Approach to Headache in Clinic Patients

E. Alexandra Brown, MD
Assistant Clinical Professor of Neurology
UCSF / ZSFG
Director, Outpatient Neurology Clinic
### Fiscal Year 2015-2016

#### Top Ten Most Frequent Diagnosis by Encounter

<table>
<thead>
<tr>
<th>Count</th>
<th>%</th>
<th>ICD10 Code</th>
<th>ICD10 Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>212</td>
<td>20%</td>
<td>G40.909</td>
<td>epilepsy, unsp, not intractable, without status epilepticus</td>
</tr>
<tr>
<td>174</td>
<td>16%</td>
<td>G43.909</td>
<td>migraine, unsp, not intractable, without status migrainosus</td>
</tr>
<tr>
<td>135</td>
<td>13%</td>
<td>R51</td>
<td>headache</td>
</tr>
<tr>
<td>109</td>
<td>10%</td>
<td>G62.9</td>
<td>polyneuropathy, unspecified</td>
</tr>
<tr>
<td>102</td>
<td>10%</td>
<td>R56.9</td>
<td>unspecified convulsions</td>
</tr>
<tr>
<td>92</td>
<td>9%</td>
<td>G20</td>
<td>parkinson's disease</td>
</tr>
<tr>
<td>68</td>
<td>6%</td>
<td>G35</td>
<td>multiple sclerosis</td>
</tr>
<tr>
<td>65</td>
<td>6%</td>
<td>I63.9</td>
<td>cerebral infarction, unspecified</td>
</tr>
<tr>
<td>60</td>
<td>6%</td>
<td>G43.109</td>
<td>migraine with aura, not intractable, w/o status migrainosus</td>
</tr>
<tr>
<td>50</td>
<td>5%</td>
<td>Z53.21</td>
<td>proc/trtmt not crd out d/t pt lv bef seen by hlth care prov</td>
</tr>
</tbody>
</table>

Clinic code: NEURO, NEUROST

35% of our outpatient neurology visits are for headache = #1 diagnosis seen in neurology

Data collected from ZSFG neurology clinic dashboard
Objectives

By the end of this talk, you will be able to:

- Identify features by history and exam that are suspicious for secondary causes of headache (red flags)
- Understand when to perform neuroimaging in headache
- Distinguish the primary headache disorders
- Identify when preventive medications should be offered
- Prescribe medications for acute and chronic migraine using most current guidelines
- Counsel headache patients effectively
Part 1: DIAGNOSIS OF HEADACHE DISORDERS
How to approach headache

History:
- Focus on gathering information (“red flags”) that may indicate an underlying cause of the headache is present (“secondary headache”).
- Assess for coexisting conditions (such as heart disease, pregnancy, and uncontrolled HTN) which may limit treatment choices.

Physical:
- Neuro exam for any focal deficits
- Fundoscopic exam to assess for papilledema (concerning for increased intracranial pressure)
Case #1: Mr. HK

- 63 year old man with history of lung cancer s/p chemo and radiation presents with more frequent headaches. Patient says his cancer is “in remission” and that he suspects that his headaches are due to stress.

- Are you reassured?
Red flags

What features should worry you for a secondary headache?

- Systemic symptoms (fevers, chills, weight loss, HIV, cancer)
- New headache in an older patient >50 y.o.
- Abrupt onset reaching maximum intensity in < 1 minute (thunderclap)
- Exacerbated by positioning or Valsalva
- Abnormal neuro/fundoscopic exam

Case #2: Ms. RB

- 20 year old female college student with no medical history presents to clinic for headache complaints. She experiences a **severe throbbing** bilateral headache, occasionally causing her to **miss class** and **spend the day in bed** with the **lights off**. Headaches come on without much warning, progress to a **10/10 in severity** within 1-2 hours. Neurological exam including fundoscopic exam is normal.

- *Does she fulfill criteria for migraine?*
Migraine Without Aura

**ICHD-3 Criteria**

Diagnostic criteria:

A. At least five attacks\(^1\) fulfilling criteria B–D

B. Headache attacks lasting 4-72 hours (untreated or unsuccessfully treated)\(^2,3\)

C. Headache has at least two of the following four 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)

D. During headache at least one of the following:
   1. nausea and/or vomiting
   2. photophobia and phonophobia

E. Not better accounted for by another ICHD-3 diagnosis.

*Cephalalgia* 2013;33:629-808.
Migraine with Typical Aura

Visual aura has both positive and negative features:

Positive = Fortification spectrum ("C" shape that is angular)

Negative = scotoma (area of central blindness)

*Cephalalgia* 2013;33:629-808.
Case #3: Mrs. TR

- 26 year old woman with no medical history presents for a life-long history of occasional mild-moderate headaches, that are annoying to her but she is able to function and does not miss work. She denies nausea, vomiting, light or sound sensitivity, or throbbing quality. She feels stress brings them on. Neurological exam including fundoscopic exam is normal.

What is her diagnosis?
Tension-type Headache

ICHDA-3 Criteria

- Lasting from 30 minutes to 7 days
- At least two of the following four characteristics:
  1. bilateral location
  2. pressing or tightening (non-pulsating) quality
  3. **mild or moderate intensity**
  4. not aggravated by routine physical activity such as walking or climbing stairs
- Both of the following:
  1. **no nausea or vomiting**
  2. **no more than one of photophobia or phonophobia**

Distinguished from migraine by its relatively milder intensity and LACK of migraine features or any accompanying “aura-like” symptoms

*Cephalalgia* 2013;33:629-808.
Case #4: Mr. DC

- 35 year old man with no medical history presents with frequent unbearable headaches occurring 5-6 times per day every several months. The headache lasts 30 minutes and involve only the right side of his head behind his eye. Laying down worsens his pain so he paces around his room, and once while looking in the mirror noticed that his right eye was red and tearing. Pain is so severe he has even contemplated suicide during the headache.

- What is his diagnosis?
Cluster Headache

**Diagnostic criteria:**

A. At least five attacks fulfilling criteria B–D
B. Severe or very severe unilateral orbital, supraorbital and/or temporal pain lasting 15–180 minutes (when untreated)
C. Either or both of the following:
   1. at least one of the following symptoms or signs, ipsilateral to the headache:
      a) conjunctival injection and/or lacrimation
      b) nasal congestion and/or rhinorrhea
      c) eyelid oedema
      d) forehead and facial sweating
      e) forehead and facial flushing
      f) sensation of fullness in the ear
      g) miosis and/or ptosis
   2. a sense of restlessness or agitation
D. Attacks have a frequency between one every other day and eight per day for more than half of the time when the disorder is active
E. Not better accounted for by another ICHD-3 diagnosis.

*Cephalalgia* 2013;33:629-808.
Trigeminal Autonomic Cephalalgias (TACs)

- The TACs share the clinical features of headache, which is usually **lateralized**, and **often prominent cranial parasympathetic autonomic features**, which are lateralized and ipsilateral to the headache pain.
- They are distinguished based on their duration:
  - Cluster headache: 15-180 min [*most common TAC*]
  - Paroxysmal hemicrania: 2-30 min
  - SUNCT/SUNA: 1-600 seconds

Part 2: WORKUP FOR HEADACHE DISORDERS
Of the headache disorders so far discussed, which patients should undergo further workup?
When to perform brain MRI

- **Red Flags**
- **Trigeminal Autonomic Cephalalgias** [special attention to the pituitary gland]
- **Facial pain (Trigeminal Neuralgia)** [perform with Gadolinium with fine cuts through trigeminal nerves]

*imaging indications not including emergency room evaluation of patients presenting for worst headache of life, acute thunderclap headache, possible carotid or vertebral artery dissection, trauma, seizure activity*

Part 3: COUNSELING YOUR PATIENTS WITH PRIMARY HEADACHE DISORDERS
General principles of management

- Establish a diagnosis.
- Educate patient about their condition and discuss rationale for a particular treatment, how to use it, and what adverse events are likely.
- Establish realistic patient expectations.
- Empower patient to be actively involved (keep a headache diary).
- Create a formal individualized management plan.

Counseling is an essential part of the Management Plan

- **Optimize self-care**: Sleep ~same # hours each night, avoid excess caffeine, hydrate, don’t skip meals, stress reduction techniques, exercise
- **Biobehavioral therapy**
- **Relaxation training**
- **Trigger awareness and avoidance**
- **Take an abortive medication early** in the attack (evidence for better efficacy at onset of headache rather than during aura if present).
- **Use acute treatments < 9 days/month**

Counseling is an essential part of the Management Plan

- If patient has attacks of varying severity, you might consider medications from different strategies to use in different attacks (Stratified care approach).
- This is more effective than step care

Part 4: TREATMENT OF PRIMARY HEADACHE DISORDERS
In follow-up, you review patient RB’s headache diary and documented that she had 4 migraines in 1 month, 3 of which were severe enough that she was bedbound for an entire day.

*In addition to prescribing an acute option to abort the attack, should you also prescribe a preventive option to take on a daily basis?*
Headache diary

- Whether to prescribe a preventive treatment is based both on the number of headache days per month AND the degree of disability it causes the patient.

- AAN suggests offering preventive treatment when an individual reports 1+ of the following:
  - >6 headache days/month
  - >4 headache days with at least some impairment
  - >3 headache days with severe impairment or requiring bed rest

You tell Ms. RB that based on the number of headache days per month and their severity, you will prescribe both acute and preventive medications.

She is not accustomed to taking medications and asks you what the difference is between acute and preventive strategies.

What is the difference?

A review of the difference between Abortive vs. Preventive Treatment

- **Abortive treatment strategy:**
  - Treat individual acute headaches early in the attack, choosing the right drug based on the symptoms
  - Limit acute therapy to 2 headache days per week on a regular basis (otherwise at risk for medication overuse/rebound headaches)
  - Goals are to shorten the attack duration, reduce the attack severity, and restore the patient’s ability to function.
A review of the difference between Abortive vs. Preventive Treatment

- Preventive treatment strategy:
  - Administer on an ongoing basis whether or not an attack is present
  - Goals are to reduce attack frequency, severity, and disability over time; reduce reliance on acute pharmacotherapies
Ms. RB understands the difference between treatment strategies now and wants to know what acute medications are effective for migraine.

What do you tell her?
Guidelines on how to treat an acute migraine attack

For mild attacks, a nonspecific analgesic such as acetaminophen, ASA, or another NSAID may be adequate.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose (mg)†</th>
<th>Dosage Interval (If Repeated) and Maximum Daily Dose†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetaminophen</td>
<td>1000</td>
<td>Every 4 hours, max. 4000 mg</td>
</tr>
<tr>
<td>Acetylsalicylic acid (ASA) (tablet)</td>
<td>975-1000</td>
<td>Every 4-6 hours; max: 5.4 g/day (varies depending on indication)</td>
</tr>
<tr>
<td>ASA (effervescent)</td>
<td>975-1000</td>
<td>Every 4 hours; max: 8 (325 mg) tablets</td>
</tr>
<tr>
<td>Ibuprofen (tablet)</td>
<td>400</td>
<td>Every 4 h; max: 2400 mg</td>
</tr>
<tr>
<td>Ibuprofen (solubilized)</td>
<td>400</td>
<td>Every 4 hours; max: 2400 mg</td>
</tr>
<tr>
<td>Naproxen sodium‡</td>
<td>500-550</td>
<td>Twice a day; max: 1375 mg</td>
</tr>
<tr>
<td>(up to 825 mg)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diclofenac potassium (tablet)</td>
<td>50</td>
<td>3-4 times a day; max: 150 mg</td>
</tr>
<tr>
<td>Diclofenac potassium (powder for oral solution)</td>
<td>50</td>
<td>Single dose recommended for migraine attack</td>
</tr>
</tbody>
</table>

Guidelines on how to treat an acute migraine attack

For moderate-severe migraine attacks, a migraine-specific medication **Triptan** is recommended.

**DHE** also an option but older drug, less-well tolerated (nausea), and non-oral formulations only.

**Combination of Acetaminophen/ASA/Caffeine** also effective [but careful with caffeine].

Before prescribing a medication for migraine, what contraindications should you watch out for?
Contraindications to be aware of

**Do not use Triptans or DHE in patients with:**
- coronary artery disease
- history of stroke
- peripheral vascular disease
- uncontrolled HTN
- hemiplegic migraine
- migraine with brainstem aura
- concurrent use of MAOIs (avoid triptans within 14 days of MAOI)
- Do not use both Triptan and DHE within 24 hours
  - **caution** if Triptan prescribed in combination with SSRI or SNRI (risk for serotonin syndrome)

Contraindications to be aware of

**Do not use NSAIDs in patients with:**

- peptic ulcer disease
- history of GI bleeding
- renal disease
- concurrent use of anticoagulants
- cardiovascular disease (may increase the risk of cardiovascular events)

How to choose the right treatment strategies

- Other factors to consider when prescribing acute treatments:
- Is there significant nausea/vomiting early in the attack that may limit use of oral medications?
Acute migraine treatment guidelines: Nausea/Vomiting

- **Presence of significant nausea/vomiting or rapid onset:**
  - Consider using **other formulations of Triptans:**
    - Subcutaneous Sumatriptan 6 mg
    - Nasal spray (available for Sumatriptan 20 mg, Zolmitriptan 5 mg)
    - Orally dissolving/rapid melt tablet that does not require water (available for Rizatriptan and Zolmitriptan)

Acute migraine treatment guidelines: Nausea/Vomiting

- **Presence of significant nausea/vomiting or rapid onset:**
- Consider adding antiemetics to regimen:
  - **Oral Metoclopramide 10 mg**
  - Less preferable options are Prochlorperazine 10 mg or Domperidone 10 mg
  - Note lack of data available for Ondansetron for efficacy in migraine-related nausea so Ondansetron is not recommended

*Avoid daily use of antiemetics due to risk of extrapyramidal side effects with Metoclopramide and QT prolongation with Domperidone*

You prescribe Sumatriptan 100 mg tabs which the patient takes at the onset of the headache pain. The medication works very well but she experiences recurrence of her pain. 

How should you counsel her?
Acute migraine treatment guidelines: Recurrence

**Scenario 1:** If initial substantial headache relief from a triptan, but moderate-severe headache returns:
- Take a *second dose of the same triptan* (>2 hours apart)
- If this is a regular issue, consider *adding Naproxen sodium 500 mg* to triptan in combination.
- If this is a regular issue, consider *switching to Eletriptan or Frovatriptan* in future attacks (triptans with relatively low recurrence rates)

Acute migraine treatment guidelines: Recurrence

- **Scenario 2**: If patients do not respond to their triptan during the attack:
  - Do not take a second dose of a Triptan since it is unlikely to be of additional benefit.
  - A rescue medication from another drug class is usually recommended in this situation

You diagnosed case #4 Mr. DC with cluster headache.

He wants to know what treatment options are available to him.

*How do you counsel him?*
## Cluster Headache Acute Treatment Evidence

### Table 1.—Efficacy, Adverse Events, Level of Evidence and Recommendations for the Acute Therapy of Cluster Headache

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Study Population</th>
<th>Efficacy</th>
<th>Adverse Events</th>
<th>Level of Evidence</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Positive evidence</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sumatriptan (subcutaneous)</td>
<td>Episodic and chronic CH</td>
<td>Sumatriptan 6 mg is effective in improving headache response</td>
<td>Nonserious: injection site reactions, nausea and vomiting, dizziness, fatigue, paresthesias</td>
<td>Two class I randomized, controlled trials</td>
<td>Level A: established as effective</td>
</tr>
<tr>
<td>Zolmitriptan (nasal spray)</td>
<td>Episodic and chronic CH</td>
<td>Zolmitriptan 5 mg and 10 mg are effective in improving headache response</td>
<td>Nonserious: unpleasant taste, nasal cavity discomfort, somnolence, dizziness, nausea, throat/neck tightness</td>
<td>Two class I randomized, controlled trials</td>
<td>Level A: established as effective</td>
</tr>
<tr>
<td>Oxygen</td>
<td>Episodic and chronic CH</td>
<td>100% oxygen 6-12 L/min is effective in improving headache response</td>
<td>Not reported</td>
<td>Two class I randomized, controlled trials</td>
<td>Level A: established as effective</td>
</tr>
</tbody>
</table>

Cluster Headache Preventive Treatment Evidence

Table 2.—Efficacy, Adverse Events, Level of Evidence and Recommendations for the Prophylactic Therapy of Cluster Headache

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Study Population</th>
<th>Efficacy</th>
<th>Adverse Events</th>
<th>Level of Evidence</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive evidence</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Suboccipital steroid injection</td>
<td>Episodic and chronic CH</td>
<td>Suboccipital single injection or injection series with corticosteroids is effective in reducing attack frequency</td>
<td>Nonserious: transient injection site pain, headache</td>
<td>Two class I randomized, controlled trials</td>
<td>Level A: established as effective</td>
</tr>
<tr>
<td>Verapamil</td>
<td>Episodic and chronic CH</td>
<td>Verapamil 360 mg daily is effective in reducing attack frequency</td>
<td>Nonserious: constipation, reduced blood pressure, reduced heart rate</td>
<td>One class II and one class III randomized, controlled trials</td>
<td>Level C: possibly effective</td>
</tr>
</tbody>
</table>

Note: Verapamil is generally regarded as the maintenance prophylactic therapy of choice for cluster headache (dosed TID), despite only Level C recommendation (there is discordance between the evidence base and expert opinion)

Case #5: Mr. KJ

- 51 year old woman with depression and chronic pain presents with daily headache. Some nausea when pain is very severe, but holocephalic and not throbbing. She can manage but is very uncomfortable all day and has tried every over-the-counter including opiates prescribed for her knee pain. She needs medication every day. Neuro exam is normal.

- *What is the diagnosis and treatment?*
Medication Overuse and Chronic Migraine are hard to distinguish

- High headache frequency with overuse of acute medications leads to medication overuse headache and chronic (“transformed”) migraine.
- Prevent this by using acute treatments no more than 9 days per month.
- Avoid Opioids and Barbiturate-containing agents (Fiorinal, Fioricet) which very frequently lead to medication overuse headache/chronic migraine.

Avoid opiates and Barbiturate-containing agents

The American Headache Society “Choosing Wisely” Recommendations

4. Don’t prescribe opioid or butalbital-containing medications as first-line treatment for recurrent headache disorders

American Academy of Neurology’s Top Five Recommendations

3. Don’t use opioids or butalbital for treatment of migraine, except as a last resort.

Lipton, RB. Continuum 2015;21:1118-1131.
Medication Overuse Headache and Chronic Migraine Treatment

- From a therapeutic perspective, treat chronic migraine with medication overuse and medication-overuse headache **the same way:**
  - Discontinue the overused acute treatment [Avoid abrupt withdrawal of Butalbital-containing combination tablets or opioids which can cause severe withdrawal symptoms]
  - Initiate a migraine preventive therapy
  - Counseling as previously discussed
For patients who are hesitant to reduce their overused acute treatment, consider adding a bridge therapy short-term:

- Naproxen bridge 500 mg BID
- Triptans (Naratriptan 2.5 mg BID)
- Steroids (Prednisone 60 mg daily x 3 days and then taper by 10 mg daily to zero)
American Headache Society and American Academy of Neurology Guidelines

Recommended Dosages:

- Depakote 500-1500 mg/day
- Topiramate 50 mg BID
- Metoprolol 50-200 mg/day
- Propranolol 60-240 mg/day
- Amitriptyline 20-150 mg/day
- Nortriptyline 20-100 mg/day

Antiepileptic drugs
- Divalproex sodium
- Sodium valproate
- Topiramate
- B-Blockers
- Metoprolol
- Propranolol

Antidepressants/SSRI/SSNRI/TCA
- Venlafaxine
- B-Blockers
- Atenolol
- Nadolol
- Triptans (MRM)
- Timolol
- Naratriptan
- Triptans (MRM)
- Zolmitriptan

Triptans (MRM)
- Frovatriptan

The patient is interested in starting a preventive medication but is worried that by starting this medication, it would mean that it would be life-long.

*How do you counsel him on the use of preventive medications?*
● Patients who respond to preventive approaches **may be able to taper or discontinue therapy after 6-12 months** of successful treatment.

● Patients should be reassured that the need for prevention will be reassessed several times per year.

Lipton RB. Headache 2015;55;S2:103-122.
Are there other treatments for chronic migraine?

- Nutraceuticals (complementary and alternative medicines classified as supplements):
  - Riboflavin (vitamin B2) 400 mg daily (level B)
  - Magnesium 400-600 mg day (level B)
  - Coenzyme Q10 (CoQ10) 100 mg TID (level C)
  - Feverfew 100 mg daily (level B)

Rajapakse T, Pringsheim T. Headache 2016 April: 808-816.
Are there other treatments for chronic migraine?

- OnabotulinumtoxinA injection every 3 months (Botox) has level A evidence for prevention of chronic migraine


**Recommendations.** OnaBoNT-A should be offered as a treatment option to patients with CM to increase the number of headache-free days (Level A) and should be considered to reduce headache impact on health-related QOL (Level B).

References

References

References

THANK YOU

Happy to answer questions