Trial of Amitriptyline, Topiramate, and Placebo for Pediatric Migraine

SCIENCE

Clinical Research

Key Take-Away:

No considerable efficacy of Amitriptyline and Topiramate over placebo in reducing the number of headache days in pediatric patients was shown.

ABSTRACT:

Background:

The prevalence of migraine in children and adolescents in the United States is quite high affecting quality of life of patients significantly. This disease is also taking a toll on the U.S. economy of approximately $36 billion. The clinical practice guidelines for the management of pediatric migraine are not evidence-based, with no Food and Drug Administration (FDA) approved migraine prevention medication for children younger than 12 years of age.

Amitriptyline and Topiramate were found to be the most common drugs used as preventive medications, based on a survey of pediatric headache specialists. "The Childhood and Adolescent Migraine Prevention (CHAMP)" trial was conducted to compare the effectiveness of Amitriptyline and Topiramate in pediatric migraine.

Rationale behind the research

The medication which can be used for migraine prevention in pediatric patients has not been established yet.

Objective

To compare the effects of Amitriptyline and Topiramate with placebo in pediatric migraine patients.

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Methods:

Note: This was a phase 3, multicenter, double-blind, placebo-controlled trial

Study outcomes measures

Primary Outcomes: Relative reduction of 50% or more in the number of headache days in the comparison of the 28-day baseline period with the last 28 days of the 24-week trial.

Secondary Outcomes: Four secondary outcomes were

- Headache disability, as measured by absolute change in the PedMIDAS score
- The absolute reduction in the number of headache days, from the 28-day baseline period to the final 28-day period of treatment

- Number of trial completers, as assessed by the percentage of patients who completed the 24-week treatment period
- Serious adverse events during treatment

Time Points: 28-day baseline period and the last 28 days of a 24-week trial

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Results:

Outcomes

Primary Outcomes: The percentage of patients with a relative reduction of 50% or more in the number of headache days was 52% in the Amitriptyline group, 55% in the Topiramate group, and 61% in the placebo group when the 28-day baseline period was compared with the last 28 days of the 24-week trial. There was no significant difference in effect when the two active drugs were compared with each other.

In sensitivity analyses using headache data obtained at baseline and week 24, there were 264 patients available for analysis. The percentage of patients with a relative reduction of 50% or more in the number of headache days was 66% with Amitriptyline, 71% with Topiramate, and 68% with placebo. By combining these approaches, the total relative reduction of 50% or more was found in 52 to 66% of the patients in the Amitriptyline group, 55 to 71% of the patients in the Topiramate group, and 61 to 68% of the patients in the placebo group.

Figure 1: Patients with a relative reduction of 50% or More in the Number of Headache Days

- **Secondary Outcomes:**

- **Headache-Related Disability:** The baseline PedMIDAS score did not differ significantly among the three trial groups (p=0.77). The absolute change in the score was −22.5 with Amitriptyline, −26.8 with Topiramate, and −22.6 with placebo.
- **Headache Days:** In the comparison of the number of days on which patients had a headache in the 28-day baseline period and the 28 days preceding week 24, patients with both measurements showed an absolute change of −6.7 days with Amitriptyline, −6.7 days with Topiramate, and −5.9 days with placebo.
- **Trial Discontinuation:** The percentage of randomly assigned patients who completed the 24-week treatment phase was 80% with Amitriptyline, 78% with Topiramate, and 89% with placebo.
- **Serious Adverse Events:** 12 serious adverse events appeared during treatment (6 in the Amitriptyline group, 4 in the Topiramate group, and 2 in the placebo group), occurring in 11 patients.

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Conclusion:

This trial demonstrated that neither of two preventive medications for pediatric migraine was more effective than placebo in reducing the number of headache days over a period of 24 weeks.

This trial demonstrated that neither of two preventive medications for pediatric migraine was more

effective than placebo in reducing the number of headache days over a period of 24 weeks. Patients who received Amitriptyline or Topiramate had higher rates of adverse events than those who received placebo. In this trial, a high placebo response rate similar to the rate reported in previous headache and pain trials was observed. These findings also recommend that the adult model of headache treatment, in which Amitriptyline and Topiramate have been useful, may not apply to pediatric patients.

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Therapeutic, Amitriptyline, Topiramate, Migraine, Head, Tricyclic Antidepressants, Anticonvulsants, Randomized, Double-blind, Placebo-controlled Trial, Efficacy, PedMIDAS score, syncope, Altered Mood