Pediatric Migraine: An Update
PROJECT ECHO
October 27, 2023

Dr. Rebecca Barmherzig, MD, FRCPC
Dr. Marissa Lagman-Bartolome, MD, FRCPC, FAHS
DECLARATION OF DISCLOSURE

Dr. Barmherzig
  • *Speakers Bureau/honoraria:* Miravo, TEVA

Dr. Lagman
  • *Advisory Board:* TEVA, Pfizer, Lundbeck, Miravo
  • *Research/Unrestricted Educational Grant:* Amgen, Lundbeck, TEVA, Abbvie (submitted to WCH Centre for Headache & HSC)
  • *Royalties as author:* Canadian Pharmacists Association

➢ We will only present the published data on any medications from these companies

➢ None of these companies contributed to the content of this presentation

➢ The off-label use of some therapies in the management of pediatric migraine will be discussed
LEARNING OBJECTIVES

1. Recognize the scope, distribution, and burden of diagnosed and undiagnosed headache disorders and migraine in children and youth

2. Review updates on acute and preventive therapies in the treatment of pediatric migraine

3. Apply evidence-based strategies for managing and preventing disability related to migraine in children and adolescents
I am comfortable managing children and youth with headache.

A. Yes, I usually feel confident managing these patients
B. No, I usually feel uncomfortable managing these patients
C. I often feel uncertain as to how to manage these patients
Migraine is a legitimate brain disease

Patients with headache are motivated to maintain their disability

ALL IN YOUR HEAD
WHO Global Burden of Disease

1st
Most expensive brain disorder

2nd
Leading cause of medical disability worldwide

3rd
Most common medical condition worldwide

GBD 2019 Diseases and Injuries Collaborators. Lancet (2020)
Prevalence

- **Pediatric migraine:** 7.7%
- **Chronic migraine:** 0.8% - 1.8% among children (12 - 17)

Impact

• Quality of life (QoL) measure studies have likened the impact of QoL in children with migraine to that in children with diabetes, arthritis, and cancer

Figure 4: Global years of life lived with disability (YLD) rate per 100 000 population due to migraine and tension-type headache by age, 2016
Shaded areas show 95% uncertainty intervals. Values are plotted at the midpoint of 5-year age categories.
Goals for pediatric migraine treatment

- Reduce disability
- Develop adaptive pain coping strategies
- Improve health-related quality of life
- Reduce risk of disease progression

CASE 1: Ethan

15y M with episodic migraine without aura since age 10

• Migraine attacks: moderate to severe, bilateral frontal pressure headache
• Frequency/duration: 2-3 days a month/ lasting 7-10 hours

• Associated features:
  • light and sound bothersome
  • prefers to rest during attacks when severe
  • nausea within 10-15 mins from headache onset

• Medications: acetaminophen and ibuprofen (no longer working)

• Past medical history: asthma, motion sickness, infant colic
• Exam: unremarkable
What would you offer him for acute therapy?

A. Sumatriptan nasal spray
B. Almotriptan tablet
C. Rizatriptan tablet
D. Zolmitriptan nasal spray
E. None of the above *(I am not comfortable trying any of these options)*
What are acute therapies?
Why are they important?

Modifiable risk factors for progression:

• Headache frequency
• Headache-related disability
• Ineffective acute treatment
• Opioids/barbituates

» Excessive opioid use is a risk factor for migraine progression to chronic migraine

Effective acute treatment

1. Rapid and consistent freedom from pain and most bothersome symptoms (MBS) without recurrence

2. Restored ability to function

3. Minimal need for repeat dosing or rescue medications

4. Optimal self-care and reduced subsequent use of resources (e.g. ED visits)

5. Minimal or no adverse effects
Challenges

• Heterogeneous population
• Difficulty with case definitions
• Outcome measures
• Confounders, confounders, confounders
• Placebo/ nocebo effects
Challenges in children

• Heterogeneous population
• Difficulty with case definitions
• Outcome measures
• Confounders, confounders, confounders
• Placebo/ nocebo effects – as high as 65%

Where to start?

Stratified care

• Severity
• Onset
• Associated symptoms/ MBS
• Duration of attacks

RED: I have to STOP

YELLOW: I have to SLOW down

GREEN: I can GO

Views and Perspectives

The Traffic Light of Headache: Simplifying Acute Migraine Management for Physicians and Patients Using the Canadian Headache Society Guidelines

Laguna-Bartalena AM, Lay C. Headache (2019)

2019 AAN/AHS Pediatric Migraine Treatment

**TRIPTANS: (level B)**

For ≥ 6 yo
- Rizatriptan ODT

For ≥ 12 yo
- Almotriptan tablet
- Rizatriptan
- Sumatriptan-Naproxen tablet
- Sumatriptan nasal spray
- Zolmitriptan nasal spray

**NSAIDs**
- Ibuprofen

**Anti-emetics**
It is important to treat early!!:

Treatment success drops from 80% to 50% as central sensitization occurs within 30-60 minutes from attack onset.


TGVS: Trigeminovascular system
CSD: cortical spreading depression
TNC: trigeminal nucleus caudalis

Early treatment
- greater % of patients achieving a 2-hour pain-free response (60% vs 32%)\(^3\)
- lower recurrence rate (13% vs 33%)
- lower adverse event rate (14% vs 29%)
## Resource

### Pediatric Migraine Action Plan - headachejournal.onlinelibrary.wiley.com/doi/epdf/10.1111/head.13681

<table>
<thead>
<tr>
<th>Green Zone – Prevent more headaches</th>
</tr>
</thead>
<tbody>
<tr>
<td>Do or take this every day to help prevent YOUR headaches:</td>
</tr>
<tr>
<td>- Get enough sleep; keep a regular schedule</td>
</tr>
<tr>
<td>- Eat healthy foods; don’t skip meals</td>
</tr>
<tr>
<td>- Drink enough water; avoid caffeine</td>
</tr>
<tr>
<td>- Get regular exercise; manage your weight</td>
</tr>
<tr>
<td>- Learn ways to relax; manage your stress</td>
</tr>
<tr>
<td>It may take 4-6 weeks to see a big change, so stick with it! Visit <a href="http://www.headachejournal.com">www.headachejournal.com</a> to manage your headaches.</td>
</tr>
</tbody>
</table>

### Yellow Zone – Don’t wait. Act fast to treat your headaches

- Go to school nurse or health office right away. Take your quick-relief medicine as soon as your headache starts:
  - Take: __________
  - Route: __________
  - Dose: __________
  - May repeat after __________ hours.

- Drink some water or sports drink if you can.

- Rest in a dark, quiet place for 30 minutes and practice your relaxation exercises (e.g., deep breathing, guided imagery). If you can:
  - You may need a different P3 activity, dark glasses, or a quiet place to work for a while.

### Red Zone – Time to get more help

- Contact your provider’s office if:
  - Your headache is much worse, lasting much longer than usual
  - Go to the Emergency Room if:
    - You have new and very different symptoms like loss of vision, unable to move one side of your face or body, trouble walking or talking, very confused or unable to respond

- Call 9-1-1 if child loses consciousness or has stroke-like symptoms

### I authorize the quick-relief medication(s) listed in the Yellow Zone:

- Provider’s Signature: __________ Date: __________
- Parent/Guardian’s Signature: __________ Date: __________
- [ ] to be administered by school personal
- [ ] to be self-administered by student
- [ ] to be administred only by parent

### Pediatric Migraine Action Plan (PedMAP): Headache Toolbox

#### Tools for life

- Children and adolescents with headaches need to learn how to manage life with headaches at home, at school and with friends.

- CBT teaches you new ways of thinking about pain and new ways of responding to it by setting goals, pacing activity, and using your brain to turn down your body’s pain response. Visit http://www.foundationuk.org to learn more about CBT and find a therapist.
Therapeutic Management of Acute Migraine in Pediatrics (PeCaHN) - https://migrainecanada.org/medication-dosing-advice/

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Dosage</th>
<th>Interval</th>
<th>Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ibuprofen</td>
<td>16 mg/kg/dose</td>
<td>q6-8 h pm</td>
<td>600 mg/dose, 40 mg/kg/day or 2400 mg/day</td>
</tr>
<tr>
<td>Naproxen</td>
<td>5-7 mg/kg/dose</td>
<td>q8-12 h pm</td>
<td>500 mg/dose, 10 mg/kg/day or 1900 mg/day</td>
</tr>
<tr>
<td>Acetaminophen</td>
<td>15 mg/kg/dose</td>
<td>q4-6 h pm</td>
<td>1000 mg/dose, 75 mg/kg/day or 4000 mg/day</td>
</tr>
</tbody>
</table>

## Specific Treatment of Migraine Attacks for Patients

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Dosage</th>
<th>Interval</th>
<th>Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rizatriptan Tablets &amp; ODT</td>
<td>≤ 40 kg: 5 mg</td>
<td>Can repeat in 2 hours, max 2 doses/24 hours</td>
<td>≤ 40 kg: 10 mg, ≤ 40 kg: 20 mg</td>
</tr>
<tr>
<td>≥ 40 kg: 16 mg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zolmitriptan Tablets, ODT &amp; nasal spray</td>
<td>≤ 40 kg: 2.5 mg PO</td>
<td>Can repeat in 2 hours, max 2 doses/24 hours</td>
<td>≤ 40 kg: 5 mg, ≤ 40 kg: 10 mg</td>
</tr>
<tr>
<td>≥ 40 kg: 5 mg PO</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sumatriptan nasal spray</td>
<td>≤ 40 kg: 5 mg</td>
<td>Can repeat in 2 hours, max 2 doses/24 hours</td>
<td>≤ 40 kg: 10 mg, ≤ 40 kg: 20 mg</td>
</tr>
<tr>
<td>≥ 40 kg: 20 mg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Almotriptan</td>
<td>≤ 40 kg: 6.25 mg PO</td>
<td>Can repeat in 2 hours, max 2 doses/24 hours</td>
<td>≤ 40 kg: 12.5 mg, ≤ 40 kg: 25 mg</td>
</tr>
<tr>
<td>≥ 40 kg: 12.5 mg PO</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sumatriptan/Naproxen combined tablet</td>
<td>≤ 40 kg: Do not use due to the SDE of naproxen which is too high</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

## Anti-Nausea Medication

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Dosage</th>
<th>Interval</th>
<th>Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ondansetron liquid, tablets and ODT</td>
<td>0.03-0.2 mg/kg/dose PO</td>
<td>q8 h pm</td>
<td>8 mg/dose</td>
</tr>
<tr>
<td>Metoclopramide liquid, tablets</td>
<td>0.1-0.3 mg/kg/dose PO</td>
<td>q6-8 h pm</td>
<td>10 mg/dose</td>
</tr>
<tr>
<td>Prochlorperazine tablets and suppositories</td>
<td>0.1 mg/kg/dose PO/PR</td>
<td>q6-8 h pm</td>
<td>10 mg/dose</td>
</tr>
</tbody>
</table>
Back to our case…. 6 months later

- Migraine attacks: no change over the past 6 months, persist at frequency of 2-3 days a month and can last up to a full day
- +++ severe and nausea within 10-15 mins from headache onset
- Medications: sumatriptan and zolmitriptan NS, almotriptan, rizatriptan, naproxen (no response, persistent vomiting with attacks)
- Exam: unremarkable
Which of the following off-label treatments would you recommend next?

A. Lidocaine nasal spray
B. CGRP antagonists (oral gepants)
C. Neuromodulation device
D. Nerve block
E. None of the above *(I am not comfortable trying any of these options)*
The landscape is changing

Rethinking known targets
Advancing technology
Evaluating new targets
Original Article

A randomized controlled pilot study of intranasal lidocaine in acute management of paediatric migraine and migraine-like headache

Kate Maki MD¹,², Quynh Doan MDCM¹,², Kendra Sih PharmD¹, Karly Stillwell BSc², Alaina Chun BSc², Garth Meckler MDS¹,²

¹Department of Pediatrics, University of British Columbia, Vancouver, British Columbia, Canada
²BC Children’s Hospital Research Institute, Vancouver, British Columbia, Canada
SPG blockade

Barre Method
https://practicalneurology.com/articles/2021-may/sphenopalatine-blocks-without-catheter/pdf
Triptan/ NSAID Combination

Sumatriptan + naproxen 85/500 mg

- Approved by FDA in 2008
- Approved by Health Canada in September 2020
- For acute migraine treatment in adults and adolescents (ages 12-17)
  - Pain free at 2h: 24% vs 10% (37 % vs 18%, adolescents)
  - Significant improvement of nausea, photophobia, phonophobia at 2h

New 5-HT1 target

**Lasmiditan** - selective 5-HT1F agonist
- FDA approved October 2019 in adults

**Systematic review and meta-analysis in adults**¹
- 79.2% ≥1 cardiovascular risk factor at baseline
- Significant pain and most bothersome symptom freedom at 2h (200 mg superior efficacy >100 mg)

**Safety and tolerability in pediatric migraine patients**²
- 100 mg (<40 kg) and 200 mg (>40-55kg): no safety or tolerability issues
- Peak at 1.5h and T1/2 is 4h

*Precautions*: risk of driving impairment, CNS depression (sedation, dizziness)

➢ **Pediatric phase 3 RCT in progress: ~completion January 2025**
  https://clinicaltrials.gov/ct2/show/NCT04396236

CASE 2: Penny

16y F athlete with infrequent migraine without aura since age 13

- Jan 2023: gradual increase in headache frequency to 4-5 days a week (duration: 4-12 hours)
- Headache RED flags: none
- Recent diagnosis of severe depression

- Previous failed headache medications: ibuprofen, naproxen, almotriptan, zolmitriptan, sumatriptan, rizatriptan

- Current medications: sumatriptan-naproxen
- Exam: unremarkable
When do you start migraine preventive treatment?

Consider and discuss preventive treatment in pediatric migraine patients with the following:

- frequent headache (>4 headache days a month or 3-4 migraine attacks a month for ≥3 months) and migraine-related disability (PedMIDAS score ≥30) or both (Level B)

- medication overuse (taking triptans, ergot, opioids and combination analgesics > 9 days/months or taking OTC analgesics >14 days/month for ≥3 months) (Level B)

Oskoui M, et al, Neurology, 2019
How do we counsel parents about preventive medications?

• Inform patients and caregivers: Majority of preventive meds are NOT superior to placebo (Level B)\(^1\)

• Shared decision making → use of short-term treatment trials for a minimum of 2 months (Level B)\(^1\)

Her mother is asking if we can start with non-prescription therapies?

<table>
<thead>
<tr>
<th>Nutraceutical</th>
<th>Recommendation</th>
<th>Strength</th>
<th>Level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coenzyme Q10</td>
<td>Use</td>
<td>Weak</td>
<td>Low</td>
</tr>
<tr>
<td>Magnesium</td>
<td>Use</td>
<td>Weak</td>
<td>Low</td>
</tr>
<tr>
<td>Butterbur</td>
<td>Do not use</td>
<td>Weak</td>
<td>Low</td>
</tr>
<tr>
<td>Other petasites formulations</td>
<td>Do not use</td>
<td>Weak</td>
<td>Low</td>
</tr>
<tr>
<td>Polyunsaturated fats</td>
<td>Do not use</td>
<td>Weak</td>
<td>Low</td>
</tr>
<tr>
<td>Ginkgolide B</td>
<td>Do not use</td>
<td>Weak</td>
<td>Low</td>
</tr>
<tr>
<td>Riboflavin (Vitamin B2)</td>
<td>Do not use</td>
<td>Weak</td>
<td>Low</td>
</tr>
</tbody>
</table>

Since 2014: Two more reviews, conclusions basically the same – insufficient evidence all around, most promise for prevention is for Coenzyme Q10 and magnesium.

---

Back to our case…

• She took Magnesium citrate and Coenzyme Q10 for 3 months.
• Partial response: 15 days a month (less disabling)

• What is your next step?
Goals for preventive treatment

≥ 50% ↓ in frequency
AND/OR
≤ 4 days/month

2019 AAN/AHS Pediatric Migraine Treatment

Level B recommendation
- Propranolol
- Topiramate
- Amitriptyline + CBT

Off label treatment:
- Onabotulinum toxin A
- Venlafaxine
- Duloxetine
- Candesartan
- Cinnarizine
- Valproic acid
- Gabapentin
- Flunarizine
- Cyproheptadine
- Nadolol/Metoprolol

QUESTION:
Which prevention therapy would you recommend for Penny?

A. Amitriptyline
B. Propranolol
C. Topiramate
D. Onabotulinum toxin A
E. None of the above (I am not comfortable starting any of the above medications for this patient)

Penny is 16 yo
- Jan 2023: 4-5 days a week 4-12 hours
- Recent diagnosis of severe depression
- Previous failed headache medications: ibuprofen, naproxen, almotriptan, zolmitriptan, sumatriptan, rizatriptan
- Current medications: sumatriptan-naproxen
## Tips on how to choose the preventative treatment for your patient

<table>
<thead>
<tr>
<th>Disorder + Migraine</th>
<th>Consider</th>
<th>Avoid or Caution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depression</td>
<td>Venlafaxine*, Sertraline*, Duloxetine*</td>
<td>B-blocker, Topiramate, Amitriptyline (increase suicidal risk in adolescents)</td>
</tr>
<tr>
<td>Anxiety</td>
<td>Amitriptyline, Venlafaxine*, Propranolol, Gabapentin*</td>
<td>Sertraline (lower doses may worsen anxiety)</td>
</tr>
<tr>
<td>Sleep disturbance</td>
<td>Amitriptyline, Gabapentin*, Melatonin</td>
<td>Topiramate</td>
</tr>
<tr>
<td>Obesity</td>
<td>Topiramate, Candesartan*</td>
<td>Amitriptyline, Valproate</td>
</tr>
<tr>
<td>Epilepsy</td>
<td>Topiramate, Valproate*, Gabapentin*</td>
<td></td>
</tr>
</tbody>
</table>

*Off-label treatment
Penny is asking how long she has to take her preventive medication?

A. 1-2 months  
B. 3 months  
C. 4 months  
D. 6-12 months  
E. I am not comfortable answering her question

2. Powers SW. JAMA Netw Open 2021;4(7):e2114712
When do you taper off her preventive medication?

• Monitor for medication effectiveness and side effects → stop once good migraine control is established for 6-12 months² (Level B)¹

2. Powers SW. JAMA Netw Open 2021;4(7):e2114712
Back to our case…. 1 year later

- Headache frequency: daily and constant
- 70% ++ migraine features
- No headache RED flags
- **Previous failed headache medications:**
  - **ACUTE:** ibuprofen, naproxen, diclofenac, almotriptan, zolmitriptan, sumatriptan, rizatriptan
  - **PREVENTIVE:** topiramate and amitriptyline (worsened depression), gabapentin, nadolol, flunarizine
- **Current medications:**
  - **ACUTE:** sumatriptan-naproxen, lidocaine NS, Cefaly (partial response)
  - **PREVENTIVE:** venlafaxine 150 mg/day
- Exam: unremarkable
What preventive therapy option would you recommend for this patient next?

A. CGRP targeted therapy
B. Neuromodulation therapy
C. Onabotulinum toxin A
D. Weekly pericranial nerve blocks
E. None of the above (I am not comfortable starting this patient with any of the above options)
What is the role of interventional headache procedures in pediatric migraine treatment?
## Interventional Procedures

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Pediatric data</th>
<th>Level of pediatric evidence</th>
<th>Approvals</th>
</tr>
</thead>
</table>
| Onabotulinum toxin A (chronic migraine) 1,2,3 | ✓              | • Open-label case series  
• Parallel-group RCT of one injection series (N=125) *Negative trial*  
• Cross-over RCT of one injection series (N=15)  
• Several retrospective review/case series: decrease in pain intensity, cumulative benefit, 50% decrease HA frequency | X         |
| Nerve blocks4,5,6                      | ✓              | • Chronic migraine, status migrainosus, chronic refractory migraine, NDPH using Lidocaine  
• Open-label case series (4 with ONB; 1 with SPG)  
• 53-70% improvement (partial to complete)  
• Reduction in pain scores by 2.4 | X         |

What is the role of emerging therapies in pediatric migraine management?
<table>
<thead>
<tr>
<th>Neuromodulation devices</th>
<th>Pediatric Data</th>
<th>Level of evidence</th>
<th>Approvals/clearances</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-invasive vagal nerve stimulation (GammaCore)</td>
<td>✓ (acute)</td>
<td>• Prospective observational open-label acute study (N=9)</td>
<td>US + CA ≥12yo</td>
</tr>
<tr>
<td>Electrical trigeminal nerve stimulation (Cefaly)</td>
<td>✓</td>
<td>• Retrospective study (N=154 visits): reduce intensity</td>
<td>✗</td>
</tr>
<tr>
<td>Remote electrical neuromodulation (Nerivo)</td>
<td>✓ (acute)</td>
<td>• Prospective open-label acute study (N=71)</td>
<td>US ≥12yo</td>
</tr>
<tr>
<td>Single pulse transcranial magnetic stimulation (sTMS mini)</td>
<td>✓</td>
<td>• Prospective open-label study (N=21)</td>
<td>US ≥12yo</td>
</tr>
</tbody>
</table>

* Available in Canada

Why target CGRP for pediatric migraine treatment?

CGRP levels are elevated in pediatric migraine patients

**Plasma CGRP levels (pg/ml) in pediatric patients**

<table>
<thead>
<tr>
<th></th>
<th>Migraine-NA</th>
<th>Migraine-A</th>
<th>Non-migraine headache</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Migraine</td>
<td>291</td>
<td>240</td>
<td>51</td>
<td>53</td>
</tr>
</tbody>
</table>

# Emerging Pediatric Migraine Therapies

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Pediatric Data</th>
<th>Level of evidence</th>
<th>Approvals/clearances</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CGRP targeted therapies</strong></td>
<td></td>
<td>• Phase III trials underway for ubrogepant, rimegepant &amp; atogepant</td>
<td>✗</td>
</tr>
<tr>
<td>Gepants</td>
<td>✗</td>
<td>• Retrospective observational studies (N=112 with mixed mAb and N=9 with eptinezumab)</td>
<td>✗</td>
</tr>
<tr>
<td>CGRP mAbs</td>
<td>✓</td>
<td>• Phase III trials underway for all 4 antibodies</td>
<td>✓</td>
</tr>
</tbody>
</table>

## CGRP targeted migraine therapies

<table>
<thead>
<tr>
<th>Medications</th>
<th>Mechanism</th>
<th>Indication</th>
<th>Route</th>
<th>Adult Dose</th>
<th>Pediatric Trial</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zavegepant</td>
<td>receptor antagonist</td>
<td>acute</td>
<td>nasal</td>
<td>prn</td>
<td>✗</td>
</tr>
<tr>
<td>Rimegepant</td>
<td>receptor antagonist</td>
<td>acute and preventive</td>
<td>po</td>
<td>50-100 mg prn/EOD</td>
<td>✓</td>
</tr>
<tr>
<td>Ubrogepant*</td>
<td>receptor antagonist</td>
<td>acute</td>
<td>po</td>
<td>50-100 mg prn</td>
<td>✓</td>
</tr>
<tr>
<td>Atogepant*</td>
<td>receptor antagonist</td>
<td>preventive</td>
<td>po</td>
<td>daily</td>
<td>✗ ✓</td>
</tr>
<tr>
<td>Erenumab*</td>
<td>mAb (receptor)</td>
<td>preventive</td>
<td>SC</td>
<td>70-140 mg monthly</td>
<td>*** ✓</td>
</tr>
<tr>
<td>Galcanezumab*</td>
<td>mAb (ligand)</td>
<td>preventive</td>
<td>SC</td>
<td>240, 120 mg monthly</td>
<td>✓</td>
</tr>
<tr>
<td>Fremanezumab*</td>
<td>mAb (ligand)</td>
<td>preventive</td>
<td>SC</td>
<td>225/675 mg monthly/quarterly</td>
<td>✓</td>
</tr>
<tr>
<td>Eptinezumab*</td>
<td>mAb (ligand)</td>
<td>preventive</td>
<td>IV</td>
<td>100-300 mg quarterly</td>
<td>✗ ✓</td>
</tr>
</tbody>
</table>

*Available in Canada

**Pediatric trials in Children’s Hospital, LHSC

**Pediatric trial in Sickkids and Children’s Hospital, LHSC
### Suggested indications, contraindications and monitoring for use of CGRP monoclonal antibodies in children and adolescents with migraine

<table>
<thead>
<tr>
<th>Indications</th>
<th>Contraindications</th>
<th>Monitoring</th>
</tr>
</thead>
</table>
| • ≥8 HA days/month  
• PedMIDAS score >30  
• Failure >2 preventive meds  
• Post-pubertal adolescent, or pre-pubertal child in carefully selected cases | • Disturbed BBB  
• Severe cardiovascular disease, recent stroke  
• Pregnancy, planned pregnancy or breast feeding | • BP and HR  
• Pubertal status  
• Bone health  
• Linear growth  
• Weight/BMI  
• Infections  
• Pregnancy status |

Szperka C, et al.. Headache (2018)
Future/Ongoing pediatric migraine trials\textsuperscript{1,2}

**ACUTE treatment:**
- Intranasal sphenopalatine ganglion block 2\% Lidocaine: phase 3 recruiting
- Propofol infusion: open label, recruiting
- Sumatriptan nasal powder: phase 3, recruiting
- Dexamethasone IV: phase 1
- Nitrous oxide
- Occipital nerve blocks
- Prochlorperazine vs Prochlor + Ketorolac
- Intranasal lidocaine
- VPA and DHE
- IV fluids
- IV Ketorolac and Metoclopramide
- Oral Dexamethasone for acute migraine recurrence in ED

**Preventive treatment:**
Alpha lipoic acid (ALA) 300 mg VS Flunarizine 5 mg: phase IV, open label, recruiting

\textsuperscript{1} Iannone LF et al, Life. (2022)  
\textsuperscript{2} clinicaltrials.gov
Natural history of pediatric migraine

Factors with favorable outcome

- Age of onset after 6 years old
  Earlier onset < 6y: 4.2 times >> risk of unfavorable outcome
  Onset 6-10y: 82% good outcome, 12% + prophylaxis

Male gender is associated with remission

Early developmental disorders
  Associated with persistence of migraine

Key Recommendations

- Recognize, diagnose and start migraine treatment early
- Counsel that lifestyle factors can influence frequency
- Inform re: placebo effect
- Discuss evidence for:
  - CBT + Amitriptyline (chronic migraine)
  - Topiramate
  - Propranolol
- Monitor effectiveness & counsel re: risks/benefits of stopping preventative medications
- Screen and manage comorbidities (i.e., mood and anxiety symptoms & disorders, etc)

© SOrr, Modified

Oskoui et al. Neurology 2019. 59(8);1144-1157.
Key Takeaways

- The importance of migraine management in children of adolescents
  - Education
  - Shared-decision making
  - Individualized treatment

- Always review 4 key aspects of treatment
  - Acute treatment
  - Preventive treatment
  - Education and Self-management
  - Comorbidity management
“We are now in an era where we understand what is happening in migraine inside of the brain. Based on our understanding, we’re designing treatment options.”

- Pediatric RCTs and novel trial designs needed *(crossover design, single-blind placebo lead-in)*
- When in doubt: be guided by clinical characteristics, stratify approach
A child’s brain is no place for migraine

https://headaches.org/pediatric-migraine-studies/ (modified)
Become a member!
Open to all health care professionals

Access to:
Educational Events | Clinical Forum | Quarterly Newsletters

info@headachesociety.ca
www.headachesociety.ca
@CanHeadacheSoc
Any questions?
Appendix
**SHARED: Lifestyle changes to promote headache health**

<table>
<thead>
<tr>
<th><strong>Headaches in Kids and Teens: SHARED Model of Care</strong></th>
</tr>
</thead>
</table>
| **Supplements** | **Magnesium citrate** (9 mg/kg/day): 150-450 mg/day  
**Coenzyme Q10** (1-3 mg/kg/day): 100-200 mg/day |
| **Screen time** | **Screen** exposure (high level >4 hours/day): may trigger migraine, negatively impacts sleep  
**Screen overuse** >2 hours/day: linked to mood and anxiety symptoms, decreases activity level |
| **Hydration** | **Increase water**, limit caffeinated drinks, no energy drinks, avoid sugary drinks |
| **Headache diary** | Use **headache diary** to identify triggers, headache pattern, response to treatment (Level C) |
| **Activity and Avoid triggers** | Out everyday, socialize (face to face)/school, physiotherapy, limit screen/computer activity |
| **Routine sleep** | Regular sleep and wake time, avoid naps  
3-5 yo: 10-13 hours  
6-12 yo: 9-12 hours  
13-18 yo: 8-10 hours |
| **Eating** | **NO** skipped meals, high protein for breakfast, whole>frozen>canned food, monitor foods which can trigger headaches (MSG, caffeine, alcohol, cured and preserved meats, aspartame) |
| **Downtime** | Stress management and relaxation (**CBT**, mindfulness, biofeedback therapy) |

**Focus on function >>**

*Note:  Monsour D, Lay C, Ansari T, Lagman-Bartolome AM, Curr Neurol Neurosci Rep, 2020; 20:53*