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Sodium Valproate is More Effective than Pizotifen in the Prophylaxis of Migraine Patients

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Abstract:

Background and objectives: *Migraine is now ranked as number 19 among all diseases causing disability by WHO[1] which is characterized by recurrent attacks of various combinations of headache and neurological, gastrointestinal and autonomic symptoms[2] accompanied by photophobia, phonophobia and vomiting[3]. The treatment of migraine involves acute, preventive drugs and non-pharmacological strategies. The basic principle in management of migraine is avoiding the trigger factors, blocking the mediators and splinting the end organ[4]. Though there is no significant curable treatment but there are some internationally proven and well accepted prophylactic medication which reduces headache severity, frequency, duration and risk for rebound[5]. Sodium valproate and pizotifen are commonest of them[6], where sodium valproate is more effective than pizotifen in the prophylaxis of migraine patients.* ***Methods:*** *This study was a single blind randomized clinical trial carried out in the neurology outpatient department of Bangabandhu Sheikh Mujib Medical University, Dhaka (BSMMU) for the period of 2 years, among adult patients between the age of 16-50 years.* ***Results:*** *A total of 120 patients were included & divided into two groups such as group-A(60 patients) treated by sodium valproate & group-B(60 patients) treated by pizotifen for a period of 6 months and followed up every two months for 3 times and showed sodium valproate is more effective than pizotifen.* ***Conclusion:*** *This study permit to conclude that efficacy of sodium valproate is more than pizotifen in the prophylaxis of migraine patients.*

Key words: *migraine ,sodium valproate, pizotifen, prophylaxis.*

Introduction:

Migraine is now ranked by the World Health Organization as number 19 among all diseases causing disability world-wide[1]. The exact cause is unknown but a number of factors trigger a migraine headache e.g. sensory stimuli, streneous exercise & physical exertion, inadequate posture or stress in neck, hormonal fluctuation, foods-drinks & additives, dehydration, insufficient sleep & skipping or missing meal[7]. The exact pathogenesis is still unclear but following possible theories are responsible like vascular theory, neural theory, 5-HT theory, dopamine theory & some other theories[8-10]. It is an episodic primary headache disorder characterized by recurrent attacks of various combinations of headache and neurological, gastrointestinal and autonomic symptoms[2]. Migraine is a common condition, annually affecting

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12% of the United states population, including 18% of women, 6% of men and 4% of children. Lifetime prevalence of migraine in women in the United States exceeds 25%. The prevalence of migraine has not changed since 1989, which was based on evidence from three large studies: American Migraine study-I, American Migraine Study-II and American Migraine Prevention and prevalence study. The basic principle in management of migraine is avoiding the trigger factors, blocking the mediators[4]. Sodium valproate and pizotifen can be used in the prophylaxis of migraine and the potential effectiveness of sodium valproate in migraine prophylaxis is well established.

Materials and Methods:

This study was a single blind randomized clinical trial carried out in the department of neurology at BSMMU, Dhaka from January 2010 to December 2011 for a duration of two years among patients of both sexes between 16-50 years who presented with migraine and were enrolled in this study. Migraine patient were selected according to INTERNATIONAL HEADACHE SOCIETY (IHS) criteria who were not on prophylactic medication & patients having hepatic or renal impairment, pregnancy and prostatism were excluded from the study.

Observation and Results:

A total of 120 patients were included as study population and were divided into two groups, group-A (60 patients) and group-B(60 patients). The group-A took sodium valproate (400-1200 mg/day) and the group-B took pizotifen (0.5-3.00 mg/day) for total 6 months duration.

Table-I

Distribution of the patients by age (n=120)

Age (y)	Group		p value
	Group A (Sodium valproate)	Group B (Pizotifen)	
<20	14 (23.3)#	15 (25.0)	
20 – 29	23 (38.3)	22 (36.7)	
30 – 39	16 (26.7)	17 (28.3)	
40 and above	7 (11.7)	6 (10.0)	
Total	60 (100.0)	60 (100.0)	0.983*

*t test was done to measure the level of significance.
#Figure within parentheses indicates percentage

Table II

Distribution of the patients by sex (n=120)

Sex	Group A (Sodium valproate)	Group B (Pizotifen)	p value
Male	11(18.3)#	11 (18.3)	1.000
Female	49(81.7)	49 (81.7)	
Total	60 (100.0)	60 (100.0)	

*Chi-square test was done to measure the level of significance.
#Figure within parentheses indicates percentage.

Table III

Distribution of the patients by severity before treatment

Severity	Group A (Sodium valproate)	Group B (Pizotifen)	p value
Moderate	21 (35.0)	19 (31.7)	0.699
Severe	39 (65.0)	41 (68.3)	
Total	60 (100.0)	60 (100.0)	

*Chi-square test was done to measure the level of significance.
Figure within parentheses indicates percentage

Table-I shows in group A majority were in the age group of 20 – 29 years which was 23 (38.3%), followed by 30 – 39 years which was 16 (26.7%) and less than 20 years was 14 (23.3%). Only 7 (11.7%) cases were in the age group of 40 years and above. In group B majority were in the age group of 20 – 29 years, which was 22 (36.7%) followed by group 30 – 39 years which was 17 (28.3%) and less 20 years was 15 (25.0%) cases. Only 6 (10.0%) cases were in the age group of 40 years and above.

Table II shows in both groups females were predominant which was 49(81.7%) and 49(81.7%) cases respectively and statistically significant.

Table III shows in group A moderate was in 21 (35.0%) cases and severe in 39 (65.0%) cases. In group B moderate was in 19 (31.7%) and severe in 41 (68.3%) cases.

Table-IV

Distribution of the patients by duration of episode before treatment (n=120)

Duration of episode	Group		p value
	Group A (Sodium valproate)	Group B (Pizotifen)	
Minutes	1 (1.7)	0 (.0)	0.341
Minutes to hours	40 (66.7)	35 (58.3)	
Hours to days	19 (31.7)	25 (41.7)	
Total	60 (100.0)	60 (100.0)	

*Chi-square test was done to measure the level of significance.

Table-V

Distribution of the patients by frequency of migraine

	Frequency of attack			
Group	Frequency of attack per month before treatment	Frequency of attack per month after 2 months of treatment	Frequency of attack per month after 4 months of treatment	Frequency of attack per month after 6 months of treatment
Group A (Sodium valproate)	7.40 ± 5.1 (3 - 25)	4.69 ± 3.46 (2-20)	2.51 ± 2.20 (1-15)	1.60 ± 1.87 (1 - 10)
Group B (Pizotifen)	9.25 ± 7.21 (2 - 30)	6.56 ± 5.14 (1-20)	3.88 ± 2.83 (1.12)	2.76 ± 1.98 (1 - 8)
p value	0.107	0.022	0.004	0.023

Figure within parentheses indicates percentage.

Table VI

Distribution of the patients by severity after treatment

Severity	Group		p value
	Group A (Sodium valproate)	Group B (Pizotifen)	
Before treatment			0.699
Moderate	21 (35.0)	19 (31.7)	
Severe	39 (65.0)	41 (68.3)	
Total	60 (100.0)	60 (100.0)	
After 2 months of treatment			0.667
Mild	4 (6.7)	2 (3.3)	
Moderate	43 (71.7)	43 (71.7)	
Severe	13 (21.7)	15 (25.0)	
Total	60 (100.0)	60 (100.0)	
After 4 months of treatment			0.234
Mild	44 (77.2)	39 (67.2)	
Moderate	13 (22.8)	19 (32.8)	
Total	57 (100.0)	58 (100.0)	
After 6 months of treatment			0.006
Mild	24 (96.0)	24 (66.7)	
Moderate	1 (4.0)	12 (33.3)	
Total	25 (100.0)	36 (100.0)	

*Chi-square test was done to measure the level of significance.
Figure within parentheses indicates percentage.

Table-VII

Distribution of the patients by duration of episode after treatment (n=120)

Severity	Group		p value
	Group A (Sodium valproate)	Group B (Pizotifen)	
Before treatment			0.341
Minutes	1 (1.7)	0 (0.0)	
Minutes to hours	40 (66.7)	35 (58.3)	
Hours to days	19 (31.7)	25 (41.7)	
Total	60 (100.0)	60 (100.0)	
After 2 months of treatment			0.128
Minutes	26 (44.1)	18 (30.0)	
Minutes to hours	33 (55.9)	40 (66.7)	
Hours to days	0 (0.0)	2 (3.3)	
Total	59 (100.0)	60 (100.0)	
After 4 months of treatment			0.007
Minutes	36 (90.0)	29 (60.4)	
Minutes to hours	4 (10.0)	18 (37.5)	
Hours to days	0 (0.0)	1 (2.1)	
Total	40 (100.0)	48 (100.0)	
After 6 months of treatment			0.010
Minutes	22 (88.0)	20 (51.3)	
Minutes to hours	3 (12.0)	18 (46.2)	
Hours to days	0 (0.0)	1 (2.6)	
Total	25 (100.0)	39 (100.0)	

*Chi-square test wa-s done to measure the level of significance.
#Figure within parentheses indicates percentage.

Table IV shows in group A duration of episode in minutes was in 1 (1.7%) case, minutes to hours in 40 (66.7%) and hours to days in 19 (31.7%). In group B duration of episode in minutes to hours in 35 (58.3%) and hours to days in 25 (41.7%) cases.

Table V shows frequency of attack per month before treatment was 7.40 ±5.1 and 9.25 ± 7.21 in group A and group B respectively (p=0.107). Frequency of attack per month after 2 months treatment was 4.69 ± 3.46 and 6.56 ± 5.14 in group A and group B respectively (p=0.022). Frequency of attack per month after 4 months of treatment was 2.51 ± 2.20 and 3.88 ± 2.83 in group A and group B respectively (p=0.004). Frequency of attack per month after 6 months of treatment was1.60 ± 1.87 and 2.76± 1.98 in group A and group B respectively (p=0.023). and statistically significant.

Table VI shows in group A moderate and severe were 35.0% and 65.0% and in group B moderate and severe were 31.7% and 68.3% respectively (p=0.699). After 2 months of treatment severity was recorded in group A mild, moderate and severe 6.7%, 71.7% and 21.7% cases and in group B mild, moderate and severe 3.3%, 71.7% and 25.0% of cases respectively (p = 0.667). After 4 months of treatment severity was recorded in group A mild and moderate 77.2% and 22.8% of cases respectively and in group B mild and moderate 67.2% and 32.8% of cases respectively (p = 0.234). After 6 months of treatment severity was recorded in group A mild and moderate 96.0% and 4.0% and in group B mild and moderate 66.7% and 33.3% of cases respectively (p = 0.006) and was statistically significant.

Table VII shows, the duration of episode before treatment in group A minutes, minutes to hours and hours to days 1.7%, 66.7% and 31.7% and in group B minutes, minutes to hours and hours to days 0.0%, 58.3% and 41.7% respectively (p=0.341). After 2 months of treatment duration of episode was recorded in group A minutes, minutes to hours and hours to days 44.1%, 55.9% and 0.0% and in group B minutes, minutes to hours and hours to days 30.0%, 66.7% and 3.3% respectively (p=0.128). After 4 months of treatment duration of episode was recorded in group A minutes, minutes to hours and hours to days 90.0%, 10.0% and 0.0% and in group B minutes, minutes to hours and hours to days 60.4%, 37.5% and 2.1% respectively (p=0.007). After 6 months of treatment duration of episode was recorded in group A minutes, minutes to hours and hours to days 88.0%, 12.0% and 0.0% and in group B minutes, minutes to hours and hours to days 51.3%, 46.2% and 2.6% cases respectively (p=0.010) and was statistically significant

Discussion:

In this present study a total of 120 patients were studied and divided into two groups, group-A and group B. The group-A took the sodium valproate and group-B took the pizotifen given with definite doses & duration. In group-A majority were in the age group of 20-29 years which was 23 (38.3%) followed by 30-39 years which was16(26.7%) and less than 20 years which was 14 (23.3%). Only 7 (11.7%) cases were in the age group of 40 years and above. In group-B majority were in the age group of 20 - 29 years which was 22 (36.7%) followed by age group of 30 - 39 years which was 17 (28.3%) and less 20 years which was 15 (25.0%) cases. Only 6 (10.0%) cases were in the age group of 40 years and above. It was reported in a study that migraine usually develops in childhood, adolescence or adulthood[11]. In a study[12] it was also reported that headache intensity declined from 40 years to 74 years with change in headache frequency or duration which is consistent with this study and also consistent with the previous study done in Bangladeshi population[13] .

In both groups female was predominant which was 49(81.7%) cases in group A and 49 (81.7%) cases in group B. Pietrobon D and Striessnig J. reported that female was more vulnerable than male in respect to migraine which is consistent with this present study[11]. Russell et. al.[14] found that there was a significant preponderance of females of all the subtypes of migraine which is also consistent with the present study and also consistent with the previous study done in Bangladeshi populations[13]. The pain severity before treatment revealed that, in group A moderate severity was in 35.0% cases and severe was in 65.0% cases & in

group B moderate was in 31.7% cases and severe was in 68.3% cases (p=0.599). Duration of episode was recorded and it was revealed that in group A minutes was in 1.7% case, minutes to hours was in 66.7% cases and hrs. to days was in 31.7% case. In group B minutes to hours was in 58.3% cases and hours to days was in 41.7% cases. Frequency of attack per month before treatment was 7.40 ±5.1 and 9.25 ± 7.21 in group A and group B respectively (p=0.107). After 2 months of treatment severity was recorded in group A mild, moderate and severe 6.7%, 71.7% and 21.7% cases and in group B mild, moderate and severe 3.3%, 71.7% and 25.0% respectively (p = 0.667). After 4 months of treatment severity was recorded in group A mild and moderate 77.2% and 22.8% cases and in group B mild and moderate 67.2% and 32.8% respectively (p = 0.234). After 6 months of treatment severity was recorded in group A mild and moderate 96.0% and 4.0% cases and in group B mild and moderate 66.7% and 33.3% respectively (p = 0.006). The difference was statistically significant (p=0.009). After 2 months of treatment duration of episode was recorded in group A minutes, minutes to hours and hours to days 44.1%, 55.9% and 0.0% cases and in group B minutes, minutes to hours and hours to days 30.0%, 66.7% and 3.3% cases respectively (p=0.128). After 4 months of treatment duration of episode was recorded in group A minutes, minutes to hours and hours to days 90.0%, 10.0% and 0.0% cases and in group B minutes, minutes to hours and hours to days 60.4%, 37.5% and 2.1% cases respectively (p=0.007). After 6 months of treatment duration of episode was recorded in group A minutes, minutes to hours and hours to days 88.0%, 12.0% and 0.0% cases and in group B minutes, minutes to hours and hours to days 51.3%, 46.2% and 2.6% cases respectively (p=0.010). The difference was statically significant (p=0.01).

Frequency of attack per month after 2 months treatment was 4.69 ± 3.46 and 6.56 ± 5.14 in group A and group B respectively (p=0.022). Frequency of attack per month after 4 months of treatment was 2.51 ± 2.20 and 3.88 ± 2.83 in group A and group B respectively (p=0.004). Frequency of attack per month after 6 months of treatment was 1.60 ± 1.87 and 2.76± 1.98 in group A and group B respectively (p=0.023). The difference is statistically significant (p=0.023) which is consistent with the previous study done in Bangladeshi populations[13]. So, sodium valproate is more beneficial than Pizotifen in the prophylaxis of migraine.

Conclusion:

The finding of this study permit to conclude that the efficacy of sodium valproate is more than Pizotifen in the prophylactic management of migraine patient.

References:

1. Headache Classification Subcommittee of the International Headache Society (HCSIHS) (2005). The International Classification of Headache Disorders, 2nd Edition, 1st revision. Retrieved 1st August, 2009 from: http://ihs-classification.org/en/0_downloads/
2. Charles A. Advances in the Basic and Clinical Science of Migraine. Ann Neurol, 2009; 65(5): 491-8.
3. International Headache Society. 2004, Headache Classification Committee of the International Headache Society. The international classification of headache disorders. 2nd ed. Cephalalgia 2004; 24(suppl 1): 1-160.
4. Rao BS, Das DG, Taraknath VR, Sarma Y, 'A double blind controlled study of propranolol and cyproheptadine in migraine prophylaxis', Neurol India, 2000; 48: 223.
5. Leonardi M, Steiner TJ, Scher AT, Lipton RB, 'The global burden of migraine: measuring disability in headache disorders with WHO's Classification of Functioning, Disability and Health (ICF)', J Headache Pain 2005; 6(6): 429-440.
6. Goadsby PJ, Lipton RB, Ferrari MD. Migraine—current understanding and treatment. N. Engl. J. Med 2002; 346: 257–70.

7. Russell MB, Rasmussen BK, Thorvaldsen P, Olesen J. Prevalence and Sex-Ratio of the Subtypes of Migraine. Int. J. Epidemiol, 1995; 24 (3): 612-18.

8. Russell MB, Rasmussen BK, Thorvaldsen P, Olesen J. Prevalence and Sex-Ratio of the Subtypes of Migraine. Int. J. Epidemiol, 1995; 24 (3): 612-18.

9. Levy D, Strassman, AM, and Burstein R. "A critical view on the Role of Migraine Triggers in the Genesis of Migraine Pain" Headache,2009; 49(6): 953.

10. Boes CJ, Capobianco DJ, Cutter FM, Dodick, DW, Eross, EJ, Swanaon, JW. Headache and other craniofacial pains. In: Bradly WG, Daroff RB, Fenichel GM, Jankovic J, editors. Neurology in clinical practice. Vol. II, 4th ed. Philaldiphia: Butterworth-Heinemann, 2004; 2055-106.

11. Pietrobon D, Striessnig J. Neurobiology of Migraine. Neuroscience 2003; 4: 386-98.

12. Camarda R, Monastero R, Santangelo G, Migraine headaches in adolescents: A five-year follow-up study. *Headache* 2002; 42: 1000-5.

13. Hannan MA, Hasan MK, Begum A, Haque A, Ullah AKM, Khan RK et al. Study of epidemiological features of primary headache patients in a tertiary centre in Bangladesh. Bangladesh Journal of Neurosciences 2007; 23:13-20.

14. Russell MB, Rasmussen BK, Thorvaldsen P, Olesen J. Prevalence and Sex-Ratio of the Subtypes of Migraine. Int. J. Epidemiol, 1995; 24 (3): 612-18.