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Original Research Article

A Study on Comparison of Efficacy of Sodium Valproate and Nortriptyline in the Management of Migraine

Komala R.[1], Amudhan Arvind E[2], Femi Retna J.[3]

[1]Assistant Professor, Department of Pharmacology, Government Medical College Krishnagiri

[2]Senior Assistant Professor, Department of Pharmacology, Government Medical College Krishnagiri

[3]Assistant Professor, Department of Pharmacology, Government Dharmapuri Medical College, Dharmapuri

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Corresponding author: Dr Femi Retna. J

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Abstract

Introduction: Migraine is a common disabling neurological disorder that affects men and women equally. Often recurrent, severe, disabling and long-lasting migraine attacks needs prophylaxis for extended period. The two frequently used drug in prophylaxis are Nortriptyline and Sodium valproate. Therefore, we planned this study to evaluate effectiveness and acceptability of above drugs in prophylaxis of migraine.

Material & Methods: This Prospective observational study was done in 200 patients. The basic features of all patients were noted which included incidence of headache and severity of migraine pain assessed using VAS score. Efficacy was assessed by noting the reduction in number of migraine attacks and severity of pain at different timelines. The adverse drug reactions were noted in due course.

Results: At the end of three and six months of drug therapy patients displayed noteworthy progress in alleviation of migraine symptoms. 50 percent of patients in Nortriptyline group and 70% of patients in sodium valproate group had > 50% improvement at three months. Similarly the reduction at six months was 63% and 82% respectively. ADR was higher in valproate group with 67% incidence.

Conclusion: Sodium valproate had superior effectiveness at the end of 3 months and 6 months. In terms of acceptability, nortriptyline was better in comparison with sodium valproate.

Keywords: Prophylaxis, Nortriptyline, Sodium Valproate.

Introduction

Migraine is one of frequently encountered neurological illness that disturbs both genders. Many works proposes that about 10-12% of the people grieve from migraine [1]. Migraine also has an adverse influence on quality of life. William Gower indicated that migraine and epilepsy are the mutual illnesses that might co-occur in a same patient. Migraine also exacerbates the epileptic seizure [2], thus, migraine treatment is a significant health problem. Management modes for migraine includes pharmacological and non- pharmacological approaches. Non-pharmacological treatment comprises behavioral and way of life modifications that comprises evading of initiating factors, reassurance and follow-up. Drug preferences for migraine contain of prophylactic and symptomatic management. Symptomatic treatment

includes simple analgesics like NSAID or triptans. But the often repetitive, severe, incapacitating and long-lasting migraine attacks needs chronic prophylaxis.

The prophylactic treatment comprises of Beta-blockers, CCBs, TCAs and anti-epileptics like valproate, topiramate. These medications are highly efficacious in prophylactic treatment. Also sometime they may have some adverse reactions and concomitant illnesses which may interfere in treatment. Although extensive range of medications are accessible, the two most frequently used prophylactic agents are Nortriptyline and Sodium valproate. There are only few works relating the effectiveness and ADR profile of Nortriptyline and Sodium valproate in migraine prophylaxis. Therefore we planned this study to evaluate effectiveness and acceptability of above drugs in prophylaxis of migraine and also to monitor related ADRs.

Methodology

This was done as a Prospective observational study at tertiary care teaching hospital for a period of one year. Patients detected with migraine based on international headache society criteria of age more than 18 years who had more than 4 migraine attacks per month, and was on sodium valproate or nortriptyline prophylactic treatment were included in the study

Patients on other drugs and not willing to take part in the study and with comorbidities and known drug allergy were excluded. The study was approved by the Institutional Human Ethics Committee. Written informed consent was acquired before registering them into study. The basic features of all patients were noted which included incidence of headache and severity of migraine pain assessed using VAS score. Efficacy was assessed by noting the reduction in number of migraine attacks and severity of pain at different timelines. The adverse drug reactions were noted in due course, causality was evaluated using WHO Causality assessment scale.

The severity of pain, frequency of headache and functional disability at baseline, 3 months and 6 months were evaluated using ANOVA, Chi-square test. The relation was considered significant if P-value was less than 0.05. The statistical analysis was executed using SPSS version 24.

Results

This study was done in 200 patients with diagnosis of migraine who were prescribed with Nortriptyline (n=100) and sodium valproate (n=100), age ranged from 18-70 years. Most common age group was 21-40 years. 88% in Nortriptyline group and 87% of Sodium valproate group was in this age range. Among 200 patients 123 were female and rest 67 were male and usage of both drugs was similar in both groups. In nortriptyline 61% were female and sodium valproate group 62% were females.

In our study group migraine signs was present for duration ranging from 1 to 6 years and at least 4-12 headache attacks per month. MIDAS score was applied to evaluate severity of migraine attack. In nortriptyline group 70 percent had mild disability, 28 percent had moderate disability and only one patient had severe disability. Where as in sodium valproate group, 20 percent had attack with mild disability, 58 percent with moderate disability and 22 percent with severe disability.

Visual analogue scale was used to assess the severity of pain. 98 percent of migraine attacks in nortriptyline group severe pain score and in sodium valproate group, 95 percent of attacks had severe pain with VAS score stretching from 7-10.

The patients were monitored at the end of 3 months and 6 months. Their pain severity and general progress in headache frequency were evaluated, at third month, 56% patients in nortriptyline group and 71% of

patients in sodium valproate had > 50% improvement in overall headache frequency, while at six months, 68% patients in nortriptyline group and 82 in sodium valproate had > 50% improvement in headache frequency.

Table1: Improvement in VAS score, Severity of headache at the end of 3 months and 6 months

Timeline	Improvement	Nortriptyline	Sodium valproate	p value
Severity of headache				
3 mon	> 50%	60	76	<0.0001
	< 50%	40	24	
6 mon	> 50%	78	87	<0.0001
	< 50%	22	13	
VAS score				
3 mon	> 50%	82	91	<0.0001
	< 50%	18	9	
6 mon	> 50%	88	95	<0.0001
	< 50%	12	5	

The severity of headache was reduced in both the treatment modalities, 60 patients at 3 months and 78 at 6 months in nortriptyline group had more than 50% improvement, while in sodium valproate group, it was 76 and 87 at 3rd and 6 months. At three months, 82 patients and at 6 months 88 patients at the end of 6 months had > 50% improvement in VAS score in nortriptyline group. In sodium valproate group 91 patients and 95 had improvement in VAS score at the end of 3 months and 6 months respectively which was significant statistically.

In our study 36 in nortriptyline group and 67 in sodium valproate group had adverse reactions. Most common ADR was sedation followed by menstrual irregularities and weight gain in nortriptyline group at 3 months, whereas at 6 months along with above dry mouth was also seen in most of patients. In sodium valproate group weight gain was most common followed by sedation and at 6 months along with above two reactions menstrual disorders were also seen commonly in fact more than sedation. We did evaluate all ADRs using WHO-UMC causality assessment scale, in Nortriptyline group at 3 months most commonly it was possible ADR with 85% having that, while 12% were probable and 3% was unlikely, while at 6 months there was not much difference with 79% possible, 14% probable and 7% unlikely. Same way in valproate group at 3 months most commonly it was possible ADR with 78% having that, while 14% were probable and 8% was unlikely, while at 6 months there was not much difference with 75% possible, 18% probable and 7% unlikely.

Discussion

In our study of 200 patients with diagnosis of migraine we found that management with Nortriptyline and Sodium valproate was more in women which is similar to the study done by Kalita J *et al* [3]. The reason may be during active reproductive period there is hormonal fluctuations which may cause this. Few researchers have opinion that it is due to genetic influence [4]. In our study 21 to 40 years was the most frequently encountered age group. This is similar to study done by Bigal *et al* [5]. This is due to exposure to range of triggering elements like stress, hormonal imbalance, high fat diet, lack of nutrition, sunlight exposure, etc [6]. There is a general improvement in incidence of headache and VAS score in comparison with before and after treatment at 3rd and 6th month. This was statistically significant too. This imitates a research work done by Kalita J *et al* [3]. we also compared between groups and sodium valproate had better effectiveness at 6th month too. In contrast to this when compared between groups at end of study period in Kalita J *et al* [3]. there was no significant difference. This may be due to multiple factors like genetic alterations,

pharmaceutical dissimilarity and schedule and dosing frequency. Because compared to our study the dosing was higher in study done by Kalita J *et al* [3].

In our study our next main objective was to evaluate the adverse drug reaction happened due to above drugs. Nortriptyline had a superior tolerability among both drugs with less side effects in comparison. It was 36 in Nortriptyline group in comparison with 67 in valproate group.

Most common ADR was sedation followed by menstrual irregularities and weight gain in nortriptyline group at 3 months, whereas at 6 months along with above dry mouth was also seen in most of patients. Goncalves AL *et al* [7] did a study which had similar results. In sodium valproate group weight gain was most common followed by sedation and at 6 months along with above two reactions menstrual disorders were also seen commonly in fact more than sedation.

This was similar to study done by T Mansoureh *et al* [8]. No life threatening adverse events happened in both treatment modalities. We used WHO-UMC causality assessment scale to evaluate severity. Most of ADR in the both groups had possible ADR at both timelines. There are not much previous studies to compare these results. Evaluation of causality helps to reinforce the association between exposure and consequence.

Conclusion

Sodium valproate had better effectiveness for longer period when given as prophylactic drug. In terms of acceptability, nortriptyline was better in comparison with sodium valproate. Hence if a drug is to be decided for prophylactic use in migraine sodium valproate can be the choice as even though nortriptyline has better safety profile there is not much life threatening adverse events which may be considered by risk benefit ratio. Anyway future evaluation is needed in bigger sample size to assess the acceptability of both drugs.

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