Common Migraine Myths

1. A MIGRAINE IS JUST A BAD HEADACHE
2. MIGRAINE IS CAUSED BY PSYCHOLOGICAL FACTORS, SUCH AS STRESS AND DEPRESSION
3. MIGRAINE IS NOT LIFE THREATENING, JUST ANNOYING
4. ANY DOCTOR WILL RECOGNIZE AND PROPERLY TREAT MIGRAINE

Migraine: The Basics

- Primary headache disorder
  - Begins at puberty, most common in ages 25-55
  - Recurrent, life-long, characterized by attacks
- Attack feature
  - Pounding or throbbing headache of moderate-severe intensity
  - One-sided
  - Nausea and vomiting, abdominal pain
  - Aggravated by routine physical activity
  - Sensitivity to light, noise, and odors
  - Loss of appetite
  - Fatigue, dizziness, blurred vision
  - Duration of 4 hours to 2-3 days
- Attack frequency between once a year and once or twice a week

WHO 2012, AAN 2013

Types of Migraines

Migraine without aura
- "Common migraine"
- May experience vague symptoms before onset
  - Anxiety, depression, fatigue
- 20%-30% experience aura
  - Can occur 1 hour before attack of pain and last 15 minutes to an hour

Migraine with aura
- "Classic migraine"
- Aura: physiological warning sign for migraine beginning
  - Bright dots, blind spots, vision loss/distortion, wavy/jagged lines, tinnitus, changes in smell, taste, or touch
- 20%-30% experience aura
  - Can occur 1 hour before attack of pain and last 15 minutes to an hour

Types of Migraines

Episodic
- <15 headache days per month, some migraines
- Menstrual associated migraine (MAM)
  - Hormone-related 2 days before onset of or first 2 days of menses
  - More severe, frequent, and resistant to therapy

Chawla 2013, Headache Classification H1998

Chronic
- >15 headache days per month, headache >4 hours for at least 3 months, some migraines
- Medication overuse headache (MOH)
  - Transition from episodic
  - Analgesic or triptan overuse
  - Unresponsive to preventative medications

Chawla 2013, Reddy 2013

Migraine Epidemiology

- Highly prevalent
  - Over 37 million Americans
    - 18% of women
    - 7% of men
    - 19% of veterans of the Iraq war
- Substantial prevalence and burden even in the least affected subgroup of males ≥75 years
  - 4.6% reported experiencing severe headache or migraine in the previous 3 months

AAN 2013
Migraine Prophylaxis

**Epidemiology**
- Epidemiologic studies suggest ~38% need preventative therapy
  - Only 3-13% use it
- Preventative therapies can decrease the occurrence of migraines by 50-80% and reduce severity and duration of migraines that do occur
- 12 million office visits → 6 million prescriptions issued for antimigraine drugs
  - Mostly triptans

**Mini Case**
KD is a 25 year old female who experiences 5 headaches per month, 2 of which are pounding and unilateral in nature and induce nausea, vomiting, and photophobia. Prior to experiencing an attack, she notices fatigue but denies vision changes.

Current medications include: albuterol inhaler (ProAir), norgestimate and ethinyl estradiol tablets (MonoNessa), rizatriptan (Maxalt). She consumes one cup of coffee or one soda daily and notes headaches occur most frequently when temperatures dramatically increase or when dehydrated after a workout.

1. What type of migraine headache does she have?
   - Common or Classic?
   - Chronic or Episodic?
2. What are her risk factors and triggers?

### Vascular Theory
- Blood vessels in the brain contract and expand inappropriately
  - Ischemia induced by intracranial vasoconstriction → aura
  - Rebound vasodilation & activation of perivascular nociceptive nerves → headache

### Neurovascular Theory
- Neurogenic process
  - Secondary changes in cerebral perfusion
  - State of neuronal hyperexcitability in cerebral cortex, especially in occipital cortex

- Explains susceptibility of migrainous brain to headaches
  - **Think**: parallels patients with epilepsy who similarly have interictal neuronal irritability

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**Migraine Risk Factors and Triggers**
Cortical Spreading Depression (CSD)

• Wave of neuronal excitation in the cortical gray matter
  – Cellular depolarization → aura phase
  – Activates trigeminal fibers → headache
    • Activation stimulates release of plasma proteins
      and pain-generating substances
      - Calcitonin gene-related peptide, Substance P,
        vasoactive intestinal peptide, neurokinin A
    • Alters permeability of blood brain barrier

Serotonin

• Serotonin receptor (5-HT) = most important receptor in headache pathway
  – Low serotonin levels in the brain →
    • Constriction and dilation of the blood vessels
      which trigger a migraine

  Currently available triptans are selective 5-HT1B/D full agonists
  Decrease headache by
  • Abolishing neuropeptide release
  • Blocking trigeminocephalic complex neurotransmission

Treatment

• Migraine treatment may be classified as:
  1) Prophylactic - chronic treatment of migraine
  2) Intermittent prophylaxis - only when migraine is expected (during menstruation)
  3) Symptomatic (abortive) - only during an attack (i.e. triptans, NSAIDs)

• Excessive use of symptomatic medications on a daily basis may result in chronic migraines (MOH)

Who are good candidates for preventive migraine medication?

• Migraine quantity and quality
  – > 2 headaches/month, but fewer than 8
  – Less frequent but more prolonged (>2 days duration)
  – Severe attacks leading to substantial disability

• Medications and comorbidities
  – Poor or refractory response to abortive treatment
    – Therapies for acute attacks are intolerable, contraindicated, or overused (>2 per week)
    – Health issues prevent use of symptomatic agents

• Certain types of migraines respond well to preventative therapy
  – Predictable in occurrence
  – Prolonged aura or hemiplegic migraine

EPISODIC MIGRAINE
Evidence-Based Guideline Update for Episodic Migraines

- American Academy of Neurology (AAN)
  - Old: 2000
  - New: 2012 → Pharmacologic treatment for episodic migraine prevention in adults
    - NSAIDs and other complementary treatments for episodic migraine prevention in adults
  - New clinical studies on efficacy and safety of migraine preventative therapies

- American Headache Society (AHS)

Analysis of Evidence

- Evaluation of new clinical studies
  - Published studies from June 1999 - May 2009
  - Excluded
    - Acute treatment
    - Migraine aura treatment/prevention
    - Nonpharmacologic treatment
    - Quality of life measures
    - Nonstandardized outcomes as primary efficacy endpoints
    - Drugs not available in US

- Revised evidence classification criteria to include study completion rates
  - Downgraded if completion rates < 80%

Category Classifications

2000

- Group 1: High efficacy, good strength of evidence, and minimal moderate side effects
- Group 2: Lower efficacy than group 1 or limited strength of evidence, and minimal moderate side effects
- Group 3: Clinically efficacious based on consensus and clinical experience, but no scientific evidence of efficacy
- Group 4: Medium-high efficacy, good strength of evidence, but with side effect concerns
- Group 5: Evidence indicating no efficacy above placebo

2012

- Level A: Medications with established efficacy (≥2 Class I studies)
- Level B: Medications that are probably effective (1 Class I or 2 Class II studies)
- Level C: Medications that are possibly effective (1 Class II study)
- Level D: Inadequate or conflicting data to support or refute medication use

Established as effective

Should be offered to patients requiring prophylaxis

Level A

- Antiepileptic Drugs
  - Topiramate 25-200 mg daily (upgraded from group 3)

Level B

- β-Blockers
  - Metoprolol 50-200 mg daily (upgraded from group 2)
  - Propranolol 120-240 mg daily
  - Timolol 10-15 mg BID

Level Other

- Herbs/Other
  - Butterbur 50-75 mg BID (added)

Level Other

- Other Medications that are established as possibly or probably ineffective

(1 Class I or 2 Class II studies)

(1 Class II study)

(≥2 Class I studies)

(1 Class I, II or III criteria including consensus or expert opinion)

(1 Class II study)

Other studies not meeting Class I, II or III criteria including consensus or expert opinion

Rando - Randomized, controlled trial (RCT) with masked/objective outcomes

Primary outcomes and exclusion/inclusion criteria clearly defined

Accounted for dropouts (≥90% of subjects completing the study)

Relevant equivalent baseline characteristics among treatment groups

Randomization or equivalence trials claiming to prove efficacy for one or both drugs have additional requirements

RCT lacks one criteria above OR prospective matched cohort study with masked/objective outcome assessment in a representative population that meets above criteria

All other controlled trials (including well-defined natural history controls or patients serving as own controls)

Recommended for these agents are based on the evidence reviewed in the original guideline
Divalproex sodium
Sodium valproate
- Strong consistent support for efficacy
- Mechanism: enhanced GABA inhibition
- New Class I trial: double-blind, randomized, placebo-controlled
  - Men/women, aged 16-69 with 2 headaches at baseline
  - Initiated on ER Divalproex 500 mg/day x 1 week
    - Increased to 1000 mg/day as tolerated
  - 4-week baseline; 12-week experimental; 1-week termination phase

Level A Beta Blockers
- **Propranolol**: Upgraded → Revised criteria reclassified prior studies as Class I
  - No clear evidence one Level A beta blocker is more effective than others
    - Propranolol: membrane stabilizing activity, affinity for 5-HT sites in brain, inhibits cytokines
    - **Timolol**: effective without these properties

Only identified common property = lack of partial agonist or intrinsic sympathomimetic activity

2013 Cochrane Review of Topiramate
Outcomes vs. Other Agents for Episodic Migraine Prophylaxis

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Responders (%)</th>
<th>Responders Odds Ratio (95% CI)</th>
<th>Difference in 28-day HA Frequency (95% CI)</th>
<th>Risk Ratio (95% CI)</th>
<th>NNT (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Topiramate 50-200 mg/day vs placebo (9 studies)</td>
<td>47 (26-63)</td>
<td>3.18 [1.10 to 8.82]</td>
<td>-1.2 [-1.59 to 0.00]</td>
<td>2.02 [1.57 to 2.60]</td>
<td>4 (3 to 6)</td>
</tr>
<tr>
<td>Topiramate 50-100 mg/day vs enalapril 50-100 mg/day (3 studies)</td>
<td>0.68 [0.44 to 1.05]</td>
<td>Unable to calculate</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Topiramate 50 mg vs propranolol 80-160 mg (2 studies)</td>
<td>1.32 [0.82 to 2.13]</td>
<td>Pooled: MD 0.14 [-0.83 to 0.34]</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Mechanism: Unknown; mediated by multiple sites
Decrease migraine frequency by at least 50% in almost half of patients

Level A Beta Blockers
Dosing Considerations

<table>
<thead>
<tr>
<th>Beta Blocker</th>
<th>Initial dose</th>
<th>Titrating maintenance dose range</th>
<th>Doses should be gradually increased based on individual response and tolerability</th>
<th>Treat at maximum tolerated dose and allow 6-8 weeks for adequate response</th>
<th>Maintain for at least 3 months before deeming the medication a failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Propranolol</td>
<td>80 mg/day divided every 6-8 hours; (LA: 80 mg once daily)</td>
<td>Increase by 20-40 mg/dose every 3-4 weeks to a maximum of 160-240 mg/day given in divided doses every 6-8 hours; (LA: 160-240 mg once daily)</td>
<td>20 mg/day or 20-30 mg divided</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Timolol</td>
<td>10 mg twice daily</td>
<td>Increase by 20-40 mg/dose every 3-4 weeks to a maximum of 160-240 mg/day given in divided doses every 6-8 hours; (LA: 160-240 mg once daily)</td>
<td>20 mg/day</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Abrupt withdrawal may result in severe rebound migraine attacks; taper gradually over several weeks

2013 Cochrane Review of Valproate
Outcomes for Prophylaxis of Epidemic Migraines

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Responders (%)</th>
<th>Responders Odds Ratio (95% CI)</th>
<th>Difference 28-day HA Frequency (95% CI)</th>
<th>Risk Ratio (95% CI)</th>
<th>NNT (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Divalproex sodium 500-1500 mg/day vs placebo (4 trials)</td>
<td>42 (34-49) vs 21 (14-34)</td>
<td>3.38 [1.46 to 7.67]</td>
<td>Unable to calculate</td>
<td>2.18 [1.28 to 3.72]</td>
<td>4 (2 to 11)</td>
</tr>
<tr>
<td>Sodium valproate 1000-1500 mg/day vs placebo (3 trials)</td>
<td>50 vs 18</td>
<td>4.67 [5.41 to 16.4] vs -3.11 [-4.32 to -1.90]</td>
<td>2.83 [1.27-6.31]</td>
<td>3 (2 to 9)</td>
<td></td>
</tr>
<tr>
<td>Divalproex sodium 1500 mg/day vs Propranolol 180 mg/day (2 trials)</td>
<td></td>
<td>1.15 [0.41 to 3.18] vs -4.28 [-4.77 to 0.42]</td>
<td>Unable to calculate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sodium valproate 400 mg vs Topiramate 50 mg (2 studies)</td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

Silberstein et al. 2012 (Table e-1), Loder et al. 2012
**Petasites extract (Butterbur)**

- Specific butterbur rhizome extract standardized to 15% petasin and isopetasin (Petadolex)
  - Reduce frequency (48%), intensity, and duration when used over 16 weeks

### Venlafaxine Trials

- Class I Study: prospective, randomized, double-blind study; n=60, 10-week study, venlafaxine XR 150 mg, 75 mg, placebo
  - Number of Headache Days: 150 mg group superior
  - Pain Severity: No significant difference (p=0.07)
  - Duration: No significant differences (p=0.479)

### Petasites extract (Butterbur)

- Recommend doses of at least 75 mg twice daily
  - Lower doses of 50 mg BID may not be effective
- Taper after 4-6 months
  - Long-term safety unknown
  - Petadolex = pyrrolizidine-free
- Other uses (limited efficacy)
  - Asthma (50 mg three times per day for adults)
  - Hay fever (1 tablet standardized to contain 8 mg petasin extract two to three times a day for two weeks)

### Venlafaxine Trials

**Randomized, double-blind crossover study:**
n=52, run-in, 12-week study, 4-week washout

<table>
<thead>
<tr>
<th>Efficacy (attack frequency ± SD)</th>
<th>Baseline</th>
<th>12 weeks</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Venlafaxine XR (titrated to 150 mg daily)</td>
<td>4.15 ± 2.24</td>
<td>1.77 ± 1.39</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Amitriptyline (titrated to 75 mg daily)</td>
<td>3.27 ± 1.61</td>
<td>1.54 ± 1.54</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Common adverse reactions:
- Mild gastrointestinal events, predominantly nausea

*Results were also significant in favor of 75 mg at 2, and 8 months based on this endpoint*
ACE-Inhibitor/ARB Trials

**Methods:** Double-blind, placebo-controlled, crossover study of 60 patients aged 19-59 years with 2 to 6 migraine episodes per month (Class II Study)

**Lisinopril Intervention:** Two treatment periods of 12 weeks, separated by 2 weeks of placebo washout
1. Lisinopril 10 mg daily for one week then two 10 mg tablets daily for 11 weeks
2. One placebo tablet once daily for one week and then two placebo tablets for 11 weeks

**Candesartan Intervention:** Placebo run-in period of 4 weeks, followed by two 12-week treatment periods, separated by 4 weeks of placebo washout
1. One 16-mg candesartan tablet daily in the first treatment period
2. Followed by 1 placebo tablet daily in the second period

**Mechanism:** Studies generally concluded to decrease headache intensity by 20% vs. placebo
- Not widely used for this indication

**Evidence:**
- Negative Evidence
  - Level A - Ineffective, should NOT be offered
    - Lamotrigine
  - Level B - Probably ineffective, should NOT be considered
    - Clomipramine
  - Level C - Possibly ineffective, MAY be considered
    - Acetbutolol
    - Clonazepam
    - Montelukast
    - Nabumetone
    - Oxcarbazepine
    - Telmisartan

**ACE-Inhibitor/ARB Trials: Results**

<table>
<thead>
<tr>
<th></th>
<th>Headache Hours</th>
<th>Headache Days</th>
<th>Migraine days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lisinopril</td>
<td>129 vs 162 hours</td>
<td>19.7 vs 23.7 days</td>
<td>14.5 vs 18.5 days</td>
</tr>
<tr>
<td>Placebo</td>
<td>20% (5-36) reduction</td>
<td>17% (5-30) reduction</td>
<td>21 (9-24) reduction</td>
</tr>
<tr>
<td>Candesartan</td>
<td>95 vs 139</td>
<td>13.6 vs 18.5</td>
<td>9.0 vs 12.6</td>
</tr>
<tr>
<td>Placebo</td>
<td>p &lt; 0.001</td>
<td>45.6 vs 26.3% reduction from baseline</td>
<td>p &lt; 0.001</td>
</tr>
</tbody>
</table>

Small size & single center, crossover design → prevents definitive conclusions regarding efficacy
- Generally concluded to decrease migraine days around 25% vs. placebo
- Not widely used for this indication

**OnabotulinumtoxinA; BOTOX®**

- **NOT** in 2012 AHS/AAN Guidelines
  - Identified as **ineffective for episodic migraine** in another AAN guideline (Level B Evidence)
- FDA approved for **chronic migraine** in October 2010
  - Intractable, chronic migraine with failed response to at least 3 conventional preventive medications
  - Two less headaches per month
  - Approved injections reduce chronic headaches by -10%
- **Mechanism:** blocking of sensory nerves in the head, not through paralysis of muscles

**Literature Review (JAMA 2012)**
- 27 randomized, placebo-controlled trials conducted on 5,300 patients with various headache types
- Failed to show any effects in episodic migraines or chronic tension-type headaches
- Studies reporting no effect in episodic migraine used number of migraines as the measured variable
- May reduce headache intensity

**Conflicting or Inadequate Data**

<table>
<thead>
<tr>
<th>Level</th>
<th>Antiepileptics</th>
<th>Calcium Channel Blockers</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Gabapentin (downgraded from group 2)</td>
<td>Nifedipine, nimodipine</td>
<td>Omega-3, hyperbaric oxygen, acetazolamide, warfarin, picotamide</td>
</tr>
<tr>
<td>B</td>
<td>Lamotrigine (downgraded from group 2)</td>
<td>Pindolol</td>
<td>N-acetyl cysteine</td>
</tr>
<tr>
<td>C</td>
<td>Valproate, levetiracetam</td>
<td>Verapamil</td>
<td>Pycnogenol</td>
</tr>
</tbody>
</table>

**OnabotulinumtoxinA; BOTOX®**

- Most insurance will not pay for Botox for episodic migraine and the cost of the drug is very high
General Management Principles

1) Assess coexisting conditions
   - Special concern for women of childbearing potential

2) Consider possible drug interactions & exacerbating medications
   - Stimulants, oral contraceptives/hormone therapy, nitrates, analgesic overuse

3) Continue abortive therapy
   - Rarely curative
   - Acute treatment effectiveness usually increased when used with prophylactic drugs

4) Start at low dose
   - Slowly increase (every 2 to 4 weeks) until therapeutic effect is achieved, side effects are intolerable, or max effective dose reached

5) Continue at least 2 to 3 months at maximum tolerable dose before deciding on effectiveness
   - Compliance is a major issue
   - 50% reduction in frequency deemed successful

6) Taper and discontinue if acceptable migraine control for 6 to 12 months
   - Resume therapy if attacks return

Silberstein et al. 2012 (Table e-1)

Common comorbid conditions

- Stroke
- Myocardial Infarction
- Raynaud’s Phenomenon
- Epilepsy
- Affective Disorders
- Anxiety Disorders
- Diabetes (with frequent hypoglycemia)
- Heart failure
- May exacerbate depression

Level A Evidence: First-line Agents Consider Coexisting Conditions

<table>
<thead>
<tr>
<th>Medication</th>
<th>Use Recommended</th>
<th>Caution/Avoid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beta Blockers</td>
<td>Anxiety&lt;br&gt;Essential tremor&lt;br&gt;Hypertension&lt;br&gt;Myocardial infarction</td>
<td>Asthma&lt;br&gt;Bradycardia&lt;br&gt;2nd or 3rd degree heart block&lt;br&gt;Peripheral vascular disease&lt;br&gt;Raynaud disease&lt;br&gt;Diabetes (with frequent hypoglycemia)&lt;br&gt;Heart failure&lt;br&gt;May exacerbate depression</td>
</tr>
<tr>
<td>Divalproex sodium</td>
<td>Prolonged or atypical aura&lt;br&gt;Anorexia&lt;br&gt;Epilepsy&lt;br&gt;Bipolar disorder</td>
<td>Liver disease&lt;br&gt;History of pancreatitis&lt;br&gt;Thrombocytopenia&lt;br&gt;Pregnancy&lt;br&gt;Obesity</td>
</tr>
<tr>
<td>Sodium valproate</td>
<td>Prolonged or atypical aura&lt;br&gt;Anorexia&lt;br&gt;Epilepsy&lt;br&gt;Bipolar disorder</td>
<td>Liver disease&lt;br&gt;History of pancreatitis&lt;br&gt;Thrombocytopenia&lt;br&gt;Pregnancy&lt;br&gt;Obesity</td>
</tr>
<tr>
<td>Topiramate</td>
<td>Obesity&lt;br&gt;Epilepsy</td>
<td>Anorexia&lt;br&gt;Renal stones&lt;br&gt;Cognitive impairment&lt;br&gt;First trimester pregnancy</td>
</tr>
</tbody>
</table>

Adapted from Silberstein et al. 2012 (Table e-1)

Level B, C, U Evidence: Other Agents Consider Coexisting Conditions

<table>
<thead>
<tr>
<th>Medication</th>
<th>Use Recommended</th>
<th>Caution/Avoid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium Channel Blockers</td>
<td>Hypertension&lt;br&gt;Angina&lt;br&gt;Prolonged or atypical aura: verapamil</td>
<td>Depression&lt;br&gt;2nd and 3rd degree heart block&lt;br&gt;Sick sinus syndrome</td>
</tr>
<tr>
<td>SSRIs/SNRIs</td>
<td>Depression&lt;br&gt;Anxiety</td>
<td>Serotonin syndrome in patients taking SSRIs with triptans but is rare (incidence approximately 0.03%)</td>
</tr>
<tr>
<td>TCAs</td>
<td>Insomnia: amitriptyline, doxepin</td>
<td>Epilepsy (may lower seizure threshold), suicidal ideation, cardiac arrhythmias</td>
</tr>
<tr>
<td>ACE/ARB</td>
<td>Hypertension&lt;br&gt;Myocardial infarction</td>
<td>Angioedema, pregnancy, electrolyte imbalances, impaired renal function, hypotension</td>
</tr>
</tbody>
</table>

Adapted from Silberstein et al. 2012 (Table e-2)

Mini Case

BC is a 27 year old female who experiences 4 headaches monthly, 2 of which cause substantial disability requiring her to miss several days of work.

Vitals: BP 151/93, Pulse 85, Temp 98.8, BMI 30. Current medications include: cetirizine (Zyrtec), sumatriptan (Imitrex), VitaFusion Prenatal Vitamins.

1. Is she an appropriate candidate for migraine prevention?
2. Which agent would be an optimal first-line selection for her?
   - Venlafaxine
   - Propranolol
   - Divalproex
   - Fluoxetine
Menstrually Associated Migraine

- Frovatriptan (Frova) 2.5 mg BID perimenstrually
- Naratriptan (Amerge) 1 mg BID x 5 days perimenstrually
- Zolmitriptan (Zomig) 2.5 mg BID-TID perimenstrually
- Estrogen: 1.5 mg estradiol gel daily x 7 days perimenstrually

Contraindicated
- Cardiovascular disease, uncontrolled hypertension, hemiplegic or basilar migraines, cerebrovascular or peripheral vascular disease
- Naratriptan in severe renal or hepatic impairment

Summary of Triptans in Menstrually Associated Migraine

<table>
<thead>
<tr>
<th>Dose*</th>
<th>Incidence (%)</th>
<th>Mean Number of HDP (days)</th>
<th>&gt;50% Event Reduction</th>
<th>Incidence (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frovatriptan vs placebo (2 trials)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.5 mg daily</td>
<td>52 vs 67</td>
<td>0.69 vs 0.42</td>
<td>p&lt;0.0001</td>
<td>0.69 vs 0.42</td>
</tr>
<tr>
<td>2.5 mg BID</td>
<td>45 vs 67</td>
<td>0.92 vs 0.42</td>
<td>p&lt;0.001</td>
<td>0.92 vs 0.42</td>
</tr>
<tr>
<td>Naratriptan vs placebo (1 trial)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 mg BID</td>
<td>50 vs 25</td>
<td>4.2 vs 7.0</td>
<td>p&lt;0.01</td>
<td>4.2 vs 7.0</td>
</tr>
<tr>
<td>Zolmitriptan vs placebo (1 trial)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.5 mg BID</td>
<td>54.7 vs 37.8</td>
<td>p=0.002</td>
<td>54.7 vs 37.8</td>
<td>p=0.002</td>
</tr>
<tr>
<td>2.5 mg TID</td>
<td>58.6 vs 37.8</td>
<td>p=0.007</td>
<td>58.6 vs 37.8</td>
<td>p=0.007</td>
</tr>
</tbody>
</table>

Both regimens also reduced:
- Severity (p<0.0001)
- Duration (p<0.0001)
- Use of rescue medication

*Beginning 2 days before anticipated menses and continued for 5-6 days per Menstrual Period

Preventing Transition to Chronic Migraines (CM)

- Modifiable risk factors
  - Obesity
  - Caffeine exposure
  - Snoring/Sleep apnea
  - Acute overuse of symptomatic medication

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Medication Overuse

OTC Analgesics
- Acetaminophen, aspirin, or NSAIDs
- Critical dose exposure - 8 days/month
- Effect more pronounced in men

Opiates
- Critical dose exposure - 5 days/month
- Effect more pronounced in women

Barbiturates
- Critical dose exposure - 5 days/month
- Effect more pronounced in women

Triptans
- High frequency of migraine at baseline (10-14 days/month)

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Summary

Migraine remains underdiagnosed and undertreated

Cause of migraine is unknown with many theories and triggers

Preventative medications may reduce frequency by ~50%

New 2012 guidelines based on efficacy only

Consider coexisting health conditions, medication efficacy, and side effects