Migraine Headache – Update on Diagnosis & Treatment

Charles Brock, M.D.
Diagnosing Migraine Headache

- Any severe or recurrent headache most likely is a form of migraine
- Almost all patients will have family history of migraines or at least “sick” headaches
- Only 15% have preceded or accompanied focal neurologic symptoms
  - Usually visual
    - Vision loss or distortion in one eye – ‘ocular migraine’
  - “Classic migraine”
Recurrent Headaches

- Primary
  - Migraine
  - Tension
  - Cluster
  - Other benign – cough, cold temperature, post coital, exertion
Recurrent Headaches

- Secondary (pain from complications)
  - Intracranial tumor
  - Intracranial aneurysm
  - Intracranial A-V malformation
  - Temporal arteritis
Migraine with aura – Criteria*

- At least 2 attacks with 3 of the following:
  - Fully reversible aura symptoms
  - At least 1 aura symptom develops gradually during more than 4 minutes or 2 symptoms occur in succession
  - Any aura symptom lasts less than 60 minutes
  - Headache follows the aura within 60 minutes

*International Headache Society - 2004
Migraine with aura

- Visual aura common
  - Slowly evolving scintillating scotoma that moves or passes through visual field
  - Duration of aura – 22 minutes
  - Should not be called ocular migraine if bilateral eye involvement
    - Just call them migraine with aura
## Visual aura rating scale (VARS)

<table>
<thead>
<tr>
<th>Visual Symptom</th>
<th>Risk Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration 5 - 60 minutes</td>
<td>3</td>
</tr>
<tr>
<td>Develops gradually over 5 min</td>
<td>2</td>
</tr>
<tr>
<td>Scotoma</td>
<td>2</td>
</tr>
<tr>
<td>Zigzag line (fortification)</td>
<td>2</td>
</tr>
<tr>
<td>Unilateral (homonymous)</td>
<td>1</td>
</tr>
<tr>
<td><strong>MIGRAINE with AURA DIAGNOSIS</strong></td>
<td>≥ 5</td>
</tr>
</tbody>
</table>
Migraine with aura – vascular risk?

- Migraine with aura is associated with 2 fold risk of ischemic stroke & cardiovascular event
  - Absolute risk is low (4 per 10000 women years)
  - May be indication for aggressive treatment of other risk factors
  - Unclear if more intense treatment & prevention of migraines will alter the risk
Migraine without aura – Criteria*

- At least 5 attacks (bunch of them)
- Lasting 4-72 hours untreated or unsuccessfully treated (didn’t just go away quickly)
- **Must** have one of these to be migraine:
  - Nausea or vomiting
  - Photophobia
  - Phonophobia

*International Headache Society - 2004*
Migraine without aura – Criteria*

- Then usually have at least 2 of these:
  - Unilateral pain
  - Throbbing/pulsating
  - Aggravation on movement
  - Moderate or severe intensity

- And of course to be sure not something else:
  - H & P does not suggest organic disorder
  - H & P suggests an organic disorder which is then ruled out
  - An organic disorder is present but attacks do not occur for the 1st time in close time to the disorder

*International Headache Society - 2004
Diagnosing the acute headache

• The classification criteria are best suited for a between-attack assessment of their typical headache
  • However, they are often used for the acute attack
  • Once acute pain relieved, take time to make an accurate diagnosis
• Up to 1/3 of ED patients cannot be assigned a diagnosis
  • Despite a through questionnaire-based assessment
ER Clinical Decision Rule

- “ID Migraine” – three features
  - Sensitivity to light
  - Nausea or vomiting
  - Disabling intensity of headache
    - 0 - 1 positive - low probability
    - If 2 positive higher probability of migraine
  - Criteria focus on typical attacks not the current acute attack
Epidemiology - Migraine

- Can start at any age, however,
  - Peak incidence of onset is mid-adolescence (age 13-16)
  - History of colic or motion sickness support Dx
- Median frequency - 1.5/month
- Greater increase in prevalence with aging in women
  - Females - 6.4% age 12 - 17; 17.3% age 18 - 29
  - Males - 4.0% age 12 - 17; 5.0% age 18 – 29
  - Usually more severe in women
Pathophysiology

- Migraine is a primary neural event
  - Something lowers threshold for a cortical spreading depression (CSD)
    - Which causes regional hypoperfusion (aura)
    - Release of proinflammatory neurochemicals
  - Neural event results in vasodilation
    - Which leads to pain & more nerve activation
- Migraine headache is not a primary vascular event
Why does it hurt?

- Substance of brain is largely insensate
- Pain could come from:
  - Cranial blood vessels
  - Trigeminal innervations of vessels
  - Reflex connection of trigeminal system with cranial parasympathetic flow
- No clear explanation for why it hurts
Testing Indications*

- Laboratory tests not helpful or needed to make the diagnosis
- EEG not indicated as routine evaluation
- Neuroimaging guidelines
  - Typical migraine with normal neurologic exam
    - Neuroimaging not warranted (SOR-B)
  - Insufficient evidence regarding imaging in presence of neurologic symptoms (SOR-C)

Neuroimaging - EBM

- For non-acute HA with unexplained abnormal finding on neurologic examination – obtain neuro image (SOR-B)
- If atypical features or headache does not fulfill definition of migraine – lower the threshold for obtaining imaging (SOR-C)
- CT vs. MRI?
  - Insufficient data to recommend MRI compared to CT in evaluation of migraine or other nonacute headache (Grade C)
Red Flags!

- Strongly consider neuroimaging if
  - New onset > age 50
  - Thunderclap onset
  - Focal and nonfocal symptoms
  - Abnormal signs
  - Headache with change in posture
  - Valsalva headache
  - HIV or cancer diagnosis
Prodrome (before headache)

- Some patients experience symptoms hours to days before the headache (prodrome)
  - Fatigue
  - Inattentiveness/confusion
  - Restlessness, elation, +/- irritability
  - Insomnia +/- depression
  - Joint pain
  - Hunger or food craving
  - Yawning
Treatment

- Goals of treatment
  - Reduce frequency, severity, & duration of headaches
  - Improve quality of life (QOL)
  - Avoid acute medication escalation
- Treatment Guidelines are based upon having a specific diagnosis
  - Often difficult initially to make specific Dx
  - Therefore, significant uncertainty about ‘best’ initial treatment
Treatment - Migraine

- The brain of patients with migraines does not tolerate peaks or troughs of life

- Patients should get:
  - Regular sleep
    - Go to bed and awaken same time every day
  - Regular meals
    - Eat same time every day
    - Never skip meals – fasting associated with precipitating headache
  - Regular exercise
  - Avoid peaks of stress, troughs of relaxation
  - Avoid unique dietary triggers
Migraine & Diet - EBM

- Frequency, duration & severity are NOT increased by dietary choices (SOR-A)
  - Cheese, alcohol, chocolate, citrus are not universal triggers
- Low-fat diet reduced frequency of migraines (SOR-B)
Migraine & Supplements - EBM

- Supplements reduced frequency & intensity
  - Riboflavin – 400 mg qd
    - Effect begins at 1 month, maximal @ 3 months
  - Magnesium – 600 mg qd
    - Diarrhea common - almost 20%
    - 360 mg qd during luteal phase reduced menstrual migraine
- Others
  - Butterbur 100-150 mg/d
  - CoQ10 300 mg/d
  - Feverfew 18.75 mg/d

- National Guideline Clearing House
  - SOR – A
Treatment of Acute Pain

- NSAID (SOR-A)
- Ketorolac (Toradol®) – 10 mg oral, 60 mg IM, or 30 mg IV (SOR-C)
- Combinations
  - Isomethetepn mucate, dichloralphenazone and acetaminophen (Midrin®)
  - Butalbital has not been effective in controlled trials (butalbital/acetaminophen/caffeine- 50/325/40 Fioricet®, butalbital/ASA/caffeine-50/325/40 Fiorinal®)
Treatment of Acute Pain

- NSAIDs – more effective when:
  - Taken early
  - With adequate initial dose
  - Combined with antiemetic

- ASA 1000 mg
  - Combined with metoclopramide IM (Reglan®) reduces nausea/vomiting but not better pain control
Treatment of Acute Pain

- IV fluids may benefit patients, although benefit is not well established
  - Unlikely to be harmful especially in patients with persistent GI symptoms
  - Parenteral therapy preferred due to gastric stasis & delayed absorption of oral medications
Treatment of Acute Pain

- Droperidol (Inapsine®) probably most effective of dopamine agonists
  - Pain relief at 2 hours approaching 100%
  - Ideal dose – 2.5 mg IV
  - FDA warning about QT prolongation
Treatment of Acute Pain

- Prochlorperazine (Compazine®) 10 mg IV
  - Effective with diphenhydramine (Benadryl®) – 25 mg IV [Friedman 2008]
  - Superior to SC sumatriptan in ED setting [Kostic 2010]
- Children 0.15 mg/kg IV over 15 minutes (max 10 mg)
  - If EPS develop give diphenhydramine 1mg/kg (max 50 mg)
Treatment of Acute Pain

- **Metoclopramide** (Reglan®)
  - IV – monotherapy 10 - 20 mg IV
  - IM – 10 mg adjunct to other therapies (SOR-C)

* FDA boxed warning 2/26/09 – Long-term or high-dose use of metoclopramide has been linked to tardive dyskinesia.
Treatment of Acute Pain

- Ergot alkaloids
  - Dihydroergotamine (D.H.E. 45®) – 1 mg IM/IV/SC
    - Since it may cause nausea, more effective with metoclopramide (Reglan®) to reduce nausea
  - Nasal spray effective
  - Ergotamine/caffeine (1/100) (Cafergot®)
    - Little evidence effective alone
    - High risk of overuse & rebound headache
Treatment of Acute Pain

- Sodium valproate (Depacon®)
  - 500 – 1000 mg in 10 ml normal saline IV over 30 min
  - May be effective but less than prochlorperazine (Compazine®)
Treatment of Acute Pain - EBM

- Patients with substantial disability will benefit from serotonin 5-HT$_{1B/1D}$ agonists (‘triptans’)
  - SOR – A
  - Clinical Evidence
    - http://www.clinicalevidence.com/ceweb/conditions/nud/1208/1208.jsp
Triptan Efficacy

- No one triptan is superior in all pain relief parameters
- Use one triptan for 2-3 attacks before abandoning that medication
- If one does not work try another one
## Triptans (Medical Letter 2008)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Onset of action</th>
<th>Elimination half-life</th>
</tr>
</thead>
<tbody>
<tr>
<td>Almotriptan (Axert®)</td>
<td>30 - 60 min</td>
<td>3 - 4 hours</td>
</tr>
<tr>
<td>Eleetroptan (Relpax®)</td>
<td>30 - 60 min</td>
<td>3 - 4 hours</td>
</tr>
<tr>
<td>Frovatriptan (Frova®)</td>
<td>~ 2 hrs</td>
<td>~ 25 hrs</td>
</tr>
<tr>
<td>Naratriptan (Amerge®)</td>
<td>1 - 3 hrs</td>
<td>~ 6 hrs</td>
</tr>
<tr>
<td>Rizatriptan (Maxalt®)</td>
<td>30 - 60 min</td>
<td>2 - 3 hrs</td>
</tr>
<tr>
<td>Sumatriptan (Imitrex®)</td>
<td></td>
<td>~ 2 hrs</td>
</tr>
<tr>
<td></td>
<td>tablets</td>
<td>30 - 60 min</td>
</tr>
<tr>
<td></td>
<td>nasal spray</td>
<td>10 - 15 min</td>
</tr>
<tr>
<td></td>
<td>SC injection</td>
<td>~ 10 min</td>
</tr>
<tr>
<td>Zolmitriptan (Zomig®)</td>
<td></td>
<td>2 - 3 hrs</td>
</tr>
<tr>
<td></td>
<td>tablets</td>
<td>30 - 60 min</td>
</tr>
<tr>
<td></td>
<td>nasal spray</td>
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Triptans – Cautions

- Contraindicated with CAD, uncontrolled hypertension or cerebrovascular disease, hemiplegic migraine
- Should not be taken within 24 hrs of another triptan or ergotamine-containing/ergot-type medication
- Taking them with an SSRI or SNRI can cause life-threatening serotonin syndrome
Combining Medications

- Sumatriptan 85 mg & Naproxen 500 mg (Treximet®) more effective than either alone for acute pain relief
  - Unknown effect of taking 2 separate pills (not tested)
  - The combination may have some increased benefit in mild/moderate pain but no evidence of need for fixed dose combination (Medical Letter 2008)
Early Recurrence

- Up to 75% of patients will experience a recurrence of pain within 48 hours
  - Naproxen (500 mg) or sumatriptan (100 mg) equally effective treating the recurrence [Friedman 2010]
  - Naproxen prophylactically can prevent recurrence (NNT – 3)
  - Triptans should not be used prophylactically
Preventing Early Recurrence

- Parenteral dexamethasone (10-25 mg IV)
  - Produced 26% relative reduction in recurrence within 72 hours [Colman 2008]
  - Modest benefit in the ED – prevented 1 in 10 patients from experiencing moderate or severe recurrence [Singh 2008]
  - Later trials failed to find benefit with oral dexamethasone or prednisone
Acute Pain & Parenteral Opioids

- Should not be used as 1st line therapy
  - International Headache Consortium
  - Canadian Association of Emergency Physicians
  - American Academy of Neurology
New Treatments Acute Pain

- Diclofenac oral solution (Cambia®) – dissolve contents in water
- Sumatriptan patch (Zelrix™) – similar levels to SC
New Treatments Acute Pain

- DHE inhaled (Levadex®) – patients not responding to triptans or more than 6 hours into headache?
- Calcitonin gene-related peptide (CGRP) antagonist (telcagepant) – as effective as zolmitriptan 5 mg oral
- Single-pulse transcranial magnetic stimulation (sTMS)
  - More effective than placebo in pain-free at 2 hours (39% vs 22%)
After the Migraine - Postdrome

- Some patients may have:
  - Mood changes
  - “Hangover”
  - Tired
  - Weak
  - Disoriented
  - “Not right”
Chronic Migraine (CM) or Medication Overuse Headache (MOH)

- Chronic migraine previously called ‘transformed migraine’
- Consider medication overuse if ≥ 2 days/week for > 3 months analgesic use
- Over period of time (months to years) can become almost daily headache
  - Resembles mixture of tension & migraine
  - Occasionally called ‘tension-vascular’
  - Hint – if awaken with headache consider medication overuse
CM Modifiable Risk Factors

- Risk factor associated with increased risk of developing CM
  - Stressful life events
  - Sleep disturbance (i.e. Snoring/sleep apnea)
  - Obesity
  - Baseline headache frequency
  - Medication overuse
CM & MOH

- Treatment
  - Must stop acute medication to determine
    - Headaches will go away in a few days if medication overuse is etiology
  - No controlled trials of medication withdrawal
  - May get severe withdrawal headache
    - Severe withdrawal headache can be treated with short course of prednisone
  - Randomized trial found no difference with steroid compared to placebo
Preventive Medication

- Candidates:
  - Unresponsive to acute attack medication & disabling headache
  - ≥ 2 attacks/month
  - Increasing frequency of attacks
  - Migraines with potential neurological sequelae
  - Patient preference (just wants to use medication to prevent headaches)
Prevention therapy - EBM

- First line treatment should be:
  - Propranolol (Inderal®)
    - 20 – 240 mg/day
  - Timolol
    - 10 – 30 mg/day
    - Less evidence to support other beta-blockers
  - Amitriptyline
    - 10 – 150 mg/day
Prevention therapy - EBM

- First line treatment should be:
  - Divalproex sodium (Depakote®)
    - 125 – 500 mg BID
  - Topiramate (Topamax®)
    - 50 - 100 mg BID
    - May be as good as propranolol
  - Anti-epileptic drugs had greater suicidal ideation vs. placebo (0.43% vs 0.22%)
Prevention therapy

- Second line (SOR-B)
  - Gabapentin - pregnancy category D
  - Carbamazepine* - pregnancy category D

* FDA Alert 12/12/07 – Dangerous or even fatal skin reactions can be caused by Carbamazepine therapy in patients with a particular HLA-B*1502 allele.
Prevention Therapies - EBM

- Relaxation training (SOR-A)
  - Progressive muscular relaxation
  - Breathing exercises
  - Directed imagery
- Cognitive-behavioral (SOR-A)
  - Combined with medication (SOR-B)
- Acupuncture appears to be effective (SOR-A)
  - Sham acupuncture just as effective as real [Linde 2009]
- Thermal biofeedback with relaxation training
Prognosis of Migraines

- Study with 10 year follow-up of 11-14 year olds at onset of migraines
  - 40% no longer had headache
  - 20% had episodic tension headache
  - 20% had migraine type that was different from the original diagnosed headache
- Frequency & intensity usually decreases after menopause
- Two fold increased risk of CVA [Spector 2010]
  - May influence how aggressive to be with other therapies to reduce risk of CVA
Key Points

- Diagnosis of migraine headache is clinical
  - Almost always positive family history
- Triptans are preferred treatment for frequent migraines
- Discuss preventive therapy with all patients
- Provide treatment plan for breakthrough pain
What Questions do you have?
References


References


References
