<td>63%</td>
</tr>
<tr>
<td>Nausea</td>
<td>63%</td>
</tr>
<tr>
<td>Weather Associated</td>
<td>57%</td>
</tr>
<tr>
<td>Pulsating</td>
<td>53%</td>
</tr>
<tr>
<td>Phonophobia</td>
<td>40%</td>
</tr>
<tr>
<td>Vomiting</td>
<td>20%</td>
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</table>

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Schreiber CP, Cady RK Poster presentation at 10th IHC; June 2001 NYC
IHS International Classification of Headache Disorders for Sinus Headaches

• A. Frontal HA accompanied by pain in one or more regions of the face, ears, or teeth.
• B. Clinical, nasal endoscopic, CT or MRI, or laboratory evidence of acute or acute-on-chronic rhinosinusitis.
• C. Headache and facial pain develop simultaneously with onset or acute exacerbation of rhinosinusitis.
• D. Headache or facial pain resolve within 7 days after remission or successful Rx of acute or acute-on-chronic rhinosinusitis.

Cephalgia, 24(suppl 1), 2004
When a “sinus” headache isn’t

• A cross sectional study enrolled 100 patients (78% female), 18-81 yrs of age who responded to an advertisement seeking people with:
  – self-diagnosed “sinus” headaches.

• A neurologist used the 2004 HIS criteria classify headache:
  – sinus HA vs. migraine

Schreiber et al, Arch Int Med 164:1769-72, 2004
When a “sinus” headache isn’t

• 86% of pts reclassified as migraine or probable migraine HA
  – only 3 retained the sinus HA diagnosis
  – remaining 11 patients suffered from other headache types

Schreiber et al, Arch Int Med 164:1769-72, 2004
NON-DROWSY
SUDAFED
DECONGESTANT tablets
Pseudoephedrine hydrochloride

12

Unblocks your nose & sinuses
Relieves sinus pressure
Clears catarrh

12 HOUR RELIEF

Clears stuffy noses fast
Soothes as it relieves

1 FL OZ (30 mL)

ORIGINAL
ANEFRIN NASAL SPRAY
Oxymetazoline HCl 0.05%
Nasal Decongestant

SOOTHING
When an antibiotic is prescribed:

• In 2007, amoxicillin was the preferred antibiotic when the incidence of beta-lactamase-producing organisms was low.

• 2012 Infectious Diseases Society of America guidelines recommends:
  – “amoxicillin-clavulanate 875 mg/125 mg bid for 7-10 days should be the first choice for most adults”
  – use the 2 gram/125 mg bid dose for pts who fail the initial therapy

When an antibiotic is prescribed:

- If the patient is allergic to penicillin, use:
  - doxycycline
  - levofloxacin
  - moxifloxacin
- due to increased resistance, do not use:
  - amoxicillin plain
  - macrolides
  - TMP/SMX
  - most cephalosporins

Neck Pain Is Seen With Meningitis and Tension Type HAs ....and

Frequently in All Phases of Migraine

Kariecki et al, Poster Presentation at 10th DHC. 6/29-7/2/01; NY, NY
Pathophysiology of Migraine

NEJM 346(4):266, 1/24/02
Migraine Related Aura
reversible focal neurologic symptoms that usually
develop gradually over 5-20 mins and
lasts less than 60 mins

• fully reversible dysphasic speech disturbance
• sensory symptoms that are fully reversible, including positive features (pins and needles) and/or negative features (numbness)
• visual symptoms are fully reversible including: positive features: flickering lights, spots, lines
• negative features: loss of vision

International Headache Society, HIS Classification, ICHD-II
Migraine with aura and increased risk of CVD in women

- Women’s Health Study, 27,840 women, aged 45 yrs or > with no prior hx of CVD
  - 5125 had migraines
  - 1434 reported migraine with aura
- 18 additional major CVD events for every 10,000 women per yr migraine with aura,
  - no increased CVD event in women with migraines without aura

WHO Guidelines 2007

- combination oral contraceptives are contraindicated in:
  - women with migraine with aura
  - women with migraine (without aura) over age 35 years

[link](http://www.who.int/reproductive-health/publications/mec/index.htm)
Relative Risk of Stroke in Women with Migraine

<table>
<thead>
<tr>
<th>Migraine conditions</th>
<th>RR Stroke (per 100,000 women-yrs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women &lt;45 years</td>
<td>3.0</td>
</tr>
<tr>
<td>With aura</td>
<td>6.0</td>
</tr>
<tr>
<td>Plus OCPs</td>
<td>10-17</td>
</tr>
<tr>
<td>Plus OCPs plus smoking</td>
<td>34</td>
</tr>
</tbody>
</table>

The Female Patient Vol 34:33, Feb 2008
Headache – Mortality in Men and Women

• 18,725 men and women with midlife migraine
  – Icelandic population, mean age 53, f/u 25.9 years
  – 11% reported migraine
    • 8% of the 11% with migraine had aura
• people with migraine with aura vs. migraine without aura/non-migraine HA:
  – All cause mortality: 1.21
  – Cardiovascular disease: 1.27
    • Coronary heart disease: 1.28
    • Stroke: 1.40

BMJ 341:3966, August 2010
Potential Triggers for Migraine

• medications:
  – estrogen: OCs or ERT
    • change in levels of estrogen
  – vasodilators – nitrates
    • dihydropyridine CCBs
      – amlodipine, felodipine, nifedipine
• stress
• diet
The headache exam!

• You need to do a 5 component neurologic exam when you are evaluating a non-classic headache presentation.
  – mental status
  – cranial nerves
  – motor including cerebellar
  – sensory
  – reflexes

• And then you need to document it in the chart!
Neuroimaging Commonly Ordered for HA Evaluation, Despite Rec Against It

- ACR recs vs: neuroimaging for uncomplicated HA
- neuroimaging is ordered in 10% of office visits for HA in U.S.
  - administrative data 2007 to 2010, 50 million office visits for HA to PCPs (50%), neurologists (20%).
- either MRI or CT ordered in 12% of HA visits and 10% of migraine visits.
  - estimated cost: $3.9 billion over 4 years
  - yield of significant abnormalities on neuroimaging in patients with chronic HAs:
    - 1 to 3%

JAMA Int Med 173, March 14, 2014
Non-pharmacologic Strategies for Migraine Headaches

- cognitive restructuring
- biofeedback & visualization
- physical therapy & massage
- OMT (osteopathic manipulative therapy)
- acupuncture
Migraine HA Treatment
Abortive Medications

- simple (OTC) analgesics
- NSAIDs
- barbiturates (butalbital: Fiorinal, Fioricet)
- antiemetics (incl. metoclopramide)
- ergot preparations (DHE 45)
- serotonin agonists (triptans)
- narcotics (pregnancy if severe)
Treating Migraine
But what about metoclopramide?

• The 2013 Cochrane review:
  – the addition of metoclopramide reduces nausea and vomiting,
    • but offers little if any benefit for headache/pain relief
    • tardive dyskinesia caution

Triptans: $T_{1/2}$

- Suma 100 mg: 2.0 hours
- Zolmi 5 mg: 3.0 hours
- Nara 2.5 mg: 5.5 hours
- Riza 10 mg: 2.0 hours
- Almo 12.5 mg: 3.1 hours
- Frova 2.5 mg: 25.7 hours
- Ele 40 mg: 6.3 hours

Common Triptan Side Effects

- tingling
- warmth
- flushing
- chest discomfort
- sensations of pressure
- dizziness, somnolence
New migraine treatments

Zecuity

sumatriptan iontophoretic transdermal system
6.5 mg/4 hours

FDA approved – but not marketed at time slide set provided to NPACE
Transcranial Magnetic Stimulator for Migraine Treatment

• Cerena: FDA approved for 18 years or older, but never available
  – Spring TMS, available and smaller
• indicated for migraine with aura
• magnetic stimulation: occipital cortex
• patients with moderate to severe migraine with aura
• pain free at 2hrs: 38% with device
  17% with controls
Possible Future Migraine Rx

- calcitonin gene-related peptide antagonist
  - lacks vasoconstrictor effects of triptans
- 2014 American Academy of Neurology Mtg
  - 2 new clinical trials
    - ALD403
    - LY2951742
    - need trials comparing efficacy to triptans
  - prior CGRP antagonists led to abnormal LFTs
Preventing HEADACHES
The latest research offers new hope for all of us
American Migraine Prevention Study: Migraine Prevention Is Underutilized

40% of migraine sufferers may be eligible for prevention

13% of all migraine sufferers currently receive prevention

Guidelines for Initiating Migraine Preventive Therapy

- frequency of headache $\geq 2$ per month with disability $\geq 3$ days per month
- recurring migraines that, in the patient’s opinion, significantly interfere with daily routines
- overuse of acute medication (>2 times per wk)
- acute medications contraindicated, not tolerated, or ineffective
- presence of uncommon migraine conditions
  - attacks with risk of permanent neurologic damage

Adapted from American Academy of Family Physicians/American College of Physicians–American Society of Internal Medicine Recommendations. 2006
Goals of Migraine Preventive Therapy

• reduce attack:
  – frequency, severity, and duration by 50% or more
  – improve function & reduce disability

• reduce:
  – use of acute medication
  – potential for rebound headache

• improve:
  – responsiveness to treatment of acute attacks

Migraine Headache Severity

• more than 50% of patients have migraines that cause severe impairment:
  – resulting in an average loss of 4-6 workdays/year

Hu, XH et al, Arch Int Med 159:813-18, 1999
Am Academy of Neurology and Am Headache Society Guidelines on Migraine Prophylaxis

- effective and should be offered:
  - most antiepileptic drugs:
    - divalprox sodim, topiramate, sodium valproate
  - certain beta blockers
    - metoprolol, propranolol, timolol
  - one triptan:
    - frovatriptan

Neurology 78:1337, April 23, 2012
Am Academy of Neurology and Am Headache Society Guidelines on Migraine Prophylaxis

• **probably effective and should be considered:**
  – antipdepressants:
    • amitriptyline, venlafaxine
  – other beta blocker:
    • atenolol, nadolol
  – other triptans:
    • naratriptan, zolmitriptan

• **not effective and should not be given:**
  – lamotrigine

Neurology 78:1337, April 23, 2012
• probably effective and should be considered:
  – several NSADS:
    • fenoprofen, ibuprofen, ketoprofen, naproxen
  – riboflavin
  – magnesium
  – feverfew
• effective to offer: petasites (butterbur)
  – a complementary medication

Neurology 78:1337, April 23, 2012
Migraine Prevention Device

- Cefaly transcranial electrical nerve stimulation (TENS) device is intended to be used:
  - once daily for 20 minutes
  - adults with migraine
- User applies electrode to center of forehead
  - electrical current stimulates trigeminal system branches

Cost: $349, then $25/3 electrodes
Requires a prescription
Menstrual Migraines

appears to be due to estrogen withdrawal with accompanying increased prostaglandin levels
Menstrual Migraine (MM) Rx

• continuous oral contraceptive pills for 3-4 months (21 day pack x 4) - 84 days
• most common reason for d/c extended-duration OCP use:
  – breakthrough bleeding/spotting
• avoid using in women with migraine with auras because of increased risk of stroke

Prescribers Letter, p 70, Dec 2007
Triptans: $T_{1/2}$

- Suma 100 mg: 2.0 hours
- Zolmi 5 mg: 3.0 hours
- Nara 2.5 mg: 5.5 hours
- Riza 10 mg: 2.0 hours
- Almo 12.5 mg: 3.1 hours
- Frova 2.5 mg: 25.7 hours
- Ele 40 mg: 6.3 hours

Tension-Type HA
Characteristics

• occur more often: females
• usually bilateral, band-like
• mild to moderate intensity without limiting activity
• usually begins during day
  – especially during work week
  – often subsides at night
• no nausea or vomiting

Am Fam Physician 83(3):271-80, Feb 1, 2011
Tricyclics and HA Burden in Pts with Migraine and Tension HAs

- meta-analysis, 37 randomized trials
  - average duration: 10 weeks
  - nearly 3200 pts
  - 73% women, mean age: 40 yrs

- tricyclics (primarily amitriptylline 10 mg start slowly 1 tab up slowly to 3-5 tabs before bed) compared with:
  - placebo, SSRIs, beta-blockers
  - Rx for: migraine and tension headaches

Jackson et al, BMJ 341:5222, Oct 20, 2010
Tricyclics and HA Burden in Pts with Migraine and Tension HAs

- tricyclics compared with placebo in 20 trials
  - tricyclics reduced the mean number of headaches monthly
    - 1.4 for migraine (from baseline of 4.7)
    - 6.9 for tension HA (from baseline of 16.9)
  - tricyclics were more likely to result in:
    - at least 50% improvement in pts HAs
    - fewer doses of analgesics
  - beneficial effect strengthened with time

Jackson et al, BMJ 341:5222, Oct 20, 2010
Tricyclics and HA Burden in Pts with Migraine and Tension HAs

- 8 trials: tricyclics were compared with SSRIs
  - tricyclics were more likely to result in 50% improvement in both types of HAs
- 3 trials: tricyclics compared with beta blockers
  - both classes similarly effective

Jackson et al, BMJ 341:5222, Oct 20, 2010
Cluster Headache
a prospective clinical study

- 230 British pts. from community
- 79% episodic, 21% chronic, 72% male
- pain experienced:
  - 92% retro-orbital, 70% temporal
  - also: teeth, forehead, jaw, cheek
  - pain duration: minimum – 72 mins
    maximum – 159 mins
- <50% had tried: inject sumatriptan or O₂ Rx

Babra et al, Neurology 58:354-61, Feb 2002
Cluster Headache

• is associated with at least one of the following signs that have to be present on the pain side:
  – lacrimation
  – facial/forehead sweating
  – rhinorrhea
  – nasal congestion
  – miosis
  – ptosis
  – eyelid edema
  – conjunctival injection

Treatment of Acute Attack of Cluster Headache

• oxygen 100%, non-rebreather face mask 12 L/min x 15-20 mins.
• sumatriptan 6 mg SQ or 20 mg nasal spray (off-label)
• zolmitriptan 5 mg nasal spray (off-label)
• lidocaine 10% solution 1 ml total to both nostrils with cotton swab x 5 minutes

Key References


• Am Fam Physician 83(3):271-80, Feb 1, 2011

• BMJ 341:3966, August 2010

• Neurology 78:1337, April 23, 2012
Thank You!
Questions