Cognitive Behavioral Therapy and Amitriptyline in Pediatric Chronic Migraine: A Randomized Clinical Trial

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Chronic Migraine in Youth

- 15 or more headache days/month
- Meet ICHD-II migraine criteria
- Typically severe level of disability
- No evidence-based treatments
Chronic Migraine in Youth

- In general population, ages 12-17, affects about 1%
- Yet, 60% of youth with CM have not seen a headache provider in past year
- But, up to 2 out of 3 patients that do seek headache specialty care
- Youth with migraine become adults with migraine
Trial Rationale

- Real world, treatment seeking sample
- Ethical and practical considerations/Choice of control arm
- Choice of prevention medication
- CBT based upon proven protocol & specific headache treatment evidence
Trial Design

- Amitriptyline (Goal Dose: 1 mg/kg/day)
- Cognitive Behavioral Therapy
- Attention Control and Education Therapy

Two Arms:
1. CBT + A
2. ATT + A
Cognitive Behavioral Therapy

• Headache Management Principles
• Biofeedback-Assisted Relaxation Training
• Activity Pacing
• Recognizing Negative Thoughts and Using Calming Statements
• Problem-Solving Skills
• Parent Coaching & Reinforcement of Coping
Inclusion Criteria

• Chronic Migraine by ICHD-II criteria

• 15 or more headaches/month based upon prospective diary

• Male or Female between ages 10-17

• PedMIDAS Disability Score > 20, indicating at least moderate disruption in daily activities
Exclusion Criteria

- Abortive Medication Overuse
- Present or Lifetime psychiatric diagnosis meeting DSM-IV criteria for bipolar disorder, major depressive disorder, or psychosis (based upon K-SADS interview)
- PedMIDAS Score > 140, indicating need for multi-systemic therapies to address very significant level of disability
Exclusion Criteria

- No other current prophylactic antimigraine medication
- Other chronic pain condition such as fibromyalgia, complex regional pain syndrome-II
- Abnormal findings on ECG
- Disallowed Medications: opioids, antipsychotics, antimanics, barbituates, benzodiazepines, muscle relaxants, sedatives, tramadol, herbal products
Trial Time Line

• Medical Assessment and Screening
• Psychosocial Assessment and Screening
• Randomization

• Treatment Phase (Total of 20 weeks)
  – Weekly for 8 weeks
  – Monthly for 3 months

• Follow-Up Phase (Total of 12 months)
  – Every 3 months
Aims

• Evaluate Safety

• Evaluate Efficacy
  – Reduction of Headache Days
  – Reduction of Disability
  – Clinical Impact: ≥ 50% Headache Day Reduction & Disability Grade of Mild to None

• Evaluate Durability
### Demographics

<table>
<thead>
<tr>
<th></th>
<th><strong>CBT + A</strong> (N=64)</th>
<th></th>
<th><strong>ATT + A</strong> (N=71)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>14.4 ± 1.9</td>
<td><strong>Gender</strong></td>
<td>79.7% female</td>
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</tr>
<tr>
<td><strong>Headache Days</strong></td>
<td>21.4 ± 5.4</td>
<td><strong>Disability</strong></td>
<td>21.2 ± 5.1</td>
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<tr>
<td><strong>Disability</strong></td>
<td>67.3 ± 29.8</td>
<td>(PedMIDAS)</td>
<td>69.2 ± 33.8</td>
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<tr>
<td></td>
<td>(Severe Grade)</td>
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<td>(Severe Grade)</td>
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</tbody>
</table>
Outcomes

- Average final dose of amitriptyline = 1.01 mg/kg/day
- No serious, related, and unexpected Adverse Events
- Total AEs = 199
Outcomes

• **Primary Endpoints:** Headache Days & Disability

• Treatment Credibility and Integrity (Both arms had high levels of credibility to participants and parents)
50% or More Headache Days Reduction

Proportion of Participants

Baseline

ATT+A

CBT+A
PedMIDAS < 20%

Baseline

Proportion of Participants

ATT+A

CBT+A
HEADACHE CENTER

Headache Days

Headache Days Per Month (Mean)

Baseline
Posttest
3 Month
6 Month
9 Month
12 Month

ATT+A
CBT+A

Cincinnati Children's
PedMIDAS Score (Mean)

- **ATT+A**
- **CBT+A**

Baseline | Posttest | 3 Month | 6 Month | 9 Month | 12 Month
---|---|---|---|---|---
PedMIDAS Score (Mean) | | | | | |
50% or More Headache Days Reduction

Proportion of Participants

Baseline  3 Month  6 Month  9 Month  12 Month

ATT+A

CBT+A
Conclusions

• CBT + Amitriptyline is safe, well tolerated, credible, efficacious, & durable

• 1st RCT to demonstrate clinically significant impact in pediatric chronic migraine
Conclusions

• Outcomes compare favorably to only FDA approved therapy for adults with chronic migraine (onabotulinumtoxin A)

• Need to test CBT + Placebo
Implications

• Given measured clinical impact, suggests a new standard of care

• Translation to practice in Cincinnati – A work in progress
Application in Current Practice

- Manualized treatment that can be basis of training

- Need for more trained providers and integration with neurology practice

- Evidence-based care needs to be reimbursed
Questions

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• Participants
• NINDS (R01NS050536)
• Cincinnati Children’s Headache Center
• Powers’ Lab Team