

Cyproheptadine versus propranolol in the prevention of migraine headaches in children

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ABSTRACT

Objective: There are conflicting results on the efficacy of propranolol and cyproheptadine in the prevention of migraine headaches in children. Therefore, in this study, we evaluated the efficacy of propranolol versus cyproheptadine in the prevention of migraine headaches.

Methodology: This was a randomized, double-blind trial. Sixty children aged 8-15 yrs with migraine headaches were randomized to be treated with either propranolol (40-80mg per day) or cyproheptadine (8-12mg per day) for 4 weeks. The patients were requested to record the severity and duration of their headaches during a 2-week period before starting the intervention. The patients were followed at 2-week intervals for a period of 1 month after starting treatment. The headache diary was analyzed for each patient and was compared with baseline using SPSS software and statistical tests including the student's t-test.

Results: Out of 60 patients at baseline, nine patients in the cyproheptadine group and six patients in the propranolol group did not appear at the appropriate time for follow-up visits and therefore were excluded from the study. The mean age in the cyproheptadine group was 11.9 ± 2.23 years and in the propranolol group was 10.7 ± 2.33 years. Based on the diaries, the results showed that propranolol and cyproheptadine decreased headaches by 54.61% and 70.53% ($p < 0.05$), respectively, at the end of four weeks of treatment.

Conclusion: Overall, the results of our study suggest that cyproheptadine is a good choice for prevention of migraine headache in pediatric group although more prolonged study with higher number of the patient is recommended.

KEY WORDS: Migraine, Pediatric, Propranolol, Cyproheptadine, Prophylactic.

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INTRODUCTION

The prevalence rate of migraine headache has been estimated to be between 4-11%,^{1,2} and this prevalence is lower in children and higher in teens. It is estimated that 1.4-5% of children and 5.5-10.6% of teens are affected by migraine.^{3,4} The migraine prevalence rate has increased in the past 10-30 years, which may be due to changes in eating habits, social stresses and lifestyle changes.⁵ Migraine headaches may severely restrict personal and social activities, so much so that about one-third of patients have lost one day at school or work in the last 3 months.⁶

CT scan and MRI are now commonly performed on patients with migraine headaches and they are recommended for those children that have signs of focal neurologic disorders. They are

also recommended for patients with increased intracranial pressure, decreased consciousness or a history of seizures, and for patients who experience changes in their headache pattern.⁷

Drug treatments for migraine headaches can be divided in two groups: those for acute attacks and for prophylactic treatment. For the treatment of an acute attack, drugs such as ibuprofen, acetaminophen, sumatriptan nasal spray or zolmitriptan are usually used. For prophylactic treatment, drugs such as felonasin, topiramate, sodium valproate, lotirasam, ciproheptadine, amitriptylin and propranolol have been suggested.⁸

There are conflicting results on the efficacy of propranolol and cyproheptadine in the prevention of migraine headaches in children. Therefore, in this study, we evaluated the efficacy of propranolol versus cyproheptadine in the prevention of migraine headaches.

METHODOLOGY

This was a randomized, double-blind trial that was performed between 2007-2010 in Al Zahra Hospital, Isfahan Iran. In this study, 60 children aged 8-15 years with migraine headaches were randomized to be treated with either propranolol (40-80mg per day) or cyproheptadine (8-12mg per day). Only patients who had at least a 6-month history of migraine headaches (according to the definition of pediatric migraine of the International Headache Society (IHS) criteria) were selected.⁹

Exclusion criteria were co-existence of tension headache with migraine, a history of using prophylactic medication during the last three months, abnormal CT scan, abnormal neurological and optic nerve examination, and history of severe head trauma or asthma.

The patients were requested to record the severity and duration of their headaches during a 2-week period before starting the intervention and were asked to use the least analgesic possible. Headache severity was measured using Visual Analogue Scale (VAS).

The headache diary result was calculated for each patient as: Headache diary result = duration of headache × frequency of headache. Brain CT scans were also performed on all participants. The patients were followed at 2-week intervals for a period of one month after starting treatment.

RESULTS

Out of 60 patients at baseline, nine patients in the cyproheptadine group and six patients in the propranolol group did not appear at the appropriate time for follow-up visits and therefore were excluded from the study. The mean of age in the cyproheptadine group was 11.9 ± 2.23 years and in the propranolol group it was 10.7 ± 2.33 years. According to the results (Table-I), propranolol and cyproheptadine decreased the headache diary result by 54.61% and 70.53%, respectively.

The mean duration of headaches in the propranolol group was 16.91 ± 4.95 hours, which decreased to 12.20 ± 4.28 hours after two weeks of treatment and to 8.85 ± 3.37 after four weeks of treatment. The values in the cyproheptadine group were 15.90 ± 5.60 at baseline, which after two weeks of treatment decreased to 12.90 ± 6.07 and 6.83 ± 5.22 hours after four weeks.

The average headache severity in the propranolol group was 6.18 ± 1.15 at baseline, 5.69 ± 0.99 after two weeks and 5.16 ± 1.18 after four weeks. These values in the cyproheptadine group were 6.26 ± 0.70 at baseline, 4.95 ± 0.72 after two weeks and 3.67 ± 1.34 after four weeks.

DISCUSSION

Prophylactic treatment of migraine headaches in children is usually indicated when there are at least three attacks per month.¹⁰ Propranolol and other beta-blockers in adults have shown satisfactory results¹¹, but in several studies performed on children, beta-blockers have been associated with varying results.¹²

Until recently, at least 17 different drugs have been studied. Topiramate, sodium valproate,

Table-I: Comparison of mean headache severity at baseline and during treatment in the Cyproheptadine and Propranolol group.

Type of treatment	Mean headache diary result at baseline	Mean headache diary result after 2 weeks of treatment	Mean headache diary result after 4 weeks of treatment
Cyproheptadine	98.10 ± 34.90	33.37 ± 66.50	28.92 ± 29.01
Propranolol	101.5 ± 33.5	72.39 ± 27.84	55.43 ± 25.81
P-value	>0.05	0.09	0.01

flurazepam, amitriptyline and cyproheptadine have demonstrated effects in all studies. Propranolol and pizotifen show some effects and other drugs, such as gabapentin and Trazodone are being studied. In children, no therapeutic effect with clonidine and nimodipine has been shown.¹³

Lewis and colleagues have shown that 53% of children with migraine headaches are placed on prophylactic treatment. Amitriptyline and cyproheptadine are the most commonly prescribed agents. Over a 6-month follow-up, the response to amitriptyline was 89% and to cyproheptadine was 83%. In patients on treatment with cyproheptadine, there was a reduction in severity, duration and frequency of headache attacks, and co-administration of propranolol with cyproheptadine was more effective than cyproheptadine alone.¹⁴

Three major studies have been performed on propranolol. In the first, propranolol had a very good effect.¹⁵ In the second study, 120-80 mg of propranolol had no therapeutic effect and the mean duration of headaches was even increased.¹⁶ In the third study, propranolol, in a dosage of 3 mg/kg per day, had no therapeutic effects.¹⁶ In contrast, a study in 1999 suggested that although cyproheptadine was frequently prescribed for children, it is not as effective as amitriptyline and propranolol.¹⁷

Our findings suggest that for prevention of pediatric migraine headaches, cyproheptadine achieves a better therapeutic effect than propranolol. The greatest advantage seems to be in reducing the severity of headaches, and according to our findings, if the child has a severe headache, it is better not to select propranolol as first-line treatment. Patient tolerance to the medications in both groups was adequate. In the cyproheptadine group, parents complained of their children's drowsiness, but in most cases these side effects were tolerated.

Another notable finding was that the effectiveness of cyproheptadine in this study was 70.53%, which is lower than the 83% mentioned in a similar study.¹⁴ Overall, the results of our study suggest that cyproheptadine is a good choice for prevention of migraine headaches in children, although a longer study with a higher number of patients is recommended.

Ethical Approval: The study was approved by the Ethics committee of the Research Department of Isfahan University of Medical Sciences.

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