Brainstorm: A Symposium on Migraine Treatment and Management

Faculty

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Disclosures

- Jeff Unger, MD, ABFM, FACE serves as a speaker for Novo Nordisk, Teva and Janssen. Dr. Unger also serves as a stock owner, consultant and researcher for Novo Nordisk.
Learning Objectives
After participating in the proposed educational activities, clinicians should be better able to:

1. Discuss the epidemiology and pathogenesis of migraine headaches
2. Discuss ways by which migraine can be diagnosed by PCPs
3. Discuss clues which may differentiate migraine from “secondary headache” disorders
4. Outline preventative, acute, abortive and rescue interventions for migraine

PRE-TEST QUESTIONS

Pre-test ARS Question 1
On a scale of 1 to 5, please rate how confident you would be in the diagnosis and management of a patient with Migraines:

1. Not at all confident
2. Slightly confident
3. Moderately confident
4. Pretty much confident
5. Very confident
Pre-test ARS Question 2
Migraine headaches are the result of which pathologic mechanism?

1. Vascular dilatation within the vessels of the cerebral cortex
2. Excitation and activation of the trigeminal nerve via neurological triggers
3. Neuroinflammation
4. The mechanism of migraine is unknown

Pre-test ARS Question 3
A 52 year old man presents with severe, throbbing and burning retro-orbital pain, tearing, and nasal congestion. His headaches awaken him at the same time each day and last 45-60 minutes before resolution. This most likely diagnosis for this patient is:

1. Migraine without aura
2. Cluster migraine
3. Acute cluster headaches
4. Stress headaches

Pre-test ARS Question 4
A 32 year old female claims she has a reoccurrence of her sinus headaches. These headaches appear acutely, and are associated with nausea, photophobia and nasal congestion. Pain is in the right side of her face. She is unable to work for up to 3 days with these headaches. This is her “3rd episode of sinusitis this month.” Your treatment should be:

1. Amoxicillin 500 mg TID x 7 days
2. Oxycodone 10/350 Q 6 hours as needed for pain
3. Sumatriptan iontophoretic transdermal system 6.5 mg/4 hours at onset of headache
4. Refer to ENT for consideration of surgical intervention
Pre-test ARS Question 5
Which of the following statements about migraine is FALSE:

1. 36 million Americans experience migraine
2. 1/9 adults in the average PCP waiting room have experienced a migraine in the past year
3. Migraine is an acute disease process
4. The most common manifestations of acute migraine include pulsatile pain, photophobia, phonophobia, nausea and disability

Pre-test ARS Question 6
Which of the following patients should be treated with migraine prophylaxis?

1. A surgeon who experiences 1 episode of migraine with aura every 8 months
2. A professional football player who experiences migraine without aura
3. A 10 year old who misses 2 days of school monthly due to basilar migraine
4. A patient who experiences more than 4 episodes of acute migraine each month
5. All of the above
Migraine is a very common medical disorder. 1-Year prevalence rates; population-based studies; IHS criteria (or modified).

Migraine has an estimated worldwide prevalence of ~10%.

Migraine in the primary care setting:
- 1/3 of patients in primary care waiting rooms have migraine.
- Half of migraineurs have not been diagnosed.

Prevalence of headache in the general population:
- Prevalence of any form of headache was 93% in men and 99% in women.
- Among men, 8% had, at some point, experienced migraine compared with 25% of women.

Patients With a Complaint of Headache Seen in Primary Care: A Prospective Diary Study

If a patient visits the doctor with a chief complaint of headache, there is greater than a 50% chance that the patient has migraine.

Most patients seeking care for a headache have migraine.

Migraine Prevalence Depends on Age and Gender

Where Do Migraine Sufferers Seek Medical Care?
Migraine Is More Common Than Asthma and Diabetes


- Migraine
- Osteoarthritis
- Asthma
- Diabetes
- Rheumatoid Arthritis
- Epilepsy

Migraine Pathogenesis

- Migraine has a genetic basis.
- Migraineurs are born with a very sensitive nervous system. Environmental triggers can activate the trigeminal nerve inducing a migraine event.
- Migraine is NOT due to vasoconstriction or vasodilatation.
- Trigeminal activation induces all headache disorders including migraine.
- Migraine has 5 phases:
  - Prodrome
  - Aura
  - Headache phase
  - Postdrome
  - Recovery

Migraine Pathogenesis And Phases
Clinical Rules:
Diagnostic Criteria for Migraine

- Attacks lasting 4–72 h (untreated or unsuccessfully treated)
- Two of the following:
  - Unilateral
  - Pulsating
  - Moderate or severe intensity
  - Aggravated by or causing avoidance of routine physical activity
- One of the following:
  - Nausea or vomiting
  - Photophobia and phonophobia
  - Not attributed to another disorder
- Aura not in diagnostic criteria

ID Migraine
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. Your headaches limited your ability to work, study, or do what you needed to do?
   Yes __________ No __________

Heather History
- Recurrent disabling headaches
- Light Sensitivity
- Nausea
- Vomiting
- + Family History
- Lasts 4-72 hours


2/3 for migraine
Sensitivity: 0.81
Specificity: 0.75
Red Flags Suggesting Secondary Headaches

- First or worst headache of your life
- Abrupt onset of headache without any warning or build-up
- Fundamental change in the pattern of recurrent headaches
- Headache beginning at unusual ages
  - ≤ 5 years old
  - ≥ 50 years old
- The presence of cancer, HIV, pregnancy
- Abnormal physical exam
- Headache onset:
  - with seizure or syncope
  - with exertion, sex or Valsalva (squeezing)

Imaging Patients With Migraine: The Yield

Findings from large meta-analysis:
0.18% of patients with migraine and normal neurological exam will have significant intracranial pathology (tumor, infection, hemorrhage, ICP).
Is This Migraine

52 y/o with 40 + headaches daily x 5 years unresponsive to therapy

-45 y/o man with nightly headaches x 2 weeks. Pain so severe he extracted his own teeth!

Why Is Migraine Frequently Mistaken for Sinus Headache?

- Pain is often located over the sinuses
- Migraine is frequently triggered by weather changes
- Tearing and nasal congestion common during attacks
- Sinus medication may help migraine

Does Peter Have Sinus Headaches?
Diagnosis of Sinusitis Is Based on The Presence of At Least 2 Major or 1 Major + > 2 Minor Symptoms

<table>
<thead>
<tr>
<th>Major Symptoms</th>
<th>Minor Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Purulent nasal discharge</td>
<td>Headache</td>
</tr>
<tr>
<td>Nasal congestion or obstruction</td>
<td>Ear pain, pressure or fullness</td>
</tr>
<tr>
<td>Facial congestion or fullness</td>
<td>Halitosis</td>
</tr>
<tr>
<td>Facial pain or pressure</td>
<td>Dental pain</td>
</tr>
<tr>
<td>Loss of taste or smell</td>
<td>Cough</td>
</tr>
<tr>
<td>Fever (acute sinusitis only)</td>
<td>Fever (for subacute or chronic sinusitis)</td>
</tr>
</tbody>
</table>

Strategies for Migraine Treatment

**Acute Treatment**
To stop pain and prevent progression

**Preventive Treatment**
To decrease frequency & severity

Behavioral Approach To Migraine Management

- Standardize sleep schedule
- No meal skips
- Limit analgesics to no more than 2 treatments per week and 24 pills per month
- Treat early after headache onset
- Exercise
- Stop smoking
- Avoid known triggers
- Relaxation exercises (biofeedback)
- Have a written treatment plan for acute attacks
Acute Migraine Treatment Goals

- Headache free in 2 hours
- Back to full function in 2 hours
- Little to no side-effects from medication
- Headache does not come back for 24 hours
- Relief of associated symptoms
- Acute medication not needed >2 times/week

Treatment Tips for Acute Management

- If acute treatment still inadequate:
  - Change dose or formulation
  - Treat early while headache is mild
  - Add adjunctive therapy (eg, NSAID)
  - Try dihydroergotamine (nasal spray, injection)
  - Add preventive therapy
  - Try additional therapies such as using ice or heat, resting, going to a quiet room, etc.
  - Screen for exacerbating/interfering factors such as caffeine or acute medication overuse

How to Use Preventive Treatment

- Start with low dose and increase slowly
- Try therapy for ≥6 wk
- Set realistic expectations (Goal 50% reduction in severity/frequency of headaches)
- Avoid drug overuse and interfering drugs
- Evaluate therapy
  - Use diary
  - Decision to discontinue or taper once headaches are well controlled should be individualized
**Oral Therapies - First Line Therapy**

- Nontriptan
- NSAIDS
  - Diclofenac potassium solution*
- Combinations
  - Acetaminophen/aspirin/caffeine
- Analgesics
- Antiemetics
- Triptans
- Ergotamines

* FDA approved

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**Triptans**

- Sumatriptan
  - Oral – 25, 50, 100 mg
  - Nasal – 5, 20 mg
  - Auto-injector – 4 or 6 mg
  - Needle-free injector – 6 mg
- Zolmitriptan
  - Oral – 2.5, 5 mg
  - ODT – 2.5, 5 mg
  - Nasal – 5 mg
- Naratriptan
  - Oral – 1, 2.5 mg

- Rizatriptan
  - Oral – 5, 10 mg
  - ODT – 5, 10 mg
- Almotriptan
  - Oral – 6.25, 12.5 mg
- Frovatriptan
  - Oral – 2.5 mg
- Eletriptan
  - Oral – 20, 40 mg
- Sumatriptan/Naproxen
  - Oral – 85 mg/500 mg

ODT, orally disintegrating tablet

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**Sumatriptan Iontophoretic Transdermal System**

Once applied delivers 6.5 mg sumatriptan transdermally via an activated transdermal iontophoretic system

Best for patient who has significant migraine + nausea

Patient applies patch at onset of headache. If no improvement in two hours can use another form of sumatriptan (nasal, oral, injection)
Pharmacokinetics and Efficacy of Transdermal Sumatriptan

Pharmacokinetics of transdermal sumatriptan

Zecuity package insert. Teva Pharmaceuticals, 2014

Rescue Therapies

- Triptans
- Subcutaneous
- DHE
- NSAIDs
- IM/IV
- Rectal
- Antihistamines
- Steroids
- Magnesium
- Anti-emetics
- Olanzapine 10 mg or sertraline 100 mg
- Occipital nerve block


When to Consider Preventive Therapy

- Migraine significantly interferes with patient’s daily routine, despite acute treatment
- Attack frequency >1/wk
- Acute medication ineffective, contraindicated, overused, or not tolerated
- Patient preference
- Presence of uncommon migraine conditions

Preventive Drugs for Frequent Episodic Migraine

- **Level A**
  - Divalproex sodium*: Oral 125 – 1000 mg
  - Sodium valproate*: Oral 125 – 1000 mg
  - Topiramate*: Oral 50 – 200 mg
  - Metoprolol
  - Oral 50 – 200 mg
  - Propranolol*: Oral 80 – 240 mg
  - Timolol*
  - Oral 20 – 60 mg
  - Frovatriptan (MRM)
  - Oral 2.5 mg
  - Butterbur
  - Oral 75 mg bid

- **Level B**
  - Amitriptyline
  - Oral 20 – 150 mg
  - Venlafaxine
  - Oral 12.5 – 75 mg
  - Atenolol
  - Oral 50 – 100 mg
  - Nedrol
  - Oral 40 – 320 mg
  - Naratriptan (MRM)
  - Oral 1, 2.5 mg
  - Zolmitriptan (MRM)
  - Oral 2.5, 5 mg
  - ODT 2.5, 5 mg
  - Nasal 5 mg

* FDA approved

Herbal Preventives

- Butterbur (Petadolex) 75 mg twice a day
- B2 (Riboflavin) 400 mg a day
- Magnesium 400-600 mg a day
- Feverfew 3 dried leaves daily
- Coenzyme Q-10 150-300 mg a day

Episodic Migraine

Frequent Episodic Migraine

- Impact During Attack
- Incapacity
- Normal
- Time to Recover

Transforming Migraine

- Attacks less distinct 6-14 days of HA per month
- Return to baseline function does not always occur between migraine attacks
- Evidence of physiological and/or psychological dysfunction often present
Classification of Migraine

- **Episodic Migraine**
  - <15 headache days per month = EM
  - Without aura
  - With aura

- **Chronic Migraine**
  - ≥15 headache days per month X 3 months = CM
  - HA day = 4 or more hours of moderate-to-severe HA or response to migraine-specific medications

EM: episodic migraine
CM: chronic migraine

Chronic Migraine Risk Factors

**Modifiable**
- Attack frequency
- Obesity
- Snoring/obstructive sleep apnea
- Stressful life events
- Medication overuse
- Caffeine overuse

**Not Modifiable**
- Age
- Female gender
- Low education or socioeconomic status
- Genetic factors
- Head injury

Sandra
Chronic Migraine Treatment

- Goal to transform back to episodic migraine
- Focus on effective preventive management
- Treatment often combination of preventive medications, procedures, addressing medication overuse, and attention to comorbid conditions
- Multidisciplinary approach desirable

Opioids May Result In Neuroinflammation

Activated Microglial Cells

Stress

Peripheral/Central Sensitization

Glutamine, IL-6

Glutamine, IL-6

Glutamine, IL-6

Adapted from: Unger J. Diabetes Management in Primary Care - 2nd Ed. Lippincott. 2012.
Occipital Nerve Block

- Bupivacaine 0.5 % 4 cc + triamcinalone 200 mg (1cc) injected into ipsilateral occipital notch
- 21 g needle
- 5 cc syringe

CPT Codes for Nerve Blocks

- CPT 64405 if unilateral
- CPT 64405-50 if bilateral
- Vary, but average $100-$194 if unilateral and $200-$294 if bilateral
- Best to not charge office visit if charging and billing for procedure
- Procedure can be done in 5 minutes

Injection Pattern for OnabotulinumtoxinA

A. Corrugator: 5 units each side
B. Procerus: 5 units (one site)
C. Frontalis: 10 units each side
D. Temporalis: 20 units each side
E. Occipitalis: 15 units each side
F. Cervical paraspinals: 15 units each side
G. Trapezius: 15 units each side

0.1 mL = (5 Units/site)
Summary

- Migraineurs are born with an inherently weak pain protective mechanism
- Migraine headaches are recurrent and disabling
- Migraine may be accurately diagnosed in patients who experience nausea, photophobia and/or disability during their headaches
- Migraine interventions include lifestyle changes, preventative therapies, abortive drugs, and rescue therapies
- Avoid prescribing opioids to migraineurs as they may induce neuroinflammation
- Sinus headache? Treat for migraine...

Post-test ARS Question 1

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Post-test ARS Question 7

Which of the statements below describes your approach to participating in diagnosing and treating Migraines?

1. I do not participate in the diagnosis and treatment of Migraines, nor do I plan to this year.
2. I did not participate in the diagnosis and treatment of Migraines before this course, but as a result of attending this course I’m thinking of doing this now.
3. I do participate in the diagnosis and treatment of Migraines and I now plan to change my treatment methods based on completing this course.
4. I do participate in the diagnosis and treatment of Migraines and this course confirmed that I don’t need to change my methods.