

# Comparison between Topiramate and Sodium Valproate Efficacy in the Treatment of Migraine

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## ABSTRACT

**Background:** Migraine is a headache, a neurological disorder associated with significant impairment in the quality of life in patients as well as disability. Topiramate (TPM) and Sodium valproate are used as preventive therapies for migraine. Studies comparing the efficacy of these agents are scarce.

**Aim:** To compare the efficacy of topiramate with sodium valproate in terms of reduction of frequency in migraine in patients with migraine.

**Methods:** This randomized controlled trial study was carried at MU-IV, DHQ Hospital, Faisalabad over a period of six months from 1<sup>st</sup> January 2017 to 30<sup>th</sup> June 2017 and comprised 90 cases. The patients were divided in two groups; Group A (Sodium valproate) and Group B (Topiromate). Each group comprised equal number of cases.

**Results:** In our study groups A and B, 20(44%) and 18(40%) cases in were found to be between 12-40 years of age, compared to 25(55.5%) and 27(60%) aged 41-55 respectively. Mean age was similar in both groups with 39.55±9.29 in A vs 42.11±8.91 years in B. 11(24.44%) in Group-A and 14(31.11%) in Group-B were male while 34(75.56%) in Group-A and 31(68.89%) in Group-B were females. Comparison of efficacy of topiramate with sodium valproate in terms of reduction of frequency in migraine in patients with migraine showed efficacy of 29(64.44%) in Group-A and 16(35.56%) in Group-B, p value was 0.006 which shows a significant difference between the two groups.

**Conclusion:** Sodium valproate as compared to topiramate is significantly better for reduction of frequency in migraine in patients with migraine.

**Keywords:** Migraine, Topiramate, Sodium valproate, Efficacy

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## INTRODUCTION

Migraine is a benign disorder comprised of headache associated with symptoms of neurological dysfunction in varying admixtures<sup>1</sup>. Migraine affects 18and 6 of women and men respectively aged 25-55 years and is frequently reported to be an under recognized disorder worldwide<sup>2</sup>. Migraine headaches can be unilateral or generalized, are dull or throbbing in character. Anorexia, nausea, vomiting, photophobia, phonophobia are common associated symptoms, although cognitive impairment and blurred vision are also found in cases<sup>3</sup>.

Stressful events, use of oral contraceptives, hypertension, mood disorders and the use or over use of certain drugs are the factors that can increase the frequency of migraine headache while diet, regular and sound sleep, exercise or other physical activity, and relaxation techniques are observed to decrease the frequency of headache episodes.<sup>4</sup> Epidemiologic studies suggest approximately 36% of migraineures need prevention therapy but only 3%-13% currently use it<sup>5</sup>. Its management consists of

three pronged strategies which include health, patient education, acute drug therapy (NSAIDS, Triptans) and prophylaxis (via anticonvulsants, beta blockers and anti-depressants)<sup>6</sup>.

Valproate is affective in migraine prophylaxis by increasing GABA levels via inhibition of gamma aminobutyric acid transaminases which degrade GABA as there is imbalance between GABA and glutamic acid in patients with migraine. Topiramate is a new broad spectrum antiepileptic drug which exerts a multitude of effects on CNS including blockage of the excitatory pathways via inhibition of sodium, calcium, and glutamate channels.<sup>7</sup> In one of previous studies divalproex sodium shows reduction in migraine frequency in 72.7% patients.<sup>7</sup> Another study shows reduction in migraine frequency of 46.3% in patients using topiramate<sup>8</sup>. Both sodium valproate and topiramate are used in migraine but evidence is lacking which one is superior to other. The study will explore the clinical improvement in patients with chronic migraine on sodium valproate compared with topiramate. This will help us in modifying the prophylaxis of migraine resulting in better patient care.

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## SUBJECTS AND METHODS

This randomized controlled trial study was carried at MU-IV, DHQ Hospital, Faisalabad over a period of six months from 1<sup>st</sup> January 2017 to 30<sup>th</sup> June 2017 and comprised 90 cases. The patients were divided in two groups; Group A (Sodium valproate) and Group B (Topiramate). Each group comprised equal number of cases. Both male and female of any race between 18 and 55 years of age and subjects who met the criteria for migraine were included. Female subjects who are pregnant determined by urine dip stick method, or planning to become pregnant during the time frame of study. Individuals with history of headache disorders other than migraine as cluster headache (periodic unilateral headache along with lacrimation, nasal congestion and conjunctival injection), tension headache (dull headache of constant character for weeks on months) and history of alcohol or overuse of acute medication were excluded. The patients were divided in two groups; Group A (Sodium valproate) and Group B (Topiramate). Patients were asked to take study drug in the morning and evening with water for up-to six weeks. Group A was given 1000mg sodium valproate per day in two divided doses. Group B was given topiramate 100mg per day in two divided doses. Baseline migraine episodes were recorded in last month and patients were given questionnaire to record the number of episodes of migraine. 50% reduction after 6 weeks in number of episodes of migraine attacks from baseline was considered significant. Patients were followed up by keeping telephonic contacts of patients by me.

## RESULTS

Age distribution of the cases shows that in group A and B, 20(44%) and 18(40%) cases were between 12-40 years of age, compared to 25(55.5%) and 27(60%) in 41-55 age group respectively. Mean age was similar in both groups with 39.55±9.29 in A vs 42.11±8.91 years in B (Table 1). Gender distribution showed that 11(24.44%) in Group-A and 14(31.11%) in Group-B were male while 34(75.56%) in Group-A and 31(68.89%) in Group-B were females (Table 2). Mean episodes of episodes of migraine at baseline were calculated as 3.64±1.19 in Group-A and 3.55±1.22 in Group-B (Table 3). Mean episodes of episodes of migraine after treatment were calculated as 1.733±0.61 in Group A and 1.311±0.46 in Group B (Table 4). Comparison of efficacy of topiramate with valproate in terms of reduction of frequency in migraine in patients with migraine showing efficacy in 29(64.44%) in Group-A and 16(35.56%) in Group-B while remaining 16(35.56%) in Group-A and

29(64.44%) in Group-B could not manage effectively, p value was calculated as 0.006 which shows a significant difference between two groups (Table 5).

Table 1: Frequency of age (n = 90)

Age (years)	Group A (n=45)		Group B (n=45)	
	No.	%	No.	%
18-40	20	44.44	18	40.0
41-55	25	55.56	27	60.0
Mean±SD	39.55±9.29		42.11±8.91	

Table 2: Frequency of genders (n=90)

Gender	Group A (n=45)		Group B (n=45)	
	No.	%	No.	%
Male	11	24.44	14	31.11
Female	34	75.56	31	68.89

Table 3: Mean episodes of episodes of migraine at baseline (n=90)

Episode	Group A (n=45)		Group B (n=45)	
	Mean	SD	Mean	SD
	3.64	1.19	3.55	1.22

Table 4: Mean episodes of migraine after 6 weeks of treatment (n=90)

Episode	Group A (n=45)		Group B (n=45)	
	Mean	SD	Mean	SD
	1.73	0.61	1.31	0.46

Table 5: Comparison of efficacy of topiramate with sodium valproate in terms of reduction of frequency in migraine in patients with migraine (n=90)

Efficacy	Group A (n=45)		Group B (n=45)	
	No.	%	No.	%
Yes	29	64.44	16	35.36
No	16	35.36	29	64.44

P value = 0.006

## DISCUSSION

Eighteen percent of women and 6% men are affected by migraine in United States, with approximately half of these patients requiring bed rest and 57% suffering from moderate-severe disability. Certain neuromodulators, most importantly topiramate (TPM) and sodium valproate are effective prophylactic agents for migraine.

In our study, comparison of efficacy of topiramate with sodium valproate in terms of reduction of frequency in migraine in patients with migraine showed efficacy of 29(64.44%) in Group-A and 16(35.56%) in Group-B. P=value was calculated as 0.006 which shows a significant difference between the two groups. Our findings are in agreement with previously studies showing that divalproex sodium shows reduction in migraine frequency in 72.7% patients<sup>9</sup>. Another study shows reduction in migraine frequency of 46.3% in patients using topiramate<sup>10</sup>.

In a study by Bartolini et al<sup>11</sup>, the comparison of efficacy between valproate and topiramate was carried out for prophylaxis of chronic migraine. They recorded that at baseline the number of headache days per month and mean of MIDAS scores, the migraine disability assessment index, were similar. When treatment period ended, a reduction in frequency of headache per 30-days as well as ( $P<0.00001$ ) MIDAS scores ( $P<0.00001$ ) were observed compared with baseline. It appears that both of these drugs were able prevent the chronic migraine successfully without considerable differentiation in efficacy or tolerability. While they compared mean MIDAS score, we compared no. of episodes of migraine<sup>12,13</sup>.

Another study<sup>14</sup> by Shaygannejad and colleagues compared the relative efficacy of same two drugs (topiramate vs valproate) in the prevention of migraine and concluded that both significantly prevented future migraine headache attacks. The effects of both topiramate and sodium valproate has previously been elucidated in migraine prevention, and it has been postulated that they may have a similar benefit<sup>15-17</sup>.

We found not much data in the favour of significant effective results of sodium valproate but the findings of our study in comparison of other two studies<sup>7-8</sup> are justifying the hypothesis that "Sodium valproate is effective in reducing the frequency of migraine headache as compared to topiramate". However, some other trials are required to authenticate our findings and modifying the treatment for prophylaxis of migraine resulting in better patient care.

## CONCLUSION

We concluded that sodium valproate as compared to Topiramate is significantly better for reduction of frequency in migraine in patients with migraine.

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