Disclosures

None
Overview

- Diagnostic criteria: Migraine, Cluster & Tension type headache

- Discuss novel treatment approaches

- Controversial Topics in Headache Medicine:
  1) Is medication overuse headache a real thing?
  2) Can patients with migraine aura take birth control pills?
  3) Would you give a triptan to a patient who is pregnant?
Whats more common?

Chronic Pain/Headache
Heart Disease
Cancer
Diabetes
Why headache matters

- Headache is the most prevalent neurologic symptom

- Global lifetime prevalences:
  - Headache 66%
  - Migraine 14%
  - Tension 46%
  - Chronic migraine 3-4%

- Great economic burden

- Complex and obscure pathophysiology

- Lack of academic and clinical interest
People can be understanding but not always.....

“Can I sign your cast?”
“Do you need help with that?”

“What is wrong with you?”
“I get headaches too but I can still work, why can’t you?”
Diagnostic Criteria
What is Migraine?

- Chronic disorder with episodic attacks
- Attacks 4-72 hours:
  - Unilateral, throbbing
  - Photophobia, phonophobia
  - Nausea/vomiting
  - Function disability
- In-between attacks:
  - Anxiety
  - Predisposition for future attacks
Migraine

- Episodic Migraine <15 headache days/month
- Chronic Migraine >15 headache days/month
- Aura (<60min)
- Prodrome/Postdrome
Migraine Pathophysiology

Migraine Medications

**Antidepressants**
- Tricyclics
  - Amitriptyline
- MAOIs
- SSRIs
- Fluoxetine
- Sertraline
- Paroxetine

**Antiepileptics**
- Divalproex sodium*
- Gabapentin
- Topiramate*
- Lamotrigine
- Tiagabine
- Zonisamide
- Levetiracetam

**Beta blockers**
- Propranolol*
- Nadolol
- Atenolol
- Timolol*
- Metoprolol

**Ca channel blockers**
- Verapamil
- Amlodipine
- Diltiazem
- Nifedipine
- Nimodipine

**5-HT2 antagonists**
- Cyproheptadine
- Methysergide*
- Methylergonovine‡

**Alternative therapies**
- Riboflavin
- Magnesium
- Feverfew, petasites

**Others**
- ACE inhibitors:
  - Lisinopril
- ARBs
- Candesartan,
- Telmisartan
- Quetiapine
- Tizanidine
- Onabotulinum toxin A*

**NSAIDs**
- Naproxen
- Meclofenamate
- Ibuprofen
- Ketoprofen
- Flurbiprofen

**Triptans**
- Sumatriptan
- Rizatriptan
- Eletriptan
- Zolmitriptan
- Almotriptan
- Naratriptan
- Frovatriptan
- Treximet

**Other**
- Midrin
- Butalbital compounds
- Migranal
- Opioids
- Tramadol
What is Cluster headache?

- “Horton’s Headache” or “Histamine Headache”
- <1 in 500 people
- Men > Women
- Severe, unilateral pain
- Autonomic features
- Restlessness/Agitation
- Pain episodes: 15-180 minutes
- Triggers: Alcohol, REM sleep
Cluster headache
Cluster headache treatments

• **Acute Treatments:**
  – 15 liters 100% oxygen via non-rebreather mask
  – Triptans (nasal spray or injectable forms)
  – Steroids
  – Occipital nerve blocks

• **Prevention Treatments:**
  – Verapamil
  – Depakote
  – Lithium
What is Tension type headache?

• Bilateral headache
  – Pressure or tightening (not throbbing)
  – Non-debilitating
  – No nausea/vomiting
  – No photophobia or phonophobia

• Basically....
Tension type headache treatments

• NSAIDs

• Try a Triptan!

• Review healthy life style choices

• Ergonomic evaluation

• Physical therapy / craniosacral therapy
Summary of key features

- Migraine:
  - Don’t want to move
- Cluster:
  - Can’t stop moving
- Tension:
  - Indifferent

Comparison
- Frequency: TTH > Migraine > Cluster
- Pain:
- Sex Ratio: F > M
Novel treatments
Historical treatments

- Historically, treatments consisted of:
  - Trephination
  - Applying a hot iron to the site of pain
  - Blood letting
  - Inserting a clove of garlic through an incision in the temple
Daith Piercing
Foods and Migraine

• Disorders highly associated with migraine that occur at a rate greater than chance:
  – IBS
  – Gastritis
  – Peptic Ulcer Disease
  – H. Pylori
  – GERD
  – Colitis
IgG Elimination diet

56 patients with migraine

More IgG food allergens seen

Elimination diet

108 food allergens measured by enzyme immunoassay

Control group without migraine

Few IgG food allergens seen

IgG Food Antibody Assessment

Patient: JENNIFER
DOB: [redacted]
Sex: F
MRN: [redacted]

IgG Food Antibody Results

<table>
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<tr>
<th>Dairy</th>
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<th>Fish/Shellfish</th>
<th>Nuts and Grains</th>
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Poultry/Meats

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<td>3+</td>
<td>Beef</td>
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Miscellaneous

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<tr>
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<td>Yeast</td>
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</table>

Total IgE

- The performance characteristics of all assays have been verified by Genova Diagnostics, Inc. Unless otherwise noted with *, all urinary 5HIAA and OVA results are for Research Use Only.
- Total IgE level may vary with clinical significance regardless of specific antibody levels.
- Increasing levels of antibody detected suggest an increasing probability of clinical reactivity to specific foods.
- The True Relief diet is specific to IgG results only. Allergens inducing IgE response should be avoided.
Peripheral nerve blocks

- Occipital Nerve blocks
- Supraorbital nerve blocks
- Auricotemporal nerve blocks
- Trigger point injections
Peripheral nerve blocks

- Occipital nerve block
- Trigger point injections
- Supraorbital nerve block
- Auriculotemporal nerve block
Sphenopalatine ganglion nerve block

- SPG has nociceptive and autonomic activity
  - Lacrimation
  - Facial fullness
  - Rhinorrhea
Sphenopalatine ganglion nerve block
OnabotulinumtoxinA (Botox)

- FDA approval in 2010 for Chronic migraine

- >15 headache days/month x 3 month, lasting >4 hours

- Medication overuse headache not excluded in PREEMPT trials

- Patient should be refractory to 3 classes of medications
  - Anticonvulsant
  - Antihypertensive
  - Antidepressant
OnabotulinumtoxinA (Botox)

BOTOX® Injection Sites

*Injections are on both the right and left side of the head.*
Boswellia Serrata

- Ayurvedic herb
- Anti-inflammatory properties
- Structurally similar to Indomethacin, better tolerated!
- Reduces Prostaglandin synthesis (Lipoxygenase inhibitor)
- Brand name (Gliacin) 375mg-750mg BID
Boswellia Serrata

Boswellic acid

Indomethacin
Zonisamide and Trokendi XR

• **Zonisamide:**
  - Similar migraine benefit as Topamax?
  - Less cognitive side effects
  - Typical dose is 50-200mg qhs

• **Trokendi XR:**
  - Recently approved for migraine prevention
  - Better tolerated than Topamax
  - Easy Transition from Topamax
  - Weight reduction still present
Candesartan

- “Beta blocker alternative”

- Typically dosed 4-16mg daily
  - Candesartan 16mg ?= Propranolol 160mg (Cephalalgia 2014)

- Well tolerated
  - No fatigue
  - No weight gain
  - No effect on mood
  - Less blood pressure effect
  - Category D
In the pipeline...2018
Lasmiditan

- Lasmiditan (Eli Lilly)
  - Highly selective 5-HT1F receptor agonist
  - No vasoconstriction observed!

- Spartan Study
  - Statistically significant improvement in pain relief compared to placebo at 2 hours after 1 dose

- Adverse events: Dizziness, paresthesia, fatigue, nausea and lethargy
## In the pipeline...2018

### Anti-CGRP monoclonal antibodies

<table>
<thead>
<tr>
<th>“mabs” against CGRP molecule</th>
<th>“mabs” against CGRP receptor</th>
<th>Episodic migraine</th>
<th>IV monthly</th>
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<td>Eptinezumab (Alder)</td>
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<td>Fremanezumab (Teva)</td>
<td>Episodic &amp; Chronic migraine</td>
<td>SQ q4 weeks</td>
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<tr>
<td>Fremanezumab (Teva)</td>
<td>Erenumab (Amgen)</td>
<td>Episodic migraine</td>
<td>SQ q4 weeks</td>
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</table>

- Adverse events: Injection site reactions
- No cardiovascular effects have been seen to date

Summary of novel treatment

• Piercings are becoming more popular

• Foods impact headache

• Procedures are good alternative to medication

• Botox is only FDA approved treatment for chronic migraine

• Think about herbal remedies/supplements

• CGRP antibodies and Lasmiditan are new medications 2018
Controversial Topics in Headache

1) Is medication overuse headache a real thing?

2) Can patients with migraine aura take birth control pills?

3) Would you give a triptan to a patient who is pregnant?
Topic 1 - Medication Overuse Headache

- Is this a marker of headache progression or separate entity?
Topic 1 - Medication Overuse Headache

- Prevalence: 1-2% of population
- 25-50% of chronic headache patients
- More common in:
  - Lower socioeconomic class
  - Females
  - Co-existing psychiatric disease
- Bifrontal headache
**Box 1 | Diagnosis of medication-overuse headache**

According to the ICHD-3 beta diagnostic criteria, each of the criteria A–C need to be filled for the diagnosis of medication overuse headache:

A
- Headache on ≥15 days/month
- Pre-existing headache disorder

B
- Overuse of acute and/or symptomatic headache drugs for >3 months*

C
- Not better accounted for by another ICHD-3 diagnosis

*Regular intake of drugs on ≥10 days/month for ergotamines, triptans, opioids and combination analgesics and on ≥15 days/month for paracetamol (also known as acetaminophen), acetylsalicylic acid and NSAIDs.

**General comment:**

In the criteria set out below for the various subtypes, the specified numbers of days of medication use considered to constitute overuse are based on expert opinion rather than on formal evidence.
Daily Triptan for Migraine Prevention

- 27 patients with chronic migraine
- Naratriptan
  - 1.25mg – 2.5mg bid
- 6 months:
  - 65% reverted to episodic migraine
- 12 months:
  - 55% episodic migraine
  - 5% relapsed to chronic migraine

In Canada and Europe.....

Sumatriptan 50mg available over the counter in several European countries
Treatment of Medication Overuse Headache

- Stop offending agent
- Consider starting prophylactic agent
- Steroid taper/Procedures
- Education

My opinion: Medication Overuse Headache is a marker of disease progression, and not a separate clinical entity
Topic 2 - OCPs and migraine with aura
Topic 2 - OCPs and migraine with aura

- Oral hormonal therapy in women with a diagnosis of migraine with aura
  - Is it safe?
  - Should you modify treatment?
Topic 2 - OCPs and migraine with aura

• 2010 – Centers for Disease Control statement:
  – Migraine with Aura:
    • Complete avoidance of combined oral contraceptives
    • Regardless of age
    • Regardless of dose

  “the condition represents an unacceptable health risk if the contraception method is used”

99% of combined hormonal OCPs are “low-dose” (<50μg estrogen)

Low-estrogen preparations do not appear to increase stroke risk

- Low-dose OCPs (<30 μg EE)
- Ultra low-dose OCPs (<15 μg EE)

OCP still restricted by current guidelines due to concerns of increased stroke risk

Concerns that originated over half a century ago in era of HIGH DOSE contraceptives
Topic 2 - OCPs and migraine with aura

- My opinion: Low dose hormonal therapy is a reasonable option in women with migraine aura.
  - Cessation of tobacco
  - No active hypertension/stroke risk factors
  - No high dose estrogen

- Consider alternative birth control options if you have concerns
Topic 3 - Triptan use in pregnancy
Topic 3 - Triptan use in pregnancy

• Migraine affects 25% of the female population during childbearing years (age 18-49)

• Rule of 1/3’s

• ~50% of pregnancies are unplanned so inadvertent fetal exposure to medications is likely

• No increased complications in migraneurs

# FDA Pregnancy Categories

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<th>Pregnancy Category</th>
<th>Description</th>
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<tr>
<td>A</td>
<td>Controlled human studies fail to demonstrate risk</td>
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<tr>
<td>B</td>
<td>Animal studies show no risk, unknown human risk. Chance of fetal harm is remote but remains a possibility.</td>
</tr>
<tr>
<td>C</td>
<td>Animal studies have shown risk, adequate controlled human studies are lacking. Risk to humans cannot be ruled out.</td>
</tr>
<tr>
<td>D</td>
<td>Positive evidence of risk to humans from human studies or post-marketing data.</td>
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<tr>
<td>X</td>
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# Acute Treatments

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<td>B</td>
<td>Acetaminophen, NSAIDs (Ibuprofen, Naproxen), Metoclopramide, Benadryl</td>
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<tr>
<td>C</td>
<td>Aspirin, Butalbital (Fioricet, Esgic), Codeine (hydrocodone, Tylenol with Codeine), Isometheptene, Phenothiazines, Triptans</td>
</tr>
<tr>
<td>X</td>
<td>Ergots</td>
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</table>
Topic 3 - Triptan use in pregnancy

- Caffeine
  - FDA category: C
  - High doses may be associated with:
    - Infertility
    - Spontaneous abortion
    - Prematurity
    - Low birth weight

Physician Desk Reference, 2002
Topic 3 - Triptan use in pregnancy

- Sumatriptan / Naratriptan Pregnancy Registry:
  - Sumatriptan: Risk of birth defects for first trimester exposure 4.2%
  - Risk of birth defects for general population is 3-5%
  - Naratriptan: Sample size insufficient to calculate a risk

My opinion: Sumatriptan is a safe option to use in pregnancy and posses similar risks as Fioricet or Tylenol #3

[2] CDC unpublished data
Summary

• Migraine vs Cluster vs Tension
• Headache is being treated with more then tablets
• Headache may get worse independent of how often medications are used
• Migraine aura patients can probably continue OCPs
• Sumatriptan will hopefully be considered category B soon
Thank You!