

## Triptans for Kids

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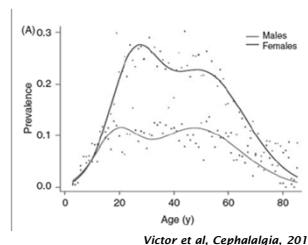
Some off-label uses of medications will be discussed

## 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



## Diagnostic Criteria for Migraine

- At least 5 attacks
- Duration 1-72 hours
- At least two of:
  - Pounding quality
  - Moderate or severe intensity
  - Unilateral or **bil**ateral location
  - Movement sensitivity
- At least one of: (can be inferred from behavior)
  - Photophobia and phonophobia
  - Nausea and/or vomiting
- Not attributable to another disorder

ICHD-II, Cephalalgia, 2004

## Disability from Migraine

- Disability from headache can be measured using PedMIDAS
- Areas of disability:
  - Missed school<sup>1</sup>
  - Impaired performance in school<sup>1</sup>
  - Impaired ability to participate in sports and other extra-curricular activities
- Impact on Quality of Life
- Impact on other family members (parents, sibs)

<sup>1</sup>Arruda, 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**

### Triptans

- 5HT<sub>1B/1D</sub> 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

### 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:
  - A) Refer her to Neurology for treatment recommendations
  - B) Curbside Neurology regarding which triptan would be appropriate in her age group and what dose
  - C) Prescribe a triptan
  - D) Prescribe another class of medication

### When to consider a triptan

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

### 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

### Question #2

- You would like to try a triptan to treat the 15 year old patient from Question #1. Which one would you choose?
  - A) Sumatriptan PO
  - B) Sumatriptan NS
  - C) Frovatriptan PO
  - D) Zolmitriptan NS
  - E) 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.

## Sumatriptan NS

Ages studied	Dose Used	Pain Relief
6-9 years <sup>1</sup>	20 mg	86% at 2 hours
12-17 years <sup>2</sup>	5-20 mg	66% at 2 hours
8-17 years <sup>3</sup>	10-20 mg	64% at 2 hours

· 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"<sup>4</sup>

<sup>1</sup>Ueberall, *Neurology*, 1999  
<sup>2</sup>Winner, *Pediatrics*, 2000  
<sup>3</sup>Ahonen, *Neurology*, 2004  
<sup>4</sup>Lewis, *Neurology*, 2004

## 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<sup>1</sup>

<sup>1</sup>Linder, *Headache*, 2008

## 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<sup>1</sup>
- Second RCT: higher 2 hour pain freedom rate in rizatriptan vs. placebo.<sup>2</sup>

<sup>1</sup>Ahonen, *Neurology*, 2006  
<sup>2</sup>Ho, *Cephalalgia*, 2012

## Zolmitriptan

- Off label for pediatric use
- Nasal spray formulation: better absorption than sumatriptan NS
- Positive trials:

Ages studied	Dose Used	Pain Relief
6-18 years <sup>1</sup>	2.5 mg PO	62% at 2 hours, 64% in those <13
12-17 years <sup>2</sup>	5 mg NS	58% at 1 hour

- Negative trial: A second oral trial was negative, placebo response rate very high (58%)

<sup>1</sup>Evers, *Neurology*, 2006  
<sup>2</sup>Lewis, *Pediatrics*, 2007

## 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?
  - A) There's no way to decrease the likelihood of recurrent headache
  - B) Take a second dose of rizatriptan before bed
  - C) 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<sup>1</sup>
- 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<sup>2</sup>
- Likely an NSAID/triptan class effect, so could substitute FDA-labeled triptans for the sumatriptan

<sup>1</sup>Brandes, JAMA, 2007  
<sup>2</sup>McDonald, 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?
- A) Sumatriptan PO  
B) Almotriptan PO  
C) Sumatriptan NS  
D) 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***

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