Headache – A Practical Approach

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Disclosures: none
Learning Outcomes

At the conclusion of this activity, you should be able to

1) Assess for and identify headache red flags/worrisome symptoms
2) Discuss medication overuse/MOH headache
3) Correctly diagnose common headache disorders and initiate treatment
4) Review general principles of headache management for migraine and tension-type headache
Neurosciences Pain Development Team

A coordination of efforts to reduce opioid misuse across neurosciences including for the treatment of headache, neck pain, LBP, and neuropathy

Goals for 2018 include a 40% decrease in opioid prescriptions

• Acute cluster headache treatment guideline
• Injectable and non-injectable acute migraine treatment guideline
• Painful peripheral neuropathy flashcard
• LBP flashcard update
• Neck pain and LBP CPM update to reflect opioid reduction goals and PAMA imaging support
What is a headache?

Headache is defined as pain in the head that is located above the eyes or the ears, behind the head (occipital), or in the back of the upper neck.
Headaches

Secondary headaches – a headache due to some underlying cause
• Medication overuse/medication overuse headache

Primary headaches
• Migraine*
• Tension-type headache*
• Cluster headache and other trigeminal autonomic cephalalgias
• Other primary headaches
Red Flags

Systemic symptoms (fever, weight loss) or Secondary risk factors (HIV, cancer)
Neurologic symptoms or Neurologic signs including level of arousal
Onset: sudden, abrupt, or split-second
Older: new-onset or progressive headache, especially in middle age
Previous headache history or lack thereof / Pregnancy / Papilledema / Progression

Medication Overuse and Medication Overuse HA

Use combination therapies sparingly and with caution as most contain caffeine (caffeine withdrawal headache)

Acute treatments can contribute to HA frequency:
- NSAIDs when taken more than 14 days per month
- Triptans when taken more than 10 days per month
- Opioids and opioid-like medications (e.g., tramadol) > 6 days per month
- Butalbital-containing compounds > 4 days per month
Epidemiology
One-year period prevalence

MIGRAINE 10-13%

CLUSTER HEADACHE 0.14%

TENSION-TYPE HEADACHE 38.3-74%

CHRONIC MIGRAINE 1.3-2.4 %

Migraine

A chronic condition with episodic manifestations
Familial disorder with a genetic component
Monogenic forms are rare and include hemiplegic migraine and other complicated migraine disorders.

Environmental triggers

Episodic or chronic migraine based on attack frequency
- Episodic < 15 days/month
- Chronic ≥ 15 days/month for at least 3 months

The most important categories are migraine with and without aura
Migraine without Aura

At least two of the following characteristics:

- Unilateral location
- Pulsating quality
- Moderate or severe intensity
- Aggravation by routine physical activities

Headache duration
4-72 hours

At least one of the following:

- Nausea and/or vomiting
- Photophobia and phonophobia
Migraine with Aura

- Migraine with aura is seen in 20% of patients with migraine
- Attributed to the phenomenon of cortical spreading depression (Ward 2012)
- Fully reversible visual symptoms (flickering lights, spots or lines and/or loss of vision)
- Fully reversible sensory symptoms (pins and needles and/or numbness)
- Fully reversible dysphasic speech disturbance
- No motor weakness
Migraine with Aura

ICHD-2 Diagnostic Criteria for Typical Aura

a. At least two attacks fulfilling criteria B-E
b. Fully reversible visual and/or sensory and/or speech symptoms but no motor weakness
c. At least two of the following
   a. Visual symptoms including positive features (i.e. flickering lights, spots and lines) and/or negative features (i.e. loss of vision) and/or unilateral sensory symptoms including positive features (i.e. pins and needles) and/or negative features (i.e. numbness)
   b. At least one symptom develops gradually over $\geq 5$ min and/or different symptoms occur in succession
   c. Each symptom lasts $\geq 5$ min and $\leq 60$ min
d. A headache that meets criteria for migraine without aura begins during the aura or follows aura within 60 min
e. Not attributed to another disorder
Trigeminovascular System

TGVS activated

PAIN

Dura

CSD

TNC

Trigeminal nerves

Ashina 2011
Migraine Pathophysiology: Trigeminovascular System

Goadsby et al. NEJM 2002
Migraine Treatment

**Triptans** are first-line treatment for moderate-to-severe attacks

Specific 5-HT1 (serotonin) agonists at the neurovascular junction

- Available subcutaneous (SC), PO, nasal spray (NS)
- Early treatment is key

**Ergots (e.g. dihydroergotamine or DHE)**

- Non-specific 5-HT1 agonist at the neurovascular junction
- Available IV, IM, SC, NS
- Do not use within 24 hours of a triptan

* Both are contraindicated in vascular disease, uncontrolled hypertension, hemiplegic/basilar migraine, and pregnancy
<table>
<thead>
<tr>
<th>Generic</th>
<th>Brand</th>
<th>Formulations</th>
<th>Doses(^a)</th>
<th>Maximum Daily Dose</th>
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</thead>
<tbody>
<tr>
<td>Sumatriptan</td>
<td>Imitrex</td>
<td>Tablet, Nasal spray, Subcutaneous injection, Fixed-dose combination tablet</td>
<td>25 mg, 50 mg, <strong>100 mg</strong> 5 mg, <strong>20 mg</strong> 4 mg, <strong>6 mg</strong> 85-mg sumatriptan + 500-mg naproxen sodium</td>
<td>200 mg 40 mg 12 mg 2 tablets</td>
</tr>
<tr>
<td>Sumatriptan + Naproxen sodium</td>
<td>Treximet</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Zolmitriptan</td>
<td>Zomig</td>
<td>Tablet, Orally dissolving tablet, Nasal spray</td>
<td>2.5 mg, 5.0 mg 2.5 mg, 5.0 mg 5.0 mg</td>
<td>10 mg 10 mg 10 mg</td>
</tr>
<tr>
<td></td>
<td>Zomig-ZMT</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Zomig</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Rizatriptan</td>
<td>Maxalt</td>
<td>Tablet, Orally dissolving tablet</td>
<td>5 mg, <strong>10 mg</strong> 5 mg, <strong>10 mg</strong></td>
<td>30 mg(^b) 30 mg(^b)</td>
</tr>
<tr>
<td></td>
<td>Maxalt-MLT</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Naratriptan</td>
<td>Amerge</td>
<td>Tablet</td>
<td>1.0 mg, 2.5 mg</td>
<td>5 mg</td>
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<td>Almotriptan</td>
<td>Axert</td>
<td>Tablet</td>
<td>6.25 mg, <strong>12.5 mg</strong></td>
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<td>Frovatriptan</td>
<td>Frova</td>
<td>Tablet</td>
<td>2.5 mg</td>
<td>7.5 mg</td>
</tr>
</tbody>
</table>

\(^a\) Optimal dose, when known, is bolded.

\(^b\) 15 mg if also on propranolol.

Coming Soon… CGRP Monoclonal Antibodies

The evidence for…

• A potent vasodilator released during migraine attacks
• Persistent elevation in CM
• CGRP infusion triggers migraine in migraine patients
• Triptans normalize CGRP levels
• CGRP antagonists (“gepants”) abort acute attacks
CGRP mAbs in Development

Humanized antibodies
LY2951742/galcanezumab (SQ) $t_{1/2} = 28h$
ALD403/eptinezumab (IV) $t_{1/2} = 31h$
TEV-48215/fremanezumab

Fully human mAb
AMG-334/erenumab (SQ) $t_{1/2} = 21h$
*Proven efficacy, tolerability and few AEs in phase 2 randomized control trials.
Treatment of Refractory Migraine

Oral abortive treatments

- Naproxen sodium 440-550 mg twice a day with food
- Metoclopromide (MTC) 10 mg to 20 mg, prochlorperazine (PCZ) 5 mg to 10 mg, OR promethazine 25 mg with Benadryl +/- NSAID morning and bedtime for 6 doses
- Dexamethasone 4 mg TID, BID, once (6 total tabs over 3 days)
- Naratriptan 2.5 mg twice a day for 5 days
Indications for Prevention

Recurring attacks that interfere with patient’s daily routine despite appropriate acute treatment

> 3 attacks per month

Trouble with or limited acute therapies

Patient preference

Missed work, family, and/or social events due to headache

Frequent, prolonged, or bothersome aura

HM, basilar migraine, migrainous infarction
Migraine Preventive Drugs

Start at a low dose and titrate slowly. May take up to 3 months at target dose for clinical effect

- Amitriptyline can be helpful at right dose after 7-10 days
- OnabotulinumtoxinA can begin to work at 3-4 weeks, but works better with subsequent treatments (over at least a 5-yr period)
- Nerve block and trigger point injections work quickly and can be done serially for prevention
Migraine Preventive Treatments by Grade

Level A: (established efficacy)

• Divalproex sodium (250 to 1500 mg daily)
  ▪ Common side effects include weight gain, tremor, and hair loss
  ▪ Monitor for potential liver and blood abnormalities
  ▪ Known teratogen

• Topiramate (25 to 150 mg daily)
  ▪ Paresthesias may occur early
  ▪ Cognitive side effects are dose dependent
  ▪ Known teratogen

• Metoprolol (50 to 150 mg)
• Propranolol (as little as 10 mg)
• Timolol (10 to 20 mg)
• Behavioral therapy (biofeedback, learned controlled, and progressive muscle relaxation)
Migraine Preventive Treatments by Grade

Level B: (probable efficacy)

- Amitriptyline (as little as 5 mg)
- Venlafaxine (37.5 mg to 225 mg)
- Atenolol (50-100 mg)
- Nadolol (20-160 mg)
- OnabotulinumtoxinA
- Mg, B2
- sTMS (acute treatment only), tSNS (Cefaly® device)
Migraine Preventive Treatments by Grade

Level C: (possible efficacy)

- Lisinopril (10 mg BID)
- Candesartan (16 mg daily)
- Clonidine
- Tizanidine
- Guanfacine
Migraine Preventive Treatments by Grade

Level U: (inadequate/conflicting data)

• Gabapentin
• Verapamil
• Fluoxetine
• sTMS for prevention
Other Treatment Options...

Magnesium oxide - 400 mg twice a day
Riboflavin (vitamin B2) - 400 mg daily
Butterbur extract (Petadolex) - 50 mg three times a day
CoQ10
Feverfew

A comprehensive treatment plan should also include
• Education and reassurance
• Identifying and avoiding triggers to prevent attacks
• Non-pharmacologic treatments
  o Relaxation, Biofeedback, cognitive-behavioral therapy
  o Lifestyle regulation
• Physical and alternative medicine when appropriate
• Periodic reassessment of the plan
Tension-Type Headache

The most common of all primary headache disorders with lifetime prevalence estimated between 30 to 78%

Both migraine and TTH are long-duration headache disorders with episodic and chronic (≥ 15 days of headache/month) forms.

Pathophysiology is poorly understood (Schwartz et al 1998). Pericranial myofascial mechanisms are likely as is central sensitization in the chronic form.

Genetic and environmental factors may also play a role.
Tension-Type Headache

ICHD-2 Diagnostic Criteria for TTH

Headache lasting from 30 min to 7 days

HA has ≥ 2 of the following characteristics

• Bilateral location
• Pressing/tightening (non-pulsating) quality
• Mild or moderate intensity
• Not aggravated by routine physical activity

Both of the following

• No nausea or vomiting
• No more than one of the following: photophobia and phonophobia

Not attributable to another disorder
Treatment of TTH

Acute treatment with simple analgesics is generally effective
- Acetaminophen 500 – 1000 mg
- Aspirin 500 – 1000 mg

NSAIDs are considered the acute-treatment drug of choice
- Ibuprofen 200 – 800 mg no more than every 6 hours
- Naproxen 375 – 550 mg no more than every 12 hours
- Ketoprofen 25 – 50 mg no more than every 8 hours

Consider headache prevention in patients with chronic TTH (≥15 days/month):
- Amitriptyline
  - A non-selective serotonin reuptake inhibitor
  - 10 mg to 75 mg per day
- Mirtazapine and venlafaxine are other options for prevention
  - Mirtazapine up to 30 mg/day
  - Venlafaxine up to 150 mg/day
Goals of Preventive Treatment

- Reduce frequency and severity of attacks
- Improve function and reduce disability (ictal and inter-ictal)
- Improve acute treatment response
- Consider comorbid condition(s)
Opioids are best avoided for headache as they can sensitize the CNS to pain

- Known to contribute to headache frequency when taken more than 6 days per month
References


Kelley NE & Tepper DE. Rescue therapy for acute migraine, Part 3: opioids, NSAIDs, steroids, and post-discharge medications. *Headache* 2012;52:467-482.


