

# **An observational study on safety and efficacy of Topiramate as an add-on drug therapy in seizures among children of India**

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## **Abstract**

Topiramate is an antiepileptic drug with anti-seizure properties around the board. It has been shown to be successful in the treatment of both partial and generalised seizures. Topiramate's effectiveness in epilepsy syndromes such as West syndrome, myoclonic-astatic epilepsy and Dravet syndrome, as well as refractory status epilepticus, has been demonstrated. Topiramate may also be used as a supplement to other treatments for Lennox-Gastaut syndrome. However, there are few studies on Topiramate's long-term efficacy, especially in children, that have lasted longer than 24 months. In this open-label, retrospective research, we looked at the safety and long-term efficacy of topiramate in a group of children with drug-resistant epilepsy for more than 24 months. The Fisher's exact test and the Chi-square test for non parametric data were used for statistical evaluation. Apart from intermittent minor side effects such as hyperactivity in ten percent of population, anorexia in four percent, sleeplessness in four percent, sedation in ten percent, hypohidrosis in eight percent, and vomiting symptoms in two percent, no significant systemic side effects were observed; none of the participants stopped TPM due to its side effects. Before and after the analysis, all haematological, hepatic, and renal parameters were normal.

**Keywords:** Topiramate, safety in children, seizures, India, therapy.

## **INTRODUCTION:**

Topiramate (TPM), also known as 2,3,4,5-bis-O-(1-methylethylidene)-beta-D-fructopyranose sulfamate, is an antiepileptic drug that works by blocking sodium channels, increasing GABA-induced chloride influx, and inhibiting kainate/AMPA glutamate receptors [1,2]. TPM has been shown to be successful in adult patients with refractory partial and generalised seizures (primarily tonic-clonic, myoclonic, and tonic) [3, 4]. Topiramate is an antiepileptic drug with anti-seizure properties around the board. It has been shown to be successful in the treatment of both partial and generalised seizures [5, 6]. Topiramate's effectiveness in epilepsy syndromes such as West syndrome, myoclonic-astatic epilepsy and Dravet syndrome, as well as refractory status epilepticus, has been demonstrated [7, 8]. Topiramate may also be used as a supplement to other treatments for Lennox-Gastaut syndrome [9]. However, there are few studies on Topiramate's long-term efficacy, especially in children, that have lasted longer than 24 months[10].

Seizures affect about ten percent of all children. Epilepsy affects 0.5–1% of the population, with 60% of cases beginning in childhood[11]. Seizures remain uncontrolled in 10–20 percent of all children with epilepsies through treatment with conventional antiepileptic medications (AEDs). Because of its wide range of service, efficiency, and ease of availability, TPM is favoured among newer AEDs [12]. It is inexpensive, has few side effects, and is approved by the FDA for use in children[13]. Complex partial seizures (CPS), partial seizures with secondary generalisation (PSSG), generalised tonic clonic seizures (GTCS), myoclonic jerks (MJ), Lennox Gastaut Syndrome (LGS), West Syndrome (WS)/Infantile Spasms (IS), mixed, and absence seizures are among the partial seizures treated with it [14, 15].

### **AIMS & OBJECTIVES:**

In this open-label, retrospective research, we looked at the safety and long-term efficacy of topiramate in a group of children with drug-resistant epilepsy for more than 24 months.

### **METHODOLOGY:**

The study population was drawn from patients at a South Indian tertiary care hospital's Pediatric Neurology Outpatient Department. We have collected the patient details from respective hospitals from February 2018 to January 2020. TPM was introduced as an add on drug to standard AEDs, orally as tablets, beginning in small divided doses (1–3 mg/kg/day) and steadily rising at regular weekly intervals until the most effective/best-tolerated dose (maximum of 9 mg/kg/day) was reached, and then continued for the remainder of the study.

### **Inclusion criteria:**

The research included forty children aged 0–12 years old who had seizures and were already taking multiple standard AEDs at the highest clinically tolerable daily dose.

### **Exclusion criteria:**

- Paroxysmal non-epileptic disorders
- Chronic metabolic/toxic/infectious events that tend to be ongoing
- Significant systemic/progressive neurological/current psychiatric disorders may occur together.
- Those with a history of nephrolithiasis and those who are acidosis-prone

### **Statistical Analysis:**

The Fisher's exact test and the Chi-square test for non parametric data were used for statistical evaluation.

### **RESULTS & DISCUSSION:**

Almost half of the participants were between the ages of 1 and 5. The youngest of the group was a 9-month-old baby. There were a total of 21 boys and 19 girls in the group. Microcephaly afflicted 50%, developmental delay afflicted 62 percent, mental retardation afflicted 54 percent, and focal neurological

deficits afflicted 36 percent. Idiopathic/cryptogenic seizures affected 12 patients, while symptomatic seizures affected 23 others. Tuberous sclerosis was seen in 6 patients, LGS in five people, WS was in three, and Dravet syndrome was seen in three people were among the fourteen children who had specific epileptic syndromes in two people. The Chi-square test was used to analyse SIS using two parameters: the initial dose and the dose at the end of the sixth month. The starting dose and the SIS position have a relationship ( $X^2=13.45$ ,  $df=4$ ,  $p0.05$ ). Maximum favourable scores of 3 and 4 and unfavourable scores of 1 and 0 were obtained at starting doses of 1–2 mg/kg/day and 2–3 mg/kg/day, respectively. The dose at the end of the sixth month (optimum maintenance dose) is related to the SIS status ( $X^2=7.0$ ,  $df=1$ ,  $p0.05$ ) (Table 1). SIS scores of 3 and 4 were obtained at optimum doses of 2.5 to 7.5 mg/kg/day.

**Table 1: Efficacy of TPM based on seizure frequency**

6th Month end dose level (mg/kg/day)	Number of patients	Seizure improvement scale in the study population					
		-1	0	1	2	3	4
Stopped	9	4	3	2	0	0	0
<2.5	2	0	0	0	0	0	2
2.5-5	7	0	0	0	0	3	4
5-7.5	12	0	0	2	3	2	5
>7.5	10	0	0	4	3	2	1
<b>Number of patients</b>		<b>4</b>	<b>3</b>	<b>8</b>	<b>6</b>	<b>7</b>	<b>12</b>

Apart from intermittent minor side effects such as hyperactivity in ten percent of population, anorexia in four percent, sleeplessness in four percent, sedation in ten percent, hypohidrosis in eight percent, and vomiting symptoms in two percent, no significant systemic side effects were observed; none of the participants stopped TPM due to its side effects. Before and after the analysis, all haematological, hepatic, and renal parameters were normal.

### CONCLUSION:

During the study period, none of the participants experienced any significant systemic manifestations apart from mild side effects. Two patients had hypohidrosis, which was reversed by drinking plenty of water. There were no kidney stones or metabolic acidosis in any of the participants. TPM has been shown in many studies to have no significant systemic side effects, including in children.

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