Pediatric Migraines

CURRENT MANAGEMENT AND CONTROVERSIES IN THE EMERGENCY DEPARTMENT

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Faculty/Presenter Disclosure

• **Faculty**: Lawrence Richer

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• **Potential for conflict(s) of interest:**
  ◦ None to disclose
Mitigating Potential Bias

- All recommendations made without RCT supporting evidence in pediatrics is declared and only offered as a consideration.
Objectives

Review some migraine physiology
Review current evidence for the treatment of migraine in the ED (pediatric and some adult)
Consider some controversies, unanswered questions, and ‘best practices’ generally in the absence of supporting evidence in pediatrics
Phases of migraine

Aura and Cortical Spreading Depression
Cortex via cortical spreading depression (i.e. aura)

Hypothalamus

Arachnoid membrane

Trigeminovascular (neurovascular) unit

Parasympathetic output (pterygopalatine ganglion)

Migraine Generator
Brainstem activation as measured with PET in spontaneous human migraine without aura attacks
Executive resting-state network connectivity in migraine without aura.

Practice variation in Canada

- Dopamine antagonists (39.5%)
- Metoclopramide > prochlorperazine
- Fluid bolus (24.3%)
- Parenteral NSAIDS (9.8%)
- Significant variation between sites with all treatments

When should I image?
Abnormalities in 68 (21.0%)
When to image?

- Focal motor findings
  - Bilateral headache location associated with higher odds of secondary cause
- Other prolonged aura > 1 hour
- Risk factors for stroke
- Altered level of consciousness
- New and rapid (< 4 mins) onset headache
  - “First”, “Worst”, thunderclap
- Hypertension

Intravenous fluid bolus?
Fluid study

- Headache relief = VAS decrease > 20 mm
- Three (n=3; 6%) returned to the ED in 24 hours

First line therapy?
ED visits in pediatric health centers

• 35 pediatric EDs (2009–2012) - 32,124 children with migraine
  ◦ 5.5% had a return ED visit within 3 days
• Meds - nonopioid analgesics (66%); dopamine antagonists (50%) – metoclopramide or prochlorperazine; diphenhydramine (33%); ondansetron (21%); Triptans and opiate medications (3% each)
• Metoclopramide had a 31% increased odds for an ED revisit within 3 days compared with prochlorperazine.
  ◦ Ondansetron had similar revisit rates to those receiving dopamine antagonists.
• Diphenhydramine with dopamine antagonists was associated with 27% increased odds of an ED revisit

Prochlorperazine vs. Ketorolac

- n=62
- All received 10 ml/kg NS bolus over 30 mins
- Discharged with naproxen sodium for 24 hours

**Metoclopramide**

<table>
<thead>
<tr>
<th>Study</th>
<th>Metoclopramide</th>
<th>Placebo</th>
<th>Odds ratio (95% CI random)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coppola 1995&lt;sup&gt;15&lt;/sup&gt;</td>
<td>12/24</td>
<td>7/24</td>
<td>2.43 (0.74 to 7.98)</td>
</tr>
<tr>
<td>Tek 1990&lt;sup&gt;13&lt;/sup&gt;</td>
<td>16/24</td>
<td>5/26</td>
<td>8.40 (2.31 to 30.60)</td>
</tr>
<tr>
<td>Tfelt-Hansen 1980&lt;sup&gt;12&lt;/sup&gt;</td>
<td>19/40</td>
<td>18/47</td>
<td>1.46 (0.62 to 3.43)</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td>47/88</td>
<td>30/97</td>
<td>2.84 (1.05 to 7.68)</td>
</tr>
</tbody>
</table>

Test for heterogeneity: $\chi^2=4.91$, df=2, $P=0.086$

Test for overall effect: $z=2.05$, $P=0.04$

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Phenothiazine vs. metoclopramide

Approximately 15 mm mean difference on VAS in favor of phenothiazines

Other dopamine antagonists

- **Droperidol**
  - Butyrophenone
  - Mean difference in VAS ~ 40 mm
  - Possible risk of QT prolongation

- **Chlorpromazine**
  - Associated with increased risk of hospitalization in one retrospective study
Best practice – first line therapy?

• Prochlorperazine better than metoclopramide
• Consider droperidol if prochlorperazine not available and metoclopramide not sufficiently effective
  ◦ Probable increased risk of side-effects
Diphenhydramine

Akathisia Rating Scale

Objective: 2-minute seated observation
- Inability to remain seated (is the patient shifting)?
- Any semipurposeful or purposeless leg or foot movements?

Subjective: Three questions
- Do you feel restless within, or the urge to move, especially in the legs?
- Are you unable to keep your legs still?
- Are you unable to remain still, standing or sitting?

Prochlorperazine-induced akathisia = Change in objective scale ≥1 point + change in subjective scale ≥2 points (from preprochlorperazine to postprochlorperazine assessment).

Best practice – diphenhydramine?

• Diphenhydramine may reduce symptoms of akathisia and does not significantly increase sedation in one adult study

• **Consider** administering 1 mg/kg especially if patient previously experienced side-effects
  - One retrospective study suggests possible increased risk of return to ED with diphenhydramine use
Combination therapy?
Ketorolac

- Survey (n=40)
  - 78% always or sometimes use ketorolac among Alberta pediatric ED physicians
  - 84% of those use it in combination with other medications
- Ketorolac + metoclopramide / prochlorperazine
  - Used in 36% of ED presentations in Canada
Combination therapy

• Retrospective study
• Standardized regimen of
  ◦ Normal saline bolus
  ◦ Prochlorperazine
  ◦ Ketorolac
  ◦ Diphenhydramine

Trigeminal Sensitization

Non-selective COX A/B inhibitor may still be effective

Early treatment (when pain is mild) most effective
RCT metoclopramide +/- ketorolac

- n=53 (8 to 17 years)
  - n=26 ketorolac; n=27 placebo
  - no significant difference
- 1/4 mild akathisia
- 2/3 had recurrence of headache

Richer et al., not yet published
Second line therapy?
## Mixed Treatment Analysis

<table>
<thead>
<tr>
<th>Drug</th>
<th>Mean VAS difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Combination therapy (DHE + metoclopramide/neuroleptic)</td>
<td>-41 mm</td>
</tr>
<tr>
<td>Neuroleptic (e.g. prochlorperazine, droperidol)</td>
<td>-40 mm</td>
</tr>
<tr>
<td>NSAIDS</td>
<td>-25 mm</td>
</tr>
<tr>
<td>Opiods</td>
<td>-25 mm</td>
</tr>
<tr>
<td>Metoclopramide</td>
<td>-24 mm</td>
</tr>
<tr>
<td>DHE</td>
<td>-16 mm</td>
</tr>
<tr>
<td>Sumatriptan</td>
<td>-12 mm</td>
</tr>
<tr>
<td>MgSO⁴</td>
<td>-10 mm</td>
</tr>
</tbody>
</table>

Agency for Health Research and Quality.  
2012; Comparative Effective Review Number 84.
Dihydroergotamine – side effects

- skin reactions (29 percent) and/or local reactions (22 percent)
- sedation (20 percent)
- digestive issues (12 percent)
- nausea or vomiting (11 percent)
- chest symptoms (9 percent)
Best practice

• Combination therapy of DHE and metoclopramide or prochlorperazine
  ◦ Considered second line given side-effects
What next?
Magnesium

- Magnesium sulfate 30 mg/kg IV (max 2000 mg)
  - Infused over 30 min
  - 1000 mg dose diluted in 50–100 mL of 5% dextrose water or normal saline
  - Cardiorespiratory monitor
### Propofol

<table>
<thead>
<tr>
<th>Triage/Discharge</th>
<th>VAS Pain Score</th>
<th>Pain Reduction, %</th>
<th>No. Propofol Boluses</th>
<th>Total Dose, mg/kg</th>
<th>Disposition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient 1</td>
<td>8/0</td>
<td>100</td>
<td>3</td>
<td>0.81</td>
<td>Discharge</td>
</tr>
<tr>
<td>Patient 2</td>
<td>7/4</td>
<td>43</td>
<td>5</td>
<td>1.71</td>
<td>Admit</td>
</tr>
<tr>
<td>Patient 3</td>
<td>10/0</td>
<td>100</td>
<td>2</td>
<td>0.53</td>
<td>Discharge</td>
</tr>
<tr>
<td>Patient 4</td>
<td>9/0</td>
<td>100</td>
<td>3</td>
<td>0.86</td>
<td>Discharge</td>
</tr>
<tr>
<td>Patient 5</td>
<td>9/0</td>
<td>100</td>
<td>2</td>
<td>1.99</td>
<td>Discharge</td>
</tr>
<tr>
<td>Patient 6</td>
<td>9/2</td>
<td>78</td>
<td>3</td>
<td>3.72</td>
<td>Admit</td>
</tr>
<tr>
<td>Patient 7</td>
<td>10/6</td>
<td>40</td>
<td>4</td>
<td>2.32</td>
<td>Discharge</td>
</tr>
</tbody>
</table>

VAS pain score indicates 1 to 10 self-reported headache severity; pain reduction, percentage reduction in pain score from time of presentation to time of discharge.

Propofol avg bolus = 0.56 mg

Ketamine

- Small RCT (n=18)
- Intranasal ketamine 25 mg
- Reduced duration and severity of aura in patients with prolonged aura
When to admit?
When to admit?

- Partial response in ED
- Repeated visits to ED
- Dehydration, intractable vomiting
- Co-morbidities
  - Psychological
  - Other medical (e.g. hypertension)
- Further investigation
Dihydroergotamine

Side Effects
Chest pain (more common with sumatriptan), nausea (more common with DHE), drowsiness, flushing, neck stiffness, vertigo, weakness, and injection site reactions


- 70% response
- repeated dosing may be more effective (IN and IV)
- 3 and 6 day protocols
- nausea is a limiting SE
- sumatriptan SC may be superior initially, but DHE more likely to sustained pain free
Best practice - admission

• Admission may be associated with better outcomes when treating chronic daily headache
  ◦ Consult other disciplines (e.g. psychiatry)
• Hydration and carbohydrate replacement
• Consider
  ◦ Repeated dosing of DHE with neuroleptic / metoclopramide
  ◦ Intravenous lidocaine?

How can I prevent headache recurrence?
Dexamethasone

Best practice - recurrence

- Dexamethasone may reduce headache recurrence although no data available in children
- Consider dexamethasone 0.5 mg/kg IV (max 25 mg) single dose prior to discharge especially if known to experience recurrence
  - Adult studies support IV delivery, but PO bioavailability is high as well
Summary

• Migraine is a complex brain-based disorder

• Treatment of migraine in the ED is highly variable

• Neuroleptics (e.g. prochlorperazine) and combination therapy with DHE are likely most effective
Acknowledgements

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Hypothalamic activation during migraine attack

Non-traditional acute therapies

- Transcutaneous magnetic stimulation
- Vagal nerve stimulation
- Sphenopalatine ganglion stimulation