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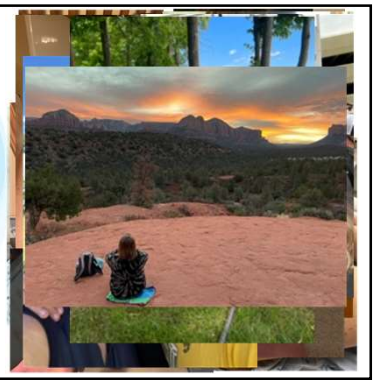
Global Treatment Strategy for Chronic Migraine

Disclosures

- No disclosures

Who I Am

Why Am I Talking About Migraine?



Why I Am Talking About Migraine

- Migraine can significantly impair ones' functional ability
- With proper diagnosis and prompt treatment the negative impacts can be minimized for most
- Majority of visits for migraine take place in primary care

Educational Objectives

1) List the practical applications of pharmacologic preventative and abortive treatments
2) Be cognizant of complimentary and alternative treatments for chronic migraine
3) Assess the clinical outcome of migraine treatment plan on patient quality of life

True or False

Migraine is the second most disabling condition

TRUE

The Burden of Migraine

- Migraine affects over 40 million people in the USA (18% of women, 6% of men)
- 2nd most disabling condition per the World Health Organization (WHO)
- Over half (52.8%) of all visits for migraine take place in primary care settings
  - Under-diagnosed
  - Under-treated
    - ~40% need preventive therapy
    - 13% receiving preventative therapy

Test Our Knowledge

Migraine is most prevalent in which age group?

A. Teenage years
B. 20s
C. 30s
D. 40s

C. 30s

Top Migraine Stats for 2022

- Most prevalent in people aged 30–40
- Prevalence with female to male ratio of 3:1
- 90% of migraineurs are unable to function normally during attacks
- Migraineurs are five times as likely to have depression and anxiety
- Suicide rates are 42.9%
- Nearly one out of every two people are never diagnosed

First, We Must Diagnose: Headache ICHD-3 Classification

3 Broad Categories

- **Primary headaches**
  - **Migraine**
- **Secondary headaches**
  - **8 categories and 46 subcategories**
- **Neuropathies and Facial Pains**

First, We Must Diagnose: Migraine ICHD-3 Criteria

A. Have had five attacks **AND**
B. Lasting 4–72 hrs (when untreated or unsuccessfully treated) **AND**
C. Has at least two of these characteristics:
   1. Unilateral location
   2. Pulsating quality
   3. Moderate or severe pain intensity
   4. Aggravation by or causing avoidance of routine physical activity (e.g., walking or climbing stairs)
   5. AND
D. Has at least one of these during the HA:
   1. Nausea and/or vomiting
   2. Photophobia and phonophobia
   3. AND
E. Not better accounted for by another diagnosis

First, We Must Diagnose: Chronic Migraine ICHD-3 Criteria

A. Migraine on ≥15 days/month for >3 months that fulfill criteria B AND C

B. at least 5 attacks fulfilling criteria B-D for migraine without aura and/or criteria B and C for migraine with aura

C. On ≥8 days/month for >3 months, fulfilling any of the following:

1. Criteria C and D migraine without aura
2. Criteria B and C for migraine with aura
3. Believed by patient to be migraine at onset and relieved by a triptan or ergot derivative

D. Not better accounted for by another diagnosis

To Image or Not To Image, That is The Question

- **Not necessary** with headaches **consistent with migraine** with a **normal neurologic examination**
  - Grade A (strong recommendation, high quality evidence).
- Neuroimaging **may be considered** for presumed migraine for the **following reasons**:
  - Unusual, prolonged, or persistent aura
  - Increasing frequency, severity, or change in migraine clinical features
  - First or worst migraine
  - Migraine with brainstem aura
  - Confusional migraine
  - Hemiplegic migraine
  - Late-life migrainous accompaniments
  - Migraine aura without headache
  - Side-locked migraine
  - Posttraumatic migraine
- Most of these are **consensus based** with **little or no literature support**
- Grade C (strong recommendation, low quality evidence)

The American Headache Society Systematic Review and Evidence-Based Guideline

When to Get Labs & What Labs to Get

- Initially
- Worsening or change in headache pattern
- CMP, CBC, TSH, Vit B12, MMA, Vit D
- Usually low yield

Headaches: On a Continuum or Distinct Conditions?

- Controversial among neurologists
- HA days/month usually > Migraine days/month
- More consistent with mixed headache picture
- But not always, few have migraine or nothing but much less common
- Common to have cervicogenic component as a contributing factor

Diagnosing Secondary Headaches

- HA is a symptom of another underlying disorder
- Approximately 18% of people who experience a headache have a secondary headache disorder
- Underlying conditions can be life-threatening or disabling and may require a completely different therapeutic approach than a primary headache disorder
- Detailed history taking, physical examination, and recognition of diagnostic red flags are crucial to diagnosis
- SNNOOP10 - mnemonic used to diagnose secondary headaches

Red Flag Detection Tool for Secondary Headaches

Table 1 SNNOOP10 list of red and orange flags

	Sign or symptom	Related secondary headaches (most relevant ICHD-3b categories)	Flag color
1	Systemic symptoms including fever	Headache attributed to infection or nonvascular intracranial disorders, carcinoid or pheochromocytoma	Red (orange for isolated fever)
2	Neoplasm in history	Neoplasms of the brain; metastasis	Red
3	Neurologic deficit or dysfunction (including decreased consciousness)	Headaches attributed to vascular, nonvascular intracranial disorders; brain abscess and other infections	Red
4	Onset of headache is sudden or abrupt	Subarachnoid hemorrhage and other headaches attributed to cranial or cervical vascular disorders	Red
5	Older age (after 50 years)	Giant cell arteritis and other headache attributed to cranial or cervical vascular disorders; neoplasms and other nonvascular intracranial disorders	Red
6	Pattern change or recent onset of headache	Neoplasms, headaches attributed to vascular, nonvascular intracranial disorders	Red
7	Positional headache	Intracranial hypertension or hypotension	Red
8	Precipitated by sneezing, coughing, or exercise	Posterior fossa malformations, Chiari malformation	Red
9	Papilledema	Neoplasms and other nonvascular intracranial disorders; intracranial hypertension	Red
10	Progressive headache and atypical presentations	Neoplasms and other nonvascular intracranial disorders	Red
11	Pregnancy or puerperium	Headaches attributed to cranial or cervical vascular disorders; postdural puncture headache; hypertension-related disorders (e.g., preeclampsia); cerebral sinus thrombosis; hypothyroidism; anemia; diabetes	Red
12	Painful eye with autonomic features	Pathology in posterior fossa, pituitary region, or cavernous sinus; Tolosa-Hunt syndrome; ophthalmic causes	Red
13	Posttraumatic onset of headache	Acute and chronic posttraumatic headache; subdural hematoma and other headache attributed to vascular disorders	Red
14	Pathology of the immune system such as HIV	Opportunistic infections	Red
15	Painkiller overuse or new drug at onset of headache	Medication overuse headache; drug incompatibility	Red

Abbreviation: ICHD-3b = International Classification of Headache Disorders 3b.
An overview of signs and symptoms, their related secondary headache, and distribution in red and orange flags.

Diagnosing Take-Aways

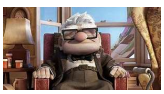
- The most crucial aspect of headache diagnosis is the history and physical exam
- Primary headache disorders are not diagnoses of exclusion but rather are based on supportive clinical features
- The presence of atypical features or red flags should raise concern for secondary headaches

The 3 Types of Patients

1. Am I Dying?
2. I want as little as possible….the majority ☺
3. I want everything, just fix me!!!

Migraines are Like a Cantankerous Person

- They are set in their ways
- Don't like changes in routine
- To keep them at bay, try to keep a steady state
  - Stay hydrated
  - Eat regularly
  - Keep a regular sleep pattern
  - Avoid stress
  - Maintain Mood
- Some changes we can't avoid
  - Weather
  - Travel
  - Good Stress



Preventative Treatment

- Many oral treatments have:
  - Limited to moderate efficacy
  - Moderate to high rates of adverse events (AEs)
  - Contraindications
  - Interactions
- Explains in part why few patients use preventive treatment (3–13%)
- Even though nearly 40% of those with episodic migraine, and almost all with chronic migraine would benefit

Preventative Treatment: Indications

- Attacks significantly interfere with patients' daily routines despite acute treatment
- Frequent attacks (≥4 monthly HA days)
- Patient preference
- Contraindication or adverse event to, failure, or overuse of acute treatments

Preventative Treatment: Acute Treatment Overuse Definition

- **10 or more days per month** for ergot derivatives, triptans, opioids, combination analgesics, and a combination of drugs from different classes that are not individually overused
- **15 or more days per month** for nonopioid analgesics, acetaminophen, and nonsteroidal anti-inflammatory drugs (NSAIDs [including aspirin])

Identifying Patients for Preventative Treatment

Prevention should be…	Headache days/month	Degree of disability required*
Offered	6 or more	None
	4 or more	Some
	3 or more	Severe
Considered	4 or 5	None
	3	Some
	2	Moderate

*As measured by scores on the Migraine Disability Assessment scale

Preventative Treatment: Goals

- Reduce attack frequency, severity, duration, and disability
- Improve responsiveness to and avoid escalation in use of acute treatment
- Improve function and reduce disability
- Reduce reliance on poorly tolerated, ineffective, or unwanted acute treatments
- Reduce overall cost associated with migraine treatment
- Enable patients to manage their own disease to enhance a sense of personal control
- Improve health-related quality of life (HRQoL)
- Reduce headache-related distress and psychological symptoms

Preventative Treatment: Developing a Plan

- Individualized education and lifestyle modification recommendations
- Use Evidenced Based Preventative Treatments
- Start Low and Titrate
- Reach a Therapeutic Dose
- Give an Adequate Trial
- Establish Realistic Expectations
- Optimize Drug Selection
- Maximize Adherence

Factors in Optimal Drug Selection of Prevention

Evidence of efficacy	Medical Professional Experience
Tolerability	Patient preference
Headache Subtype (episodic or chronic)	Comorbid and coexistent illnesses
Concomitant medications	Physiological factors (heart rate, blood pressure, etc)
Body habitus	Pregnancy or the potential for pregnancy among women
Ease of use	Response to previous treatments
Contraindications/Allergies	Cost/Insurance coverage

Preventative Treatments With Evidence of Efficacy in Migraine Prevention

Established efficacy	Probably effective
Monoclonal antibodies: **Eptinezumab** **Galcanezumab** **Fremanezumab** **Erenumab**	Antidepressants: Amitriptyline Venlafaxine
CRGP inhibitors: Rimegepant	Beta-Blockers: Atenolol Nadolol
Antiepileptic drugs: Divalproex sodium Valproate sodium Topiramate	ACE inhibitors: Lisinopril
Beta-blockers: Metoprolol Propranolol Timolol	Alzheimers/Dementia: Memantine
Triptans: Frovatriptan (menstrual migraine only)	
OnabotulinumtoxinA	OnabotulinumtoxinA +CGRP mAb
Angiotensin receptor blockers: Candesartan	

Monoclonal Antibodies

- Collection of identical proteins
- Target either CGRP or the CGRP receptor
- Given by SC injection or IV infusion
- Because they are large molecules, they take longer to start working
- May achieve rapid treatment effects over days to weeks
- Work in the lining of the brain rather than in the brain itself
- Tend to have few drug interactions
- Unlikely to cause liver or kidney damage
- Effective in patients who have failed prior preventive treatment, as well as in those on concurrent oral preventive treatments

Monoclonal Antibodies: -mAbs

- **Eptinezumab**: IV infusion every 3 months
- **Galcanezumab**: SC injection monthly, loading dose
- **Fremanezumab**: SC injection monthly or every 3 months, no loading dose
- **Erenumab**: SC injection monthly (2 different doses available), no loading dose
  - Constipation with serious complications
  - Hypertension

Monoclonal Antibodies: Indications for Initiating Treatment

- Use is approved when **ALL** of the following are met:
- Patient is at least 18 years of age
- Diagnosis of migraine with or without aura (4-7 monthly HA days) and both of the following:
  - Inability to tolerate (due to SE) or inadequate response to a 6-week trial of at least 2 RX from table 1:
  - AND
  - At least moderate disability (MIDAS>11, HIT-6>50)
- Diagnosis migraine with or without aura (8–14 monthly HA days) AND inability to tolerate (due to SE) OR inadequate response to a 6-week trial of at least 2 RX from table 1:
- Diagnosis of chronic migraine and EITHER a or b:
  a) Inability to tolerate (due to SE) OR inadequate response to a 6-week trial of at least 2 RX from table 1:
  b) Inability to tolerate or inadequate response to a minimum of 2 quarterly injection (6 months) of onabotulinumtoxinA

Table 1
1. Topiramate
2. Divalproex sodium/valproate sodium
3. Beta-blocker
4. Tricyclic antidepressant
5. Serotonin-norepinephrine reuptake inhibitor
6. Other Level A or B treatments (established efficacy or probably effective) according to AAN-AHS guideline

Monoclonal Antibodies: Reauthorization After Initial Use

A. Reduction in mean MHDs or headache days of at least moderate severity of ≥50%
B. A clinically meaningful improvement in ANY of the following validated migraine-specific patient-reported outcome measures:
   a) MIDAS
      i. Reduction of ≥5 points when baseline score is 11–20
      ii. Reduction of ≥30% when baseline score is >20
   b) MPFID
      i. Reduction of ≥5 points
   c) HIT- 6
      i. Reduction of ≥5 points

Preventative Treatment: Measuring Response

- Use patient-centric and validated outcome measures that evaluate the effect of treatment on:
  - Functional Capacity
  - Disability
  - Quality of life
- Help guide clinical decision-making for:
  - Changes in dose
  - Adding additional preventive treatment
  - Or switching to an alternative treatment

The Migraine Disability Assessment Test (MIDAS)

Asks "over the last 3 months:"

- How many days miss work or school?
- How many days was productivity reduced by half or more?
- How many days did you not do household work?
- How many days was productivity in household word reduced by half or more?
- How many days did you miss family, social, or leisure activities?
- How many days did you have a headache?
- On a scale of 0-10, on average how painful were they?

MIDAS Scoring

MIDAS Grade	Definition	MIDAS Score
I	Little or No Disability	0-5
II	Mild Disability	6-10
III	Moderate Disability	11-20
IV	Severe Disability	21+

Microsoft Word - MIDAS-1.doc (headaches.org)

Abortive/Rescue Treatments

- All patients should be offered a trial of acute treatment
- Treat at the first sign of pain
- Mild-to-moderate:
  - NSAIDs
  - Nonopioid analgesics
  - Acetaminophen
  - Caffeinated analgesic combinations
- Moderate or severe and mild-to-moderate that respond poorly to NSAIDs or caffeinated combinations: Use migraine-specific agents
  - Triptans
  - Ergotamine derivatives
  - CGRP inhibitors
  - Ditans

Abortive/Rescue Treatments: Goals

- Rapid and consistent freedom from pain and associated symptoms without recurrence
- Restored ability to function
- Minimal need for repeat dosing or rescue medications
- Optimal self-care and reduced subsequent use of resources
- Minimal or no adverse events
- Cost considerations

Assessment of Acute Treatment for Migraine

Established efficacy	Probably effective
Triptans	Ergotamine and other forms of DHE
Ergotamine derivatives	
Gepants	
Lasmiditan	NSAIDs: flurbiprofen, ketoprofen, IV & IM ketorolac
NSAIDs: aspirin, **celecoxib oral solution**, diclofenac, ibuprofen, naproxen	IV Magnesium: *in migraine with aura*
Combination analgesic: acetaminophen + aspirin + caffeine	Isometheptene-containing compounds
Consider **neuro-modulatory devices** for patients who prefer nondrug treatments or in whom treatment is ineffective, intolerable or contraindicated	Antiemetics: chlorpromazine, droperidol, metoclopramide, prochlorperazine, promethazine

What is CGRP? & What are CGRP inhibitors?

CGRP

- Calcitonin Gene-Related Peptide – a small protein
- Highly prevalent in sensory nerves that supply the head and neck
- Involved in pain transmission and levels increase during migraine attack
- May also play a role in the induction of migraine attacks

CGRP inhibitors

- First drugs developed specifically for migraine prevention
- Block effect of CGRP by either targeting CGRP itself or the CGRP receptor
- 2 types
  - Gepants
  - Monoclonal antibodies

CRGP inhibitors: -Gepants

- Fewer restrictions than triptans
- Great side effect profile
- Do NOT cause overuse or rebound headaches
- Well covered by insurance, except Medicare
- Insurance covers if fail two triptans
- Can take triptans & other OTC abortive medications along with them
- Some drug interactions and possibility of liver damage, metabolized by CYP system
- Rapidly penetrate the brain so work quickly
- All oral
- **Ubrogepant**
  - abortive only
- **Atogepant**
  - abortive only
- **Rimegepant**
  - abortive and preventative

Ditans

- **Iasmiditan**
- In a class by itself
- Works on serotonin 5-HT 1F receptor subtype
- BUT does NOT cause vasoconstriction
- Safe for patients with hx CAD & PVD
- Does cause dizziness and sedation
- Can NOT drive for 8 hours after administration

Non-Pharmacologic Treatments

True or False

Combined drug and non-pharmacological therapy can produce better outcomes than either modality alone

TRUE

Neuromodulation

- Devices that can enhance or suppress the activity of the nervous system
- Modulates pain mechanisms by stimulating the nervous system centrally or peripherally with an electric current or a magnetic field
- Most require prescription
- One device now OTC

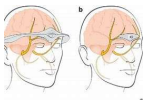
Neuromodulation: Indications

- All patients with migraine may be offered treatment
- All four devices that have received FDA clearance (eTNS, nVNS, REN, and sTMS) can be used alone or together with pharmacotherapy for acute treatment
- Three devices are cleared for use as monotherapy or adjunctive therapy for preventive migraine treatment: eTNS, nVNS, and sTMS
- Three devices (nVNS, REN, and sTMS) are also cleared for the acute and preventive treatment of migraine in adolescents between 12 and 17 years of age
- May be an especially important alternative for patients who prefer nondrug therapies and those who have failed to respond to, have contraindications to, or have poor tolerability with pharmacotherapy

Neuromodulation: Device Types

- Single Pulse Transcranial Magnetic Stimulator (sTMS) is a handheld device that works by generating a magnetic impulse that affects electrical signaling in the brain
- Transcutaneous Vagus Nerve Stimulator (nVNS) is a noninvasive handheld tool that uses electrical stimulation to target the vagus nerve in the neck
- Remote electrical neuromodulation (REN) stimulates peripheral nerves in the arm, goal of blocking pain signals from reaching the brain

Neuromodulation: Device Types



- Transcutaneous Supraorbital Neurostimulator (eTNS) uses electrical stimulation to stimulate the supraorbital nerves. Now OTC.
- Non-invasive multi-channel brain neuromodulation system (eTNS) is worn as a headset and targets multiple nerves on the head. Shown to reduce pain and other migraine-related symptoms like sensitivity to light and sound

Behavioral Health: What We Know

- Combined pharmacologic & behavioral therapy can produce better outcomes than either modality alone
- But it can be used as an alternative to pharmacologic treatment
- The effects of treatment tend to get better the more you use it

Behavioral Health: Barriers

- Lack of knowledge regarding non-pharmacologic treatment options
- Limited availability of clinicians trained in non-pharmacologic treatment
- Belief that behavioral interventions are for longstanding or complex headache patients who have failed pharmacotherapies
- Perception that behavioral treatments are stigmatic

Behavioral Health: Treatment Types

- Cognitive Behavioral Therapy (CBT)
  - identifying and challenging negative thoughts and behaviors
  - helps develop and use coping skills to manage pain
- Biofeedback
  - learn how to understand and control body functions that used to be considered involuntary (muscle tension, HR, BP)
  - helps manage your body's reaction to stress
- Progressive Muscle Relaxation
  - consciously concentrate on tensing and then relaxing every muscle in your body
  - Reducing muscle tension can lead to lower migraine pain
- Mindfulness Meditation
  - involves learning to become aware of the present moment no matter what is happening
  - effective in reducing the duration and intensity of Migraine attacks

Physical Therapy

- Passive Physical Therapies
  - Hot/Cold Packs
  - Massage
  - Steroid Creams
  - Ultrasounds
  - TENS
  - Dry Needling
  - Graston Technique
  - Cupping Therapy
- Active Physical Therapies
  - Stretching
  - Pain-relief and ROM exercises
  - Low-impact aerobic conditioning
  - Strengthening exercises
- Biopsychosocial model vs Biomechanical model

Self-Care & Trigger Avoidance

- Self- Care: The practice of taking action to preserve or improve one's own health
- Consistency is the key in diet, sleep, movement and stress
- The Migraine Brain Hates Change
- Common triggers
  - Food
  - Personal (stress, sleep)
- Grace and Forgiveness

Nutraceuticals

- Magnesium
  - Oxide and Citrate most studied, Pilodate has best pharmokinetic profile
  - Most useful for menstrual migraine
  - SE: diarrhea
  - Dose: 600 mg/day
- Riboflavin (Vitamin B2)
  - May lower frequency and need for medications
  - Common dose 400 mg daily
- Vitamin D
  - Useful for decrease in frequency and severity
- Omega 3
  - limited information available about the relationship between migraine and fish oil.
- Coenzyme Q10
  - Studies show useful for reducing frequency but not severity
  - Deficiency widespread
- Phycocyanin (Palmitoyl ethanol amide (PEA))
  - Pilot study on migraine with aura had significantly significant reduction of days with pain and # of attacks/ month
- Butterbur
  - Decent evidence for preventative treatment
  - Safety concerns due to contamination
- Feverfew
  - Limited evidence/studies

Acupuncture

- Can be recommended as an alternative or adjunct to drug treatment
- Multiple studies noted at least non-inferior to standard drug therapy and had some levels of superiority over sham acupuncture
- Further clinical trials are still needed to strongly present an evidence-based strategy

Chiropractic Care

- Spinal manipulation may reduce migraine frequency
- Not many high-quality, large studies on the benefit of chiropractic treatment in migraine
- Pilot randomized controlled trial in 2020 with preliminary data that supports a definitive trial for use of multimodal chiropractic care for migraine
- SE are generally temporary and may include:
  - Headaches
  - Tiredness
  - Soreness or discomfort where the chiropractic manipulation took place
- Rare serious SE include stroke, pinched nerves, and further damage to already herniated disks, but the cause-and-effect has not been proven.
- Find a chiropractor with proper credentials

Take-Aways for the Primary Care Provider Caring for Patients With Migraine

- Get treatment started promptly with both preventative and abortive/rescue medication
- Consistency is key
- Combined drug and non-pharmacological therapy can produce better outcomes than either modality alone
- Use disease specific tool to evaluate outcome of treatment plan

The Teacup Theory

Questions??

Thank You!

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