Emerging Challenges in Primary Care: 2018

Managing Migraine: Primary Care for Primary Headaches

Faculty

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Disclosures

- Jeff Unger, MD, FAAFP, FACE has no financial relationships to disclose.
Learning Objectives

1. Utilize evidence-based strategies to diagnose patients presenting with headache.
2. Identify associated conditions (e.g. depression), and red flags for potentially life threatening causes of headache.
3. Use evidence-based recommendations to prescribe treatment for patients presenting with acute or emergent headache pain.
4. Develop collaborative management plans, emphasizing patient education on avoiding triggers that cause headache, and adherence to prescribed treatment strategies.
5. Discuss newer pharmacologic targets for managing patients with Chronic Migraine.

PRE-TEST QUESTIONS

Pre-test ARS Question 1
How confident are you in your ability to treat patients with chronic migraine?
1. Not at all confident
2. Slightly confident
3. Moderately confident
4. Pretty much confident
5. Very confident
Pre-test ARS Question 2

How often do you consider a diagnosis of migraine in a patient presenting with a chief complaint of headache?

1. Never
2. Rarely
3. Sometimes
4. Often
5. Always

Pre-test ARS Question 3

Intravenous infusion of CGRP into an asymptomatic patient with migraine will result in which of the following events:

1. Hypotension
2. Syncope
3. Acute migraine
4. Cardiac arrhythmia

Migraine Fact Check

- 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.
- Migraine is one of the world's 10th leading cause of disability
- Migraine is a leading cause of ED visits in the US
- < 13% of all migraineurs receive prophylactic treatment
- Migraine is considered a long-term, chronic disease


Primary and Secondary Headaches

Primary:
- Migraine
- Cluster
- Tension-type

Secondary:
- Traumatic
- Vascular
- Infectious
- Metabolic
- Oncologic
  - Primary
  - Secondary
  - Inflammatory

Primary And Secondary Headache Disorders

Primary
- H/A is idiopathic
- No identifiable cause
- No specific diagnostic tests
- Defined clinically
- Dx based on ruling out specific pathologic events

Secondary
- H/A is a symptom reflective of underlying pathology
- Diagnostic tests useful
- Diagnosis based on defining pathology

Diagnostic Red Flags and Comfort Signs

Red Flags:
- First or worst
- Abrupt onset
- Fundamental change in pattern
- New headache onset in patients ≤ 5 or ≥ 50 years of age
- Cancer, HIV, pregnancy
- Neurological dysfunction + headache
- HA onset with seizure or syncope
- HA onset with exertion, sex or Valsalva
- Abnormal vital signs
- In children, HA get progressively worse over time

Comfort signs:
- Stable pattern ≥ 6 months
- Long history of same headaches
- In children-recurring, INTERMITTENT
- Normal neurologic exam
- Occur with menstruation
- +FH of same
- Known consistent triggers
Migraine Prevalence: Age and Gender

Migraine prevalence peaks in the 25-55 age range


Definition of Migraine

- A stable pattern of recurrent disabling headaches without evidence of underlying cause.
- Migraineurs have a genetic sensitivity towards severe, disabling headaches.
- Migraineurs are born with a very sensitive nervous system.
- The goal of migraine management is to allow the migraineur to learn to reduce their neurological sensitivity.
- Migraine events disrupt normal neurologic brain function which increases the likelihood of having additional events.

- Unger J. Migraine prophylaxis. The Pain Practitioner. 17 (1). 32-36. 2007
Migraineurs Are Born With A Genetically Predisposed Sensitive Neurological System

- Triggers:
  - Stress
  - Hormonal changes
  - Skipping meals
  - Specific food (cheap red wine, caffeine)
  - Sleep disruptions
  - Medications and med overuse
  - Weather
  - Minor head trauma

- Protective factors:
  - Standardized sleep patterns
  - Regular meals
  - Exercise
  - Stress management
  - Pro-active treatment for menstrual migraine and prodromes
  - Post-menopause treatment
  - Avoidance of triggers
  - Reduction caffeine usage

Phases of a Migraine Attack

Prodrome: Symptoms

- Irritability - 48%
- Nausea - 43%
- Muscle pain/tenderness - 38%
- Change in energy level - 30%
- Change in mood - 24%
- Change in appetite - 21%
- Yawning - 21%

Adapted from Cady RK. Headache. 2008;48(9):1415-1416.

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Migraine: Spreading Cortical Depression and Aura

Patient Describing Aura

Neck Pain During Migraine

- Prevalence
  - 75% of subjects
- Descriptions
  - 69% - tightness
  - 17% - stiffness
  - 5% - throbbing
  - 5% - other

82% had previously been given a diagnosis of tension-type headache.
“Even My Hair Hurts” (allodynia)

- Cutaneous allodynia
  - “Hair hurts”
  - Painful when:
    - Shaving
    - Combing hair
    - Touching scalp
    - Resting head on pillow
    - Pulling hair back (wearing a ponytail)
    - Wearing eyeglasses or contact lenses
    - Wearing hat or head band


Migraine Pathogenesis

- Genetic predisposition
- Triggers evoke aberrant firing of neurons resulting in cortical spreading depression (CSD)
- CSD activates the release of neurokinins and CGRP causing vascular dilation and increased platelet adhesiveness.
- Neuronal flow into the nucleus caudalis can eventually cause nausea, vomiting, dizziness, and severe head pain


Diagnosis Of Migraine (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 ___

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

Barriers and Pitfalls In Primary Headache Diagnosis

- Headaches evaluated within Primary Care are rarely due to secondary causes.
- Remember, migraine is a neurologic event, not a pathologic process based upon vasodilation and constriction.
- Be cautious of patient directed diagnoses: “Sinus, stress or allergic headaches”.
- Most patients will have tried OTC meds prior to seeking professional consultation.
- “Sinus headaches” and neck pain...think migraine.

Physical Exam

- Vital signs!
- Look for any focal neurological findings
- Listen to the head!
- Feel the scalp and neck muscles

Listen to the Head!
**Headache Lab Tests**

- CBC
- ESR
- T4, TSH, Thyroid Peroxidase Antibody

**Heather History**

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

**Diagnostic Evaluation**

- Primary Headache
- Secondary Headache
- Atypical Features
- Danger signs present?
- Investigations

Adapted from Silberstein et al. (eds.) Headache in Clinical Practice. 1999.
Primary Vs. Secondary Headache Disorders

Imaging Patients With Migraine: The Yield

Findings from large meta-analysis: 6.18% of patients with migraine and normal neurologic exam will have significant intracranial pathology (tumor, infection, subarachnoid hemorrhage 2.8%)

Is This Migraine?

-45 y/o man with nightly headaches x 2 weeks. Pain so severe he extracted his own teeth!
Cluster Headache: AKA “Suicide Headaches”

- Usually no aura
- Peak pain in 10 to 15 minutes
- Duration 15 minutes to 2 hours
- Unilateral, side-locked—rarely switches sides
  - Ipsilateral conjunctival injection and/or lacrimation
  - Ipsilateral nasal congestion and/or rhinorrhea
  - Ipsilateral miosis and/or ptosis
- 1 - 3 attacks per day. Awaken at night
- Described as excruciating, boring, burning pain; usually non-throbbing

Cluster Headache Treatment

**Acute**
- High flow O₂, 10-12 or 12-15L/m by NRBm
- Parental/Nasal DHE-Triptan
  - Oral meds aren’t fast enough
  - Zolmitriptan 10 mg (off label)

**Preventive**
- Steroid Burst (Decadron 12 mg day 1, 8 mg day 2, 4 mg day 3)
- Occipital Nerve Block with Steroids
- Verapamil—must be instant release
  - Start @ 80-120 BID – Increase to TID
  - Titrate up until cluster stops or side effects intolerable
- EKG 3 days after dose increases >360mg & yearly

One Nerve Pathway: Multiple Symptoms of Migraine
10/9/18

Does Peter Have Sinus Headaches?

Diagnosis of Sinusitis Is Based on The Presence of At Least 2 Major or 1 Major + > 2 Minor Symptoms

- Purulent nasal discharge
- Nasal congestion or obstruction
- Facial congestion or fullness
- Facial pain or pressure
- Loss of taste or smell
- Fever (acute sinusitis only)
- Headache
- Ear pain, pressure or fullness
- Halitosis
- Dental pain
- Cough
- Fever (for subacute or chronic sinusitis)
- Fatigue


Nasal Endoscopy

No Headache

With a moderate to severe "sinus" headache

1 hour after treatment with sumatriptan 6mg SC


Photos courtesy of Jeff Unger, MD
Strategies for Migraine Treatment

Lifestyle Interventions

Acute Treatment

Preventive Treatment

When all else fails!

1. No meal skips
2. Exercise
3. Sleep hygiene
4. Avoid triggers
5. Stop smoking
6. Stop analgesics > 2 times weekly
7. 2 cups java per day
8. Relaxation exercises
9. Have a written plan!!

Behavioral Approach to Migraine

Educate Patient Regarding The Diagnosis of Migraine

- Emphasize biologic and behavioral aspects of migraine.
- Reassure patient regarding migraine pathogenesis.
- Discuss treatment expectations: reduction in frequency, intensity, duration of headaches as well as limiting migraine disability.
- Engage patient in treatment plan.
- Answer questions.
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.

Triptans

- Sumatriptan
  - Oral – 25, 50, 100 mg
  - Nasal – 5, 20 mg
  - Auto-injector – 4 or 6 mg
  - Needle-free injector – 6 mg
  - Sumatriptan nasal powder -11 mg
- Zolmitriptan
  - Oral – 2.5, 5 mg
  - ODT – 2.5, 5 mg
  - Nasal – 5 mg
- Naratriptan
  - Oral – 1, 2.5 mg
  - ODT, orally disintegrating tablet
- Almotriptan
  - Oral – 4 or 6 mg
  - Needle-free injector – 6 mg
  - Sumatriptan nasal powder -11 mg
- Eletriptan
  - Oral – 20, 40 mg

Triptans are 5-HT1B/D/F receptor agonists that attenuate migraine in many patients. They inhibit release of CGRP within the trigeminal vascular system. However, inhibition may be short lived, and HAs can reoccur. Over 30% of patients do not respond well to triptans, especially if drugs are used when the patient experiences peripheral and central sensitization.
Triptan Dosing Strategies

- Treat early after migraine onset.
- Use highest dose formulation.
- Expect to be pain free and associated symptom free within 2 hours.
- If headache worsening after 2 hours, repeat dose x 1.
- If headache worsens typically after initial dosing, reduce dose of triptan by 50% and add NSAID.
- Can dose ondansetron 4-8 mg for nausea.
- In presence of nausea consider SQ injection or nasal spray.
- If no response to triptan use “rescue” therapy.
- Keep a migraine diary to record frequency, intensity and duration of migraine.

Early Intervention: Triptan Efficacy vs. Pain Intensity

2 Hour Pain Free Response

<table>
<thead>
<tr>
<th>Pain Intensity When HA Treated</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 Hour Pain Free Response</td>
<td>80%</td>
<td>38%</td>
<td>35%</td>
</tr>
</tbody>
</table>

Adapted from Cady RK et al. SPECTRUM Study. Headache 2000 38:173-83

When To Consider Preventive Therapy

- Migraine significantly interferes with patient’s daily routine, despite acute treatment.
- Attack frequency >1/wk.
- Acute medication ineffective, contraindicated, over-used, or not tolerated.
- Patient preference.
- Presence of uncommon migraine conditions.
Basic Rules For Migraine Prevention
Pharmacology
- Remember, drugs used for migraine prevention were NOT developed initially to minimize migraine frequency.
- 70% of patients may have intolerable side effects resulting in high rate of non-adherence after 6 months.
- Start low, advance slow (migraineurs are drug sensitive).
- Consider co-morbidities when prescribing preventative agents.
- Re-assess or increase dose of single agent after 6 weeks of use.
- Advise patient when they should expect to feel some improvement with preventative care.
- Consider tapering or discontinuing meds after 6 months.
- Goal is to reduce pain index by 50%.
- PTI= Intensity (0-10) x duration (hrs) + frequency/30 days.
  - 7 x 8 hours over 10/30 days= 66.

Selecting Appropriate Preventive Therapy
- Take advantage of drug's side effects
  - Underweight patient: pick a drug that produces weight gain
  - Overweight: select drug that is not associated with weight gain
  - Insomniac: use sedating tertiary TCAs at HS
  - Elderly or cardiac patient: use divalproex or topiramate
  - Athlete: avoid β-blockers

American Academy Neurology
American Headache Society
Preventive Recommendations

<table>
<thead>
<tr>
<th>Level A</th>
<th>Level B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Divalproex Sodium</td>
<td>Amitriptyline</td>
</tr>
<tr>
<td>Sodium valproate</td>
<td>Venlafaxine</td>
</tr>
<tr>
<td>Topiramate</td>
<td>Atenolol</td>
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<tr>
<td>Metoprolol</td>
<td>Nadolol</td>
</tr>
<tr>
<td>Propranolol</td>
<td>Naratriptan*</td>
</tr>
<tr>
<td>Timolol</td>
<td>Zolmitriptan*</td>
</tr>
<tr>
<td>Frovatriptan*</td>
<td>CGRP inhibitors</td>
</tr>
</tbody>
</table>
**Herbal Preventives**

- Butterbur (Petadolex) 75 mg twice a day
- B2 (Riboflavin) 400 mg a day
- Magnesium 250-400 mg a day
- Feverfew 3 dried leaves daily
- Coenzyme Q-10 150-300 mg a day

* Effective for pediatric migraine

**Injection Pattern for OnabotulinumtoxinA-PREEMPT Technique (155-200 Units)**

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: 10 Units each side

0.1 mL = (5 Units/site)

**Menstrual Migraine Prevention Option**

- Frovatriptan 2.5 mg BID x 6 days beginning 2 days prior to onset of period.
- Frovatriptan 10 mg at onset of period.
- Frovatriptan 2.5 mg qd x 6 days beginning 2 days prior to onset of period.
Why Patients Fail

- Not able to treat early
- Low and inconsistent oral absorption
- Unrecognized analgesic overuse
- Medical and psychiatric comorbidities
- 5HT receptor polymorphisms

Migraine Rescue Strategies

- Olanzapine 10 mg PO
- Quetiapine 100 mg PO
- Magnesium Sulfate 1 gram IV Push*
- Occipital nerve block*
- Sphenopalatine ganglion block*
- Use a “sphenocath”
- *= Office procedure by a family physician

Occipital Nerve Block

- Inject bupivacaine 0.5% 4 cc + triamcinolone 40 mg into the occipital notch on the side where patient perceives the majority of their head pain.
- Patient will note paresthesias lasting 6-12 hours on the side of the head where the injection was performed followed by significant headache relief lasting days to weeks.
**IV Magnesium-Aborting Migraine Within 15 Seconds! NO KIDDING…**

- 1 gram IV push over 1-2 minutes
- Side effect: severe hot flash lasting < 1 minute
- Eliminates migraine and migraine associated symptoms within 2-3 minutes
- Works best for HA < 24 hour duration. For HA > 24 hour duration use valproate (depakon) 500 mg IV push over 3-5 minutes

**Chronic Migraine**

- Decreased platelet 5-HT.
- Upregulation of 5-HT2A receptors, leads to increased NO synthesis.
- NO induces cerebral vasodilation and sensitized central and peripheral nociceptors.
- Increased levels of Substance P and CGRP in CSF.
- Sensitization of central neurons potentiates pain response.

**Episodic Migraine**

**Frequent Episodic Migraine**

- Impact During Attack
- Frequency
- Incapacity

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Chronic Migraine

Catalysts of Transformation

- Overuse of acute treatment (> 2/ week)
- Analgesic use with each attack
- Head or neck trauma in a migraineur
- Genetics
- Obesity (> 30 kg/m2)
- Female gender/caucasian
- Earlier age of headache onset
- Oral contraceptive use

Drugs Which Can Result In Analgesic Rebound Headache

- Caffeine
- Butalbital
- Opioids
- Ergots
- Triptans
- Acetaminophen
- NSAIDs
- OTC
- Tramadol
- Decongestants
CGRP (Calcitonin-gene related peptide) And Migraine

- CGRP is released from various locations in the body during times of physiologic or emotional stress.
- CGRP sensitizes trigeminal afferents recruiting other nerves which can potentiate migraine.
- As more nerves become sensitized, the thalamus becomes activated and patient develops central sensitization.
- CGRP levels sampled from the external jugular vein are increased during migraine compared with controls who do not have migraine.
- CGRP infusions can trigger migraine in migraineurs, but not healthy controls.
- CGRP inhibitors block migraine progression and reduce frequency, intensity and duration of migraine.
- CGRP inhibition allows brain to recover more fully from a migraine event.
- A brain which has not fully recovered from a migraine event is more reactive. Another migraine will follow.
- Frequent migraine, result in more frequent events.

CGRP And Migraine

Migraine trigger

Trigeminal Nerve activation

Pain!
CGRP Inhibitor Prevents Migraine

Migraine Trigger

Trigeminal Nerve activation

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Treatment of Chronic Migraine

- Maximize behavioral interventions
- Stop MOH agents
- Address any co-morbidities (MDD, GAD, sleep disturbances, obesity)
- Maximize acute treatment outcomes

- Consider nerve blocks
- CGRP inhibitors (not FDA approved)
- Referral for refractory patients
- Employ preventative medications:
  - AEDs, mg, beta blockers, TCAs
  - Botulinum toxin A
  - CGRP Inhibitors

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CGRP Inhibitors

<table>
<thead>
<tr>
<th>Pharmacologic target</th>
<th>ALD403</th>
<th>Erenumab-Aimovig</th>
<th>Galcanezumab-Emgality</th>
<th>Fremanezumab-Ajovy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Migraine target</td>
<td>Episodic, chronic</td>
<td>Episodic, chronic</td>
<td>Episodic, chronic</td>
<td>Episodic, chronic</td>
</tr>
<tr>
<td>Dosing</td>
<td>Single-dose IV, 1 Gram. Efficacy lasts up to 4 months</td>
<td>SC 70 and 140 mg monthly</td>
<td>SC 240 mg loading dose, then 225 mg/month</td>
<td>SC 225 mg/month, with 675 mg q 3 months (30 minute warmup time)</td>
</tr>
<tr>
<td>Notes</td>
<td>Drug inhibits action of CGRP and removes CGRP from receptors. Some patients have achieved complete remission</td>
<td>Nearly 50% reduction in episodic migraine vs PBO</td>
<td>75% reduction in headaches observed in 28% of patients vs 16% receiving PBO</td>
<td></td>
</tr>
</tbody>
</table>


Cycle Breakers For Chronic Migraine

- Stop offending agent(s)
- Frovatriptan 2.5 mg at 4 pm daily x 8 days
- Dexamethasone PO x 3 days:
  - 12 mg
  - 8 mg
  - 4 mg
- IV magnesium sulfate 1 gram stat, then 1 gram weekly x 3 doses total
- Occipital nerve block
- Sphenopalatine ganglion block
- Olanzapine 20 mg or quetiapine 100 mg x 7 days
- Dihydroergotamine

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…
- Consider use of CGRP inhibitors for patients who have failed other preventative agents.

POST-TEST QUESTIONS
**Post-test ARS Question 1**

After participating in this program, how confident are you now in your ability to treat patients with chronic migraine?

1. Not at all confident
2. Slightly confident
3. Moderately confident
4. Pretty much confident
5. Very confident

**Post-test ARS Question 2**

After participating in this program, how often will you now consider a diagnosis of migraine in a patient presenting with a chief complaint of headache?

1. Never
2. Rarely
3. Sometimes
4. Often
5. Always

**Post-test ARS Question 3**

Intravenous infusion of CGRP into an asymptomatic patient with migraine will result in which of the following events:

1. Hypotension
2. Syncope
3. Acute migraine
4. Cardiac arrhythmia
Thank You!

Questions