Case Based Headache Management

or

Everything you wanted to know about headaches but were afraid to ask

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Disclosures & Shameless Plug

• Advisory board for Allergan & MAP
• Just one blind man at the elephant
• Family Physician
• Join your County, State, & Professional Societies
• You can learn a lot at a Headache meeting
• NHF www.headaches.org
• AHS www.americanheadachesociety.org

Objectives

• Increase awareness of the burden of Headache
• Have you feel comfortable with the management of Primary Headaches
• Increase your interest in Headache management
• Make it worth your time
But What I Really Want is…

- Increase your desire to care for these patients.
- To have you believe that you can do it and not have it consume you (as it did Obi-Wan’s apprentice)
- Really if I can… Honest it’ll be easier for you
- A little background
- Consider a post residency fellowship in Headache Medicine

Limbic Influences in Migraine

- All Pain has meaning
- The Sorrow that hath no vent in tears may make organs weep— Henry Maudsley
- (When) the mind is hurt the body cries out
- Italian Proverb
- The body remembers what the mind forgets— J.L. Moreno

Not All Pain is Nociceptive

- San Francisco Spine study 1992
- Five childhood traumas: Loss of parent, Hx of Substance abuse, emotional neglect, physical abuse, sexual abuse
- No risk factors = 95% chance surgical cure
- 1-2 risk factors = 73% chance surgical cure
- 3 or more risk factors = 15% chance of a surgical cure
- Increased incidence of Chronic Daily HA in victims of Sexual Abuse.
If You Remember Just One Thing

- They Can’t Find Anything Wrong
- If you only read one book this year
- Stress Illness
- It is a practice changer

Case 1

- 61yo H ♂ TBI /c LOC >30y HAs 25/30 days
- Primarily L sided /c N/V, Allodynia, Neck Pain
- Sleep Non-restorative, Onset delayed 1 hour
- Often awakens with headaches
- No prior preventive meds. Uses APAP

Case 2

- 27yo C♀ ICU nurse. Onset @ 5y +FH
- Episodic to CDH over last 2 years
- 2 prior hospitalizations for headache no DHE
- Sleep non-restorative, Schedule erratic
- Awakens with HAs,
- N/V, Photophobia,
- Darvocet/Excedrin Migraine
- Recently started on Topirimate
Case 3

- 13yo prepubescent C♀
- Missed >15 days school in fall
- Admitted in Status Migranous
- Resolved /c Raskin protocol (IV DHE TID)
- Bridge therapy of Prednisone 7d followed by Etodolac 400mg BID
- Preventive Magnesium, Divalproic 500mg
- Still /c days of HA not responding to triptans

Why Migraine & Why Should I Care

- 6% Men, 18% women, 33-37% reproductive women, 4% CDH
- 38% Male Veterans, 58% Female, 20% CDH
- Most common 25 – 55yr (most productive years)


Severe Migraine Is Ranked in the Highest Disability* Class by WHO

<table>
<thead>
<tr>
<th>Disability Class</th>
<th>Severity Weight</th>
<th>Indicator Conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.00-0.02</td>
<td>Vitiligo of face, weight for height less than 2 SDs</td>
</tr>
<tr>
<td>2</td>
<td>0.02-0.12</td>
<td>Watery diarrhea, severe sore throat, severe anemia</td>
</tr>
<tr>
<td>3</td>
<td>0.12-0.24</td>
<td>Radius fracture in a stiff cast, infertility, erectile dysfunction, rheumatoid arthritis, angina</td>
</tr>
<tr>
<td>4</td>
<td>0.24-0.36</td>
<td>Below-the-knee amputation, deafness</td>
</tr>
<tr>
<td>5</td>
<td>0.36-0.50</td>
<td>Rectovaginal fistula, mild mental retardation, Down syndrome</td>
</tr>
<tr>
<td>6</td>
<td>0.50-0.70</td>
<td>Unipolar major depression, blindness, paraplegia</td>
</tr>
<tr>
<td>7</td>
<td>0.70-1.00</td>
<td>Active psychosis, dementia, severe migraine, quadriplegia</td>
</tr>
</tbody>
</table>

*Assessments of disease severity determined by Global Burden of Disease researchers using the person trade-off method, which includes judgments about the trade-off between quality and quantity of life. Spectrum ranges from 0 (perfect health) to 1 (death).
Headaches in Primary Care

- **Primary** – nervous system you are born with or acquire (trauma) and the environment you are in
- **Secondary** – headaches that are caused by something else
  - Migraine, Cluster, Tension Type
  - Infection, Mass, Vascular, Trauma

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**Headaches in Primary Care**

- **Primary Headaches** are the result of the nervous system you were **Born With** & the **Environment** you are in.
- **Secondary Headaches** are headaches that are **Caused by** Something

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**SNOOP4: Ruling Out Secondary Causes of Headache in Migraine**

- Systemic symptoms and signs
- Neurologic symptoms or signs
- Onset: peak at onset or <1 minute
- Older: after age 50 years
- Previous headache: pattern change
- Postural, positional aggravation
- Precipitated by valsalva, exertion, etc.
- Papilledema
Headache Pattern Recognition

<table>
<thead>
<tr>
<th>Minutes</th>
<th>Hours/Days</th>
<th>Weeks/Months</th>
<th>Months/Years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vascular</td>
<td>Infectious</td>
<td>Inflammatory, Neoplastic</td>
<td>Primary Headache</td>
</tr>
</tbody>
</table>

Secondary Headache Disorders

The Headache “Patient”

- Most likely has migraine because
  - Significant secondary headaches are infrequent
  - Episodic tension-type headache rarely produces need for medical consultation
  - Other primary headache disorders infrequently appear in a primary care office
- If the patient has migraine, they will likely be engaged with the medical system for decades...they need a good primary care physician

The Migraine Brain

- Genetic hyperexcitability:
  - Lower threshold for activation
  - Longer retention of sensory information
    - Between episodes of migraine
    - During episodes of migraine
- May have been adaptive
Until proven otherwise, A stable pattern of disabling HA that disrupts function is _____.

- A sensitive brain that doesn't like change
- Hyper-vigilant 24/7
- Always more than a headache!
- That would be ... ”What is Migraine?” Alex

Staging Migraine

- Developed by Lipton, Cady, Farmer, & Bigal
- First doctor/patient book
- Based on frequency not severity of HA
- www.managingmigraine.org

Stage 1: Infrequent Episodic

- Emphasis on acute abortive therapy
  - OTCs
  - Triptans
  - NSAIDs
- Early intervention – complete response
- Evaluation on mechanism of injury and pre-morbid biology of patient
- Education focused on resuming normal function
Stage 2: Frequent Episodic

- Acute medication limits
  - MOH is a quantity of medication associated with headache progression
- Early intervention vs. staged care
- Preventive pharmacology
- Behavioral interventions

Stage 3: Transforming Headache

- Preventive pharmacology
- Targeted use of abortives
- Strong emphasis on behavioral intervention
- Screen and treat co-morbidities
- Perpetuating Factors > Precipitating Factors

Stage 4: Chronic Daily Headache

- Behavioral intervention -- absolutely essential
- Preventive pharmacology -- unavoidable
- Screen & aggressively treat co-morbidities
- Educate, educate, educate
- Establish reasonable goals and expectations
- Targeted use of abortive medications
- Emphasis of Quality of Life
The Evolution of Episodic to Chronic Migraine

Migraine “Transformation”

- 450 episodic migraine patients followed for 1 year
- 14% developed chronic daily headache (CDH)
- Risk factors
  - Headache frequency >10 days/month (RR = 20)
  - Medication frequency >10 days/month (RR = 19)


Chronic Migraine Risk Factors

<table>
<thead>
<tr>
<th>Modifiable</th>
<th>Not modifiable</th>
</tr>
</thead>
<tbody>
<tr>
<td>Attack frequency</td>
<td>Age</td>
</tr>
<tr>
<td>Obesity</td>
<td>Female sex</td>
</tr>
<tr>
<td>Snoring/OSA</td>
<td>Low education or socioeconomic status</td>
</tr>
<tr>
<td>Stressful life events</td>
<td>Genetic factors</td>
</tr>
<tr>
<td>Medication overuse</td>
<td>Head injury</td>
</tr>
<tr>
<td>Caffeine overuse</td>
<td></td>
</tr>
</tbody>
</table>

Lessons Learned From IHS Classification of Chronic Migraine

- Chronic migraine evolves from episodic migraine
- Migraine attacks becomes less stereotypic as migraine becomes chronic
- Phenotypes of migraine respond to migraine- specific treatments
- Patients can evolve into and out of chronic migraine as part of its natural history

Headache Treatments

- **Preventive** – reduce frequency, intensity, and improve response to acute meds
- **Abortive** – pain freedom in 2 hours
- **Rescue** – when the stop medicine didn’t
Migraine Prevention Utilization

- 53% of migraineurs meet disability and frequency criteria for prevention
- < 5% of migraineurs are on preventive therapy

53% of migraineurs meet disability and frequency criteria for prevention.

Saves You Money!

- 18-month comparison study
- Acute vs acute/preventive therapies
  - Office visits ↓ 51%
  - ED visits ↓ 82%
  - CT scans ↓ 75%
  - MRI scans ↓ 88%
  - Medication costs ↓ $48 - $138/month/patient

Prevention

- Underutilized
- Consider when Migraine significantly interferes with pt's daily routine, despite acute treatment
- Attack frequency >1/wk
- Five FDA approved drugs
- Many off label choices
- Start low and titrate as tolerated
- Two-fers overrated

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Migraine Preventive Agents

<table>
<thead>
<tr>
<th>Antidepressants</th>
<th>Antiepileptics</th>
<th>Beta blockers</th>
<th>Ca channel blockers</th>
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</thead>
<tbody>
<tr>
<td>Trazodone</td>
<td>Diphenhydramine</td>
<td>Propranolol*</td>
<td>Verapamil</td>
</tr>
<tr>
<td>Amoxapine</td>
<td>Topiramate</td>
<td>Nadolol</td>
<td>Amlodipine</td>
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<tr>
<td>Desipramine</td>
<td>Tiagabine</td>
<td>Atenolol</td>
<td>Diltiazem</td>
</tr>
<tr>
<td>Nortriptyline</td>
<td>Zonisamide</td>
<td>Timolol*</td>
<td>Nifedipine</td>
</tr>
<tr>
<td>Nefazodone</td>
<td>Labetalol</td>
<td>Metoprolol</td>
<td>Nimodipine</td>
</tr>
<tr>
<td>Tranylcypromine</td>
<td>Nebivolol</td>
<td>Nebivolol</td>
<td>Niifedipine</td>
</tr>
</tbody>
</table>

NSAIDs

<table>
<thead>
<tr>
<th>NSAIDs</th>
<th>Nimesulide</th>
<th>Naproxen</th>
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</thead>
<tbody>
<tr>
<td>Meclofenamate</td>
<td>Naproxen</td>
<td>Meclofenamate</td>
</tr>
<tr>
<td>Ketoprofen</td>
<td>Naproxen</td>
<td>Ketoprofen</td>
</tr>
<tr>
<td>Flurbiprofen</td>
<td>Naproxen</td>
<td>Flurbiprofen</td>
</tr>
<tr>
<td>Celecoxib</td>
<td>Naproxen</td>
<td>Celecoxib</td>
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</table>

5-HT2 antagonists

<table>
<thead>
<tr>
<th>5-HT2 antagonists</th>
<th>Cyproheptadine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methysergide*</td>
<td>Cyproheptadine</td>
</tr>
<tr>
<td>Methylergonovine‡</td>
<td>Methysergide*</td>
</tr>
<tr>
<td>Alternatives therapies</td>
<td>Methysergide*</td>
</tr>
<tr>
<td>Riboflavin</td>
<td>Methysergide*</td>
</tr>
<tr>
<td>Magnesium</td>
<td>Methysergide*</td>
</tr>
<tr>
<td>Feverfew, petasites</td>
<td>Methysergide*</td>
</tr>
</tbody>
</table>

Prevention – Pound of Cure

- Supplements – Mg 500mg, Riboflavin Vit B2 400mg, CoQ 10 200mg BID (www.puritan.com), Butterbur (should be PA free Petadolax)
- Membrane Stabilizing medications - Valproate, Toprimate, …
- AntiHTN Beta Blockers, CCB, ACE
- TCA off label most data is with amitriptyline – SSRIs not thought to be effective
- Onabotulinumtoxin A – FDA approved for Chronic Migraine Oct 2010

Migraine preventive therapy

Possible reasons for lack of efficacy

- Inadequate trial duration (<6-8 weeks) at an optimal dosage
- Patient non-compliance (side effects, half-life, unrealistic expectations)
- Concomitant drug-induced headache
- Newly developed medical condition causing a secondary headache
**Headache Treatments**

- **Preventive** – reduce frequency, intensity and improve response to acute meds
- **Abortive** – pain freedom in 2 hours
- **Rescue** – when the stop medicine didn’t

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**Abortive Therapy**

- Goal is pain freedom in 2 hours
- Treat at mild pain (prior to central sensitization)
  - May use polypharmacy

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**Triptan Pearl: Treat @ Mild Pain Early Intervention Improve Efficacy**

![Graph showing 2 Hour Pain Free Response](Image)

- 56% Mild
- 58% Moderate
- 35% Severe

*Cady RK et al. Headache 36:175-83; Frascio J et al. Headache 42[Suppl 1]:S10-S17*
Oral Therapies

- Non-triptan
  - NSAIDS
- Combinations
  - Acetaminophen/aspirin/caffeine
  - Analgesics
- Antiemetics
- Triptans
- Ergotamines
- When to consider
  - First-line therapy
  - Adjunctive therapies

There is no medication that is perfect for all migraine attacks or all circumstances in which treatment is needed.

What I do

- Sooooo Off-Label
- 3 tablets Effervescent ASA + Mg 500mg or
- Ibuprofen 1000-1200mg + Mg
- Naproxen 500mg + Mg
- Augment /c Metoclopramide or Prochlorperazine
- Treat @ mild pain

Triptans

- Sumatriptan
  - Oral – 25, 50, 100 mg
  - Nasal – 5, 20 mg
  - Auto-injector – 4 or 6 mg
  - Needleless injector – 6 mg
- Zolmitriptan
  - Oral – 2.5, 5 mg
  - ODT – 2.5, 5 mg
  - Nasal – 5 mg
- Naratriptan
  - Oral – 1, 2.5 mg
- Rizatriptan
  - Oral – 5, 10 mg
  - ODT – 5, 10 mg
- Almotriptan
  - Oral – 6.25, 12.5 mg
- Frovatriptan
  - Oral – 2.5 mg
- Eletriptan
  - Oral – 20, 40 mg
- Sumatriptan/Naproxen

ODT, orally disintegrating tablet
Headache Treatments

- **Preventive** – reduce frequency, intensity and improve response to acute meds
- **Abortive** – pain freedom in 2 hours
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Why should I treat Acute Headaches?

- **Why Not?** – Do we only want to manage chronic diseases?
- What are other acute conditions seen in our offices: UTI, Viral Illness – upper respiratory, GI
- Lacerations, Backaches & sprains – oh my!

But Most Importantly!

- We have to keep these people out of the Emergency Department
- In reality Primary HAs are not an emergency
- Not the best place – too bright, too loud, often ignored
- More likely to V.O.M.I.T. In ED
- Can’t risk exposure to opiates
Migraine Rescue

- Evidence-based first-line treatments should replace opioids, which often do not meet current guidelines\(^1\)
- Opioids are potentially ineffective, often suboptimal\(^1\), and can lead to abuse and/or drug-seeking behaviors\(^1,2\)


Clinical Headache Rescue

- Associated Neurologist of S. CT AHS SA Poster
- Drop in HA Clinic – Prevent ED visits
- 9/05-8/07 500 pts
- Time to Present = 104 hours (8-240h)
- VAS pain: Entry 8.5 Discharge 1.5
- Txt: IVF (94%), Ketoralac (84%), Suma sq (78%), Prochlorperazine (52%), Metoclopramide (21%), DHE (8%), Mg (4%)
- Average charge $426 Average payment $272.64

Clinical Headache Rescue UAB experience

- 200 pts. Randomized Optimal Self Admin or Optimal Self Admin + Optional in-clinic Headache rescue

<table>
<thead>
<tr>
<th>Optimal Self Adm</th>
<th>Clinic Rescue</th>
</tr>
</thead>
<tbody>
<tr>
<td>423 visits</td>
<td></td>
</tr>
<tr>
<td>33.6K ($80)</td>
<td></td>
</tr>
<tr>
<td>73 ED Visits</td>
<td>27</td>
</tr>
<tr>
<td>147.9K ($2027)</td>
<td>45.3K ($1609)</td>
</tr>
<tr>
<td>79% no d/a &gt; 24'</td>
<td></td>
</tr>
</tbody>
</table>

Average charge $426 Average payment $272.64
Clinical Headache Rescue
UAB experience

- 89% very satisfied

<table>
<thead>
<tr>
<th>Drug</th>
<th># Dose</th>
<th>Drug Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Droperidol 2.75mg</td>
<td>218</td>
<td>3.00</td>
</tr>
<tr>
<td>Diphenhydramine 50mg</td>
<td>201</td>
<td>1.25</td>
</tr>
<tr>
<td>DHE 1mg</td>
<td>167</td>
<td>42</td>
</tr>
<tr>
<td>Prochlorperazine 5-10mg</td>
<td>141</td>
<td>11.5</td>
</tr>
<tr>
<td>Promethazine 50mg</td>
<td>68</td>
<td>4.0</td>
</tr>
<tr>
<td>Ketorolac 30mg</td>
<td>58</td>
<td>9 + 11 (saline)</td>
</tr>
</tbody>
</table>

Acute Headache Interventions

- IV>>IM>>PO
- Sumatriptan 6mg IM/SC
- Dihydroergotamine
- Ketorolac
- Neuroleptics – Dopamine Antagonists (Droperidol, Metoclopramide, Prochlorperazine)
- Steroids
- Others – Mg++, Valproic Acid, Diphenhydramine
- Procedures – Occipital Nerve Block, Lower Cervical Intramuscular Injections

Procedures

- Lower Cervical Intramuscular Injections
- Occipital Nerve Block
- Sphenopalentine Ganglion Block
Lower Cervical Intramuscular Injections

- Headache 10/06
- 417 ED Pts / 1 yr
- 65% relief in 15m
- Repeat injection brought additional relief
- Worsened HA in 1%

Lower Cervical Intramuscular Injections

- 3mL bupivicane 0.5%
- 25g 1.5” / 27g 1.25”
- 2-3cm lateral to the spinous processes between C6 & C7
- AE / CI
- Vasovagal, Neck stiffness, usual injection risks

Occipital Nerve Block

- Local anesthetic (bupivicaine, 0.5% xylocaine 1% --Duration of anesthesia doesn’t correlate to duration of relief
- Steroid (triamcinolone 40mg/mL) evidence doesn’t support general use
- 3mL total per side
- 25 or 27 gauge needle
- May place as a “ridge” of anesthesia, “trigger points”, or fixed.
Occipital Nerve Block

- AEs & CIs
  - Prior hx of craniotomy over injection site
  - AEs primarily related to steroid- fat atrophy, alopecia, pigment change
  - Vagal response – Happened to me X 3 in over 6000 blocks

Case 1 - 61yo H♂ /c hx TBI

- Initial placed on Magnesium, Tizanidine
- Placed B ONB
- ↓ Freq 3/7 days, + Memantine (NMDA receptor blocker)
- @ 1 yr HAs 1/7 days mild
- Severe HAs 1/60 days responds to ONB
Injectable Treatments

Subcutaneous Sumatriptan

- Dose: 6mg subcutaneous
- Contra-indications/ Cautions:
  - Cardiac risk-stratification
  - Severe hypertension
  - Pregnancy
  - Recent use
- What to expect:
  - Worsening of headache
  - Palpitations/ flushing
  - Address recurrence

Triptan Risks

Risk of a serious life-threatening cardiac event occurring with triptan administration:

Less than One in 2.5 Million
**Dihydroergotamine**

- Underutilized
- Dose, route: 0.5-1mg IV, IM, SQ
- Cautions/ contra-indications
  - Similar to sumatriptan
  - Cardiac risk factors (class effect, not specific)
  - Hypertension
  - Recent use of sumatriptan (theoretical risk)
  - Pregnancy (Category X)
- What to expect
  - Nausea. Un-treated you will throw your toenails up)

**Dihydroergotamine IV**

- Largely replaced by sumatriptan, still has a role
- Duration of headache not important consideration
- Combine with anti-emetic (usually metoclopramide)
- Dilute in 50mL NS & infuse over 30min to improve tolerability*

* SIMU

**DHE vs. Suma**

*Are you Ready 2 Rumble?*

- DHE 1mg SQ vs sumatriptan 6mg SQ
  - At 2 hours could receive second dose of same medication
  - Two hour relief: 85% Suma Vs. 73% DHE (p=0.002)
  - 24 hour relief: 77% Suma Vs. 90% DHE (p=0.004)
**Ketorolac**

- Dose: 30mg IV or 60mg IM
- Cautions/ Contra-indications:
  - Typical Non-steroidal risk
- What to expect:
  - IM shots cause localized burning pain

**Dopamine antagonists**

- Prochlorperazine (Compazine): 10mg IV SIVP
- Metoclopramide (Reglan): 10mg IV SIVP
- Droperidol: 2.75mg IM, 2.5mg IV
  - Black box warning for QT prolongation
- Haloperidol (Haldol) Drug of choice in many countries
  - 5 mg IV following 500 - 1000cc bolus of normal saline
- Olanzapene 2.5-10mg po or im prn q 6- 8 hours

Honkanen J. Headache 2006, May;46(5):781-7

**QT issues & Phenothiazines**

- Screen patients for risk factors
- Pretreatment ECG
- Follow-up ECG
- Usually only an issues with long-term repetitive dosing
- Inconsistent warnings from the FDA
Alternate / Special Groups

1. Diphenhydramine 25-100mg PO/IM/IV (pregnancy/kids)
2. MgSO4 1-2 gm IV over 30 minutes (pregnancy)
3. IV Valproic Acid 1000mg mix 50/50 in NS infuse over 7-10 or less (not pregnant)
4. Procedures -- Occipital Nerve block

Reasons not to use opioids for Migraine Rescue

• Use of oral opioids associated with likelihood of increased headache
• ED treatment with opioids associated with more refractory headaches down the road
• Does not disrupt underlying pathophysiology
• Requires multiple successive doses
• Lastly – I will hunt you down!

Case 2 – 27yo C ICU Nurse

• Dexamethasone 4mg BID X 7d
• Magnesium, CoQ10, Tizanidine, B ONB
• Metoclopramide to augment acute meds.
• No improvement placed on DHE for 10d
• Ketorolac 60mg IM rescue
• F/U HAs ↓ 3/7 days started Topirimate
• HAs reduced to 1/7 days /c severe 1-2/30d
• Titrated off Topirimate after 9m of stability

2. Jakubowski, Headache, 2005
Case 3 – 13yo C♀

- Increase Divalproic 1gm, + CoQ10
- HAs decreased over summer frequency 1-2/30d No missed school
- After 6m stability titrated of Divalproic
- After another 6m titrated off CoQ10
- HAs returned 2-3/w resumed CoQ10 placed ONB -- regained control after 4wks