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Research Article

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 Chi-square test was used to analyse SIS based on two parameters: the starting dose and the dose at the end of the sixth month. There is a relationship between the starting dose and the SIS location (X2=13.45, df=4, p0.05). At starting doses of 1–2 mg/kg/day and 2–3 mg/kg/day, respectively, favourable scores of 3 and 4 and unfavourable scores of 1 and 0 were maximally obtained. There is a connection between the dose at the end of the sixth month (optimum maintenance dose) and SIS position (X2=7.0, df=1, p0.05) (Table 1). At optimum doses of 2.5 to 7.5 mg/kg/day, favourable SIS scores of 3 and 4 were obtained. 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.

Key words: - Topiramate, Safety in Children, Seizures, India, Therapy.

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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].

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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]. Despite treatment with traditional antiepileptic medications, seizures remain uncontrolled in 10–20 percent of all children with epilepsies (AEDs). TPM is preferred by newer AEDs because of its wide spectrum of operation, effectiveness, and ease of availability [12]. It is cost-effective, has few side effects, and has FDA approval for use in children [13]. It is used to treat partial seizures such as complex partial seizures (CPS), partial seizures with secondary generalisation (PSSG), generalized tonic clonic seizures (GTCS), myoclonic jerks (MJ), Lennox Gastaut Syndrome (LGS), West Syndrome (WS)/Infantile Spasms (IS), mixed, and absence seizures [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. After receiving parental consent and Ethical Committee approval, the study was conducted from January to September 2020. TPM was added orally as tablets to traditional AEDs, starting in small divided doses (1–3 mg/kg/day) and gradually increasing at frequent weekly intervals until the most effective/best-tolerated dose (maximum of 9 mg/kg/day) was reached, and was continued for the remainder of the study period.

Inclusion criteria:

- The study involved forty children aged 0–12 years old who had seizures and were already taking more than one primary traditional AED at the highest clinically tolerable daily dosage.

Exclusion criteria:

- Non-epileptic paroxysmal conditions, apparent chronic metabolic/toxic/infectious events, concomitant severe systemic/progressive neurological/current psychiatric diseases, history of nephrolithiasis, and those at risk of acidosis, such as renal/respiratory diseases, were all removed from the study.

Statistical Analysis:

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

RESULTS & DISCUSSION:

Almost half of the participants were between the ages of 1 and 5. The tiniest of the group was a 9-month-old baby. There was 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 (6), LGS (5), WS (3), and Dravet syndrome (3) were among the fourteen children who had specific epileptic syndromes (2).

The Chi-square test was used to analyse SIS based on two parameters: the starting dose and the dose at the end of the sixth month. There is a relationship between the starting dose and the SIS location ($X2=13.45$, $df=4$, $p0.05$). At starting doses of 1–2 mg/kg/day and 2–3 mg/kg/day, respectively, favourable scores of 3 and 4 and unfavourable scores of 1 and 0 were maximally obtained. There is a connection between the dose at the end of the sixth month (optimum maintenance dose) and SIS position ($X2=7.0$, $df=1$, $p0.05$) (Table 1). At optimum doses of 2.5 to 7.5 mg/kg/day, favourable SIS scores of 3 and 4 were obtained

Table 1: Efficacy of TPM based on seizure frequency

Dose at the end of 6th month (mg/kg/day)	Total patients	Number of patients based on Seizure improvement scale					
		-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
Number of patients		4	3	9	8	10	16

Apart from intermittent minor side effects such as hyperactivity (10%), sedation (10%), hypohidrosis (8%), anorexia (4%), sleeplessness (4%), and vomiting (2%), 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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