Objectives

- Describe the EM relevance of headaches and migraines
- Discuss the rationale for steroid therapy
- Review the evidence
- Conclusions
My inspiration
Headache in the ED

- 85% of adults – at least occasionally – c/o headaches
- “Chief Complaint” of 2-5% of all ED visits
- Vast majority are primary headache disorders
  - Tension-type (~50%)
  - Migraine (~10%)
  - Mixed – Type (~30%)
- Secondary headaches ~ 10%
Headache in the ED

- ED management
  - Exclude secondary causes
    - SAH, infection, tumor, etc
  - Treat symptoms
  - Create a plan for discharge
Migraine Headache

- Recurring, unilateral headache
- Lasts 4-72 hours untreated
- Moderate to severe intensity
- Worse with activity
- Associated with N/V, photophobia, phonophobia
Migraine Headache

- Affects 25% of women
- Less common in men
- Underdiagnosed, undertreated…
- Most patients with migraines do not come to the ER
Migraine Headache in the ED

- ED use for migraine
  - “First or worst” headache
    - Needs a diagnostic evaluation for secondary cause
  - “Last straw” headache – unremitting exacerbation of headache disorder
- Frequent presenters
Migraine Headache in the ED

- Parenteral therapy better
  - GI effects of migraine – stasis and delayed absorption
- Migraine-specific therapy
  - Triptan – Sumatriptan 6mg subQ
  - Ergot – DHE 0.5-1mg IVPB
Migraine Headache in the ED

- Antiemetics
  - Dopamine antagonists are best (Reglan, Compazine)
- NSAIDs
  - Used for outpatient therapy
  - Can give Toradol IV or IM
- IV Hydration
Migraine Headache in the ED

- Opioids
  - Can be used for migraine
  - Other agents better
  - Side effects, abuse potential
  - Increased chance of revisit and recurrence
Tension-Type Headache

- Bilateral
- Pressing or tightening
- Mild-moderate intensity
- Absence of N/V, photophobia, functional disability
Tension-Type Headache

- Along the migraine spectrum?
  - Same medications work
  - Patients can fit diagnostic criteria for both

- NSAIDS
- Antiemetics
Recurrence of Benign Headache

- Within 24-72 hrs:
  - 8-66% of migraines recur
  - 20-25% of tension headaches recur
- Of all headaches, about 35-50% recur
  - Less if headache is gone at discharge
Why do we get headaches?

- Vascular changes
- Hormones
- Inflammation
  - Increasingly thought to be very important in migraine pathophysiology
Inflammation in Benign Headaches

- Traditional ED therapy treats pain and nausea (NSAID-antiemetic)
- Abortive therapy treats hormonal changes (triptans, DHE)
- Inflammation has not been targeted aggressively
The Question Today

- Does administration of steroids prior to discharge decrease the recurrence rate of benign headache?
- Controversial
- We will discuss evidence on both sides!
But first, a methodology quandary…

- We are looking at steroid administration as an adjunctive therapy as part of a discharge plan
- This is concurrent or after administration of symptom relief
But first, a methodology quandary…

- Should studies standardize headache treatment?
  - Pro: No confounding from other meds administered
  - Con: Unrealistic; may deter enrollment
- Or should therapy be at physician discretion?
  - Pro: Reflects normal practice; does not discourage physicians from enrolling patients
  - Con: Other meds may have effect on recurrence rates
CJEM 2006

- Type: RDBCT
- Setting: Two urban academic EDs in Texas
- Patients: 55
- Therapy: At physician discretion
- Intervention: 10mg IV Decadron vs placebo
- Results: Phone call 48-72h post ED discharge
- Recurrence = Worse/unchanged/returned HA
CJEM 2006 - Patients

- Convenience sample

- Inclusion: >18yo, benign headache, IV established, safe for discharge home

- Exclusion: pregnant, fever, meningismus, focal signs, allergy, active PUD, DM 1, systemic fungal infection

- Also excluded if already on steroids or already in study group
Randomized by pharmacist prior to enrollment

Either saline or Decadron 10 mg given by blinded RN

Patients contacted in 48-72h for headache recurrence and side effects
CJEM 2006 - Methods

- Patients did not differ in demographics or in other medications received
- Interim analysis with highly significant results – terminated early
CJEM 2006 - Results

<table>
<thead>
<tr>
<th></th>
<th>Study</th>
<th>Control</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache recurrence</td>
<td>9.7%</td>
<td>58.3%</td>
<td>P&lt;0.001</td>
</tr>
<tr>
<td>Severe recurrence</td>
<td>12.9%</td>
<td>33.3%</td>
<td>P=0.14</td>
</tr>
<tr>
<td>Side effects</td>
<td>19.4%</td>
<td>20.8%</td>
<td>P=1</td>
</tr>
</tbody>
</table>
CJEM 2006 - Discussion

- Strongly positive study
- Limitations:
  - Very small study
  - Convenience sample
Am J EM 2007

- Type: RDBCT
- Setting: community ED and academic ED in southeast Michigan
- Patients: 115
- Therapy: At physician discretion
- Intervention: 24 mg Decadron vs placebo
- Results: Headache recurrence 3 and 30 days after ED visit
Am J EM 2007- Methods

- Blinded randomized study packets
- Inclusion: exacerbation of migraine, meeting IHS criteria; need an IV
- Exclusion: pregnant, fever, allergy to steroids, GI bleeding, diabetes, acute neuro deficit, recent steroid use
Am J EM 2007 - Methods

- Randomized by study pharmacist
- Administered by blinded RN
- Phone followup
  - Assessed recurrence at 3 and 30 days
  - Assessed functional disability
## Results

<table>
<thead>
<tr>
<th></th>
<th>Study</th>
<th>Control</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recurrence of headache – 3 day</td>
<td>36.8%</td>
<td>42.9%</td>
<td>P=0.6776</td>
</tr>
<tr>
<td>Resolution of headache – 3 day</td>
<td>47.3%</td>
<td>35.7%</td>
<td>P=0.305</td>
</tr>
<tr>
<td>Recurrence of headache – 30 day</td>
<td>42.9%</td>
<td>47.5%</td>
<td>p=0.682</td>
</tr>
<tr>
<td>Side effect – dizziness</td>
<td>16.1%</td>
<td>2.5%</td>
<td>P=0.040</td>
</tr>
</tbody>
</table>
Negative study

All outcomes with nonsignificant trends towards improvement with Decadron

Limitations:
- Small study
- Significant number of dropouts (19/115 = 17% - more in the placebo group)
- Large dose of Decadron
Neurology 2007

- Type: RDBCT
- Setting: 4 urban EDs in NYC
- Patients: 205
- Therapy: All received IV reglan
  - Further therapy at physician discretion
- Intervention: 10 mg IV Decadron vs placebo
- Results: Persistently pain free; functional disability
Neurology 2007 – Patients

- Convenience screening by RA’s
- Inclusion: IHS migraine criteria
- Exclusion: Pregnancy, lactation, fever, focal neurological signs, LP planned, allergy/intolerance to study medication
Neurology 2007 - Methods

- Randomization by study pharmacist
- Medication or placebo given by blinded RN
- Assessment Q30min x 2 hours
- Assessment at 24h by phone
- No demographic differences
Neurology 2007 - Outcomes

- Pain rated none/mild/moderate/severe
- Outcomes
  - Persistent pain free
  - Persistent headache relief
    - Mod/severe → none/mild
### Neurology 2007 - Results

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<tr>
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<th>Study</th>
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</thead>
<tbody>
<tr>
<td>Persistent pain relief</td>
<td>25%</td>
<td>19%</td>
<td>0.34</td>
</tr>
<tr>
<td>Subgroup with HA &gt;72hours</td>
<td>38%</td>
<td>13%</td>
<td>0.06</td>
</tr>
<tr>
<td>Normal functionality</td>
<td>67%</td>
<td>59%</td>
<td>0.20</td>
</tr>
<tr>
<td>Require rescue medication</td>
<td>13%</td>
<td>13%</td>
<td>1</td>
</tr>
<tr>
<td>Side effects</td>
<td>39%</td>
<td>26%</td>
<td>0.08</td>
</tr>
</tbody>
</table>
Results with nonsignificant trend toward less headache persistence and less functional disability

Limitations:

- Standardized medication regimen
- Did not use a numerical pain scale – more subjective “none-mild-moderate-severe”
- Underpowered for degree of difference seen
Headache 2008

- Type: RDBCT
- Setting: 4 EDs in Edmonton, Canada
- Patients: 126
- Therapy: At physician discretion
- Intervention: 15 mg Decadron vs placebo
- Results: Recurrence of headache at 48-72h and 7 days
Headache 2008 - Patients

- Convenience sample
- Inclusion: >18yo, hx of migraine, IHS criteria, IV established
- Exclusion: Pregnant, diabetic, PUD, allergic to steroids, already receiving steroids, immunosuppressed
Headache 2008 - Methods

- Phone contact at 72h and at 7 days
- Rate headache
- Describe recurrence
- Describe functional impairment
# Headache Article - Results

<table>
<thead>
<tr>
<th></th>
<th>Study</th>
<th>Control</th>
<th>OR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recurrence within 72 hours</td>
<td>22%</td>
<td>32%</td>
<td>0.6 (CI 0.3-1.3)</td>
</tr>
<tr>
<td>Recurrence within 7 days</td>
<td>28%</td>
<td>40%</td>
<td>0.6 (CI 0.3-1.3)</td>
</tr>
</tbody>
</table>
Headache 2008 – Discussion

- Trend towards benefit at 3 and 7 days
- Limits:
  - Convenience sample
  - Small
  - Underpowered
EMJ 2008

- Type: RDBCT
- Setting: 3 community teaching EDs in Australia
- Patients: 63
- Therapy: Compazine/Thorazine + IVF
- Intervention: 8 mg PO Decadron vs placebo
- Results: Recurrence of headache at 48-72h
EMJ 2008 – Patients

- Convenience sample
- Inclusion: Age >17, diagnosis of migraine by a physician, exacerbation of migraine
- Exclusion: “Findings inconsistent with migraine,” pregnancy, PUD, Type 1 DM, currently on steroids, allergic to steroids, prior enrollment, active fungal infection, headache requiring hospital admission
EMJ 2008 – Methods

- Randomization by study pharmacist
- Assessment at 48-72 hr by phone
- All patients got Compazine or Thorazine and IVF
- Blinded RN administered study medication or placebo
- Recurrence if patient had return of headache or it worsened >2 points on VAS
## Results

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<tr>
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</thead>
<tbody>
<tr>
<td>Recurrence</td>
<td>27%</td>
<td>39%</td>
<td>0.47</td>
</tr>
<tr>
<td>Subgroup with headache &lt;24h</td>
<td>15%</td>
<td>45%</td>
<td>0.08</td>
</tr>
</tbody>
</table>
Nonsignificant trend towards improvement in decadron group

Limitations:
- Excluded patients who had “findings inconsistent with migraine” but did not specify – selection bias?
- Small study
- Underpowered
- Convenience study
Type: RDBCT
Setting: Suburban community hospital in New Jersey
Patients: 181
Therapy: At physician discretion
Intervention: 10 mg IV Decadron or 40 mg PO prednisone x 2 days vs placebo
Results: Recurrence of headache at 48-72h
JEM 2011 - Patients

- Consecutive patients screened
- Inclusion: >17y, clinical dx of migraine
- Exclusion: pregnancy, fever, meningismus, atypical symptoms, uncontrolled DM or HTN, PUD, allergy to lactulose or steroids
JEM 2011 - Methods

- Randomized by study pharmacist
- Administered by blinded RN
- Assessment by VAS pre/post therapy
- Phone followup 24-72h
- Resolution of headache post discharge
  - Resolution with pain = 0
  - Recurrence with pain ≥ moderate
## JEM 2011 – Results

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<th>P value</th>
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</thead>
<tbody>
<tr>
<td>Recurrence</td>
<td>22%</td>
<td>32%</td>
<td>0.21</td>
</tr>
<tr>
<td></td>
<td>Prednisone 17%</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Decadron 27%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Resolution in ED</td>
<td>51%</td>
<td>49%</td>
<td>0.56</td>
</tr>
<tr>
<td>Rescue meds</td>
<td>36%</td>
<td>44%</td>
<td>0.42</td>
</tr>
</tbody>
</table>
JEM 2011 - Discussion

- Nonsignificant trend towards improvement in both arms of study

- Limitations:
  - Convenience sample
  - Lactulose as placebo
  - Underpowered
Acad EM 2008

- Type: Meta-analysis
- Studies: Online search in multiple databases
- 7 studies found for inclusion
Inclusion:

- Blinded, randomized, controlled trial
- Addressed migraine headache
- Patients treated in the ED
- Assessed steroid vs placebo
- Evaluated for percentage/rate of headache recurrence in 24-72 hours
Acad EM 2008 - Methods

- Study validity assessed with Jadad scoring
  - Assessed for blinding and randomization
- Data extracted and pooled
- Pooled risk ratio calculated
Acad EM 2008 - Results

- Risk of recurrence 24-72 hours
- RR 0.87
- CI 0.8 – 0.95
- 9.7% risk reduction
Results become significant when all data pooled

Around 10% reduction in risk of recurrent headache

Limitations:

- Data pooled
  - Different medication protocols and doses across studies
  - Most trials were convenience-sampled
  - Most trials allowed for physician discretion for treatment plan
BMJ 2008

- Type: Meta-analysis
- Studies: Online search through several online databases
- 7 trials included
Inclusion:
- Randomized controlled trials
- Assessed parenteral steroids
- ED or urgent evaluation in headache clinic
- Patients meeting criteria for migraine
- Assessed 24-72h recurrence
BMJ 2008 - Methods

- Validity scoring
- Data extracted and pooled
BMJ 2008 - Results

- Relative risk of recurrence
- RR 0.74
- CI 0.6 to 0.9
- NNT = 9
BMJ 2008 – Dosage

- Less than 15 mg Decadron
  - RR 0.8
  - CI 0.62 – 1.04
- More than 15 mg Decadron
  - RR 0.67
  - CI 0.5 – 0.91
- Nonsignificant difference
Followup period <48h
- RR 0.86
- CI 0.66 – 1.11

Followup period >48h
- RR 0.61
- CI 0.45 – 0.84

Significant difference p=0.038
BMJ 2008 - Discussion

- Results become significant when all data pooled
- Around 26% reduction in risk of recurrent headache
- NNT = 9
- Limitations:
  - Data pooled
    - Different medication protocols and doses across studies
    - Most trials were convenience-sampled
    - Most trials allowed for physician discretion for treatment plan
    - Only assessed IV/IM steroids
Final thoughts

- Many studies address this question
- Most of the RDBCTs negative
- Most of the RDBCTs also underpowered
- Both meta-analyses show significant results when data from the RDBCTs pooled
Final thoughts

- Clinically significant results?
  - Studies with 10-48% reduction in risk of migraine recurrence
  - Meta-analyses with 10-25% reduction
  - Treat 5-10 patients to avoid 1 recurrence
  - Side effects of single dose Decadron minimal, rare and self limited in most studies
Final thoughts

- I plan to start adding this to my treatment of uncomplicated migraine pts
- Probably will still not use for pregnant, diabetic/immunocompromised
Final thoughts

Questions?

Comments?

Thank you!
References


References

- Baden and Hunter. *Intravenous dexamethasone to prevent the recurrence of benign headache after discharge from the emergency department: a randomized, double-blind, placebo-controlled clinical trial.* CJEM 2006; 8:393-400.


- Donaldson et al. *Intravenous dexamethasone vs placebo as adjunctive therapy to reduce the recurrence rate of acute migraine headaches: a multicenter double-blinded placebo-controlled randomized clinical trial.* Am J EM 2007;26:124-130.

References


- Kelly et al. *Impact of oral Decadron versus placebo after ED treatment of migraine with phenothiazines on the rate of recurrent headache; a randomized controlled trial.* EMJ 2008; 25:26-29.

