Migraine and Tension Headache: The latest treatment recommendations

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Objectives

Having completed the learning activities, the participant will be able to:
– Describe the assessment of the person with primary headache.
– Identify the most appropriate and efficacious treatment options for acute headache relief.

Objectives (continued)

Having completed the learning activities, the participant will be able to: (cont.)
– Summarize the guidelines for initiating headache prophylaxis with select medications and nutritional supplements.
### What type of headache? Primary vs. Secondary

<table>
<thead>
<tr>
<th>Primary HA</th>
<th>Secondary HA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not associated with other diseases</td>
<td>Associated with or caused by other conditions</td>
</tr>
<tr>
<td>- Migraine</td>
<td>- Tumor</td>
</tr>
<tr>
<td>- Tension-type</td>
<td>- Bleed</td>
</tr>
<tr>
<td>- Cluster</td>
<td>- Increased intracranial pressure (ICP)</td>
</tr>
<tr>
<td>- Others</td>
<td>- Others</td>
</tr>
</tbody>
</table>

### Per VA/DoD: Interchangeable terms

- Mild traumatic brain injury
- Concussion
- No universal standard criteria for definition of concussion/mTBI
- Diagnosis based primarily on the characteristics of immediate sequelae following event

### VA/DoD Evidence-based Practice: Management of Concussion/Mild Traumatic Brain Injury

VA/DoD Clinical Practice Guideline for Management of Concussion/mTBI

- "Headache is the single most common symptom associated with concussion/mTBI and assessment and management of headaches in individuals should parallel those for other causes of headache."

Post Traumatic Brain Injury (TBI) Headache

- Estimated prevalence in TBI
  - 25-78%
  - Greater HA prevalence, duration, severity post mild head injury compared with more severe trauma

Post Traumatic Brain Injury (TBI) Headache (continued)

- Comorbidity
  - Significant number of patients with preexisting headaches
  - Data conflict on whether this is risk factor for post TBI HA
Post TBI Headache

- Tension-type headaches most frequently report – 75-77%
- More than one type of headache – 27-75%
- Migraine – Post blast trauma, most common HA type reported

Source: http://www.uptodate.com/contents/postconcussion-syndrome?source=search_result&search=post concussion+syndrome&selectedTitle=1-8

Please see table for diagnostic criteria for primary headaches and information at the end of handout for VA/DoD TBI Classification.

What causes primary headache?

- Likely a complex neurovascular event
  - In health, balance between excitation, inhibition of nervous system
Genetic component?

- Polygenetic
  - Multiple mutations and variations noted
  - Twin studies = 65% prevalence
  - Likely X linked
  - Correlation with motion sickness

Genetic component? (continued)

- Migraine with aura
  - 4-fold increase risk in 1st degree relatives
- Migraine without aura
  - 1.9-fold increase risk in 1st degree relatives

Pathophysiology of Primary Headache

- Genetic disorder
- Brain disease
- Most common chronic pain condition
Should we think of migraine and tension-type headache as two different conditions or different points on the headache continuum?

Is this really a migraine/TTH or something more dangerous?

- Reassuring findings
  - Positive family history of migraine
  - Headache related to menstrual cycle
  - Headaches preceded by typical aura
  - Headaches remaining periodic and stable over time
  - Normal physical and neurologic findings

Primary Headache: True or false?

- The initial onset of TTH and migraine usually occurs in childhood or early adulthood.
- The initial onset of cluster headache usually occurs in the later part of the 3rd to early part of the 4th decade of life.
Primary Headache: True or false?

- Most people who fulfill the criteria for migraine have not received this diagnosis from a healthcare provider.
- The majority of people with primary headache have seen a healthcare provider for this condition in the past year.

Primary Headache: True or false?

- Cluster is the only primary headache type more common in men, with a ratio of approximately 3.5:1 and 2:1.
- Patients typically have a single headache type.

What about neuroimaging in nonemergency setting?
American Academy of Neurology: Imaging algorithm for non-acute headache

- Headache => 4 weeks duration and normal neurologic exam
  - Comment on neuroimaging not likely to reveal abnormalities without “alarm” findings

(continued)

- Headache => 4 weeks duration with “alarm” or other worrisome findings
  - Comment made that head MRI and CT roughly equivalent in revealing abnormalities
  - MRI better at revealing pathologic changes

AAN Encounter Kit for Headache
Encouraging HA Self-care, Avoiding ED or Urgent Care Use = Important Clinical Goal

When should you use headache abortive therapy?

- To achieve maximum effect
  - When first headache symptoms occur?
  - When headache is clearly not going away without therapy?
  - When pain severity increases?

Goals of Treating Acute Primary Headache

- Treat attacks rapidly and consistently without recurrence
- Restore the patient’s ability to function
Goals of Treating Acute Primary Headache (continued)

• Minimize the use of backup and rescue medications
  – In particular, minimize use injectable or other medications usually only available in healthcare office or emergency department as this discourages patient self care actions

Goals of Treating Acute Primary Headache (continued)

• Optimize self care and reduce subsequent use of resources
• Be cost-effective for overall management
• Have minimal or no adverse events

Acute Headache Medications

• Nonspecific: Used for a variety of painful conditions
  – Aspirin
  – NSAIDs (ibuprofen, naproxen)
  – Acetaminophen, aspirin, and caffeine (Excedrin®)
  – Opioids
Acute Headache Medications
(continued)

• Migraine specific but also used in tx of other primary HA types
  – Ergots
  – Triptans (5-HT_{1B/1D} agonists)
• Used to treat nonpain symptoms
  – Prochlorperazine
  – Other antiemetics and GI medications such as metoclopramide (Reglan®)

Who should get a triptan?

• Mild to moderate disability who do not respond to other therapies
  – Strong evidence
• Substantial disability with migraine
  – Strong evidence
• Patients who can take triptans safely
  – Contraindicated in CVD, uncontrolled HTN

What do you need to know about the triptans?

• T_{1/2}
• T_{max}
• C_{max}
• Analgesic adjuncts
Please refer to table comparing the triptans.

If one triptan does not work, should you try another product in the class?

General Triptan Advise

- With initial triptan ineffective
  - Maximize dose
  - Try on two HA attacks
- If still ineffective
  - Switch to different triptan
  - Consider subcutaneous sumatriptan
General Triptan Advise (continued)

- Triptan monotherapy remains ineffective
  - Try with other drugs, especially antiemetics or nonsteroidal anti-inflammatory drugs (NSAIDs)

Dihydroergotamine (DHE):
Nasal Spray (Migranal®) or Injection

Prescriber must be well informed of adverse effects and contraindications prior to prescribing. At the same time, helpful agent in select patient situations.

DHE: Most commonly used in patients who are...

- Experiencing severe migraine headache
- In status migrainosus or have rebound withdrawal type of headaches
- Only received opioids for severe headaches
- Have not responded to triptans in the past
- Have not received a triptan within past 24 hours or are on a CYP4503A4 inhibitor
Algorithm for DHE Use in Migraine

- American Academy of Neurology: Use of DHE in Migraine
  - Available at https://www.aan.com/Guidelines/home/GetGuidelineContent/120

Ergot Derivatives

- Mechanism of action
  - Bind to 5HT_{1B/1D} receptors
  - Similar to triptans

Dihydroergotamine (DHE 45)

- Alpha-adrenergic blocker
  - Weaker arterial vasoconstrictor and more potent venoconstrictor than ergotamine tartrate
  - Potent 5-HT_{1B/1D} receptor agonist
DHE: Precautions

• Do not use
  – Within 24 hours of administration of triptans
  – In uncontrolled hypertension (blood pressure>165/95)
  – With history of ischemic heart disease including angina
  – In Prinzmetal angina (atypical angina), peripheral vascular disease
  – During pregnancy and lactation

DHE: Precautions (continued)

• If patient has chest pain or severe anxiety following the first dose of DHE, do not repeat.
• With IV use, consider use with antiemetic and analgesic.
• Also available in nasal spray

NSAIDs

• Quick onset?
• Duration of action?
• If one fails, ditch the whole class?
Analgesic Agents in Migraine and Tension-type Headache

- Consider as first-line drug, due to safety, efficacy, cost
  - Ibuprofen, maximum dose 2.4 g/d
    - Greatest clinical effect with high dose use (i.e. =>800 mg at HA onset, repeat in 3 h if needed, do not exceed daily total dose as above)
  - Naproxen 750-1250 mg per day
    - 500 mg at HA onset, repeat in 3 h if needed, do not exceed daily total dose as above
    - Are all forms equivalent?

Additional Recommendations: Post TBI HA management

- Analgesia overuse
  - Monitor analgesic use due to high rate of analgesic overuse as contributor in 19-42%
  - Response to analgesic withdrawal as favorable as patients whose headaches were not posttraumatic

You see a woman with a chief complaint of headache.

- You can give her one tablet of any of the following. Which is the best choice?
  A. Naproxen (Naprosyn®)
  B. Naproxen sodium (Aleve®, Anaprox®)
  C. Enteric coated naproxen
In Healthy Volunteers

- Time to Cmax of naproxen forms
  - Naproxen sodium = 1 h
  - Naproxen = 1.9 h
  - EC naproxen = 4 h

Analgesic Agents in Migraine and Tension-type Headache

- If required, parenteral form
  - Ketorolac 30-60 mg IM
  - No more than 3 X week due to risk of nephrotoxicity
    - Per NHF Guidelines

Short-term Alternative to Triptans?
Butalbital, Acetaminophen and Caffeine (Fioricet®)

• “...is a combination of caffeine, butalbital, and acetaminophen. Whereas caffeine enhances the analgesic properties of acetaminophen, butalbital's barbiturate action enhances select neurotransmitter action, helping to relieve migraine and tension-type headache pain.”

Butalbital, Acetaminophen and Caffeine (Fioricet®) (continued)

• “Butalbital-containing analgesics may be effective as backup medications or when other medications are ineffective or cannot be used. Because of concerns about overuse, medication-overuse headache, and withdrawal, their use should be limited and carefully monitored.”


Systemic Corticosteroids in the Treatment of Migraine

• Indicated in intractable migraine
  — No more than 1/month

• Prednisone
  — 20 mg QID X 2-6 days

  — Source: http://www.headaches.org
Lidocaine Nasal Spray

- Virtually no systemic absorption
  - Not FDA approved for this use
- 4-10% solution
- 1 squirt to nostril on side of pain
  - Repeat q 1h
    - Alternative- Soak cotton swab (Q-tip®), leave in nostril

(continued)

Lidocaine Nasal Spray

- Efficacy
  - 50% reduction in pain by 55% patients
  - 42% relapse in 2-4 hours
- Studied in cluster with similar efficacy

NHF Guidelines for Abortive Therapies

- Position on using opioids
  - Use when other therapies have been ineffective
  - Give in adequate amounts if needed
  - Limit to 2/days/week
Use of Abortive Therapies

- Excessive use of abortive therapies can lead to rebound headache.
- Consider use of prophylactic therapy if following guidelines are exceeded.

Frequent Headaches
Prophylaxis Indications

- Two or more HA monthly
  – Absolutely indicated for 2 HA days per week
- HA duration
  – >2 days with disability
- Treatment
  – Refractory to current abortive agents
  – Intolerance to abortive agents
  – Overuse of abortive agents

True or false?

- According to recent study, about 38% of people who suffer from migraine attacks could benefit from preventive treatments.
True or false?

• Less than a third of individuals who would likely benefit from headache prophylaxis currently use these treatments.

Headache Prophylaxis: Managing expectations

• Typically need 1-2 months therapy before effect seen
• Reasonable expectation
  – 50% reduction in HA in about 2/3 of all patients
  – Possibly easier to control HA
• Rarely does headache prophylaxis eliminate headache entirely

Headache Prophylaxis (continued)

• Use prophylaxis for 3-6 months then try a taper off the medication slowly
  – Helps break headache cycle
  – Allows lifestyle modification to be used
• Eliminate, limit use of certain drugs
  – Estrogen, progesterone
  – Vasodilators
  – Many analgesic agents
Options for Headache Prophylaxis

Evidence-based Guideline Update: Pharmacologic Treatment for Episodic Migraine Prevention in Adults


Strong Evidence of Efficacy in Headache Prophylaxis

• Beta-adrenergic antagonist
  • Daily recommended doses
    – Propranolol 160-240 mg
      • Noncardioselective
      • Also mentioned in TBI guidelines
    – Metoprolol 100-200 mg
      • Cardioselective
    – Timolol 20-60 mg
      • Noncardioselective

Clinical Case Study

• You are considering prescribing beta blocker therapy for migraine prophylaxis in a 24-year-old woman with asthma. Which would be the preferred agent?
Evidence of Efficacy for Headache Prophylaxis: Other anti HTN medications

• Moderate evidence
  – Atenolol
    • Cardioselective
  – Nadolol
    • Non-cardioselective

• Weak evidence
  – Candesartan
  – Lisinopril
  – Nebivolol
    • Cardioselective
    • Non-cardioselective

• Weak evidence
  – Pindolol

Evidence of Efficacy in Headache Prophylaxis

• Moderate evidence
  – Amitriptyline 10-100 mg daily
    • Also mentioned in TBI guidelines
  – Nortriptyline 10-50 mg daily
  – Venlafaxine up to 225 mg daily
    • Commonality with these medications?

Evidence of Efficacy in Headache Prophylaxis (continued)

• Inadequate evidence
  – Fluoxetine
  – Fluvoxamine
  – Protriptyline
Evidence of Efficacy in Headache Prophylaxis: Antiepileptic drugs (AED)

• Strong evidence
  • Total daily dose
    – Divalproex sodium 500-1000 mg
    – Sodium valproate 500-1000 mg
    – Topiramate 25-100 mg

(continued)

• Weak or insufficient evidence
  – Carbamazepine
  – Gabapentin

Evidence of Efficacy in Headache Prophylaxis: Calcium channel blockers

• Insufficient evidence
  – Nicardipine
  – Nifedipine
  – Nimodipine
  – Verapamil
Evidence of Efficacy in Headache Prophylaxis: Possibly helpful

- Serotonin antagonists
  - Cyproheptadine (Periactin®)
    - 4-8 mg daily
  - Acceptable for use in children, associated weight gain

Additional information about OnabotulinumtoxinA (BOTOX®) for HA prophylaxis at end of program.

Per AAN and AHS

- “Strong evidence shows that the herbal preparation Petasites (butterbur) can help prevent migraine.”
**Petasites (Butterbur)**

- AKA sweet coltsfoot
  - Leaves used to wrap butter, hence its name
- Member of the daisy family

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**Petasites (Butterbur)**

(continued)

- Portion of plant used medicinally
  - Usually root, rhizome
- Recognized efficacy
  - When taken orally, headache, inflammation hay fever
  - When applied topically, wound healing
    - Source: http://nccam.nih.gov/health/butterbur

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**Petasites (Butterbur)**

(continued)

- Proposed mechanism of action
  - Antispasmodic effects on smooth muscle and vascular walls
  - Anti-inflammatory effects by inhibiting leukotriene synthesis
**Petasites (Butterbur):**

**Recommended use**

- Usual dose
  - 50-100 mg BID
  - 75 mg twice daily typical dose
  - Doses ≤ 50 mg per day ineffective
  - Use for 4-6 months then consider taper, monitoring for recurrence

**Petasites (Butterbur): Caution**

- Pregnancy and lactation
  - Use not recommended due to limited studies, hepatotoxic potential

**Petasites (Butterbur): Herb-drug interactions**

- Pyrrolizidine alkaloids (PA)
  - CYP450 3A4 substrates
- Theoretical drug interaction
  - CYP3A4 enzymatic inducers could increase conversion of PAs to toxic metabolites.
  - Examples: Carbamazepine (Tegretol®), phenobarbital, phenytoin (Dilantin®), rifampin, rifabutin, St. John’s wort, echinacea, others
Petasites (Butterbur):

Adverse effects

- Allergic potential
  - Cross sensitivity possible in presence of allergy to ragweed, chrysanthemums, marigolds, daisies
- Adverse effects
  - Headache, itchy eyes, GI upset, asthma, fatigue

Per AAN and AHS

- “There is moderate evidence that riboflavin (vitamin B2), the mineral magnesium, and the herbal preparation MIG-99 (feverfew) help prevent migraine.”

Per American Academy of Neurology

- Feverfew, riboflavin, and magnesium as possibly or probably preventative treatments for migraine...
  - Information on each product at http://naturaldatabase.therapeuticrosearch.com
Feverfew, Riboflavin, Magnesium

**Daily Dose**

- Typically start with riboflavin and magnesium, add feverfew if needed
  - MOA not well understood
  - Feverfew 100 mg
  - Riboflavin 400 mg
  - Magnesium 360 mg

- Available in one-tablet formulation as Migrelief®

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**Conclusion**

End of Presentation
Thank you for your time and attention.

Margaret A. Fitzgerald,
DNP, FNP-BC, NP-C, FAANP, CSP, FAAN, DCC

www.fhea.com          cs@fhea.com
OnabotulinumtoxinA (BOTOX®)

- **Indication**
  - HA prophylaxis in adults with chronic migraine who have =>15 HA per each month with HA lasting =>4 hours each day

![Injection Sites](www.botoxchronicmigraine.com)

**OnabotulinumtoxinA (BOTOX®) for Migraine**

**CLINICAL TRIALS (N = 1384)**

<table>
<thead>
<tr>
<th>Order of Injection</th>
<th>Muscle</th>
<th>Recommended Dose, Number of Sites</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Corrugator</td>
<td>12 units divided by 2 sites</td>
</tr>
<tr>
<td>B</td>
<td>Procerus</td>
<td>5 units in 1 site</td>
</tr>
<tr>
<td>C</td>
<td>Frontalis</td>
<td>20 units divided in 6 sites</td>
</tr>
<tr>
<td>D</td>
<td>Temporalis</td>
<td>60 units divided in 8 sites</td>
</tr>
<tr>
<td>E</td>
<td>Occipitalis</td>
<td>30 units divided by 6 sites</td>
</tr>
<tr>
<td>F</td>
<td>Cervical paraspinal</td>
<td>20 units divided in 6 sites</td>
</tr>
<tr>
<td>G</td>
<td>Trapezii</td>
<td>40 units divided in 6 sites</td>
</tr>
</tbody>
</table>

**Total dose**

120 units divided in 30 sites
OnabotulinumtoxinA (BOTOX®) Efficacy

• Clinical improvement
  – 8 to 9 fewer headache days per month (vs 6 to 7 days with placebo)
  – 4% discontinuation rate due to adverse events for onabotulinumtoxinA (BOTOX®) vs 1% for placebo

OnabotulinumtoxinA (BOTOX®)

• Warning
  – Effect can spread from injection area to produce symptoms consistent with botulinum toxin effects
  • Symptoms can last hours to weeks after injection, include difficulty swallowing, breathing difficulties, potentially life-threatening

Post-concussion/mTBI Related Symptoms*

<table>
<thead>
<tr>
<th>Physical Symptoms:</th>
<th>Cognitive Symptoms:</th>
<th>Behavior/ emotional Symptoms:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache, dizziness, balance disorders, nausea, fatigue, sleep disturbance, blurred vision, sensitivity to light, hearing difficulties/loss, sensitivity to noise, seizure, transient neurological abnormalities, numbness tingling</td>
<td>Attention, concentration, memory, speed of processing, judgment, executive control</td>
<td>Depression, anxiety, agitation, irritability, impulsivity, aggression</td>
</tr>
</tbody>
</table>

*Symptoms that develop within 30 days post injury
Criteria for characterizing posttraumatic headaches as tension-like (including cervicogenic) or migraine-like based upon headache features.

<table>
<thead>
<tr>
<th>Headache Feature</th>
<th>Tension-like (include cervicogenic pain)</th>
<th>Migraine-like</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain Intensity</td>
<td>Usually mild-moderate</td>
<td>Often severe or debilitating</td>
</tr>
<tr>
<td><strong>Pain Character</strong></td>
<td>Dull, aching, or pressure. Sharp pain may be present, but is not predominant</td>
<td>Throbbing or pulsatile, can also be sharp/stabbing or electric-like</td>
</tr>
<tr>
<td><strong>Duration</strong></td>
<td>Usually less than 4 hours</td>
<td>Can last longer than 4 hours</td>
</tr>
<tr>
<td><strong>Phono- or photophobia</strong></td>
<td>One but not both may be present</td>
<td>One, or both usually present</td>
</tr>
<tr>
<td><strong>Able to carry out routine activities/work</strong></td>
<td>Usually</td>
<td>Usually not, or with a decreased level of participation</td>
</tr>
</tbody>
</table>

**Classification of TBI Severity**

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Structural imaging</td>
<td>Normal</td>
<td>Normal or abnormal</td>
<td>Normal or abnormal</td>
</tr>
<tr>
<td>Loss of consciousness (LOC)</td>
<td>0-30 min</td>
<td>&gt;30 min and &lt;24 hrs</td>
<td>&gt;24 hrs</td>
</tr>
<tr>
<td>Alteration of consciousness/ment al state (AOC)*</td>
<td>A moment up to 24 hrs</td>
<td>&gt;24 hours</td>
<td>Severity based on other criteria</td>
</tr>
<tr>
<td>Post-traumatic amnesia (PTA)</td>
<td>0-1 day</td>
<td>&gt;1 and &lt;7 days</td>
<td>&gt;7 days</td>
</tr>
<tr>
<td>Glasgow Coma Scale (best available score in first 24 hours)</td>
<td>13-15</td>
<td>9-12</td>
<td>&lt;9</td>
</tr>
</tbody>
</table>

*A Alteration of mental status must be immediately related to the trauma to the head. Typical symptoms would be: Looking and feeling dazed and uncertain of what is happening, confusion, difficulty thinking clearly or responding appropriately to mental status questions, and being unable to describe events immediately before or after the trauma event.


Headache Feature          | Tension-like (include cervicogenic pain) | Migraine-like |
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Location</strong></td>
<td>Bilateral frontal, retro-orbital, temporal, cervical and occipital, or holocephalic</td>
<td>Usually unilateral and often vary in location among episodes</td>
</tr>
<tr>
<td><strong>Nausea or malaise</strong></td>
<td>Not present</td>
<td>Usually present</td>
</tr>
<tr>
<td><strong>Palpable muscle tenderness or contraction</strong></td>
<td>Pericranial muscles including temporalis, masseter, pterygoid, posterior neck muscle, sternocleidomastoid, splenius or trapezius</td>
<td>Localized muscle tenderness is not typical, muscle tenderness may be present with long duration headaches</td>
</tr>
</tbody>
</table>

All websites listed are active at the time of publication.