Neurology Update
Migraine Headaches

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Objectives

- Discuss Diagnosis of Migraine
- Review present standard of care treatment of acute migraine treatment
- Review present standard of care treatment for prevention of migraines

Diagnosis of Migraine

Acute Migraine Treatment

- Goal is to reduce disability caused by migraine
  - Shortening the attack
  - Reducing the severity
- Treatment Approaches
  - Stratified Approach
    - Medication chosen based on migraine severity and the resulting disability
    - Best medication first approach
  - Step Care Across Attack Approach
    - Less expensive/safer medications used first, working up the ladder
  - Step Care Within Attack Approach
    - May work in selected patients with graduated headaches, but need to monitor effectiveness as time delay in taking stronger medication may result in prolonged disability and headache

- Early treatment is important
- Ongoing dialogue is important as sometimes medications don’t work
- May need more than one type of treatment for more than one type of migraine in the same patient
- Medication choice based on many factors (comorbid conditions, presence of nausea/vomiting etc.)
- Two or more medications can be combined if necessary
  - sumatriptan and naproxen
  - triptan plus medication for nausea
Acute Migraine Treatment

- Overuse of acute medications for migraine needs to be avoided
- Use of NSAIDs or acetaminophen > 15 days per month
- Use of combination analgesics, opioids, ergots, or triptans 10 days per month
- Opiates generally should be avoided except in certain circumstances
- Usually less effective than other medications
- Lead to escalation of acute migraine treatment, thought to alter receptors and ultimately make headaches more refractory over time
- Lead to medication overuse

Acute Migraine Treatment

APAP and NSAIDs

- Acetaminophen may be administered in migraine headache when other meds:
  - Ketorolac 30-60 mg IM, self injection at home
  - Indomethacin 50-75 mg orally or suppository
  - Dexamethasone (4 mg tablets, drip ile: two now, two later today and if headache persists take additional one pill in the am)
  - Naprosyn with APAP
  - Combination analgesics with opiates used sparingly

Acute Migraine Treatment

Triptans

- Should be considered first line in patients with severe headaches
- There is no preferred triptan, all have strong evidence for efficacy
- Decisions based on:
  - Patient preference
  - Cost
  - Delivery method (nasal vs)
  - Type of migraine (migrainous prevention)
- Recent meta-analyses found eletriptan 40 mg (Relpax) and almotriptan 10 mg (Axert) provided highest pain relief of two hours
- Recent meta-analyses found eletriptan 40 mg (Relpax) highest 24 hour pain relief

Acute Migraine Treatment

Problem Medications

- Indomethacin 50-75 mg orally or suppository
- Combination analgesics with opiates used sparingly
- Combination analgesics with triptans used sparingly
- Combination analgesics with triptans not recommended
- Combination analgesics with triptans not recommended
- Combination analgesics with triptans not recommended

Acute Migraine Treatment

Rescue for Triptan Failures

- Ketorolac 30-60 mg IM, self injection at home
- Indomethacin 50-75 mg orally or suppository
- Dexamethasone (4 mg tablets, drip ile: two now, two later today and if headache persists take additional one pill in the am)
- Naprosyn with APAP
- Combination analgesics with opiates used sparingly

Acute Migraine Treatment

Problem Medications

- Opioids/Opiates should generally be avoided
- Thought to alter receptors and ultimately make headaches more refractory over time
- Habitual compounds (Foscavir) – high risk for escalation and overuse
- Tramadol with APAP (Valium) – high potential for abuse
Acute Migraine Treatment

**Antiemetics**
- Promethazine (Phenergan)
- Metoclopramide (Reglan)
- Sparing up to three times a day
- Prochlorperazine (Compazine)
- Sparing up to two times a day
- EKG monitoring recommended in some cases
- 10 mg up to four times per day
- May be used with other acute therapies

**Beta Blockers**
- Nonselective - propranolol
- S1 selective - metoprolol, atenolol, bisoprolol, nadolol, timolol
- Those with sympathomimetic activity not effective - pindolol (Visken), acebutolol (Sectral)
- Contraindicated in asthma, COPD, AV conduction defects, Raynaud's, PVD, severe OMI
- Up to 50% effective

Preventative Migraine Treatment

**Antiemetics**
- Recommended for recurring migraine attack that interfere with quality of life
- Frequent headaches (for or more per month or more than 8 headache days per month)
- Fulsize or contraindication, or overdose, or side effects from acute medications
- Patient preference
- Complicated migraine (hemiplegic, brainstem)

**Beta Blockers**
- Choice based on best Proven Efficacy
- Choice based on risk/benefit analysis
- Consider comorbid states and other medical factors
- Complicated migraine (hemiplegic, brainstem)
- Up to 50% effective
- Sometimes requires two medications (tricyclic at low dose for migraine, SSR or SNRI for depression)
- Prevention goal is for 6-9 months of control then slow taper and reintroduction as necessary (but relapse rate is high)

**Beta Blockers**
- Choice based on best Proven Efficacy
- Choice based on risk/benefit analysis
- Consider comorbid states and other medical factors
- Adequate treatment trial up to 2-6 months
- Realistic expectations
- Reevaluate therapy
- Always consider pregnancy risks in females
- Involve patients in their care
- Discuss side effects in advance
Efficacy is not thought to be related to treating underlying depression in most cases.

Preventative Migraine Treatment

Antidepressants

- Efficacy is not thought to be related to treating underlying depression in most cases.
- Amitriptyline is a TCA used most commonly and only one for which data supports its use. We do sometimes try or substitute other with less side effects of tricyclics.
- Need to go slow due to side effects: dry mouth, constipation, dizziness, urinary retention, blurred vision.
- SSRIs, SNRIs data is mixed, generally disappointing except with venlafaxine.
- Use with low dose tricyclics may be helpful in patients with comorbid depression.

Preventative Migraine Treatment

Calcium Channel Blockers

- Often used initially but efficacy in real studies is lacking.
- May be some benefit with brainstem migraines (anecdotal).
- No longer recommended.

Preventative Migraine Treatment

Antiepileptic Drugs

- Valproic Acid - 60-450 mg at 600-1500 mg per day across studies.
- Dose of carboxylic acid is found to be 500 mg per day.
- Can be used as monotherapy.
- Standard starting dose.
- Standard for prophylaxis.
- Toxicity: dose-limiting toxicity (e.g., liver damage).
- Side effects: nausea, vomiting, weight gain, tremors, ataxia.
- Blood pressure should not be lowered.
- Use only if not available or contraindicated/contracepted.
- May be effective in some, but not in all cases.
- Use with caution in children.

Preventative Migraine Treatment

Other Blood Pressure Medications

- ACE inhibitors - limited data but small controlled trial showed efficacy at 10-40 mg per day.
- Angiotension Receptor Antagonists (ARBs) - limited data but small controlled trial showed efficacy at 16-32 mg per day.

Preventative Migraine Treatment

Antihistamines

- Cyproheptadine - H1, H4, and muscarinic cholinergic receptor antagonist.
- Used widely in children for migraine prevention.
- Dose ranges from 12-36 mg per day.
- Shown in a small study to be as effective as propranolol 80 mg per day.
- May inhibit growth in children.
- Reduces efficacy of SSRIs.
- Side effects: sedation, weight gain, dry mouth, lightheadedness.
Preventative Migraine Treatment

Botox

- Approved for patients with 15 or more headache days per month with each headache lasting longer than 4 hours
- Efficacy in study resulting in FDA approval was 62%
- Keeping a headache calendar for up to three months prior to injection required by some insurance companies
- 31 standard injections over the scalp for 150 units then 45 units used for “follow the pain” protocol

Preventative Migraine Treatment

Other considerations

- Women with migraine with aura that use estrogen-based OCs are at 1.5 times the risk of stroke, and if they smoke and use OCs the risk is 5 times
- Women who smoke and have migraine with aura are at 2 times the risk of stroke, even without the use of OCs
- Migraine prevention in some studies has been shown to be much less effective in patients that smoke, the threshold seems to be 5 cigarettes per day

Preventative Migraine Treatment

Other Considerations

Behavioral Management

- Relaxation training, thermal biofeedback, EMG biofeedback and CBT have been shown helpful for migraine prevention (some studies average 32-65% reduction in headache scales)
- Helpful to minimize use of acute medications and in identifying triggers and relieving anxiety
- Recommended for pregnant and lactating woman
- Emerging evidence that aerobic exercise reduces headache frequency

Preventative Migraine Treatment

Other Considerations

- Lifestyle issues cannot be stressed enough to patients with migraines
- Treatment of migraines is a team sport, and if the patient isn’t on the team, it usually results in a loss
- Headache calendars are very effective for getting patients involved in their headache management
- It is important to treat the comorbid issues, especially insomnia, anxiety and depression

Nutraceuticals for Headache

- 80% of patients with headaches use complementary or alternative medications to manage headaches (supplements)
- Many patients prefer “natural” treatments over prescription
- Using non-prescription medications that are proven often adds to the doctor/patient relationship as they respect your willingness to do something other than just prescribe the regulars
- Nutraceuticals many times complement and may augment a standard treatment protocol for migraines
Nutraceuticals for Headache

Riboflavin
- Important role in mitochondrial energy production
- Riboflavin 400 mg per day in one study offered 59% of patients 50% or greater improvement in headaches as compared to 13% in placebo
- Another study compared combo of Feverfew 100 mg, Mg 300 mg and Riboflavin 400 mg vs Riboflavin 25 mg vs placebo and both treatment groups 40% of patients had 50% reduction in headaches
- AAN Guidelines: Riboflavin if probably effective for prevention of migraines
- Side effects diarrhea, polyuria rarely occur, cause bright yellow urine
- Recommended dose 400 mg per day

Magnesium
- Mg binds to and inhibits NMDA (glutamate) receptors
- Many studies demonstrate low Mg levels in migraine patients
- Data suggests Mg more effective in patient with aura
- Studies are mixed
- AAN has no recommendations on use of Mg
- Experts argue that trial of Mg for migraine with aura is reasonable in some cases, dose Mg Citrate 100 mg per day
- Side effects diarrhea, flushing, weakness

Feverfew
- Tanacetum parthenium (chrysanthemum family)
- Mechanism mostly unknown
- AAN guidelines suggest possibly effective
- Average study dose 100 mg per day
- Well tolerated but ‘post feverfew syndrome’ reported with arthralgia and mouth ulcers

Coenzyme Q10
- Evidence that migraine is associated with mitochondrial energy depletion, CoQ10 is considered
- CoQ10 is an electron carrier in the electron transport chain, cofactor in maintaining mitochondrial energy stores
- Few studies
  - 69% of 43 patients had greater than 50% reduction in headaches (200 mg per day vs 10% in placebo)
- Two pediatric studies of 1.3 mg/kg/day demonstrated statistically significant reduced migraine frequency
- AAN Guidelines: Possibly effective in treatment of migraines
- Side effects <1% anorexia, dyspepsia, nausea, diarrhea
- Dose: 100 mg TID for Adults

Butterbur (Petasites hybridus)
- Petasites has antihistamine properties, inhibits calcium channels
- Sold as Petadole since 1988
- Studies are mixed and some experts raise concern about risk/benefit due to potential liver toxicity
- Dose: 100 mg once daily
- AAN recommends use of butterbur, but many experts argue against it for safety reasons
- Side effects mild GI discomfort, cholestatic hepatitis
- If patients do use this, need liver monitoring

Melatonin
- Data is limited and conflicting
- AAN has no recommendations


References

Prietto JM: Update on the efficacy and safety of Petadolex, a butterbur extract for migraine prophylaxis. Botanics Targets Ther 2014;4:1-9


Thank You