12:50 – 1:50 PM

Headache: Meeting the Clinical Challenge

SPEAKER
Gerald W. Smetana, MD, MACP

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Learning Objectives

1. Describe recent guidelines regarding the proper role of acute treatments for migraines, cluster headaches and tension headaches

2. Outline an approach to preventive therapy for patients with disabling migraines, cluster headaches and tension headaches

3. Learn which complementary and alternative treatments are effective in the treatment of primary headache disorders

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Why is Headache Important?

- Headache is part of the human experience
- Lifetime prevalence of headache:
  - 99% in women
  - 95% in men
- One half of the population experiences headaches severe enough to prevent work in a given year

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Impact of Primary Headache Syndromes

- Source of suffering and disability
- Contributes to lost work and school days
- Decreased productivity
- Impact on quality of life
**Primary Headache Syndromes**

- Migraine without aura
- Migraine with aura
- Migraine with typical aura
- Tension-type headache
- Cluster headache

**Case Vignette: Karen**

A 24-year-old primary care patient comes to see you for management of migraines

- What lifestyle changes will help me help my migraines?
- Which acute medication is right for me?
- Should I take preventive medicine?
- Do complementary medicines work?

**Treatment of Migraine: General Principles**

- Lifestyle advice to minimize triggers for all patients
- Acute therapy at onset of migraine
- Preventive therapy for patients with frequent and/or disabling migraines
- Consider complementary and physical treatments for patients with poor Rx response or based on patient preference

**Lifestyle Approaches to Migraine: Obtain a Headache Diary**

- Ask patient to keep a headache diary for one month
- Record
  - Dates
  - Events prior to headache
  - Presence of headache
  - Type and location of pain
  - Menses
  - Sleep patterns
  - Foods, caffeine, alcohol
  - Stress
### Sample Headache Diary

<table>
<thead>
<tr>
<th>Date</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time headache began</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time headache ended</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Menses in past 2 days</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Food triggers</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hours of sleep night before</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stressful events</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intensity (1-10 scale)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preceding symptoms</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type of pain (pressure, stabbing)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other symptoms (nausea, etc.)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medication used</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disabled by headache (yes/no)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Relief with treatment (complete, partial, none)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Patient Education: Avoid Migraine Triggers

- Tailor recommendations based on headache diary
- Regular meal and sleep pattern
- Avoid oversleeping, skipping meals
- Limit caffeine intake to < 2 drinks/day
- Avoid offending foods
  - Cheese, red wine, MSG, chocolate, alcohol most common offenders
- Regular exercise

### Complementary Physical Treatments for Headache

**Migraine**
- Probably effective
  - Spinal manipulation
  - Biofeedback*
- Possibly effective
  - Electromagnetic fields
  - TENS and electrical neurotransmitter modulation

**Tension-type headache**
- Probably effective
  - Spinal manipulation
  - Possibly effective
  - Therapeutic touch
  - Cranial electrotherapy
  - TENS
  - TENS and electrical neurotransmitter modulation


### Cochrane: Acupuncture is More Effective than Meds and is Safe

- 22 trials (n=4985)
- Acupuncture vs. placebo:
  - 41% vs. 17% (at least 50% reduction)
- Acupuncture vs. sham Rx: sham nearly as effective
  - 50% vs. 41% (sham)
- Acupuncture vs. medications for prevention:
  - More effective than meds
  - 57% vs. 46%
  - Safer than meds (fewer dropouts in trials)

Acute Migraine Treatments:
General Classes

- Nonspecific
  - NSAIDs
  - Combination analgesics
  - Neuroleptics/antiemetics
- Specific
  - Ergotamine/DHE
  - Triptans

NSAIDs

- Recommended first line abortive therapy for most patients
- Ibuprofen, naproxen, and indomethacin most extensively studied
- If first doesn’t work, try another
- Treatment of choice for menstrual migraines

Triptans

- Serotonin (5HT₁) agonists
- Side effects
  - Pain at injection site
  - Flushing
  - Chest or jaw pressure
  - Nausea and bad taste (intranasal form)
- Some patients respond better to one than another triptan
- Try at least two before giving up...

Triptans: More Alike than Different

<table>
<thead>
<tr>
<th>Drug</th>
<th>Onset of Action</th>
<th>Minimum Interval Between Doses</th>
<th>Maximum Dose per 24 Hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>Almotriptan</td>
<td>30-60 min.</td>
<td>2 hours</td>
<td>25 mg</td>
</tr>
<tr>
<td>Eletriptan</td>
<td>30-60 min.</td>
<td>2 hours</td>
<td>80 mg</td>
</tr>
<tr>
<td>Frovatriptan</td>
<td>2 hours</td>
<td>2 hours</td>
<td>7.5 mg</td>
</tr>
<tr>
<td>Naratriptan</td>
<td>1-3 hours</td>
<td>4 hours</td>
<td>5 mg</td>
</tr>
<tr>
<td>Rizatriptan</td>
<td>30-60 min.</td>
<td>2 hours</td>
<td>30 mg</td>
</tr>
<tr>
<td>Sumatriptan</td>
<td>30-60 min.</td>
<td>2 hours</td>
<td>200 mg</td>
</tr>
<tr>
<td>Nasal Spray</td>
<td>10-15 min.</td>
<td>2 hours</td>
<td>40 mg</td>
</tr>
<tr>
<td>SC injection</td>
<td>10 min.</td>
<td>1 hour</td>
<td>12 mg</td>
</tr>
<tr>
<td>Zolmitriptan</td>
<td>30-60 min.</td>
<td>2 hours</td>
<td>10 mg</td>
</tr>
<tr>
<td>Nasal Spray</td>
<td>10-15 min.</td>
<td>2 hours</td>
<td>10 mg</td>
</tr>
</tbody>
</table>
**Triptan Contraindications**

**Absolute**
- Pregnancy
- MAO inhibitors
- Use within 24 hours of ergot
- Complex neurologic features during aura (migraine with typical aura)
- Coronary artery disease

**Relative**
- Post menopausal women
- Hypertension
- Obesity
- Diabetes
- Smokers
- Elevated cholesterol
- Family History CAD
- Age > 50

**Ergots**

- Ergotamine
  - Available as monotherapy or in combination with caffeine
  - Can not use during pregnancy or if pregnancy possible
  - Frequent use may cause rebound headaches, ergotism
  - Not recommended due to:
    - More side effects than NSAIDs
    - Less effective than NSAIDs

**DHE (dihydroergotamine mesylate)**

- Would consider only using in patients referred to consultant
- Given IM along with anti-emetic
- Selected patients who are non-responders to other acute Rx's:
  - Nasal spray (Migranal)
  - Pulmonary inhaler (Levadex)
- Causes less rebound headaches

**Migraine Specific Rx Formulations**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Tablet</th>
<th>Dissolving tablet</th>
<th>Nasal spray</th>
<th>Injection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Almotriptan</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eletriptan</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rizatriptan</td>
<td>✓ ✓</td>
<td>✓ ✓</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zolmitriptan</td>
<td>✓ ✓ ✓</td>
<td>✓ ✓ ✓</td>
<td>✓ ✓ ✓</td>
<td></td>
</tr>
<tr>
<td>DHE</td>
<td>✓ ✓ ✓</td>
<td>✓ ✓</td>
<td>✓ ✓ ✓</td>
<td></td>
</tr>
<tr>
<td>Ergotamine</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Acute Treatment: Anti-Emetics are Underutilized

- Particularly useful when nausea is a major feature
- Useful when nausea prevents use of PO analgesics
- Metoclopramide (Reglan)
  - PO, PR, IM
- Prochlorperazine (Compazine)
  - PO, PR, IV
- Prochlorperazine is superior to metoclopramide and potentially to other common 1st line Rx's*

*Headache 2009;49:1324

Other Acute Treatments

- Midrin (isometheptene, dichloralphenazone, acetaminophen)
  - Third line agent
- Acetaminophen, ASA, and caffeine (AAC = Excedrin Migraine)
- Butalbital
  - Best avoided due to risk of drug induced rebound headaches and habituation
  - Consider in patients with very infrequent headaches requiring only occasional use
- Opiates (Butorphanol nasal, oral opiates)
  - Last resort

American Headache Society 2015: Evidence-Based Acute Migraine Rx

**Level A: Established efficacy**
- OTC analgesics
  - ASA
- Acetaminophen, ASA, plus caffeine
- NSAIDs
- Opioids
  - Butorphanol nasal spray
- Migraine specific medications
  - Triptans: PO, nasal, patch
  - DHE: nasal or pulmonary inhaler
  - Sumatriptan + naproxen

**Level B: Probably Effective**
- Antiemetics
  - Chlorpromazine IV, IM, PR
  - Metoclopramide IV
- Ergots
  - DHE IV, IM, SC
  - Ergotamine + caffeine SL
- Others
  - MgSO4 IV
  - Isometheptene PO
  - Combinations
    - Codeine + acetaminophen
    - Tramadol + acetaminophen

Headache 2015;55:3
American Headache Society 2015: Evidence-Based Acute Migraine Rx

- Valproate IV
- Ergotamine PO
- Opioids PO, IM
- Tramadol IV
- Dexamethasone IV
- Butalbital + caffeine +/- codeine

Level C: Possibly effective

- Celecoxib PO
- Lidocaine IV
- Hydrocortisone IV

Level U: Conflicting evidence

Cost of Treating A Single Migraine Attack at Lowest Dosage

<table>
<thead>
<tr>
<th>Drug</th>
<th>Cost (USD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eletriptan 20 mg</td>
<td>$20</td>
</tr>
<tr>
<td>Naratriptan 1mg</td>
<td>$10</td>
</tr>
<tr>
<td>Sumatriptan 25 mg PO</td>
<td>$2</td>
</tr>
<tr>
<td>Sumatriptan 6 mg SC</td>
<td>$85</td>
</tr>
<tr>
<td>Sumatriptan intranasal 10mg</td>
<td>$55</td>
</tr>
<tr>
<td>DHE Nasal</td>
<td>$421</td>
</tr>
<tr>
<td>Ibuprofen 600 mg</td>
<td>$0.20</td>
</tr>
</tbody>
</table>

Case Vignette: Linda

- My headaches are terrible
- I can’t work for a day or two each time
- Acute treatments hardly touch my headache
- Can I try preventive Rx?
- Which one is right for me?

Acute Treatment of Migraines: Recommendations

- NSAIDs for mild to moderate migraine
- Triptan for moderate to severe migraine
- Consider PR prochlorperazine
- Third line option:
  - DHE nasal
- If nausea limits the use of PO meds
  1. PR prochlorperazine or indomethacin
  2. Intranasal sumatriptan, zolmitriptan or DHE
  3. SC sumatriptan
  4. Transdermal sumatriptan

Level C: Possibly effective

Level U: Conflicting evidence
Indications for Preventive Therapy

- More than 2 migraines per week
- Headache related disability for ≥ 3 days per month
- Duration > 48 hours
- Acute migraine treatments are ineffective or overused
- Attacks produce severe disability
- Prolonged aura (> 1 hour), complex aura, or migrainous infarction
- Patient preference

Principles of Migraine Prevention

- 50% or greater reduction in severity or frequency is a success
- May take 2-3 months to take effect
- Use drugs that benefit a coexisting condition when possible
- Goal is fewer headaches, less absence from work or school, less use of abortive medications

Beta Blockers

- Most commonly used prophylaxis
- Avoid if history of CHF, asthma, diabetes (relative contraindication), depression
- Propranolol best studied
  - 80-240 mg daily
- Timolol, atenolol, metoprolol also effective
- Begin low dose, may need to push to full beta blockade (i.e. HR in 50’s)
- Follow bp, HR

Divalproex Sodium

- Equivalent efficacy to beta blockers
- Doses of 500-1000 mg daily are effective
- Requires baseline and periodic laboratory monitoring:
  - LFTs, platelet count, coagulation studies
- Contraindicated during pregnancy and reproductive age women not using birth control
- Weight gain important side effect
Topiramate

- Efficacy similar to propranolol
- Side effects are common and may result in discontinuation
  - Paresthesias
  - Fatigue, poor concentration
  - Weight loss
  - Acute angle closure glaucoma (rare)
- Limit maximum dose to 50 mg bid

Amitriptyline

- Efficacy similar to propranolol in clinical practice
- Less data
  - Downgraded in 2012 by AAN to Level B
- Side effects are common and may result in discontinuation
  - Weight gain
  - Dry mouth
  - Constipation
- Equally effective in non-depressed patients
- Usual doses 10-50 mg qhs
- Helpful if coexistent chronic pain or insomnia

Other Preventive Therapies

- Verapamil
  - Particularly for exertional migraine or migraines in men
- Venlafaxine probably effective
  - Suggest use if amitriptyline fails or not tolerated
- Short term daily triptans
  - Effective for menstrual migraine
- ACE inhibitors
  - Lisinopril effective in a single study
- ARBs
  - Candesartan may be effective

Cochrane: Odds Ratio for 50% Reduction in Migraine Frequency with Anticonvulsants

Chronic, Edward P., Mulleners, Wim M. Anticonvulsant drugs for migraine prophylaxis. Cochrane Database Revised June 2013
TCAs Effective for Both Migraine and Tension Type Headache

BMJ 2010;341:c5222

Third Line Approach: Botulinum Toxin

Botulinum toxin pericranial injections
- Ineffective for episodic migraine
- Ineffective for chronic tension-type headache
- Effective for chronic migraine and chronic daily headache
- FDA approved for chronic (not episodic) migraine in 2010
- Treat every 12 weeks

AAN Guideline: Neurology 2008;70:1707

Summary of Results from 3 RCTs: Effective for Both Episodic and Chronic Migraine
(Medical Letter June 2018)

<table>
<thead>
<tr>
<th></th>
<th>Δ Migraine Days/month</th>
<th>≥ 50% Reduction Days/mo.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Episodic migraine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study 1</td>
<td>-3.2</td>
<td>43%</td>
</tr>
<tr>
<td>Study 2</td>
<td>-3.7</td>
<td>50%</td>
</tr>
<tr>
<td>Placebo</td>
<td>-1.8</td>
<td>27%</td>
</tr>
<tr>
<td>Episodic migraine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study 2</td>
<td>-2.9</td>
<td>40%</td>
</tr>
<tr>
<td>Placebo</td>
<td>-1.8</td>
<td>30%</td>
</tr>
<tr>
<td>Chronic migraine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study 3</td>
<td>-6.6</td>
<td>40%</td>
</tr>
<tr>
<td>Placebo</td>
<td>-6.6</td>
<td>42%</td>
</tr>
<tr>
<td>Placebo</td>
<td>-4.2</td>
<td>24%</td>
</tr>
</tbody>
</table>
Erenumab: Use

- Reduces migraine days by one half
- Cost comparable to Botulinum toxin and easier to administer
- Approved dose is 70 mg SC once monthly, self injected
- Can increase to 140 mg SC in selected patients
- FDA: Post marketing reports of hypersensitivity reactions
- 2 other monoclonal Ab to CGRP have since been FDA approved as well: galcanezumab, fremanezumab

Cost of Commonly Used Dose of Migraine Prevention Drugs

<table>
<thead>
<tr>
<th>Drug</th>
<th>30 Day AWP Cost (USD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Propranolol 60 mg qd</td>
<td>$12</td>
</tr>
<tr>
<td>Divalproex Sodium 250 mg bid</td>
<td>$7</td>
</tr>
<tr>
<td>Topiramate 50 mg bid</td>
<td>$6</td>
</tr>
<tr>
<td>Amitriptyline 50 mg qhs</td>
<td>$9</td>
</tr>
<tr>
<td>Botulinum toxin</td>
<td>$400</td>
</tr>
<tr>
<td>Erenumab 70 mg SC monthly</td>
<td>$575</td>
</tr>
</tbody>
</table>

Medical Letter June 2018

American Academy of Neurology 2012: Evidence Based Preventive Treatment

Level A: Established efficacy
- Anti-epileptic drugs
- Topiramate
- Divalproex sodium
- Beta blockers
- Propranolol
- Metoprolol
- Timolol
- Triptans
- Frovatriptan (menstrual migraine)

Level B: Probably effective
- Antidepressants
- Amtriptyline
- Venlafaxine
- Beta blockers
- Atenolol
- Nadolol
- Triptans
- Naratriptan
- Zolmitriptan

Level C: Possibly effective
- ACEi
- Lisinopril
- ARB
- Candesartan
- Alpha blocker
- Clonidine
- Anti-epileptic drugs
- Carbamazepine

Level U (abbreviated list): Conflicting or inadequate data
- Acetazolamide
- Warfarin
- Fluoxetine
- Gabapentin
- Nifedipine
- Verapamil

Neurology 2012;78:1137
### Summary: Preventive Migraine Rx

<table>
<thead>
<tr>
<th>Drug</th>
<th>Efficacy</th>
<th>Side effects</th>
<th>Relative contraindications</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>β-Blockers</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Metoprolol</td>
<td>4+</td>
<td>2+</td>
<td>Asthma, depression, CHF</td>
</tr>
<tr>
<td>• Propranolol</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Antidepressants</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Amitriptyline</td>
<td>3+</td>
<td>3+</td>
<td>Mania, BPH, heart block</td>
</tr>
<tr>
<td>• Venlafaxine</td>
<td>2+</td>
<td>1+</td>
<td>Mania</td>
</tr>
<tr>
<td><strong>Anticonvulsants</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Divalproex</td>
<td>4+</td>
<td>2+</td>
<td>Liver dz, bleeding disorders</td>
</tr>
<tr>
<td>• Gabapentin</td>
<td>2+</td>
<td>2+</td>
<td>Liver dz, bleeding disorders</td>
</tr>
<tr>
<td>• Topiramate</td>
<td>4+</td>
<td>2+</td>
<td>Kidney stones</td>
</tr>
<tr>
<td><strong>NSAIDs</strong></td>
<td>2+</td>
<td>2+</td>
<td>Ulcer disease, gastritis</td>
</tr>
</tbody>
</table>

### Complementary Migraine Prevention: Positive Results but Small Studies

- Coenzyme Q 100 mg tid
  - Effective in two small trials
- Magnesium citrate 300 mg daily
  - Effective in 3 of 4 small trials to date
  - Data limited
- Riboflavin 200 mg bid
  - >50% response rate in 2 small trials
- Extract of feverfew plant
  - Effective in 4 of 6 studies (n=561) included in a systematic review*
  - Small sample sizes with effect magnitude uncertain

*Cochrane 2015, April 20

### Evidence Based Complementary Treatments for Migraine Prevention

- **Level A**
  - Established efficacy
  - (None)

- **Level B**
  - Probably effective
  - Magnesium
  - MIG-99 (feverfew)
  - Riboflavin

- **Level C**
  - Possibly effective
  - Co-Q10

**Butterbur No Longer Recommended**

- Butterbur (Petasites) had been recommended by the AAN 2012 guideline
- However, many proprietary products contain pyrrolizidine alkaloids which are potentially hepatotoxic
- Carcinogenic in animal studies
- Potency of active drug also varies in products
- AAN and UpToDate **no longer** recommend Butterbur due to safety concerns

AAN Guideline: Neurology 2012;78:1346
Preventive Therapy of Migraines: My Recommendations

<table>
<thead>
<tr>
<th>First Line Rx</th>
<th>Second Line Rx</th>
<th>Third Line Rx</th>
</tr>
</thead>
<tbody>
<tr>
<td>Propranolol</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Topiramate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Divalproex Sodium</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amitriptyline</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Venlafaxine</td>
<td></td>
<td></td>
</tr>
</tbody>
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Preventive Therapy of Migraines: My Recommendations

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<td></td>
<td>Amitriptyline</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Venlafaxine</td>
<td></td>
</tr>
</tbody>
</table>

American Headache Society Choosing Wisely

1. Don’t perform neuroimaging studies in patients with stable headaches that meet criteria for migraine.
2. Don’t perform computed tomography (CT) imaging for headache when magnetic resonance imaging (MRI) is available, except in emergency settings.
3. Don’t recommend surgical deactivation of migraine trigger points outside of a clinical trial.
4. Don’t prescribe opioid or butalbital-containing medications as first-line treatment for recurrent headache disorders.
5. Don’t recommend prolonged or frequent use of over-the-counter (OTC) pain medications for headache.
Cluster Headache

- Much less common in primary care practice than migraine
- High rates of disabling pain among patients with cluster headache
- Unique pathophysiology
- Effective treatment regimens differ in important ways from treatment of migraine

Trigger Avoidance for Cluster Headache

AVOID
- Afternoon naps or changes in sleeping habits
- Alcohol
- Prolonged exposure to volatile chemicals
- Excessive bursts of anger or extreme emotion
- Prolonged physical exertion
- Extreme changes in altitude

Abortive Treatment of Cluster Headache

First line options
- O₂ 100% non rebreather at 7-10 l/min for 15 minutes
- 70% effective within 5 minutes
- Sumatriptan 6 mg SC
- No evidence of tachyphylaxis or dependency with repeated use
- Sumatriptan or zolmitriptan IN

Abortive Treatment of Cluster Headache

Second line abortive treatments
- Octreotide SC
- DHE IV, IM, or SC
- DHE Intranasal
- Intranasal lidocaine

Biondi D, Mendes P. Cluster headache. National Headache Foundation. 2004
Prophylactic Therapy for Cluster Headache

Transitional
- Prednisone (60-100 mg daily for 5 days, then taper over 10-12 days)
- Ergotamine tartrate
- DHE
- Occipital nerve block

Maintenance
- First line
  - Verapamil (240-480 mg / day)
- Second line
  - Methysergide
  - Lithium carbonate
  - Divalproex sodium
  - Topiramate
  - Melatonin

Refractory Cluster Headache

- Heroic treatments with appropriate subspecialty consultation
  - IV histamine desensitization
  - Surgical or RFA ablation of sensory trigeminal nerve
  - Glycerol injection to trigeminal cistern
  - Gamma knife radiosurgery

Levels of Evidence for Rx of Cluster Headache

<table>
<thead>
<tr>
<th>Acute Rx</th>
<th>Level of Evidence</th>
<th>Maintenance Prophylaxis</th>
<th>Level of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>100% Oxygen</td>
<td>A</td>
<td>Verapamil</td>
<td>A</td>
</tr>
<tr>
<td>Prednisone</td>
<td>A</td>
<td>Melatonin</td>
<td>B</td>
</tr>
<tr>
<td>Sumatriptan SC</td>
<td>A</td>
<td>Lithium</td>
<td>B</td>
</tr>
<tr>
<td>Zolmitriptan or Zolmitriptan IN</td>
<td>A</td>
<td>Topiramate</td>
<td>B</td>
</tr>
<tr>
<td>Zolmitriptan PO</td>
<td>B</td>
<td>Valproic Acid</td>
<td>B/C</td>
</tr>
<tr>
<td>Octreotide SC</td>
<td>B/C</td>
<td>Baclofen</td>
<td>C</td>
</tr>
<tr>
<td>Lidocaine IN</td>
<td>B/C</td>
<td>Gabapentin</td>
<td>Not rated</td>
</tr>
<tr>
<td>DHE IN</td>
<td>Not rated</td>
<td>Botulinum Toxin</td>
<td>Not rated</td>
</tr>
</tbody>
</table>

Tension-Type Headaches

- Less gratifying than treatment of migraines
- Stress reduction or biofeedback may be helpful
- Psychiatric evaluation in selected patients
- Physical therapy for tender points
- Consider TMJ or cervicogenic components to headache

EFNS Guidelines: Eur J Neurol 2006;13:1066
**Acute Treatment of Tension-Type Headaches**

- ASA or NSAIDs are mainstay
- Acetaminophen effective in some patients
- Butalbital containing medications for patients with infrequent headache
  - Risk of addiction and rebound headache

**Preventive Treatment of Tension-Type Headaches**

1st Line
- Amitriptyline
- Nortriptyline

2nd Line
- Venlafaxine
- Tizanidine
- Mirtazapine

Ineffective
- Botulinum toxin injections
- SSRIs

**Factors That Influence Rx Choice for Prevention of TTH**

<table>
<thead>
<tr>
<th>Co-existing conditions / symptoms</th>
<th>Preferred Rx options</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insomnia</td>
<td>Amitriptyline, mirtazapine</td>
</tr>
<tr>
<td>Fibromyalgia, chronic pain syndromes</td>
<td>Amitriptyline</td>
</tr>
<tr>
<td>Constipation</td>
<td>Nortriptyline, tizanidine</td>
</tr>
<tr>
<td>Worried about weight gain</td>
<td>Tizanidine, venlafaxine</td>
</tr>
<tr>
<td>Daily fatigue</td>
<td>Venlafaxine</td>
</tr>
</tbody>
</table>

**Summary**

- Avoid migraine triggers
- Acute therapies for migraine
  - NSAIDs, AAC
  - Triptans
  - DHE
  - Antiemetics
- Preventive medications for migraine
  - Propranolol
  - Divalproex sodium
  - TCAs
  - Topiramate
  - Botulinum toxin
  - Erenumab
Summary

- Complementary physical strategies for migraine
  - Acupuncture (preferred)
  - Spinal manipulation
  - Biofeedback
  - Cognitive behavioral therapy

- Complementary oral medications
  - Magnesium
  - Riboflavin
  - Feverfew
  - Co-Enzyme Q

Summary

- Acute therapy for cluster headache
  - O2
  - Sumatriptan SC
- Prophylaxis for cluster headache
  - Prednisone
  - Verapamil
  - Lithium
  - Divalproex sodium

- Acute therapy for tension-type headache
  - NSAIDs
  - ASA
- Prophylaxis for tension-type headache
  - Amitriptyline
  - Tizanidine
  - Venlafaxine
  - Mirtazapine