Triptans for Kids

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Some off-label uses of medications will be discussed

Goals

• Review Epidemiology and Diagnostic Criteria for migraine in children/adolescents
• Overview of treatment of acute migraine in children/adolescents
• Detailed review of the evidence for the use of triptans in children/adolescents

Epidemiology of Migraine

One-year period-prevalence for migraine by age and sex

Victor et al, Cephalalgia, 2010

Diagnostic Criteria for Migraine

A. At least 5 attacks
B. Duration 1-72 hours
C. At least two of:
  • Pounding quality
  • Moderate or severe intensity
  • Unilateral or bilateral location
  • Movement sensitivity
D. At least one of: (can be inferred from behavior)
  • Photophobia and phonophobia
  • Nausea and/or vomiting
E. Not attributable to another disorder

Disability from Migraine

• Disability from headache can be measured using PedMIDAS
• Areas of disability:
  - Missed school
  - Impaired performance in school
  - Impaired ability to participate in sports and other extra-curricular activities
• Impact on Quality of Life
• Impact on other family members (parents, sibs)

1Arruda, Neurology, 2012
Overview of Pediatric Acute Migraine Treatment

- **Non-pharmacologic measures:**
  - Quiet, dark environment
  - Encourage PO fluid intake

- **Pharmacologic measures:**
  1) Non-specific analgesics: Studied down to Age 4
     - Acetaminophen
     - NSAIDs: Naproxen, Ibuprofen, Ketorolac
  2) Dopamine receptor antagonists: e.g. prochlorperazine
  3) Dihydroergotamine (DHE): IM, IV, NS
  4) Opioids
  5) Barbiturate containing compounds (i.e. Fioricet)
  6) Triptans

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Triptans

- 5HT1B/1D receptor agonists
- Most efficacious taken when pain is still mild, which tends to be early in the attack
- 7 currently on the U.S. market
- 2 FDA-labeled for use in pediatric patients, and others studied
- 3 formulations: PO, nasal spray, injection
- Generally, oral formulations easiest, though not always possible due to nausea or speed of headache onset

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Question #1

You're seeing a 15 year old girl who has migraine attacks twice a month. The pain during her attacks is severe and associated with photophobia and phonophobia, but not nausea or vomiting. Naproxen (Aleve) helps a bit but she is still not able to get out of bed during an attack. Would you:

- Refer her to Neurology for treatment recommendations
- Curbside Neurology regarding which triptan would be appropriate in her age group and what dose
- Prescribe a triptan
- Prescribe another class of medication

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When to consider a triptan

- Child has moderate or severe pain with attacks
- NSAIDs or acetaminophen inadequately treat the pain

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When not to consider a triptan

- History of stroke or myocardial infarction
- Uncontrolled hypertension
- Hemiplegic or basilar-type migraine
- Pregnancy (relative contra-indication)
- In someone with triptan overuse → medication overuse headache; a risk when using triptans ≥10 triptan days/month for ≥3 months

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Question #2

You would like to try a triptan to treat the 15 year old patient from Question #1. Which one would you choose?

- Sumatriptan PO
- Sumatriptan NS
- Frovatriptan PO
- Zolmitriptan NS
- Rizatriptan MLT
**Sumatriptan**

- In clinical use in the U.S. since early 1990s
- 3 forms:
  - PO
  - Nasal spray (NS)
  - Subcutaneous injection (SC)
- Pediatric studies:
  - PO: one negative trial, but...
  - SC: Open-label use suggests efficacy
  - NS:
    - 3 positive double-blind, placebo-controlled trials
    - Labeled for use in 12-17 year-olds in the UK, now generic so unlikely to ever get labeled in U.S.

- 2004 Practice Parameter from American Academy of Neurology and Child Neurology Society:
  "Sumatriptan nasal spray is effective and should be considered for the acute treatment of migraine in adolescents"\(^4\)

### Sumatriptan NS

<table>
<thead>
<tr>
<th>Ages studied</th>
<th>Dose Used</th>
<th>Pain Relief</th>
</tr>
</thead>
<tbody>
<tr>
<td>6-9 years(^1)</td>
<td>20 mg</td>
<td>86% at 2 hours</td>
</tr>
<tr>
<td>12-17 years(^2)</td>
<td>5-20 mg</td>
<td>66% at 2 hours</td>
</tr>
<tr>
<td>8-17 years(^3)</td>
<td>10-20 mg</td>
<td>64% at 2 hours</td>
</tr>
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</table>

\(^1\)Ueberall, Neurology, 1999
\(^2\)Winner, Pediatrics, 2000
\(^3\)Ahonen, Neurology, 2004
\(^4\)Lewis, Neurology, 2004

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**Almotriptan**

- FDA-labeled for treatment of acute migraine in adolescents 12-17 years old
- Randomized, double-blind, placebo-controlled, parallel-group trial in 12-17 year olds of 6.25 or 12.5 mg PO: pain relief in 72-73% at 2 hours\(^1\)

\(^1\)Linder, Headache, 2008

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**Rizatriptan**

- FDA-labeled for treatment of acute migraine in ages 6-17
- Labeled dosing:
  - <40 kg: 5 mg MLT
  - ≥40 kg: 10 mg MLT
- Randomized, double-blind, placebo-controlled trial: 73-74% had pain relief at 2 hours\(^1\)
- Second RCT: higher 2 hour pain freedom rate in rizatriptan vs. placebo.\(^2\)

\(^1\)Ahonen, Neurology, 2006
\(^2\)Ho, Cephalalgia, 2012

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**Zolmitriptan**

- Off label for pediatric use
- Nasal spray formulation: better absorption than sumatriptan NS
- Positive trials:
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<th>Pain Relief</th>
</tr>
</thead>
<tbody>
<tr>
<td>6-18 years(^1)</td>
<td>2.5 mg PO</td>
<td>62% at 2 hours, 64% in those &lt;13</td>
</tr>
<tr>
<td>12-17 years(^2)</td>
<td>5 mg NS</td>
<td>58% at 1 hour</td>
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</tbody>
</table>
- Negative trial: A second oral trial was negative, placebo response rate very high (58%)

\(^1\)Evers, Neurology, 2006
\(^2\)Lewis, Pediatrics, 2007

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**Question #3**

- Your 15 year-old migraine patient responds within 2 hours to rizatriptan 10 mg MLT and has no side effects. However, about half the time the headache comes back the next morning. What do you tell her?
  - There’s no way to decrease the likelihood of recurrent headache
  - Take a second dose of rizatriptan before bed
  - Take naproxen with the rizatriptan
**Triptans combined with NSAIDS**

- In adults, efficacy of 85 mg sumatriptan/500 mg naproxen (pain relief at 2 hours and sustained pain relief 2-24 hrs) is greater than that of either agent alone.  

- Adolescents 12-17 (n=622) treated over 12,000 attacks open-label without any serious adverse events, providing safety data for this combination in adolescents.  

- Likely an NSAID/triptan class effect, so could substitute FDA-labeled triptans for the sumatriptan

1Brandes, JAMA, 2007  
2McDonald, Headache, 2011

**Question #4**

- You’re seeing a 7 year old whose migraine attacks are associated with significant nausea and vomiting. Prochlorperazine (Compazine) PR causes a dystonic reaction and does not relieve the headache. Which triptan might you consider for her?  

  - Sumatriptan PO  
  - Almotriptan PO  
  - Sumatriptan NS  
  - Rizatriptan MLT

**Summary Points**

- Triptans have been studied in pediatric patients, and two are now FDA-labeled for use in pediatrics.  

- For those who can tolerate oral medications during an attack: almotriptan (12-17) and rizatriptan (6-17) are both on label.  

- For those who can’t tolerate the oral route: sumatriptan NS is studied down to age 6, with zolmitriptan NS having better absorption so preferable for those >40 kg. Sumatriptan SC also an option.  

- Whenever possible, combining the triptan with an NSAID is likely to be helpful.

**Helpful References**


