Management of Adult and Pediatric Migraines in Primary Care

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Disclosures

• Speaker Bureau: Novartis, GSK, Sanofi-Pasteur, Merck, Takeda, Vivus
• Consultant: Vivus, Sanofi-Pasteur, Takeda

Objectives

• Upon completion, the participant will be able to:
  – Discuss current research regarding the etiology of primary headaches
  – Identify the signs and symptoms of migraines, tension, and cluster headaches
  – Discuss the various pharmacologic and non-pharmacologic treatments available for individuals with migraines, tension and cluster headaches

Migraine Prevalence

(American Migraine Study II)

• There are currently 28 million migraine sufferers age 12+ in the United States
  • 21 million females: approximately 18.2% of women
  • 7 million males: approximately 6.5% of men
• Migraine prevalence peaks in the 25-55 age range – These are the most productive years of the lifespan
• One in 4 households has at least 1 migraine sufferer

Prevalence of Migraines

• Children/adolescents/women suffer from migraine at a 3:1 ratio over men after puberty
  – Before puberty: 60% of all children with migraines are male
• 1 in 6 American women suffer from migraines
• Familial disorder
  – 70% of pediatric patients with migraines have a family history
Headaches in Children

- Very common complaint among children
  - 37 – 51% prevalence during elementary school years
  - 57-82% - prevalence during high school years
- Most common recurrent headache in childhood is migraine
- More common in boys before puberty
  - After puberty, headaches are more common in girls

Secondary Headaches: Prevalence

- 1% of office HA presentations
- 3.8% of ED HA presentations

Headache Diagnosis: Primary Headache Types

- Tension-type headache
- Migraine
  - Migraine without aura
  - Migraine with aura
  - Chronic migraine (complication of migraine)
- Cluster headache
- Other primary headaches
  - Cough headache
  - Exertional headache
  - Sexual activity headache
  - Hemicrania continua

Headache Diagnosis: History

- Medical history
- Headache history
  - For each headache type
    - Onset
    - Location
    - Quality
    - Intensity
    - Duration
    - Frequency
    - Associated symptoms
    - Impact on routine physical activity
Predictors of Migraine in Children

- History of motion sickness
- History of paroxysmal dizziness or vertigo
- Cyclic vomiting syndrome
- Many have premonitory symptoms
  - Irritability, fatigue

Positive Predictors of Migraine

- Predictor
  - Female gender
  - Aura
  - Higher pain severity
  - Disability during headache
  - Photophobia, phonophobia

- Don't be confused by
  - Male gender
  - Multiple headache types
  - Bilateral headache
  - Neck pain
  - Sinus symptoms
  - Patient-derived diagnosis

Features Suggestive of Secondary Headache: SNOOP

- Systemic symptoms or signs of systemic disease
  - Fever, myalgias, weight loss
  - Malignancy, acquired immunodeficiency syndrome
- Neurological symptoms or signs
  - Onset sudden (thunderclap headache)
  - Onset before age 5 years or after age 50 years
- Pattern change
  - Progressive headache with loss of headache-free periods
  - Change in type of headache

Red Flags for Secondary Headache

- Indications for HA workup
  - First/worst HA
  - Abrupt-onset HA
  - Head trauma
  - Progression or fundamental change in pattern
  - New HA in those <5 yo or >50 yo
  - New HA with cancer, immunosuppression
  - HA with syncope or seizure
  - HA triggered by exertion/Valsalva/sex
  - Neurologic symptoms >1 hour in duration
  - Abnormal general or neurologic examination

Brain Tumor
Case Study 6: JD

• 1 week history of blurred vision and worsening headache in a 46 year old male.
  – Headache is 5 on 1-10 scale; now associated with vomiting and blurred vision
  – Seen 3 days ago, diagnosed tension headache
  – No improvement despite medications
  – Had been feeling well until this began; No other symptoms

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Case Study 6: JD

• PE: VSS
  • Head: N/C; no abnormalities
  • Ears: Canals/TM’s normal; hearing intact
  • Nose: Turb/mucosa normal; no discharge, abnormalities
  • Mouth: Mucosa moist; tongue midline; Gag intact
  • Nodes: nonpalp, nontender
  • Lungs: clear bilaterally; no c/w/r

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Case Study 6: JD

• CN II – XII intact; exceptions noted
  – Papilledema
  – Conversant but slow responses to questions.
  – Neat and clean
  – Seems to stare at examiner
  – Tries to smile at times; not always appropriate for the situation

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Diagnostics

• CT with contrast ordered stat
  – MRI is the most sensitive test, particularly when gadolinium (contrast)
• Stat CT scan confirmed a large glioblastoma in the frontal region
  – Within 4 hours, underwent a debulking procedure
  – Pathology confirmed and experimental chemotherapy was initiated
  – Unfortunately, tumor was fatal with 3-4 months of presentation

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Papilledema

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Fig. 19.105 Acute papilledema, characterized by blurred disc edges, an absent physiologic cup, and intraretinal exudates.

Giant Cell Arteritis

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Case Study 7: BT

- 61 year old w.f. who presents with a 11/2 month history of “the worst headaches of my life” and a decrease in vision bilaterally
  - Initially blurred vision was present in the right eye; now bilaterally
  - Seen by nurse practitioner and MD; diagnosed with sinusitis and depression
  - No improvement with 2 courses of antibiotics and Zoloft
  - Unable to comb or wash hair for weeks, hasn’t driven in the weeks

Physical Examination Findings

- VS: BP:148/94
- Gait: unsteady-holding on wall to ambulate
- Unable to perform heel/toe ambulation
- Eyes: PERRLA; EOMI; Fund: Optic disc pallor
- ENT-normal
- Nodes: nonpalp, nontender
- Lungs: clear bilaterally; no c/w/t
- Heart: S1S2: RRR; No murmurs
- Temporal arteries: tender
- Unable to touch scalp/head due to pain
- Speech – smooth and articulate
  *A/A/O*

Giant Cell Arteritis

- Etiology
  - Systemic inflammation of the large vessels, most commonly affecting the branches of the cranial arteries
  - Most common in the elderly; 60 years or >
  - Almost always occurs in Caucasian individuals
  - Frequently associated with polymyalgia rheumatica

- Symptoms
  - Abrupt or insidious onset over months
  - Headache (2/3 of patients)
    - Usually unilateral temporal
    - Can be generalized or occipital
    - Constant, boring, intense pain that is exacerbated by contact: brushing hair/cold on the skin
  - Generally feel lousy
  - Night sweats
  - Jaw/tongue pain upon chewing (jaw claudication)
  - Visual changes-early; Blindness-late
    - May be complete blindness or altitudinal blindness
  - Scalp tenderness
  - Low grade fever
  - Fatigue/malaise
  - Weight loss and anorexia
  - Myalgias: predominantly proximal muscles

- Physical Examination Findings
  - Scalp vessels are thick and tender
  - Erythematous, edematous temporal artery
  - Pulsation may be decreased or absent
  - Optic disc-edematous first; becomes pale
  - Scalp tenderness
  - Gait disturbance
  - Polymyalgia rheumatica
  - Labs:
    - Sed rate usually > 70
    - CRP: may be more sensitive than the sed rate
    - Increased alkaline phosphatase
Giant Cell Arteritis

- Diagnosis
  - Anemia (normocytic, normochromic)
  - Leukocytosis
  - Elevated platelet count
  - Occasionally: Elevated AST
  - Temporal artery biopsy
    - Recommended within 4 days of starting steroids

- Treatment
  - Prednisone 20 – 60 mg
    - Begin immediately while arranging for biopsy
    - High risk of blindness and CVA if not treated
    - Taper according to symptoms and sed rate
  - Education
    - Disease process: Average time to disease remission is 12-24 months; Range is 1-10 years
    - Side effects of prednisone
  - Calcium 1500mg qd
  - Ophthalmologic examination

Additional Issues

- Given high/prolonged dosage of prednisone, must consider risks of osteoporosis, cataracts, glaucoma, diabetes, and obesity
- Increased incidence of depression

Waiting Room Study: Results Compared with General Population

Couch JR et al. Presented at: American Headache Society; June 19-22, 2003; Chicago, IL
The Diagnosis of Migraine Has Increased Modestly (Using IHS Criteria)

14.6 million migraine sufferers remain undiagnosed

Undiagnosed Migraine Sufferers Often Report Receiving a Diagnosis of Tension Headache

In the Presence of Neck Pain Tension Headache is Frequently Diagnosed

Stress is the Most Frequently Reported Trigger of Migraine

Migraine Can Be Triggered by Weather
Like Sinus Headache, Migraine May Present With Autonomic Symptoms

46% of patients had at least 1 autonomic symptom during migraine attacks. Of these,
• 14% had only nasal symptoms
• 41% had only ocular symptoms
• 46% had both nasal & ocular


Summary of Clinical Data

• Most patients with self-described “sinus” headache:
  – May actually have migraine and migrainous headache as defined by IHS criteria (90%)  
  – Experience sinus pain and pressure, nasal symptoms, ocular symptoms and weather as a trigger
  – Are disabled by their headaches
  – Are dissatisfied with Rx and OTC medications they are using to treat these headaches

Female Life Events That Influence Migraine

• Menarche
• Menses
• Oral Contraception
• Pregnancy
• Lactation
• Menopause
• Hormone Therapy

Migraine and Menarche

• Females suffer from migraine at a 3:1 ratio to males
• Beginning with puberty, migraine is more common in girls
• Menstrually-associated migraine begins at menarche in 33% of women
• 60-70% of female sufferers experience migraine in association with menses

Menstrual Migraine: Definitions

• Menstrually-associated migraine (MAM):
  – Women who experience attacks that occur both premenstrually and at other times of the month
  – 60-70% of female migraineurs report a menstrual relationship to their headaches
• Menstrual migraine (MM):
  – Women who experience attacks that occur only premenstrually
  – True menstrual migraine occurs in only 7-14% of female migraineurs

Characteristics of Menstrually-Associated Migraine Attacks

• Longer in duration than non-MAM attacks
• Perceived by some to be more difficult to treat than non-MAM attacks
• Predictable in some women
• Influence of co-existing PMDD (premenstrual dysphoric disorder)
Migraine Vulnerability During the Menstrual Cycle

- Can occur before, during, and after menstruation
  - Migraine may be part of premenstrual syndrome (PMS), now a part of the DSM-V criteria for Premenstrual Dysphoric Disorder (PMDD)
  - Greatest likelihood of menstrual migraine on Day -1 to Day <4, but can vary
  - Decrease in estrogen levels in the late luteal phase is a likely trigger for migraine
- Although migraine may be related to PMDD, it is important to treat migraine as an individual disorder with migraine-specific treatment

Impact of Hormones on Migraine

- Progesterone given during the menstrual cycle will postpone bleeding but not the headache
- Estrogen given during the menstrual cycle will postpone the headache but not the bleeding
- Constant levels of estrogen can prevent the migraine attack

New Insights into Migraine Pathophysiology

A Scientific Hypothesis for the “Tension-Like” and “Sinus Like” Presentation of Migraine

The Migraine Process: Activation of Nerves and Blood Vessels

The Migraine Process: Activation of the Trigeminal Nucleus Caudalis (TNC)
Trigeminal Nucleus Caudalis (TNC): Processing and Relaying Migraine Pain

Activation of the TNC can Result in Referred Pain

- Cerebellum
- Thalamus
- Trigeminal nucleus caudalis
- Sensory integration for O5, O1, O4

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Activation of the TNC May Result in Referred Pain that Could be Perceived Anywhere along the Trigeminocervical Network

- Cervical spine
- Mastoid
- Mastoid foramen
- Occiput

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 Activation of the TNC May Result in Reflex Activation of Cranial Parasympathetic Nerves Extending into Sinus Cavities and Tear Ducts

- Sphenopalatine ganglion
- Trigeminal nucleus caudalis

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Cranial Parasympathetic Activation May Explain “Sinus-Like” Symptoms in Migraine

- Lacrimation
- Rhinorrhea
- Congestion

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Pathophysiology of Migraine is No Longer Just Neurovascular: Multiple Mechanisms of Migraine Exist

Using ID Migraine™*

Prescreening Questions

a. Do your headaches limit your ability to work, study, or enjoy life?

or

b. Do you want to talk to your health care professional about your headaches?

Screening Questions

During the last 3 months, did you have the following with your headaches:

1. You felt nauseated or sick to your stomach?

   Yes____ No____

2. Light bothered you (a lot more than when you don’t have headaches)?

   Yes____ No____

3. Did your headache limit your ability to work, study, or do what you needed to do for at least 1 day?

   Yes____ No____

   a. Do your headaches limit your ability to work, study, or enjoy life?

   or

   b. Do you want to talk to your health care professional about your headaches?

*Physician disclaimer: Answering the questions in the ID Migraine™ screener is not intended to provide a medical diagnosis for migraine. Since the ID Migraine™ screener relies on self-reporting, the health care professional should verify all responses. A definitive diagnosis of migraine is made on clinical grounds by a health care professional taking into account how well the patient understood the questionnaire as well as other relevant information. ID Migraine™ is a trademark of Pfizer Inc. Patent pending.

### Episodic Migraine Without Aura: Diagnostic Criteria

At Least 5 Attacks Fulfilling the Criteria Below

- Headache attack lasting 4 to 72 hours (untreated or unsuccessfully treated)
- Not attributable to another disorder

### Episodic Migraine with Aura: Diagnostic Criteria

At Least 2 Attacks Fulfilling the Criteria Below

- Meets the IHS criteria for migraine without aura
- Not attributable to another disorder

### Episodic Tension-Type Headache: Diagnostic Criteria

At Least 10 Episodes Occurring < 1 Day/mo

- Headache lasting 30 minutes to 7 days
- Not attributable to another disorder

### Episodic Cluster Headache: Diagnostic Criteria

At Least 5 Attacks Fulfilling the Criteria Below

- Not attributable to another disorder

### We Also Need to Think….

- Sinusitis
  - Edematous turbinates, tenderness to palpation
- Head trauma
- Intracranial Masses
  - Abnormal neurologic examination
- Pseudotumor cerebri
  - Papilledema, neurologic abnormalities, 6th nerve palsy
- Epilepsy
- Meningeal irritation

### Treatments for Migraines

**Look How Far We Have Come**

- BC: trephination
- 1850: bromide
- 1883: ergotamine
- 1897: aspirin
- 1963: methysergide
- 1975: DHE
- 1993: triptans

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Selective 5-HT¹ agonists (the triptans) have emerged as the gold standard for acute migraine therapy.

5 HT 1B/1D Antagonists
- Sumatriptan (Imprex)
  - SC, Nasal Spray and tablet
- Zolmitriptan (Zomig)
  - Tablet (2.5 and 5.0mg tablets); MLT
- Naratriptan (Amerge)
  - Tablet (1mg and 2.5 mg)
- Frovatriptan (Frova)
  - Tablet (2.5 mg)
- Rizatriptan (Maxalt)
  - Tablet and MLT (5 and 10 mg)
- Almotriptan (Axert)** 12 and up
  - Tablet (6.25mg and 12.5 mg)
- Eletriptan (Relpax)
  - Tablet (20 mg and 40 mg)

Stratified Care vs Step Care
Headache Response

Early Treatment: Abortive Medications

Headache Experts Agree That the Optimal Treatment Strategy Is to Treat Early, Before Central Sensitization Occurs
Too Much of a Good Thing….

- Use of any product more than 2-3 times per week will result in rebound headaches
- Medication overuse headache
  - Worsening of headache pain caused by frequent and excessive use of immediate relief medications
  - Bilateral, diffuse headache
  - Waxes and wanes
  - Associated with fatigue, n/v, restlessness
  - Will never get better on any medications until rebounding is eliminated

AHS/AAN Migraine Prevention Guidelines


Level A Recommendations:

**Drugs**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
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<tbody>
<tr>
<td>Divalproex/sodium valproate</td>
<td>400 – 1000 mg/day</td>
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<tr>
<td>Metoprolol</td>
<td>47.5 – 200 mg/day</td>
</tr>
<tr>
<td>Petasites (butterbur)</td>
<td>50-75 mg two times daily</td>
</tr>
<tr>
<td>Propranolol</td>
<td>120 – 240 mg/day</td>
</tr>
<tr>
<td>Timolol</td>
<td>10 – 15 mg two times daily</td>
</tr>
<tr>
<td>Topiramate</td>
<td>25 – 200 mg/day</td>
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</table>

Level B Recommendations:

**Drugs**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
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<tbody>
<tr>
<td>Amitriptyline</td>
<td>25 - 150 mg/day</td>
</tr>
<tr>
<td>Fenoprofen</td>
<td>200 - 600 mg three times daily</td>
</tr>
<tr>
<td>Fendoux</td>
<td>50 mg – 300 mg two times daily</td>
</tr>
<tr>
<td>Flurbiprofen</td>
<td>1 – 10 mg subcutaneously twice weekly</td>
</tr>
<tr>
<td>Naproxen</td>
<td>200 mg two times daily</td>
</tr>
<tr>
<td>Ketoprofen</td>
<td>50 mg three times daily</td>
</tr>
<tr>
<td>Magnesium</td>
<td>600 mg daily</td>
</tr>
<tr>
<td>Naproxen/sodium naproxen</td>
<td>550 mg two times daily</td>
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Level B Recommendations:

**Drugs**

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<thead>
<tr>
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<th>Dosage</th>
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<tbody>
<tr>
<td>Riboflavin</td>
<td>400 mg daily</td>
</tr>
<tr>
<td>Nimesidase</td>
<td>150mg ER once daily</td>
</tr>
<tr>
<td>Atenolol</td>
<td>100 mg daily</td>
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Level C Recommendations: Possibly Effective

<table>
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<tr>
<th>Drug</th>
<th>Dosage</th>
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<tbody>
<tr>
<td>Candesartan</td>
<td>16mg once daily</td>
</tr>
<tr>
<td>Carbamazepine</td>
<td>600 mg daily</td>
</tr>
<tr>
<td>Clonidine</td>
<td>0.75 mg daily</td>
</tr>
<tr>
<td>Guanfacine</td>
<td>0.5-1.0 mg/day</td>
</tr>
<tr>
<td>Lisinopril</td>
<td>10 – 20 mg daily</td>
</tr>
<tr>
<td>Nebivolol</td>
<td>5 mg daily</td>
</tr>
<tr>
<td>Pindolol</td>
<td>10 daily</td>
</tr>
<tr>
<td>Flurbiprofen</td>
<td>200 mg daily</td>
</tr>
</tbody>
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AHS/AAN Migraine Prevention: Migraines Associated With Menstruation

- Frovatriptan: Level A
  - 2.5 mg two times daily perimenstrually
- Naratriptan: Level B
  - 1 mg two times daily x 5 days perimenstrually
- Zolmitriptan: Level B
  - 2.5 mg two times daily perimenstrually
- Estrogen: Level C
  - 1.5 mg estradiol in gel daily x 7 days perimenstrually

Summary Slide

- Level A
  - Antiepileptic drugs (AEDs): divalproex sodium, sodium valproate, topiramate
  - Beta-Blocking: metoprolol, propranolol, timolol
  - Triptans: frovatriptan for short-term MAMs prevention
- Level B
  - Antidepressants: amitriptyline, venlafaxine
  - Beta Blockers: atenolol, nadolol
  - Triptans: naratriptan, zolmitriptan for short term MAMs prevention

What About Cluster Headaches?

- Oxygen – 7L via mask (high flow oxygen)
- Abortive therapies
  - Avoid medications such as stadol, opioids
- Prophylaxis:
  - Lithium: best studied prophylactic medication

Common Pitfalls in Migraine Diagnosis: Importance of Medication Overuse

- MOH is common, but widely unrecognized
- MOH is almost always transformed migraine
- Ask patients about all pain medication use
MOH Diagnosis

- Patients typically overuse multiple medications simultaneously
  - Mean tablets/day = 5.2
  - Most commonly overused drugs are
    - Butalbital combinations (48%)
    - Acetaminophen (46%)
    - Opioids (33%)
    - ASA (32%)
    - Triptans (18%)


MOH Diagnosis (cont’d)

- Both diagnosis and treatment require time
  - Diagnosis is confirmed in retrospect
  - Offending medications must be stopped and prophylactic medications started

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Chronic Migraine: Diagnostic Criteria

Migraine Fulfilling the Criteria Below

- Meets the IHS criteria for migraine without aura
- Not attributable to another disorder

- Occurs ≥ 15 days per month for ≥ 3 months
- Usually begins as migraine without aura and progresses
- As chronicity develops, headache tends to lose its attack-like presentation
- When medication overuse is present, it is the likely cause of the chronic symptoms
  (Medication overuse headache – MOH)


Additional Therapy For Chronic Migraine

- onabotulinumtoxinA (Botox)
  - Chronic Migraine: Recommended total dose 155 Units, as 0.1 mL (5 Units) injections per each site divided across 7 head/neck muscles

http://www.botoxchronicmigraine.com/aboutchronicmigraine/?cid=sem_CMB_g00_s_7899 accessed 12-30-2012

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My Medication Doesn’t Work...

- Prednisone
  - 60, 40, 20 mg/day
- Or....Ketorolac
- Analgesic
- Antiemetic
  - Zofran or similar (4 mg)

http://www.botoxchronicmigraine.com/aboutchronicmigraine/?cid=sem_CMB_g00_s_7899 accessed 12-30-2012

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Sinus Headache or Migraine: *Differential Diagnosis*

- Difficult to distinguish
- Overdiagnosis of sinus headache
- Presentation overlap
- Differentiation is critical for successful management


Sinusitis: *Diagnostic Hints*

- Frontal head pain more often caused by migraine and/or tension headache than sinusitis
- Sinus headache more likely when
  - Purulent nasal discharge is present
  - Headache and sinusitis onset coincides
  - Headache location coordinates with sinus anatomy
  - Positive diagnostic test for sinus congestion
  - Headache disappears when sinusitis resolves


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