The clinical assessment of propranolol vs. divalproex sodium in the prophylaxis of migraine at a tertiary centre in Bihar

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Abstract

Background: Migraine headaches are common, with a worldwide prevalence ranging between 8 and 18%. The present study was conducted to compare propranolol and divalproex sodium in the prophylaxis of migraine.

Aims and Objectives: The present study was conducted to compare propranolol and divalproex sodium in the prophylaxis of migraine.

Materials & Methods: 80 patients of migraine were divided into 2 groups of 40 each. In group I, patients received propranolol 20 to 160 mg/day, and in group II, patients received divalproex sodium 250 to 750 mg/day for three months. The Migraine Disability Assessment Score (MIDAS) and VAS were compared. Adverse effects were also recorded.

Results: There were 18 males and 22 females in group I, and group II had 24 males and 16 females. The mean ages (mean ± SD) in years were 30.46±8.5 in group I and 35.14±9.24 in group II, respectively; MIDAS was 12.4±3.62 in group I and 10.6±3.90 in group II; VAS was 7.4±1.48 in group I and 6.5±3.02 in group II; the frequency/month of migraine was 5.02±1.26 in group I and 5.01±1.64 in group II; and the duration of migraine was 20.8±6.10 in group I and 19.2±7.2 The difference was non- significant (P> 0.05). Tremor was seen in 1 in group I, hair loss in 1 in group I, weight gain in 1 in group II, insomnia in 1 in group I and 2 in group II, dizziness was seen in 3 in group I and 4 in group II and facial swelling was seen in 1 in group II. The difference was significant (P< 0.05).

Conclusion: Both drugs were found to be equally effective in the management of migraine patients.

Keywords: migraine, propranolol, divalproex sodium.

INTRODUCTION

The prevalence of migraine headaches varies between 8 and 18% globally.[1] The International Headache Society (IHS) diagnostic criteria for migraine include having at least 5 attacks that last 4–72 hours, are unilateral, pulsating, moderate or severe in intensity, are aggravated by or cause avoidance of routine physical activity, and are also accompanied by nausea and/or vomiting, photophobia, or phonophobia.[2] There are a large number of prophylactic treatment options available; common ones include alpha antagonists, anti-convulsants, beta-blockers, botulinum-A, calcium channel blockers, serotonin agonists, serotonin reuptake inhibitors (SSRIs), and tricyclic antidepressants (TCAs).[3] Two emerging prophylactic candidates are angiotensin-converting enzymes (ACE) and angiotensin receptor antagonists (ARB). Valproic acid was first synthesised in 1882 as an analogue of valeric acid, found naturally in valerian. At room temperature, it is a liquid, but when it reacts with a base like sodium hydroxide, it turns into the solid salt sodium valproate.[4] Valproic acid, sodium valproate, or a mixture of the two (divalproex sodium according to United States Adopted Names (USAN) and valproate semisodium according to WHO International Non-proprietary Name (INN) nomenclature) are marketed under various brand names and are collectively referred to as valproate.[5] The U.S. Headache Consortium and European Federation of Neurological Societies (EFNS) Task Force guidelines on the drug treatment of migraine have established the circumstances that might warrant preventive treatment.[6,7]

Aims and Objectives

The present study was conducted to compare propranolol and divalproex sodium in the prophylaxis of migraine.

Materials & Methods

The present prospective cross-sectional study comprised 80 migraine patients of both genders. The study was carried out at department of pharmacology, Sri Krishna Medical College & Hospital, Muzaffarpur, Bihar, India, and Bhagwan Mahavir Institute of Medical Sciences, Pawapuri, Nalanda, Bihar (India) , in collaboration with the department of medicine, after receiving approval from the institutional ethical committee. All were informed about the study, and their written consent was acquired. The research was conducted from May'2019 to April' 2020.

Inclusion criteria:

- Patients who met the International Headache Society (IHS) criteria for migraine between the ages of 18 and 60, of both sexes, had at least five headache attacks lasting four to 72 hours (untreated or unsuccessfully treated), and the headache had at least two of the following features: Unilateral location. pulsating nature
- Patients who agreed to participate in the trial voluntarily, in writing, and with full disclosure were considered for inclusion.

Exclusion criteria:

- Patients with an age of less than 18 years or more than 60 years who are non-cooperative or not willing to give written consent
- Pregnant or lactating women.
- Patients with life-threatening illnesses, acute emergencies, impaired renal or hepatic function, or any organ failure

Data such as name, age, gender, etc. was recorded. Two groups of 40 patients each were created from the patients. In group I, patients received 20–160 mg/day of propranolol, and in group II, patients received 250–750 mg/day of divalproex sodium for three months. Parameters such as respiratory rate, weight, pulse rate, and blood pressure were noted. In all patients, adverse effects were recorded. The Migraine Disability Assessment Score (MIDAS) and VAS were compared in both groups. Results were subjected to statistical analysis, where a p value less than 0.05 was considered significant.

Results:

In the present study, of the total 80 patients enrolled, they were divided into 2 groups of 40 each. Among 80 patients of migraine 42 were male and 38 were female.

Table I: Distribution of patients

Groups	**Group I**	**Group II**
Agent	Propranolol	Divalproex sodium
M:F	18:22	24:16

Table I shows that there were 18 males and 22 females in group I and group II had 24 males and 16 females in group II.

Table II: Assessment of parameters

Parameters	**Group I Mean±SD**	**Group II Mean±SD**	**P value**
Mean Age (in years)	30.46±8.5	35.14±9.24	0.38
MIDAS	12.4±3.62	10.6±3.90	0.09
VAS	7.4±1.48	6.5±3.02	0.81
Frequency/month	5.02±1.26	5.01±1.64	0.92
Mean duration	20.8±6.10	19.2±7.20	0.96

Table II, graph I shows that the mean age (mean±SD) in years of were 30.46±8.5 in group I and 35.14±9.24 in group II respectively, MIDAS was 12.4±3.62 in group I and 10.6±3.90 in group II, VAS was 7.4±1.48 in group I and 6.5±3.02 in group II, frequency/month of migraine was 5.02±1.26 in group I and 5.01±1.64 in group II and duration of migraine was 20.8±6.10 in group I and 19.2±7.20 in group II. The difference was non- significant (P> 0.05).

Graph I: Assessment of parameters

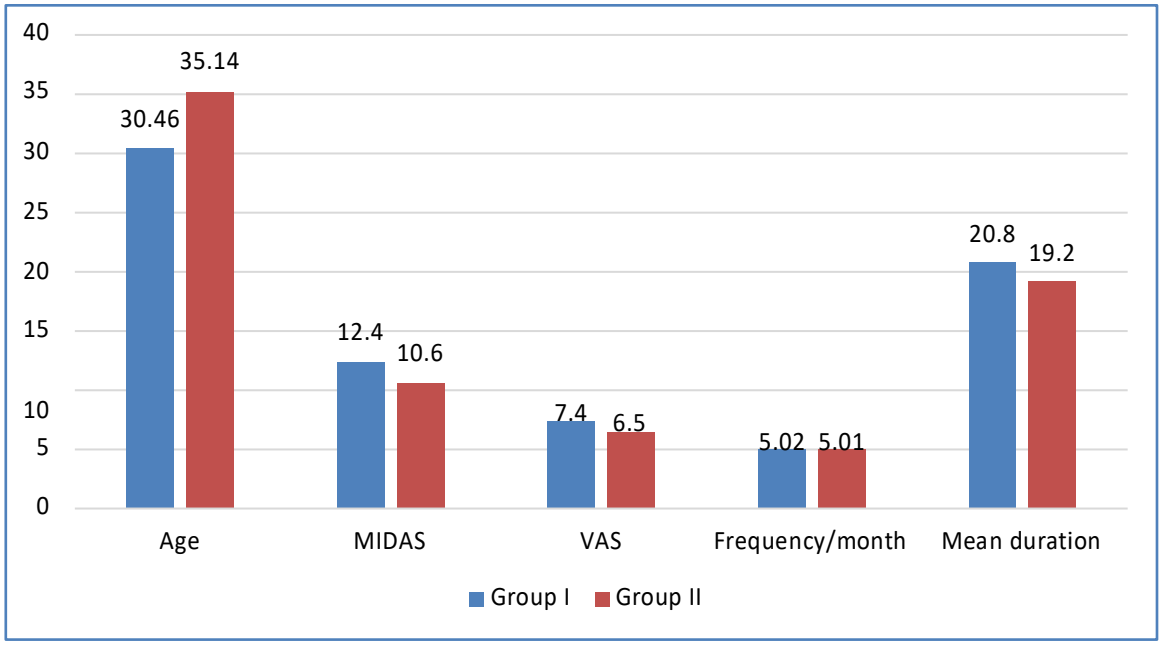


Table III: Assessment of adverse effects in both groups

Adverse effects	Group I	Group II	P value
Tremor	1	0	0.11
Hair loss	1	0	0.11
Weight gain	0	1	0.11
Insomnia	1	2	0.07
Dizziness	3	4	0.08
Facial swelling	0	1	0.11

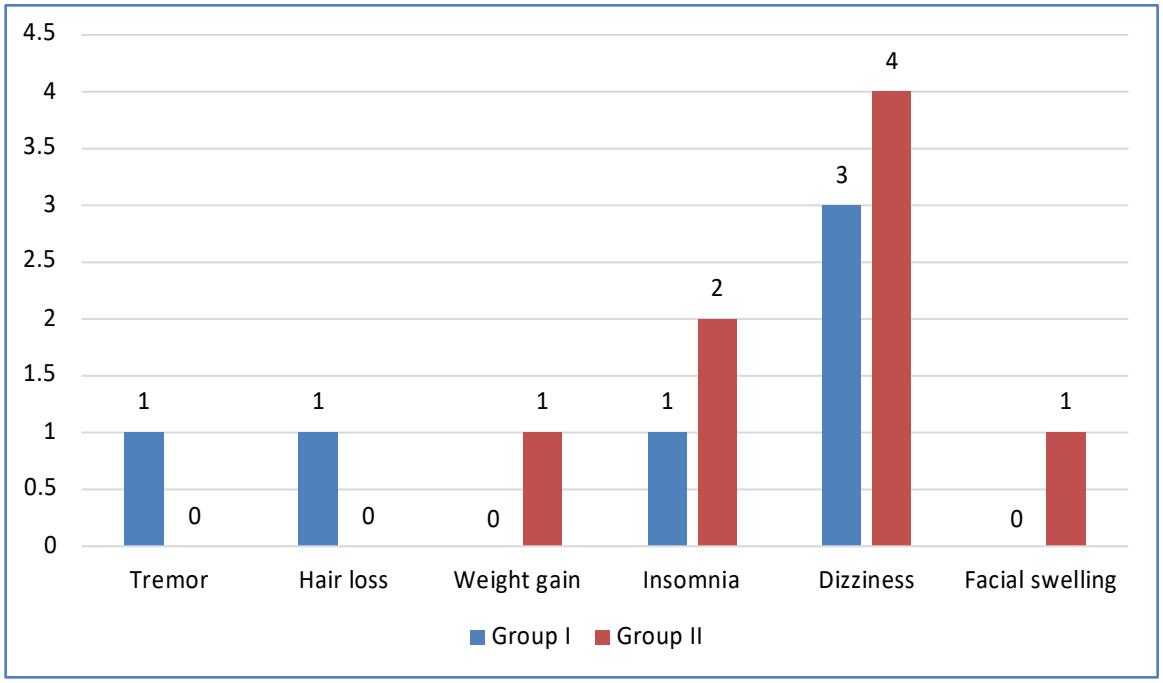
Table III, graph II shows that tremor was seen in 1 in group I, hair loss in 1 in group I, weight gain in 1 in group II, insomnia in 1 in group I and 2 in group II, dizziness was seen in 3 in group I and 4 in group II and facial swelling was seen in 1 in group II. The difference was non- significant (P> 0.05).

Discussion

Migraine is a common and disabling health problem among children and predominantly young and middle-aged adults.[8] Surveys from the main regions of the world suggest that the global prevalence of migraine is 14.7% (18.8% among women and 10.7% among men). Some of the symptoms associated with migraine are: nausea, vomiting, loss of appetite, photophobia, phonophobia, and osmophobia.[9] Spontaneous overactivity and abnormal amplification in pain and other, predominantly sensory, pathways in the brainstem lead to migraine. Current opinion favours a primarily neural cause involving feedback loops through innervation of cranial arteries in the trigeminovascular system.[10] IHS further categorises migraine as episodic or chronic, with or without an aura.Chronic migraine is defined as more than 15 migraine headaches per month for more than 3 months.[11] Chronic migraines result in significantly greater disability than episodic migraines. Treatment of headaches can be either abortive or prophylactic. Abortive treatment provides symptom relief for the acute headache, while prophylactic treatment aims to reduce the frequency or severity of headaches over time.[12,13].

The present study was conducted to compare propranolol and divalproex sodium in the prophylaxis of migraine.

Graph II: Assessment of adverse effects in both groups



We found that there were 18 males and 22 females in group I, and group II had 24 males and 16 females. In a systematic review by Linde K. and Rossnagel K.[14] ,propranolol was found to be more effective than a placebo, and no clear differences were found between propranolol and other migraine-preventing drugs like amitriptyline, flunarizine, cyclandelate, etc.

We found that the mean ages (mean±SD) in years were 30.46±8.5 in group I and 35.14±9.24 in group II; MIDAS was 12.4±3.62 in group I and 10.6±3.90 in group II; VAS was 7.4±1.48 in group I and 6.5±3.02 in group II; the frequency/month of migraine was 5.02±1.26 in group I and 5.01±1.64 in group II; and the duration of migraine was 20.8±6.10 in group I and and 19.2±7.20 in group II.

Jackson et al[15] included Beta-blockers (n = 39), calcium channel blockers (n = 12), flunarizine (n = 7), serotonin reuptake inhibitors (n = 6), serotonin norepinephrine reuptake inhibitors (n = 1), anticonvulsants (n = 32), alpha blockers (n = 9), angiotensin converting enzyme inhibitors (n = 3), angiotensin receptor blockers (n = 3), and tricyclic antidepressants (n = 11). Additionally, 53 trials comparing multiple medications were conducted. Amitriptyline (SMD: -1.2, 95% CI: -1.7 to -0.82), flunarizine (-1.1 headaches/month (ha/month), 95% CI: -1.6 to -0.67), fluoxetine (SMD: -0.57, 95% CI: -0.97 to -0.17), metoprolol (-0.94 ha/month, 95% CI: -1.6 to -0.67), fluoxetine (SMD: -0.57, 95% CI: -0.97 to -0.17), metoprolol (-0.94 ha/month, 95% CI: -1.4 to -0.46), pizotifen (-0.43 ha/month, 95% CI: -0.6 to -0.21), propranolol (-1.3 ha/month, 95% CI: -2.0 to -0.62), topiramate (-1.1 ha/month, 95% CI: -1.9 to -0.73) and valproate (-1.5 ha/month, 95% CI: -2.1 to -0.8) drugs which at least 3 trials that were more effective than placebo for episodic migraines were included.

Several effective drugs with fewer than three trials included: three ACE inhibitors (enalapril, lisinopril, and captopril), two angiotensin receptor blockers (candesartan and telmisartan), two anticonvulsants (lamotrigine and levetiracetam), and several beta-blockers (atenolol, bisoprolol, and timolol). Amitriptyline was found to be comparable to atenolol, flunarizine, clomipramine, and metoprolol in a network meta-analysis and to be superior to several other drugs, such as candesartan, fluoxetine, propranolol, topiramate, and valproate.

We observed that tremor was seen in 1 in group I, hair loss in 1 in group I, weight gain in 1 in group II, insomnia in 1 in group I and 2 in group II, dizziness was seen in 3 in group I and 4 in group II and facial swelling was seen in 1 in group II. Bhat et al[16] found that patients with history of 3 to 12 migraines a month (IHS) were divided into three groups of 30 patients to receive - propranolol 20 to 160mg/day; flunarizine 5 to 10mg/day or divalproex sodium 250 to 750 mg/day, for three months. Total 90/116 patients completed the study. Regarding the mean age or other standard migraine symptoms, there were no significant differences between the groups. The incidence, duration, and intensity of migraines were all markedly reduced by all the medications (P <0.001). For any of the efficacy parameters, propranolol, flunarizine, and divalproex sodium do not differ statistically significantly from one another. All three treatments were well-tolerated and safe.

SAMPLE SIZE

The shortcoming of the study is small sample size.

CONCLUSION

The results of this study demonstrate that both drugs were equally effective in management of migraine patients. Though various patients may experience distinct side effects and requiring individualised drug management be taken into account in accordance with the patient profile. Adverse events were comparable in both groups.

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