

Topiramate for Migraine Prophylaxis in Children

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ABSTRACT

Objective: To determine the efficacy and safety of topiramate (TPM) for prophylaxis of migraine in children

Study Design: Quasi-experimental study

Place and Duration of Study: This study was conducted at the Pediatric Department, Bahawal Victoria Hospital affiliated with Quaid e Azam Medical College, Bahawalpur from January 2018 to November 2018.

Materials and Methods: A total of 60 children with migraine, aged 5 to 15 years, fulfilling the inclusion and exclusion criteria, were enrolled. TPM as 2 mg / kg / day was used twice a day in equally divided dosage. Monthly frequency, headache's duration along with its severity and pedMIDAS score were noted prior and after three months of TPM therapy.

Results: Out of a total of 60 children, majority of the children, 35 (58.3%) were female, had migraine type without aura 37 (61.7%) and family history of migraine in 49 (81.7%). Mean age of the children was 9.77±2.8 years whereas mean age of migraine onset amongst all the children was 7.43± 2.9 years. When children with good response of TPM were compared with no good response, headache frequency (monthly), headache severity, duration of headache and headache disability (pedMIDAS) was significantly decreased after TPM treatment (p value < 0.05).

Conclusion: TPM was found to be effective and safe in children for prophylaxis of migraine. TPM reduced frequency, severity along with duration and disability of migraine headache with very few side effects.

Key Words: Headache, severity, frequency, topiramate, Migraine

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INTRODUCTION

In children, migraine is considered as a frequent neurological disorder. Prevalence of migraine varies from 5 to 17% while both male and female children are affected equally before puberty, but following puberty, its prevalence increases 2 to 3 folds in girls.¹⁻³

In the last few decades, numerous diagnostic criteria for migraine have been in practice but International Classification of Headache Disorders (ICHD-II) for children migraine published in 2004 stands well accepted around the world.⁴

Over the years, lifestyle changes have been advised including avoiding those foods along with practices and environmental factors that may initiate attack of migraine.^{5,6} It has been stated multiple times that epilepsy and migraine share some common features.^{9,10} Some new antiepileptic options like topiramate (TPM) and levetiracetam are showing reduction in frequency

of headache. TPM is proving efficient in adult populations for the prevention of migraine. Very few studies are available assessing the efficacy and safety aspects of TPM in children.⁷ Exact mechanism of action of TPM is still not clear.⁸ As TPM is given in low doses for prophylaxis of migraine, some uncontrolled trials confirmed the efficacy of TPM for prophylaxis of migraine^{7,11,12} but more work is needed to establish the efficacy and safety of TPM, especially in pediatric population so this study was planned. The objective of the study was to determine the efficacy and safety of TPM for prophylaxis of migraine in children.

MATERIALS AND METHODS

This was a quasi-experimental trial, conducted from 1st January 2018 to 30th November 2018 at Pediatric Department, Bahawal Victoria Hospital, affiliated with Quaid e Azam Medical College, Bahawalpur. The study was approved by local ethical committee. Verbal consent was acquired from parents / guardians of all the children participating in this study.

A total of 60 children with migraine headache as per ICHD-II criteria⁴ for a minimum period of 6 months prior to study, aged 5 to 15 years, history of no migraine treatment, had 1 or more migraine episodes per week, or those children who had disabling (PedMIDAS > 20) headaches, were enrolled for this study. Children with metabolic acidosis, any type of renal dysfunction or kidney stones, any type of

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systemic illness, other headache types that were not migraine were excluded from this study.

Children were given TPM as 2 mg per kg per day in equally divided 2 doses. All children enrolled in the study were asked to visit for consecutive 3 months. Information regarding frequency as well as severity, along with duration of headache (pedMIDAS scoring),¹³ duration were noted prior to the start of study period as well as after 3 months of TPM treatment. Headache's severity was evaluated by enquiring from every child as per visual analogue scale (VAS)¹⁴ according to a ten point scaling where no pain was considered as a score of zero and most severity of pain was recorded as a score of 10. A monthly pain reduction of > 50% was taken as a "good" response. The side effects of TPM during the study period were also noted. Children's parents or guardians were interviewed to collect all the relevant information.

SPSS version 20 was used for data entry and analysis. Chi square test was applied to analyze qualitative data and t test was used to analyze quantitative data. The p value < 0.05 was considered as statistically significant.

RESULTS

Out of a total of 60 children, 35 (58.3%) were female. There were 37 (61.7%) children having migraine type without aura and family history of migraine was positive in 49 (81.7%). Mean age of the children was 9.77 years with standard deviation of 2.8 years whereas mean age of migraine onset amongst all the children was 7.43 years with standard deviation of 2.9 years. Amongst all the children, 44 (73.3%) children had good response (reduction of > 50% headache frequency

monthly). There were 17 (38.6%) male and 27 (61.4%) female with good response in comparison to 8 (50.0%) male and 8 (50.0%) female children with no good response. This difference was not statistically significant (p value = 0.430) as shown in table No-1.

When children of both groups were compared for age, the mean age of children with good response was 9.64 with standard deviation of 2.7 years in comparison to 10.13 years with standard deviation of 2.9 years (p value = 0.567) as shown in table No-1.

The mean age of migraine onset in children with good response was 7.41 years with standard deviation of 2.8 years in comparison to mean of 7.50 years with standard deviation of 3.2 years in children with no good response (p value = 0.920). Type of migraine and family history of migraine amongst children of both group were also not statistically significant (p value > 0.05) as shown in table No-1.

When headache characteristics of children in both groups were compared, headache frequency (monthly) was significantly decreased after treatment with TPM (p value = 0.0001). Similarly, headache severity, duration of headache and headache disability (pedMIDAS) was also significantly decreased after TPM treatment (p value = 0.0001) as shown in table No-2.

Hyperthermia was found to be the most frequent side effects that was experienced by 8 (13.3%), followed by anorexia in 5 (8.3%), weight loss in 4 (6.7%) and paresthesias in 1 (1.67%) but these side effects resolved 4-7 days and did not cause interference in daily activities of life.

Table No.1: Frequency of Good response with regards to different characteristics studied

Characteristics		Good Response		P value
		Yes (n=44%)	No (n=16)	
Gender	Male	17 (38.6%)	8 (50.0%)	0.430
	Female	27 (61.4%)	8 (50.0%)	
Age in Years (mean+SD)		9.64 + 2.7	10.13 + 2.9	0.567
Age of Migraine onset (mean+SD)		7.41 + 2.8	7.50 + 3.2	0.920
Type of Migraine	With Aura	16 (34.6%)	7 (43.8%)	0.603
	Without Aura	28 (63.6%)	9 (56.3%)	
Family History of Migraine	Yes	37 (84.1%)	12 (75.0%)	0.421
	No	7 (15.9%)	4 (25.0%)	

Table No.2: Headache Characteristics of the children before and after TPM treatment

Headache Characteristics	Time (Mean + Standard Deviation)		P value
	Before Treatment	After Treatment	
Headache Frequency (Monthly)	13.85 + 6.2	6.10 + 2.3	0.0001
Headache Severity	7.20 + 1.6	3.97 + 1.8	0.0001
Duration of Headache (in hours)	2.06 + 0.8	1.34 + 0.7	0.0001
Headache Disability: pedMIDAS	32.28 + 5.9	17.30 + 4.5	0.0001

DISCUSSION

Prophylactic treatment of migraine has been proposed by many researchers but best treatment consists of an

individual approach tailored for an individual child including both pharmacological and non pharmacological options.^{15,16} Non pharmacologic options include following specific patterns of sleep,

diet, reduction of stress and doing recommended exercises, all these can prove helpful.^{15,17} Pharmacological options for prophylaxis of migraine include beta blockers, calcium channel as well as serotonin antagonists, anti epileptics and different anti depressants.^{18,19} TPM belongs to anti epileptics that has been found to have effectiveness and safe in the last few years.^{7, 11, 12, 18,19} Most of the trials assessing safety and efficacy of TPM in migraine prophylaxis has been conducted in adults so this study was planned to share our local experience.

Studies from around the world have noted good response of TPM varying from 55-100%.^{11, 20-23} In the current work, we noted the good response of TPM in 73.3% children. Our findings were very similar to what Fallah R et al²⁴ found where they noted the good response in 74% patients. Varying results in response to TPM could possibly be due to variation in demographic as well as difference in sample size and study methodologies.

In the present study, headache duration dropped from 2.06±0.8 hours to 1.32 + 0.7 hours. Our results in this aspect were very similar to another study conducted in Iran²⁴ where they noted it to decrease from 2.28 to 0.94 hours. It has been documented that migraine duration in children is shorter in comparison to adults.⁴

We found TPM to reduce pedMIDAS scoring significantly thus improving headache disability as well as severity of headache as per VAS scoring. These results were very similar to what Unalp A et al²⁵ and Lakshmi CV et al found in their studies.²⁶

Hyperthermia was found to be the most frequent side effects in this study that was experienced by 8 (13.3%) children with TPM, followed by anorexia in 5 (8.3%) and weight loss (6.7%). This pattern was very similar to what Fallah R and colleagues found in 2013²⁴ but our results were different from other two trials^{21, 28} where weight loss was turned out to be the commonest side effect. In another study comparing TPM with placebo found upper RTI and paresthesia as the commonest occurring side effects with TPM but none of these were of any serious concern.^{21, 23}

Our study had some limitations as it did not have placebo or any comparable group. We also did not assess the cognitive aspects of children in this study. More studies with bigger sample size are required to further establish the effectiveness and safety of TPM.

CONCLUSION

TPM was found to be effective and safe in children for prophylaxis of migraine. TPM reduced frequency, severity along with duration and disability of migraine headache with very few side effects.

Author's Contribution:

Concept & Design of Study: Syed Fawad Saleem
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Revisiting Critically: Syed Fawad Saleem,
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Conflict of Interest: The study has no conflict of interest to declare by any author.

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