Headaches
MHD – Neuroscience Module

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Famous Migraines

Super Bowl XXXII

- Terrell Davis developed a literally blinding migraine
- He still played …despite not being able to see (hooray for player safety!)
- He was given intranasal DHE at halftime, symptoms resolved (enough) and he returned to lead the Broncos past the Packers with 3 TDs while securing the game MVP

“In the second quarter, I really couldn’t see straight”– Terrell Davis to Denver Post / 1-26-98

“What do you think you’re doing on this play? Because we’re going to fake it to you on this play…”– Mike Shanahan
https://www.youtube.com/watch?v=z7XjBNGxg

DHE = dihydroergotamine

What Causes Headaches: Pain Pathways

Structures Sensitive to Pain
- The brain parenchyma itself does not produce pain.
- Intracranial lesion (tumor, hemorrhage) does not produce headache pain by itself—the swelling around it may cause headache by stretching or compressing blood vessels or cranial nerves.
- Skin, subcutaneous tissue, muscles, extracranial arteries, peristeme of the skull—produce pain.
- Delicate structures of the eye, ear, nasal cavities & paranasal sinuses
- Intracranial venous sinuses & tributaries
- Dura at the base of the brain & arteries within the dura and pia-arachnoid (ACA, MCA, ICA)
- Optic, oculomotor, trigeminal, glossopharyngeal, vagus, first three cervical nerves.
The Headaches

Primary Headache
• Condition in which headache is the primary manifestation and no underlying disease process is present

Secondary Headache
• Condition in which headache is a secondary manifestation of an underlying disease process

Most Common Headaches
• Tension-type
• Migraine & variants
• Provoked by fever or hunger
• Provoked by nasal, paranasal, ear, tooth, eye disease

The Rapid Headache Evaluation

• Classic Test Question: A 24 year old female presents for the sudden onset of the “worst headache of her life.” Her neurologic examination is notable for an enlarged and poorly reactive right pupil. What is the most likely diagnosis?
  – A. Migraine Headache
  – B. Aneurysmal subarachnoid hemorrhage
  – C. Cluster headache
  – D. Secondary pain related to acute angle closure glaucoma
  – E. Tension headache

Answer is: _____

The Rapid Headache Evaluation: Red Flags

<table>
<thead>
<tr>
<th>Signs &amp; Symptoms</th>
<th>Diagnosis to Consider</th>
</tr>
</thead>
<tbody>
<tr>
<td>Split second, unexpected, worst/not previously encountered, LOC, vertigo, vomiting</td>
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<td>Fever &amp; skin rash</td>
<td>Meningitis</td>
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<td>Immunosuppressed state</td>
<td>Crypto meningitis, toxoplasmosis</td>
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<td>Coagulopathy/anticoagulation</td>
<td>Subdural or intradural hematoma</td>
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Adapted from: Wijdicks EFM. Catastrophic Neurologic Disorders in the Emergency Department

This is my own editorial: “worst headache of my life” has somehow become pathognomonic for subarachnoid hemorrhage. However, everyone has had a “worst headache of life” if you’ve only had one headache, it was technically also the worst one you ever had. Patients with ruptured aneurysms usually report it was a very, very rapid in onset. I’ve made my point—now, don’t argue with the USMLE over this one. Back to the lecture…
Primary Headache Disorders

The Headaches

• A 28 year old male presents for complaint of visual problems and headaches. He reports the development of a shimmering light in his left visual field that gets bigger over the course of about 30 minutes, followed by a pounding left sided headache lasting several hours, associated with an upset stomach, light and sound sensitivity. What is the treatment of choice?
  – A. Lorazepam 1.0 mg
  – B. Inhaled oxygen 10 mL/min
  – C. Sumatriptan 100 mg
  – D. Methylprednisolone 1g
  – E. Butalbital-acetaminophen combination therapy
  Answer is: _____

Migraine

• A genetic condition in which a person has a predisposition to episodic headaches, GI dysfunction, or neurologic dysfunction
• Severity **NEED NOT BE** a feature

Key Clinical Questions

1. Do you have nausea or feel sick to your stomach with your HA?
2. Does light bother you more with a headache than w/o?
3. Does the HA limit you from working, studying, or doing what you need to do?

Sensitivity 0.81, Specificity 0.75 for migraine headache if all 3 are positive

“Migraine” is derived from the French words “hemi-crain” (half the head). The first two letters of “crain” dropped over time, leaving just “migraine”, which turned into “migraine.”
Migraine Symptoms

- Typical clinical symptoms
  - Periodic, usually unilateral, pulsatile
  - Begin in late childhood or early adult life ("From menarche to menopause.")
    - Pulsate: around age 40
    - 15% of women, 6% of men
  - Recur with diminishing frequency throughout life
  - It is unusual to develop late in life
  - Usually stereotypical
  - Most patients will limit activities due to/during the headache

- Typical Triggers
  - Stress
  - Lack of sleep
  - Hunger
  - Hormonal fluctuations
  - Foods (+/-)
  - Alcohol/nitrates
  - Weather changes
  - Smokes, scents, fumes

Migraine Phases

1. Prodrome: occurs hours (6) to days (48hrs) before the headache (in 60% of patients)
   - Depression
   - Irritability
   - Drowsiness
   - Fatigue
   - Yawning
   - Rhinorrhea/lacrimation
   - Hunger/thirst
     - Cravings for chocolate, nuts, bananas (controversy as cause or effect)

2. Aura: can be visual (most common), sensory (numbness/tingling), motor, brainstem (dizziness/diplopia) or cortical (aphasia)
   - Can occur before (most common) or after the HA
   - Usually develop over 5-20 minutes
   - Usually last <60 minutes
   - HA usually occurs within 60 minutes
   - May be associated with HA (acephalgic migraine)
   - May not be present (common migraine; migraine without aura)
   - Due to "spreading cortical depression"
   - More on this later and in supplement

Raskin, Headache, 1988
Evolution of a "scintillating scotoma" or "fortification phenomenon"

Not all migraine patients have an aura ("migraine without aura"), but the characteristics and associated features are otherwise identical to migraine with aura.
Migraine Phases: Aura

• Visual aura of migraine:
  – blind spot near center of vision prohibits reading, as peripheral, flashing, pulsating bands of light spread out across the visual field.

Fun Fact: In 1941, a physician who suffered from migraines studied his own scintillating scotoma and postulated that it must have been due to a change spreading over the occipital lobe at 3 mm per minute. In 1994 a patient with migraine had an attack while in a PET scanner. A spreading wave of depression was noted on the scan - at a rate of 3 mm per minute.

Migraine Phases

• 3. Pain: may be in the head (most common, by far), abdomen (abdominal migraine) or chest (precordial migraine)
  – Onset is gradual over minutes to hours
  – Duration is hours to days
  – Can be associated with:
    • Photophobia, phonophobia
    • Nausea/vomiting
    • Osmophobia, thermophobia

Osmophobia: fear, aversion or psychological aversion to odors

Migraine Phases: Spreading Cortical Depression (SCD)

• A genetically susceptible patient has a multifactorial defect in brain metabolism leading to a gain in NMDA-receptor function (an excitatory receptor)
• NMDA activation leads to a burst of focal cerebral activity causing local hyperemia, and “positive” symptoms
  – Usually in the occipital lobe
  – What triggers it is unknown (may be multiple triggers)
• Burst is followed by a loss of neuronal activity (“cortical depression”)
• Has a slow, deliberate march forward at around 3 mm/min
• Advances until there is a change in cortical architecture

Hyperemia: increased amount of blood in vessels of an organ or tissue
Migraine Phases: Trigeminovascular Reflex & SCD

- Trigeminal nerves wrap around pain sensitive structures, release local neuropeptides, and convey information to the trigeminal nucleus in the brainstem
- Associated with release of neuropeptides including CGRP, Substance P, and Neurokinin A
  - May lead to "neurogenic inflammation"
  - Evoke vasodilation of pain-producing structures
  - Creates a feedback loop with the trigeminal pathway

Migraine Phases

- 4. Postdrome: present for several hours after the event
  - Mood changes (euphoria, fatigue)
  - Impaired concentration
  - Scalp/muscle tenderness

Treatment

Optimizing the Treatment of Acute Attacks of Migraine

- Treat early in the attack when the pain is still mild (don’t “wait it out”!!!)
- Simple analgesics (usually over the counter NSAIDs) are considered first line treatment for mild to moderate migraines, followed by triptans (for more severe migraines, triptans can be used migraines)
- Use effective doses! (doctors and patients often underdose)
- Avoid medications with high medication overuse potential (MOH): especially butalbital-containing medications
- Treat the associated symptoms when needed (ie, nausea)
- Consider side effects & contraindications
- Less is more: try to minimize the use of medications as much as possible

Migraine Specific Therapies: Triptans

If a patient fails to respond to simple analgesics or has moderate to severe migraine pain, migraine-specific therapies are recommended

- All triptans are agonists at 5HT1B/D receptors
- May lead to vasoconstriction
- Range of agents available (currently 7), half-lives 3-26 hours, and routes of delivery
  - Inadequate response to one does not mean an inadequate response to all
- Most provide approx 66% headache response at 2 hours
- Most provide approx 30% pain-free response at 24 hours

If a patient fails to respond to simple analgesics or has moderate to severe migraine pain, migraine-specific therapies are recommended

- Avoid if patient has, or is at risk for, ischemic heart disease
- Avoid with uncontrolled hypertension, renal disease
- Should not be used during pregnancy
- Avoid in cases of basilar migraine, hemiplegic migraine
  - Debatable contraindication in the literature, but it's still in the literature
- Avoid within 24 hrs of use with ergotamine (these are fairly rare medications)
- Avoid if patient on MAO inhibitor

Caveats in use of Triptans

Common Theme: Avoid in those with vascular risk factors

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- Avoid with uncontrolled hypertension, renal disease
- Should not be used during pregnancy
- Avoid in cases of basilar migraine, hemiplegic migraine
  - Debated contraindication in the literature, but it's still in the literature
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Triptan Sensations (Side Effects)

- Warm/Hot sensations
- Tightness
- Tingling
- Feelings of heaviness or pressure
- Occur in nearly any part of the body
- Most commonly reported in face, limbs, and chest
- Occur with all 5-HT1B/1D agonists

Also counsel patients about duration of use: more than 10 days/month can cause Medication Overuse Headaches
Serotonin Syndrome

- Caused by excessive activation of 5-HT_1a and 5-HT_2 receptors
- Severe leg-predominant rigidity, dysautonomia (diarrhea, excessive lacrimation, hyperactive bowel sounds), and encephalopathy characterized by myoclonus, hyper-reflexia & seizures
- Usually within 24hr of med exposure/change

<table>
<thead>
<tr>
<th>Drugs and</th>
<th>Serotonin Syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reuptake inhibitors</td>
<td>SSRI, TCA</td>
</tr>
<tr>
<td>Metabolism inhibitors</td>
<td>MAO-B (selegeline)</td>
</tr>
<tr>
<td>Release enhancers</td>
<td>Tryptophan</td>
</tr>
<tr>
<td>Agonists</td>
<td>Triptans, ergotamine</td>
</tr>
<tr>
<td>Non-specific</td>
<td>Lithium, ECT</td>
</tr>
</tbody>
</table>

No reports of SS in triptan clinical trials. Cases reports of it occurring with monotherapy. Dual therapy is a risk but use is not prohibited.

Migraine Therapies: Ergot Alkaloids

- Ergotamine
  - rarely used since introduction of triptans
  - potent arterial vasoconstrictor
  - extremely nauseaing
  - causes uterine contractions
- DHE (Dihydroergotamine)
  - IV, SC and nasal spray formulations
  - arterial and venous vasoconstrictor
  - less emetic than ergotamine
  - less uterine contract than ergotamine

Contraindications and Precautions: Ergots

- Ischemic cardiac, cerebrovascular, or peripheral vascular disease,
- Collagen vascular disease or vasculitis
- Cardiac valvular disease
- Uncontrolled hypertension
- Use within 24hrs of triptan therapy
- Hemiplegic/basilar migraine
- Prior evaluation of patients with risk factors for CAD
- Renal or hepatic impairment
- Pregnancy, breastfeeding
- Age > 60
When To Consider a Preventive Therapy

• 1. Incidence of attacks ≥2-3 per month
• 2. Attacks are severe and impair normal activity
• 3. Patient is psychologically unable to cope with attacks
• 4. Optimal abortive therapies have failed or produced serious side effects

Migraine Therapies

AAN Guidelines: Preventive Therapies

<table>
<thead>
<tr>
<th>Level A</th>
<th>Level B</th>
<th>Level C</th>
<th>Level U (Inef)</th>
<th>Estab Inefll</th>
</tr>
</thead>
<tbody>
<tr>
<td>Valproic acid</td>
<td>Amitriptyline</td>
<td>Lisinopril</td>
<td>Aceinoidamide</td>
<td>Lamotrigine</td>
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<tr>
<td>Topiramate</td>
<td>Venlafaxine</td>
<td>Candesartan</td>
<td>Coumadin</td>
<td>Clonopinone</td>
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<tr>
<td>Metoprolol</td>
<td>Atenolol</td>
<td>Chlordine</td>
<td>Fluoxetine</td>
<td>Clomazepam</td>
</tr>
<tr>
<td>Propranolol</td>
<td>Nadolol</td>
<td>Carbamazepine</td>
<td>Gabapentin</td>
<td>Oxcarbazepine</td>
</tr>
<tr>
<td>Floxurinptant</td>
<td>Naratriptant</td>
<td>Pindolol</td>
<td>Verapamil</td>
<td></td>
</tr>
<tr>
<td>Zolmitriptant</td>
<td>Cyproheptadine</td>
<td>Bisoprolol</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*a for short term prophylaxis

Consider dosing other medical conditions, side effects, and dosing regimen when selecting therapies.

Alternative Therapies

• Avoid triggers
• Relaxation, biofeedback, acupuncture
• Physical therapy
• Dietary/vitamin supplementation:
  - Penadex type of Butterbar (but may cause liver failure...)
  - Vitamin B2, B6
  - St.John’s Wort
  - Ginger
  - Ginigla bileda
  - Fever few
  - Magnesium supplementation (+/-)
  - Coenzyme Q10
Alternative Therapies

- Botulinum Toxin
  - Indicated only for chronic migraine headache
  - Usually approved only after a patient has failed multiple medications and has multiple headache days per month
  - Effective after 7-10 days up to 12 weeks

Alternative Therapies

- Anti-CGRP agents
  - Monthly injections
  - Monoclonal antibody directed against the neuropeptide CGRP (which is involved in neurogenic inflammation)
  - Brand new—unlikely to be on the USMLE (but you can sound super smart and up-to-date when you talk to your friends)

“Other” Headaches
The Headaches

A 48 year old male presents for a severe boring pain in the left eye. Which of the following is considered an effective abortive therapy?
- A. Lorazepam 1.0 mg
- B. Inhaled oxygen 10 mL/min
- C. Carbamazepine starting at 200 mg BID
- D. Methylprednisolone 1g
- E. Butalbital-acetaminophen combo therapy

Answer is: _____

“Other”: Cluster Headache

One of the most severe headaches
- More common in men (4.5:1)
- Peak incidence 40-49y
- Often heavy smokers & excessive alcohol use
- More common in the spring & autumn
- Commonly occur at night
- Symptoms usually “side locked” during cluster but can switch sides in subsequent attacks

Clusters last 6-12 weeks
- Typically occur every year or two
- 85% episodic, 15% chronic/unremitting
- 1-4 attacks/day lasting 20m to 3hrs
- Rapid onset over usually 15-30 minutes (but not seconds)
- Invariably unilateral
- Alcohol nearly always triggers attacks
- Can be associated with a partial Horner’s & unilateral rhinorrhea ("Trigeminal Autonomic Cephalgia")

Cluster Headache

Acute therapies

Can be limited by headache duration (minutes to a few hours)
- Oral medications of little use

Effective medications
- Inhaled oxygen 100% by rebreather at 10-15 L/min
- Injectable sumatriptan
- Nasal spray triptans
- Intranasal lidocaine
- Intranasal DHE
The Headaches

A 62 year old female presents for a severe lightening-like pain that radiates down her jaw. Pain come in brief, but intense, spurts often triggered by talking or chewing. Which of the following is considered an effective symptomatic therapy?

- A. Lorazepam 1.0 mg
- B. Inhaled oxygen 10 mL/min
- C. Carbamazepine starting at 200 mg BID
- D. Methylprednisolone 1g
- E. Butalbital-acetaminophen combo therapy

Answer is: _____

“Other”: Trigeminal Neuralgia

A. Paroxysmal attacks of pain lasting from a fraction of a second to two minutes, affecting one or more divisions of the TN
- Peak incidence 60-70, unusual before 40
- MS is the most common assoced disease (idiopathic most common)
- Usually worse with talking or eating
- Usually end up at the dentist first for a root canal

- Treatment:
  - Carbamazepine is established as effective for controlling pain (200-1200 mg/d) (first line therapy)
  - Oxcarbazepine is probably effective (600-1800 mg/d)
  - Baclofen & lamotrigine are possibly effective

Trigeminal neuralgia usually involves the jaw and is lightening-like; cluster headaches are usually behind the eye and last much longer. Also referred to as “tic douloureux.”

Trigeminal Neuralgia

A potentially “curative” option for trigeminal neuralgia is a microvascular decompression but requires an artery from the trigeminal root.
“Other”: Tension-type Headache

- The most common form of HA (occurs in 35-75% of adults)
  - Rarely severe & thus account for <5% of visits
- Clinical features
  - Bilateral pain lasting >30 minutes, usually 4-6 hours
  - Band-like head pain with a "pressing" or "tightening" quality
  - Mild-to-moderate intensity
  - Not aggravated by routine activity
  - No nausea/vomiting
  - Phonophobia & photophobia can occur but not both
- Treatment is both pharmacologic & non-pharmacologic
  - Screen for depression and sleep disorders
  - Physiotherapy, biofeedback
  - May be responsive to TCAs (amitriptyline)

“Other”: Pseudotumor Cerebri

- Clinical Features:
  - Patients often overweight
  - ICP ≥ 250 mm H2O
  - No localizing features
  - No mass lesion or enhancement
  - Normal CSF content
  - No CVT
- Headache is the presenting feature in ≥ 75%
- Treatment: acetazolamide, topiramate, surgical intervention

“Other”: Primary Exertional Headache

- Pulsating HA last from 5 min to 48 hours, and occurring only during or after physical activity
- Younger patients (10-48 y/o), usually male
- Treatment
  - Beta-blockers
  - Indometacin
  - Can treat for 3-6 months

Jokl & Jokl (1968)
- Described “effort migraines” during the Olympic Games
  - Athletes developed scotomas, retro-orbital pain, nausea, vomiting and prostration
  - Attributed to high altitude (7000 feet above sea level), heat, & humidity
For Your Interest Only

The Rapid Headache Evaluation

Chief Complaint: Headache

- First/Worst/Rapid
- Recent Onset of Headache
- Abnormal Neuro Exam

History >1 year
- Normal Neuro Exam
- Similar HA in past

Secondary HA

Further Evaluation

Primary Headache

Migraine

Cluster

Tension

These headaches are often the most serious and concerning!

The Headaches: Further Evaluation

Worst Headache:
- CT Head

Blood

No Blood

Mass Lesion

SAH

CTA or 4-V Angio

Brain tumor, abscess

Aneurysmal SAH or Non-aneurysmal SAH
The Headaches

Worst Headache: CT Head

No Blood

Pt >50 OR
Pt >50 and ESR/CRP elevated (*)

Labs Abnormal Other
Than ESR/CRP

Suspect IFX
or SAH

Spinal Tap

MR/MRV

RBC

WBC

CTA

AVM, CTV

IFX

GCA

Systemic Illness

The Rapid Headache Evaluation:

Red Flags

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<td>Carotid artery aneurysm</td>
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<td>Carotid bruit in the young</td>
<td>Carotid artery dissection</td>
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<td>Fever &amp; skin rash</td>
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<td>Shock, Addison’s</td>
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The Rapid Headache Evaluation:

Non-Neurologic Causes

<table>
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<th>Disorder</th>
<th>Location/Type</th>
<th>Time Profile</th>
<th>Pathognomic Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute angle glaucoma</td>
<td>Eye pain, frontal</td>
<td>Acute</td>
<td>Red eye, midrange pupil, decreased vision</td>
</tr>
<tr>
<td>Temporal arteritis</td>
<td>Sharp or dull</td>
<td>Rapidly built up</td>
<td>ESR &gt;95 mU/hour</td>
</tr>
<tr>
<td>Acute sinusitis</td>
<td>Frontal and maxilla</td>
<td>Hours</td>
<td>Fever, pressure pain</td>
</tr>
<tr>
<td>Pheochromocytoma</td>
<td>Bilateral</td>
<td>Rapidly increasing</td>
<td>Sweating, pallor, SBP &gt;200</td>
</tr>
<tr>
<td>Herpes zoster</td>
<td>Eye pain, frontal</td>
<td>Hours-days</td>
<td>Rash (may be delayed), facial edema, visual loss</td>
</tr>
</tbody>
</table>

Acute angle glaucoma & temporal arteritis are at least mentioned in First Aid
Differentiating Headaches

<table>
<thead>
<tr>
<th>Type</th>
<th>Location/Type</th>
<th>Duration</th>
<th>Symptoms</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cluster</td>
<td>Unilateral/retro-orbital</td>
<td>15-20 min-3+ hours</td>
<td>Excruciating periorbital pain with lacrimation</td>
<td>Inhaled oxygen Injectable sumatriptan</td>
</tr>
<tr>
<td>Tension</td>
<td>Bilateral</td>
<td>&gt;30 min (usually hours)</td>
<td>Band-like pressure/pain</td>
<td>Sleep, Diet, Exercise Simple analgesics</td>
</tr>
<tr>
<td>Migraine</td>
<td>Unilateral</td>
<td>4-72 hours</td>
<td>Pulsating pain with photo/phono-phobia</td>
<td>NSAIDs Triptans</td>
</tr>
</tbody>
</table>

Recommended Dosages

<table>
<thead>
<tr>
<th>Drug</th>
<th>Daily Dose</th>
<th>Max Dose</th>
<th>Half-Life</th>
<th>Peak Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetaminophen</td>
<td>1000 mg/dose</td>
<td>4000 mg</td>
<td>2-3 hrs</td>
<td>+Less gastric irritation, does not affect platelet function +Less effective</td>
</tr>
<tr>
<td>Ibuprofen</td>
<td>400 mg/dose</td>
<td>2400 mg</td>
<td>2 hrs</td>
<td>+NNT 3.2 for relief at 2 hrs +Liquid-containing capsules work the fastest</td>
</tr>
<tr>
<td>Diclofenac</td>
<td>50 mg/dose</td>
<td>150 mg</td>
<td>2 hrs</td>
<td>+Fast onset (15 min)</td>
</tr>
<tr>
<td>Naproxen</td>
<td>500-625 mg/dose</td>
<td>1375 mg</td>
<td>14 hrs</td>
<td>+Longer half-life +Slower onset</td>
</tr>
<tr>
<td>Aspirin</td>
<td>875-1000 mg/dose</td>
<td>4000 mg</td>
<td>6 hrs</td>
<td>+Fast onset +Cannot use &gt;5-7 days -No data in support of use</td>
</tr>
<tr>
<td>Ketorolac</td>
<td>10 mg</td>
<td>400 mg</td>
<td>5 hrs</td>
<td>+Fast onset +Can use &gt;5-7 days</td>
</tr>
</tbody>
</table>

Characteristics of Triptans

Patients usually take one at onset of headache and one two hours later if the headache persists.

<table>
<thead>
<tr>
<th>Drug</th>
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<th>Max Dose</th>
<th>Half-Life</th>
<th>Peak Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sumatriptan (Imitrex)</td>
<td>50-100</td>
<td>300</td>
<td>2.0</td>
<td>2.5</td>
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<tr>
<td>Zolmitriptan (Zomig)</td>
<td>2.5</td>
<td>10</td>
<td>3.0</td>
<td>4.0</td>
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<tr>
<td>Naratriptan (Amerge)</td>
<td>2.5</td>
<td>5</td>
<td>5.0</td>
<td>2.5</td>
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<tr>
<td>Rizatriptan (Maxalt)</td>
<td>10</td>
<td>20</td>
<td>2.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Almotriptan (Axert)</td>
<td>12.5</td>
<td>25</td>
<td>3.5</td>
<td>2.5</td>
</tr>
<tr>
<td>Frovatriptan (Frova)</td>
<td>2.5</td>
<td>5</td>
<td>25.0</td>
<td>3.0</td>
</tr>
<tr>
<td>Eletriptan (Relpax)</td>
<td>40</td>
<td>80</td>
<td>5.0</td>
<td>2.8</td>
</tr>
</tbody>
</table>
Migraine Therapies

AAN Guidelines: Preventive Therapies

<table>
<thead>
<tr>
<th>Level A</th>
<th>Level B</th>
<th>Level C</th>
<th>Level U</th>
<th>Estab Ineffec</th>
</tr>
</thead>
<tbody>
<tr>
<td>Valproic acid</td>
<td>Amitriptyline</td>
<td>Lisinopril</td>
<td>Acetazolamide</td>
<td>Lamotrigine</td>
</tr>
<tr>
<td>Topiramate</td>
<td>Venlafaxine</td>
<td>Candesartan</td>
<td>Coumadin</td>
<td>Clomipramine</td>
</tr>
<tr>
<td>Metoprolol</td>
<td>Atenolol</td>
<td>Chloride</td>
<td>Fluoxetine</td>
<td>Clonazepam</td>
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<tr>
<td>Propranolol</td>
<td>Nadolol</td>
<td>Carbamazepine</td>
<td>Gabapentin</td>
<td>Ocarbazepine</td>
</tr>
<tr>
<td>Frovatriptan*</td>
<td>Naratriptan*</td>
<td>Pindolol</td>
<td>Verapamil</td>
<td></td>
</tr>
<tr>
<td>Zolmitriptan*</td>
<td>Cyproheptadine</td>
<td>Bupropiol</td>
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</table>

a=for short term prophylaxis

Preventive Therapy for Migraine

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Selected Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Valproic Acid</td>
<td>800-1200</td>
<td>Tiredness, weight gain, hair loss, liver and hematologic abnormalities, teratogenecity</td>
</tr>
<tr>
<td>Topiramate</td>
<td>25-200</td>
<td>Confusion, paresthesia, weight loss, angle closure glaucoma, renal stones (&quot;Dopamax&quot;)</td>
</tr>
<tr>
<td>B-adrenergic receptor antagonists (β-blockers)</td>
<td>40-240</td>
<td>Reduced energy, tiredness, postural symptoms, dizziness, weight gain, impotence</td>
</tr>
<tr>
<td>Propranolol</td>
<td>100-200</td>
<td></td>
</tr>
<tr>
<td>Metoprolol</td>
<td>100-320</td>
<td>Constipation, leg swelling, atrioventricular conduction disturbances</td>
</tr>
<tr>
<td>Amitriptyline</td>
<td>25-75</td>
<td>Dryness, weight gain, dry mouth</td>
</tr>
<tr>
<td>Venlafaxine</td>
<td>100-320</td>
<td>Constipation, leg swelling, atrioventricular conduction disturbances</td>
</tr>
<tr>
<td>SSRI</td>
<td></td>
<td>Anxiety, insomnia</td>
</tr>
<tr>
<td>Gabapentin</td>
<td>900-1800</td>
<td>Tiredness, dizziness</td>
</tr>
<tr>
<td>Tizanidine</td>
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<td>Fatigue</td>
</tr>
</tbody>
</table>

End