Migraine, Tension, and Cluster Headache: Primary Care for Primary Headaches

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• Experimental therapies will also be discussed. The audience will be informed about unapproved drug interventions.

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.
Associated Sessions

- Migraine, Tension, and Cluster Headache: PBL

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.

Primary and Secondary Headaches

- Primary:
  - Migraine
  - Cluster
  - Tension-type
- Secondary:
  - Primary:
  - 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
  - Classic H/A: pregnancy
  - Neurological dysfunction + headache
  - H/A onset with seizure or syncope
  - Abnormal vital signs
  - In children, H/A get progressively worse over time
- Comfort signs:
  - Stable pattern x 6 months
  - Long history of same headaches
  - In children-recurring, INTERMITTENT
  - Normal neurologic exam
  - Occur with menstruation
  - +FH of same
  - Known consistent triggers
Headache Time Course

Migraine Prevalence: Age and Gender

Definition of Migraine

- A stable pattern of recurrent disabling headaches without evidence of an 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.

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 menopausal treatment
  - Avoidance of triggers
  - Reduction caffeine usage

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%

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 neuropeptides 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

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

A patient consulting a PCP for headaches has a 94% chance of having migraine.
< 2% will have a secondary headache disorder.
Consults for tension-type headaches are rare.
Diagnostic Evaluation

Primary Headache

Secondary Headache

Investigations

Primary Vs. Secondary Headache Disorders

Imaging Patients With Migraine: The Yield

Is This Migraine?

Cluster Headache: AKA “Suicide Headaches”

Cluster Headache Treatment

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

References:


One Nerve Pathway:
Multiple Symptoms of Migraine

Major 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)

Major Symptoms
- Headache
- Ear pain, pressure or fullness
- Halitosis
- Dental pain
- Cough
- Fever (for subacute or chronic sinusitis)
- Fatigue

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

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)

Strategies for Migraine Treatment

- Acute Treatment
- Preventive Treatment
- Preemptive Treatment

BEHAVIORAL APPROACH TO MIGRAINE

- No meal skips
- Exercise
- Sleep hygiene
- Avoid triggers
- Stop smoking
- Stop analgesics > 2 times weekly
- 2 cups java per day
- Relaxation exercises
- Have a written plan!!
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
- Zolmitriptan
  - Oral – 2.5, 5 mg
  - OD – 2.5 mg
- Naratriptan
  - Nasal – 5 mg

Triptans

- Triptans are 5-HT1B/D/F receptor agonists that attenuate migraine in many patients
- Inhibit release of CGRP within the trigeminal vascular system
- However, inhibition may be short-lived. HAs can reoccur
- 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

Adopted 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, overused, or not tolerated
- Patient preference
- Presence of uncommon migraine conditions

Basic Rules For Migraine Prevention Pharmacology

- 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 Preventive Treatment

Use Drug Best for Patient

- 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

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
G. Trapezius: 15 Units each side

0.1 mL = (5 Units/site)

Liberini et al. NeurolSci. 2014 May;35 Suppl 1:41‐3

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 co-morbidities
• 5HT receptor polymorphisms

Migraine Rescue Strategies

• Olanzepine 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 (marcaine) 0.5% 4 cc + triamcinolone (Kenalog) 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

• 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 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

Severity

Frequent Episodic Migraine

Time to Recover

Incapacity

Normal


Transforming Migraine

- Transforming Migraine

Frequency

Severity

Normal


Catalysts of Transformation

- Overuse of acute treatment (> 2/ week)
- Analgesic use with each attack
- Head or neck trauma in a migraineur
- Genetics
- Female gender/caucasian
- Earlier age of headache onset
- Previous ineffective prophylaxis
- Occurrence of vomiting
- Attack onset upon awakening
- Family history of coronary artery disease

Drugs Which Can Result In Analgesic Rebound Headache

- Caffeine
- Butalbital
- Opioids
- Ergots
- Triptans
- Acetaminophen
- NSAIDs
- OTC
- Tramadol
- Decongestants
CGRP 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 are increased during migraine.
- CGRP injections can trigger migraine.
- 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.
- Frequent migraine results in more frequent events.

Mechanism of Action

- Onabotulinum toxin A
  - Inhibits neurogenic inflammation by attenuating neurotransmitter release of glutamate, substance P and CGRP.
  - Reduces peripheral and central sensitization.
  - Injected in face and neck every 3 months.
  - 50% reduction in Chronic migraine.

CGRP Inhibitors In Pipeline (Not FDA Approved)

- ALD403
- AMG 334
- LY2951742
- TEV-48125

Pharmacologic target
- CGRP receptors which modulate pain during migraine.
- Can actively remove CGRP from receptor sites.
- Reduce vasoconstriction.
- Reduce mass cell extravasation of neuropeptides.
- CGRP levels are chronically elevated in patients with chronic migraine.
- Can be given SQ or IV monthly or once every 6 months. Rapid response to therapy.

- Minimal side effects (injection site rxs)
- Some patients experience complete resolution of their headaches.

CGRP Receptor Structure And Targeted Action Sites

- Blocks vasodilation of meningeal arteries.
- Stops release of neuropeptides which potentiate migraine.
- CGRP inhibition:
  - Blocks vasodilation of meningeal arteries.
  - Stops release of neuropeptides which potentiate migraine.

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.

Notes

- Drug inhibits action of CGRP and removes CGRP from receptors from chronic or episodic conditions of migraine.
- Nearly 90% reduction in episodic migraine.
- Nearly 70% reduction in chronic migraine.
- 75% reduction in headaches observed in 30% of patients vs 16% reduction in PBO.

CGRP Receptor Inhibitors (Not FDA Approved)

- CGRP inhibition:
  - Blocks vasodilation of meningeal arteries.
  - Stops release of neuropeptides which potentiate migraine.

Free Iron Deposition in The PAG In a Patient With CDH
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

Practice Recommendations

- Imaging studies are not needed in patients with intermittent disabling headaches (ie. Migrane). (SOR A)
- Patients presenting with the complaint of “sinusitis” should be considered as having a migraine unless symptoms are associated with fever, discolored nasal secretions, halitosis and loss of smell. (SOR A)
- Avoid the use of chronic opioids in patients with headache disorders. (SOR A)

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…

Thank You!

Questions