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Original Article

The Role of Topiramate in the Prevention of Migraine

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ABSTRACT

Aims and Objectives: *To see the efficacy of topiramate in migraine prevention* ***Methods & Materials:*** *This prospective randomised control clinical trial was conducted in the Department of Medicine, Sylhet M.A.G. Osmani Medical College Hospital from 1st July 2009 to 30th June 2010. Fifty patients with migraine of more than 15 years of age were selected according to inclusion and exclusion criteria and divided randomly into two groups by lottery method. Patients of group-A were treated with topiramate 100mg/day and NSAIDs and prochlorperazine symptomatically; and patients of group-B (control group) were treated symptomatically with same NSAIDs and prochlorperazine.* ***Results:*** *The mean age of 27.640 ± 9.772 years in topiramate group and 28.320 ± 10.846 years in control group (p=0.817). In topiramate group, 24.0% of patients were male, 76.0% were female; whereas 36.0% patients were male and 64.0% were female in the control group (p=0.538). The frequency of migraine attack was decreased from 6.240 ±1.451 to 3.400 ± 1.041 in the topiramate group (p < 0.001) and from 6.000±1.608 to 5.840±1.491 in the control group (p< 0.103 and more reduction in topiramate group (p<0.001). The duration of migraine attack was decreased from 6.240±1.451 to 2.560± 0.290 in the topiramate group (p<0.001) and from 6.000±1.451 to 4.760± 0.321 in the control group (p < 0.001) but more decreased in topiramate group (p <0.001). The intensity of headache was decreased from 7.000± 1.259 to 3.400± 1.041 in the topiramate group (p < 0.001) and from 7.080±1.383 to 5.040±1.136 in the control group (p < 0.001) but marked reduction in topiramate group (p < 0.001). The physical disability was decreased from 12.800±5.447 to 5.920±2.691 in the topiramate group (p <0.001) and from 13.600± 5.686 to 8.440±4.154 in the control group (p<0.001) but more in topiramate group (p<0.014). The mental disability was decreased from 3.200±1 to 1.600 ± 0.763 in the topiramate group (p< 0.001) and from 3.360±1.221 to 2.400±0.957 in the control group (p<0.001) but more marked in topiramate group (p<0.002). The side effects such as nausea, anorexia, weight loss and taste perversion did not differ significantly in two groups (p>0.05) but paresthesia was significantly more in topiramate group (p=0.022).* ***Conclusion:*** *The efficacy and safety of topiramate 100mg/day in migraine prevention is established in this study.*

Keywords: *Topiramate, Prevention, Migraine*

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INTRODUCTION

Migraine, the second most common cause of headache, afflicts approximately 15% of women and 6% of men. [1] It is most common in the third decade of life and in lower socioeconomic groups and is associated with an increased prevalence of depression and panic attacks.[2] Migraine is a recurrent headache.[3] It can be divided as migraine with aura and migraine without aura. The typical migraine headache is unilateral and pulsating, lasting from 4 to 72 hours. [4] It starts with a nonspecific prodrome of malaise and irritability followed by the 'aura' of a focal neurological event and then a severe, throbbing, hemicranial headache with photophobia and vomiting.[5] Migrainous headaches may be lateralized or generalized, may be dull or throbbing. [6] The brain of the migraineur is particularly sensitive to environmental and sensory stimuli. This sensitivity is amplified in females during the menstrual cycle. Headache can be initiated or amplified by various triggers, including glare, bright lights, sounds, or other afferent stimulation; hunger; excess stress; physical exertion; stormy weather or barometric pressure changes; hormonal fluctuations during menses; lack of or excess sleep; and alcohol or other chemical stimulate.In the familial hemiplegic migraine the patient experiences typical migraine headache either preceded or accompanied with unilateral reversible limb weakness and/or sensory difficulties and/or speech difficulties. Abdominal migraine is a recurrent disorder of unknown origin, principally affecting children; episodes feature nausea, vomiting, and moderate-to-severe central, abdominal pain. Menstrual migraine is distinct from other migraines and is two forms, menstrually related migraine and pure menstrual migraine.[4] Effective migraine-prevention drugs can be expected to achieve at least 50% reduction in

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headache frequency.[7] Topiramate 100 mg/day has efficacy in migraine prevention. The goals of migraine-prevention therapy are to: reduce the frequency, severity and duration of attacks. By choosing a drug with the highest level of evidence-based efficacy and the lowest potential for adverse effects in an individualpatient is important for reaching such goal.[8] So, this study is to find out the role of topiramate in the prevention of migraine type headache.

MATERIALS AND METHODS

This was a randomized controlled clinical trial conducted at the department of Medicine, Sylhet M.A.G. Osmani Medical College Hospital, Sylhet from 1st July 2009 to 30th June 2010 for a duration of one year. An approval of study protocol was obtained from the Ethical Review Committee before the commencent of the study. Adults with migraine of more than 15 years of age were selected as study population. Exclusion criteria were sudden severe headache, headache with persistent neurological deficit, migraine with pregnancy. Simple random sampling was done. A total number of 50 cases were enrolled, each migraine patient was given an arbitrary number, every odd number of patients was taken as group-A and even number of patients as group-B, each consists of 25 cases. Group-A (study group) patients were treated with topiramate (upto 100 mg daily) and NSAIDs (symptomatically) and prochlorperazine. Group B (control group) patients were treated symptomatically with same NSAIDS and prochlorperazine. This selection was done by guide and investigator assessed the results. All the patients were assessed by taking complete history and clinical examination. Necessary investigations such as Complete Blood Count, CT scan of brain, MRI of brain, X-ray PNS etc. were done in selected cases in whom headache pattem has changed recently.Follow up of the patients was done for four months. Outcome variableswere frequency of attack, duration of attack, intensity of headache, physical disability and mental disability. Data were collected in a preformed questionnaire. Data were processed and analyzed with the help of computer program SPSS (Statistical package for social sciences) 16 version. Quantitative data were analyzed by mean and standard deviation; comparison was done between two groups by unpaired t-test. Qualitative data were analyzed by rate, ratio and percentage; comparison was done between two groups by Chi-Square (x^2) test. A probability (p) value of < 0.05 was considered statistically significant. All the participants in the study were informed about the purpose of the study and written consent was taken. All information was collected confidentially with complete respect to the patient's wish and without any force or pressure.

RESULTS

50 patients with migraine were selected according to inclusion and exclusion criteria. They were divided into two groups, the study group (group-A) and Control group (group-B) each consists of 25 patients. The maximum patient age in both groups was between 26-35 years, mean age was 27.640±9.772 in group-A and 28.320±10.846 in group-B, most was female and housewife in both groups. Light sensitivity, stress sensitivity, sound sensitivity, insomnia, menstrual sensitivity and alcohol intake was more in group –B. There was no statistically significant difference of these parameters between two groups.

Table – I: Distribution of the patients according to demographic variables

Parameters	Group -A	Group -B	p-value
Age			
15-25 years	10 (40.0)	13 (52.0)	
26-35 years	11 (44.0)	6 (24.0)	
36-45 years	3 (12.0)	5 (20.0)	0.373
46-55 years	1 (4.0)	0 (0.0)	
56-65 years	0 (0.0)	1 (4.0)	
Mean±SD	27.640± 9.772	28.320± 10.846	0.817
Sex			
Male	6 (24.0)	9 (36.0)	0.538
Female	19 (76.0)	16 (64.0)	
Occupation			
House wife	14 (56.0)	8 (32.0)	
Student	7 (28.0)	11 (44.0).	0.463
Service	3 (12.0)	4 (16.0)	
Business	1 (4.0)	2 (8.0)	
Others			
Light sensitivity	19 (76.0)	22 (88.0)	0.463
Stress sensitivity	17 (68.0)	21 (84.0)	0.321
Sound sensitivity	15 (60.0)	19 (76.0)	0.364
Insomnia	6 (24.0)	11 (44.0)	0.274
Menstrual sensitivity	10 (55.5)	13 (76.5)	0.289
Alcohol Intake	1 (4.0)	2 (8.0)	1.000

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Table – II: Distribution of patients by frequency of migraine attack

Study group	Frequency of migraine attack/month		p† value
	Before treatment	After treatment	
Group-A (n = 25)	6.240 ± 1.451	3.400 ±1.041	<0.001
Group-B (n = 25)	6.000±1.607	5.840±1.491	
P* value	0.582	<0.001	0.103

*Unpaired t test was employed to analyze the data.
†Paired t test was employed to analyze the data.

Before treatment, there was no statistically significant difference between the groups in relation to frequency of migraine attack (p = 0.582). After treatment it decreased significantly in group-A (p <0.001) and more than group-B (p < 0.001) (Table-II). Before treatment, duration of migraine attack was identical in both groups (p = 0.901). After treatment it decreased significantly in both groups (p < 0.001), and more marked in group-A (p < 0.001) (Table-III).

Table – III: Distribution of patients by duration of migraine attack

Study group	Duration of attack in days/month		p† value
	Before treatment	After treatment	
Group-A (n = 25)	6.240 ± 1.451	2.560 ± 0.290	<0.001
Group-B (n = 25)	6.000 ± 1.451	4.760 ± 0.321	
P* value	0.901	<0.001	<0.001

*Unpaired t test was employed to analyze the data. †Paired t test was employed to analyze the data.

Table – IV: Distribution by intensity of headache

Study group	Intensity of headache††		p†value
	Before treatment	After treatment	
Group-A (n = 25)	7.000 ±1.259	3.400±1.041	<0.001
Group-B (n = 25)	7.080 ±1.383	5.040±1.136	
P* value	0.831	<0.001	<0.001

*Unpaired t test was employed to analyze the data. †Paired t test was employed to analyze the data. ††Visual analogue scale (Appendix, xix) was used to measure the intensity of headache

Table – V: Distribution of patients by physical disability

Study group	Physical disability		p†value
	Before treatment	After treatment	
Group-A (n = 25)	12.800 ± 5.447	5.920 ± 2.691	<0.001
Group-B (n = 25)	13.600± 5.686	8.440 ± 4.154	
P* value	0.614	<0.014	<0.001

*Unpaired t test was employed to analyze the data. †Paired t test was employed to analyze the data. Before treatment, the intensity of headache did not reach the level of significance between the groups (p = 0.831). After treatment it reduced significantly in both groups (p <0.001) but more reduction in group-A (<0.001) (Table-IV). Before treatment, physical disability between the groups did not show any statistical significance difference (p=0.614). After treatment it decreased significantly in both groups (p<0.001) and more in group-A (p=0.014) (Table-V).

Table – VI: Distribution of patients by mental disability

Study group	Mental disability		p† value
	Before treatment	After treatment	
Group-A (n = 25)	3.200 ± 1.000	1.600± 0.7638	<0.001
Group-B (n = 25)	3.360 ± 1.221	2.400± 0.957	
P* value	0.614	0.002	<0.001

* Unpaired t test was employed to analyze the data. †Paired t test was employed to analyze the data. #SF-36 Health survey (Appendix, xviii) was used to measure the mental disability.

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Table – VII: Distribution of patients by side effects

Side effect	Study Subjects		p-value
	Group-A (n = 25)	Group-B (n = 25)	
Paresthesia	6 (24.0)	0 (0.0)	0.022*
Nausea	7 (28)	5 (20.0)	0.742†
Anorexia	8 (32.0)	4 (16.0)	0.321*
Weight loss	3 (12.0)	0 (0.0)	0,235†
Taste perversion	2(8.0)	0(0.0)	0.490†

*x^2 (Chi-square) test employed to analyze the data. †Fisher's Exact test employed to analyze the data.

Before treatment, mental disability was almost similar in both groups (p=0.614). After treatment mental disability reduced in both groups (p<0.001) but more reduction in group-A (p=0.002) (Table-VI). Paresthesia was more marked in group-A (p=0.022); other side effects such as nausea, anorexia, weight loss and taste perversion did not vary statistically significant between the groups (p=0.742; p=0.321; p=0.235 and p=0.49 respectively) (Table-VII).

DISCUSSION

The goals of managing migraine are to reduce migraine frequency, severity and disability; reduce reliance on poorly tolerated, ineffective or unwanted acute pharmacotherapies; improve quality of life; reduce headache-related distress and psychologic symptoms; educate patients and enable them to manage their disease; and avoid dose escalation of acute medications. [8] Recent studies suggest that habitual overuse of acute medications, including triptans, ergots and other analgesics can lead to the development of chronic daily headaches.[9] Preventive medications can serve an important role in the treatment of migraine by reducing migraine frequency and by ameliorating dose escalation and the potential for overuse of acute pharmacotherapies. Recent research suggests that topiramate may modulate trigeminovascular signaling, which could affect migraine pathogenesis [10] and several studies indicated the role of topiramate in migraine prophylaxis. [11-16] The age of the patients was ranging from 15 to 55 years with the mean age of 27.640 ± 9.772 years in topiramate group; whereas the age of the control group wasranging from 15 to 60 years with the mean age of 28.320 ± 10.846 years. In the present study 24.0% of patients were male and 76.0% were female in topiramate group whereas 36.0% patients were male and 64.0% were female in control group. This result is supported by another study. [11] In the present study the frequency of migraine attack was decreased from 6.240 ± 1.451 to 3.400 ± 1.041 in the topiramate group (p < 0.001). This result is supported by other studieswhich showed that monthly migraine frequency decreased for patients treated with topiramate at 100 mg/d. [12,13] In the current study the duration of migraine attack was decreased from 6.240 ± 1.451 to 2.560 ± 0.290 in the topiramate group. This result was correlated with other studies which showed thatthe mean reduction in the monthly number of migraine days was statistically significant for the topiramate at 100 mg/d group. [12-14]. In this study the intensity of headache was decreased from 7.000 ± 1.259 to 3.400 ± 1.041 in the topiramate group. This result was concordance with another study which showed that the mean headache intensity decreased significantly in the topiramate group. [11] In present study physical disability was decreased from 12.800 ± 5.447 to 5.92±2.691 in the topiramate group. This result is supported by another study which found that topiramate significantly improved physical component scores.[17] Mental disability was decreased from 3.200±1.000 to 1.600± 0.7638 in the topiramate group. This result is supported by another study which found that topiramate significantly improved mental component scores.[17] The side effects observed in this study were paresthesia, nausea, anorexia, weight loss and taste perversion in topiramate group. Rate of side effects in this study was lower than other studies. [13,14] This may be due to geographical and racial variation of the study population.

CONCLUSION

The efficacy and safety of topiramate in migraine prevention is established in this study. This study was conducted in tertiary hospital and did not represent the actual situation of the country. Sample size in this study was small and may not give the actual conclusion. Follow up period in this study was short. A prospective study involving multicenter, large sample size and at least one year follow up should be conducted to evaluate long term efficacy and safety of topiramate in the prevention of migraine.

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