

## ORIGINAL ARTICLE

## TOPIRAMATE FOR MIGRAINE PROPHYLAXIS AMONG CHILDREN AGED 5 TO 15 YEARS

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**Background:** Migraine is known to be a common neurological disorder among children. Newer anti-epileptic agents like topiramate (TPM) have shown to decrease the frequency of headache but not much work about safety and efficacy of TPM is seen in the paediatric population with migraine. This study was aimed to find out the efficacy and safety of TPM for migraine prophylaxis among children aged 5–15 years. **Methods:** A total of 132 children having migraine headache according to ICHD-II criterion for duration of at least 6 months, from 5–15 years of age were enrolled. Frequency of headache, severity of headache and duration of headache were compared before and after 3 months of TPM treatment. Side effects of TPM treatment were also observed. **Results:** In a total of 132 children, 80 (60.6%) were female and 52 (39.4%) males. Mean age was 9.52±2.5 years. Good response of TPM treatment was observed in 102 (77.3%) children. Significant decrease ( $p$  value <0.05) was noted in headache frequency, severity and duration following TPM treatment. No serious side effects of TPM treatment were noted. **Conclusion:** Topiramate is noted to be effective and safe for migraine prophylaxis among children. Reduction in headache frequency, severity as well as duration and disability scores are recorded after TPM treatment.

**Keywords:** Headache frequency; Good response; Side effects; Topiramate; Treatment

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## INTRODUCTION

Migraine is known to be a common neurological disorder among children.<sup>1</sup> In children, prevalence of migraine is between 5–17%. Before puberty, both genders are equally affected but after puberty, girls are more affected (2–3 times more).<sup>2–4</sup> Menstrual cycle induced triggered effects in girls are considered to be the reason behind increased incidence of migraine in girls.<sup>1</sup>

Commonest symptoms comprise of episodes of headache with nausea, photophobia and phonophobia.<sup>3</sup> Migraine affects quality of life frequently.<sup>3,4</sup> Various diagnostic criteria are in use around the world for the diagnosis of migraine but “International Classification of Headache Disorders (ICHD-II)” for children released in 2004 is considered to be the most authentic worldwide.<sup>5</sup>

Lifestyle modifications including avoidance foods, activities and environmental factors that can trigger attacks of migraine are advised as part of the management.<sup>6,7</sup> As we know that common features are found among patients of migraine and epilepsy,<sup>8,9</sup> newer antiepileptic drugs such as TPM as well as levetiracetam are seen to impart decrease in the frequency of headache<sup>10</sup>. The relevant mode of action of TPM credited for good migraine prophylaxis is yet to be determined but TPM is found effective among adults for the management of migraine. Very little data exists

regarding efficacy as well as safety of TPM among paediatric population suffering with migraine.<sup>7,11</sup>

For prophylaxis of migraine, TPM is usually prescribed in low dose and some researchers have found TPM to be effective.<sup>12,13</sup> Scarcity of local data exists when we look for the role TPM for the prophylaxis of migraine especially in children, this study was aimed to find out the efficacy and safety of TPM for prophylaxis of migraine among children aged 5–15 years.

## MATERIAL AND METHODS

This quasi-experimental study was done at Outpatient Department of Children's Hospital and The Institute of Child Health, Multan from June to November 2019. Approval from Institutional Ethical Committee sought while written consent was taken from parents or guardians of all the children participating in the study.

A total of 132 children having migraine headache according to ICHD-II criterion for a duration of at least 6 months, from 5–15 years of age, no prior history of migraine treatment, having one or more than one migraine episodes weekly, or children who were having disabling headaches as Paediatric Migraine Disability Assessment (PedMIDAS) score of more than 20, were enrolled during the study period.<sup>14–16</sup> Those children who had metabolic acidosis, renal abnormalities or

renal stones, any sort of systemic diseases, or headache types other than migraine, were not included.

All the study information including name, age, gender, type of migraine, family history of migraine, monthly headache frequency, headache severity, duration of headache (in hours) and headache disability pedMIDAS score were noted on a predesigned proforma. All study participants were prescribed TPM as 3 mg/kg/day in equally divided 2 dosages.<sup>16</sup> Study participants were advised to visit after every month for consecutive 1<sup>st</sup> three months. Frequency of headache, severity of headache, duration of headache (hours) and pedMIDAS score before and after three months of TPM treatment in all the study participants were noted. Side effects of TPM treatment were also observed. Headache severity was assessed employing visual analogue scale (VAS) in each study participant. VAS consisted of 10 points from 0–10 where zero highlighted no pain whereas severe pain was denoted as a score of 10. At the end of 3 months follow up from every study participant, efficacy of TPM was labelled as good response if more than 50% reduction in monthly headache frequency at the end 3 months TPM treatment (in comparison to before treatment) was noted or efficacy of TPM was labelled as not good if less than 50% reduction in monthly headache frequency was noted. Interviews from Child and parents/guardians were conducted to note relevant study information.

Chi square test was employed to compare sex, type of migraine and family history of migraine with respect to response of TPM treatment while independent sample t test adopted for comparison of mean age and mean age of onset of migraine. Paired sample t test employed for comparison of monthly headache frequency, headache severity, duration of headache and headache disability score before and after the TPM treatment. *p*-value <0.05 was considered as carrying statistical significance.

## RESULTS

Out of 132 children, there were 52 (39.4%) male and 80 (60.6%) females. Male to female ratio was 0.65:1. Mean±SD age was 9.52±2.5 years. Mean±SD age of onset of migraine was 7.62±2.6 years. Positive family history of migraine was observed among 103 (78.0%) children.

Table-1 compares characteristics of patients having good response (n=102) and not good response (n=30). There were 40 (39.2%) male and 62 (60.8%) female who showed good response in comparison to 12 (40.0%) male and 18 (60.0%) females with not good response (*p* value =0.9384). Likewise, mean age was noted as 9.31±2.4 years among children with good response versus 9.92±2.7 years with not good response (*p* value =0.2366). Similarly, age of onset of migraine was 7.31±2.3 years among children with good response versus 8.02±3.0 years among children with not good response (*p* value =0.1693). There was no statistical difference between children having good or not good response in terms of migraine type (*p* value = 0.3899) or family history of migraine (*p* value = 0.2796).

Table-2 shows that when children were compared for headache characteristics before and after TPM treatment, significant decrease (*p* value <0.05) in terms of monthly headache frequency, headache severity (VAS score) as well as duration of headache (in hours) and headache disability (pedMIDAS) score were observed.

Table-3 shows frequency of various side effects of TPM treatment noted among study participants. No serious side effects of TPM treatment were noted. Hyperthermia was the commonest side effect, noted among 20 (15.2%) whereas anorexia and weight loss were seen in 14 (10.6%) and 6 (4.5%) children respectively. Treatment discontinuation was not required in any of the patients due to side effects while all side effects disappeared after 1 to 2 weeks after starting TPM treatment.

**Table-1: Distribution of response of TPM treatment with respect study variables**

		Good response		<i>p</i> -value
		Yes (n=102)	No (n=30)	
Sex	Male	40 (39.2%)	12 (40.0%)	0.9384
	Female	22 (60.8%)	18 (60.0%)	
Age (mean±SD) in years		9.31±2.4	9.92±2.7	0.2366
Age of Migraine onset (mean±SD)		7.31±2.3	8.02±3.0	0.1693
Type of Migraine	With Aura	33 (32.4%)	11 (36.7%)	0.3899
	Without Aura	69 (67.6%)	19 (63.3%)	
Family History of Migraine	Yes	81 (79.4%)	22 (73.3%)	0.2796
	No	21 (20.6%)	8 (26.7%)	

**Table-2: Headache characteristics of study participants before and after TPM treatment**

	Before treatment	After treatment	p-value
Monthly headache frequency	12.81±6.6	7.18±2.6	< 0.0001
Headache Severity	7.74±1.9	4.21±1.8	< 0.0001
Duration of headache (in hours)	2.18±0.6	1.48±0.5	< 0.0001
Headache disability pedMIDAS score	34.24±6.3	19.01±4.8	< 0.0001

**Table-3: Side effects of topiramate treatment observed in study participants**

Side effects	Number (%)
Hyperthermia	20 (15.2)
Anorexia	14 (10.6)
Weight Loss	6 (4.5)
Drowsiness	4 (3.0)

## DISCUSSION

Prophylactic treatment of migraine is considered a popular choice by many clinicians around the world.<sup>17,18</sup> TPM is an anti-epileptic drug that has been known to be useful and safe.<sup>20,21</sup> Majority of the studies conducted on TPM in migraine prophylaxis are done in adult populations, this is why we felt there was a need to conduct a research like the present one, to assess safety as well as efficacy of TPM in migraine prophylaxis among children. TPM has shown lots of variability in terms of good response. Worldwide studies done on TPM have shown lots of variability like 55–100% good response in migraine prophylaxis.<sup>22–24</sup> In the present study, 77.3% children reported good response after TPM treatment. Our results in terms of good response were consistent with those of another local study where authors noted 73% of the children to have good response of TPM treatment for migraine prophylaxis.<sup>25</sup> Fallah R and colleagues also reported good response of TPM treatment in migraine prophylaxis among 74% of their patients, again showing very similar results to what we noted.<sup>14</sup> Variability in response to TPM treatment for migraine prophylaxis could be due to difference in demographical aspect while lots of variety is also seen in terms of sample size in studies conducted worldwide.

In the current work, duration of headache decreased significantly from a mean of 2.18±0.6 to 1.48±0.5 hours among study participants which correlate very well with another local study where authors noted a drop in headache duration from a mean of 2.06±0.8 hours to 1.32±0.7 hours.<sup>25</sup> Researchers from Iran<sup>14</sup> also observed good efficacy of TPM in terms of duration of headache that decreased from a mean 2.28±1.55 hours before starting TPM treatment to 0.94±0.35 hours after TPM treatment (*p* value=0.002).

Significant reduction in pedMIDAS score as well as headache severity in terms of VAS score were recorded among study participants after TPM

treatment, which correlates to findings of other local and international studies.<sup>14,25–27</sup>

No serious side effects of TPM treatment were noted. Hyperthermia was the commonest side effect, noted among 20 (15.2%) whereas anorexia and weight loss were seen in 14 (10.6%) and 6 (4.5%) children respectively. Treatment discontinuation was not required in any of the patients due to side effects while all side effects disappeared after 1 to 2 weeks after starting TPM treatment. Hyperthermia and anorexia are known to be common side effect as seen by others.<sup>25</sup> Our results were different to those of Fallah R and coworkers<sup>14</sup> where they noted weight loss to be the commonest side effect of TPM treatment for migraine prophylaxis. Other researchers have also noted upper respiratory tract infections and paraesthesia as the most common side effects occurring after TPM treatment but no study reported any serious side effects that needed any emergency or critical care.<sup>18,28</sup>

There were few limitations of this study as well. Our study did not have any comparator or placebo to compare our findings. We also did not evaluate any kind of cognitive aspects in the present study. Further studies involving different set of paediatric populations along with bigger sample size will further add to the knowledge we have about the role of TPM among children for migraine prophylaxis.

## CONCLUSION

Topiramate is noted to be effective and safe for migraine prophylaxis among children. Reduction in headache frequency, severity as well as duration and disability scores is recorded after TPM treatment. Hyperthermia, anorexia and weight loss are the most frequent side effects in few of the patients but no major side effect reported.

## AUTHORS' CONTRIBUTION

MKS: Literature review, drafting. MY: Study idea, data collection. NA: Data interpretation. SK: Data analysis. GH, SH: Data collection.

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