Cognitive Behavioral Therapy plus Amitriptyline for Chronic Migraine in Children and Adolescents: A Randomized Clinical Trial

BACKGROUND

- Migraine is ranked in the 2010 Global Burden of Disease Study as the eighth leading cause of years lived with disability
- There are currently no interventions approved by the FDA for the treatment of chronic migraine in young persons; thus clinical practice is not evidenced based and is quite variable
- A high priority research need in headache medicine is the testing of multimodal treatments against pharmacotherapy alone

OBJECTIVE

- To determine the benefits of cognitive behavioral therapy (CBT) when combined with amitriptyline vs headache education plus amitriptyline in youth aged 10-17 diagnosed with chronic migraine

METHODS

- **Design:** randomized, single-blind, parallel-group, single-centered, clinical trial
- **Inclusion criteria:** diagnosis of chronic migraine made by a board-certified headache specialist using the ICHD-II criteria, 15 or more dats with headache per month measured by a prospective 28-day headache diary, and Pediatric Migrain Disability Assessment Score (PedMIDAS) of greater than 20 points, indicating at least moderate disability
- **Exclusion criteria:** medication overuse, current use of amitriptyline or other prophylactic antimigraine medication within a period equivalent to less than 5 half-lives before study screening, other chronic pain condition such as fibromyalgia or complex regional pain syndrome II, abnormal electrocardiogram, severe orthostatic intolerance or dysregulation, documented developmental delay or impairment, severe psychiatric comorbidity, PedMIDAS of greater than 140 points, pregnancy or being sexually active without use of medically accepted form of contraception, and use of disallowed medications including opioids, antipsychotics, antimanics, barbiturates, benzodiazepines, musclerelaxants, sedatives, tramadol, or herbal products
- **Primary outcome measure:** change in days with headache per month (28-days) collected via prospective headache diary
- **Secondary outcome measure:** change in total PedMIDAS score (0-10 [little to no disability]; 11-30 [mild disability]; 30-50 [moderate disability]; and > 50 [severe disability])

RESULTS

- Primary outcome – CBT resulted in a decrease of 11.5 days with headache vs 6.8 days with headache education (score difference, 4.7[95% CI, 1.7-7.7] days; p=0.002.
    - Clinical – 66% of the CBT group had a 50% or greater reduction in headache days vs. 36% in the headache education group (OR 3.45 [95% CI, 1.66-7.15]; p<0.001)
- Secondary outcome – PedMIDAS was decreased by 52.7m points with CBT vs 38.6 points with headache education (score difference, 14.1[95% CI, 3.3-24.9] points; p=0.01)
    - Clinical – 75% of the CBT group had a PedMIDAS score of less than 20 points vs 56% of the headache education group (OR 2.36 [95% CI, 1.10-5.10], p = 0.02)

STRENGTHS

- Randomized controlled trial study design
- Use of clear and standardized diagnostic criteria
- Full power to test hypothesis
- Stratified Random assignment

LIMITATIONS

- Study therapists were unblinded
- No mention of how the subjects were recruited
- No mention of the use of abortive medications
- No data provided for compliance with amitriptyline
- More total and upper-level adverse events in the headache education vs CBT group
- Did not include a study arm concerning CBT plus placebo

CONCLUSION

- Cognitive Behavioral Therapy plus amitriptyline resulted in a statistically and clinically meaningful reduction in days with headache per month and total headache disability compared to headache education plus amitriptyline
    - Primary and secondary outcomes showed improvements using CBT vs headache education
    - More importantly, CBT provided better clinical outcomes vs headache education
    - Less CNS and possibly respiratory related adverse events with CBT compared to headache education

- Future research:
    - Post-hoc analysis over a 12-month follow-up were included but not statistically analyzed, which proposes the need for further research including long-term outcomes
    - Investigation of CBT alone compared to those with CBT plus an active medication can give some further insight to the utility of the psychological intervention
    - Investigation of the possible relationship between increased adverse events with headache education compared to CBT interventions

Reference: Powers SW, Kashikar-Zuck SM, Allen JR, LeCates SL, Slater SK et al. Cognitive Behavioral Therapy Plus Amitriptyline for Chronic Migraine in Children and Adolescents: A Randomized Clinical Trial. 2013;(310)24:2622-2630.

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