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Original Research

Propranolol vs divalproex sodium in prophylaxis of migraine

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ABSTRACT:
Background: Migraine is a common and disabling health problem among children and predominantly young and middle-aged adults. The present study compared propranolol and divalproex sodium in prophylaxis of migraine. **Materials & Methods:** 94 patients of migraine of both genders were divided into 2 groups of 47 each. In group I patients received propranolol 20 to 160 mg/day and group II patients received divalproex sodium 250 to 750 mg/days for three months. Treatment-emergent adverse effects were recorded. Migraine Disability Assessment Score (MIDAS) and VAS was compared. **Results:** There were 18 males and 10 females in group I and group II had 12 males and 16 females in group II. The mean frequency/month of migraine was 5.07 in group I and 5.01 in group II. The mean duration of migraine was 20.5 in group I and 18.1 in group II, MIDAS was 11.8 in group I and 10.2 in group II and VAS was 7.9 in group I and 7.1 in group II. Dizziness was seen in 1 in group I, facial swelling was seen in 1 in group I, tremors in 1 in group II, hair loss in 1 in group I and 2 in group II, weight gain in 2 in group I and 3 in group II and insomnia in 1 in group II. The difference was non-significant (P> 0.05). **Conclusion:** Both drugs found to be equally effective in management of migraine patients.
Key words: Divalproex sodium, Migraine, propranolol

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INTRODUCTION:

Migraine is a common and disabling health problem among children and predominantly young and middle-aged adults.[1] 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, osmophobia.[2] Spontaneous overactivity and abnormal amplification in pain and other, predominantly sensory, pathways in the brainstem, leads to migraine. Current opinion favours a primarily neural cause, involving feedback loops through innervation of cranial arteries in the trigeminovascular system.[3]

Valproic acid (2-Propylpentanoic acid) was first synthesised in 1882 as analogue of valeric acid, found naturally in valerian. It is a liquid at room temperature, but it can be reacted with a base such as sodium hydroxide to form the salt sodium valproate, which is solid.[4] Valproic acid, sodium valproate, or a mixture of the two (divalproex sodium according to United States Adopted Names (USAN), valproate semisodium according to WHO International Nonproprietary 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] The present study compared propranolol and divalproex sodium in prophylaxis of migraine.

MATERIALS & METHODS

The present study was conducted in 94 patients of migraine of both genders. All were informed regarding the study and their written consent was obtained.

Data such as name, age, gender etc. was recorded. Patients were divided into 2 groups of 47 each. In

group I patients received propranolol 20 to 160 mg/day and group II patients received divalproex sodium 250 to 750 mg/days for three months. Parameters such as respiratory rate, weight, pulse rate, blood pressure were noted. Treatment-emergent adverse effects were recorded. Migraine Disability Assessment Score (MIDAS) and VAS was compared. Results were subjected to statistical analysis, where p value less than 0.05 was considered significant.

RESULTS

Table I Distribution of patients

Groups	Group I	Group III
Drug	Propranolol	Divalproex sodium
M:F	18:10	12:16

Table I shows that there were 18 males and 10 females in group I and group II had 12 males and 16 females in group II.

Table II Assessment of parameters

Parameters	Group I	Group II	P value
Frequency/month	5.07	5.01	0.17
Mean duration	20.5	18.1	0.21
MIDAS	11.8	10.2	0.14
VAS	7.9	7.1	0.81

Table II, graph I shows that mean frequency/month of migraine was 5.07 in group I and 5.01 in group II. The mean duration of migraine was 20.5 in group I and 18.1 in group II, MIDAS was 11.8 in group I and 10.2 in group II and VAS was 7.9 in group I and 7.1 in group II. The difference was non- significant (P> 0.05).

Graph I Assessment of parameters

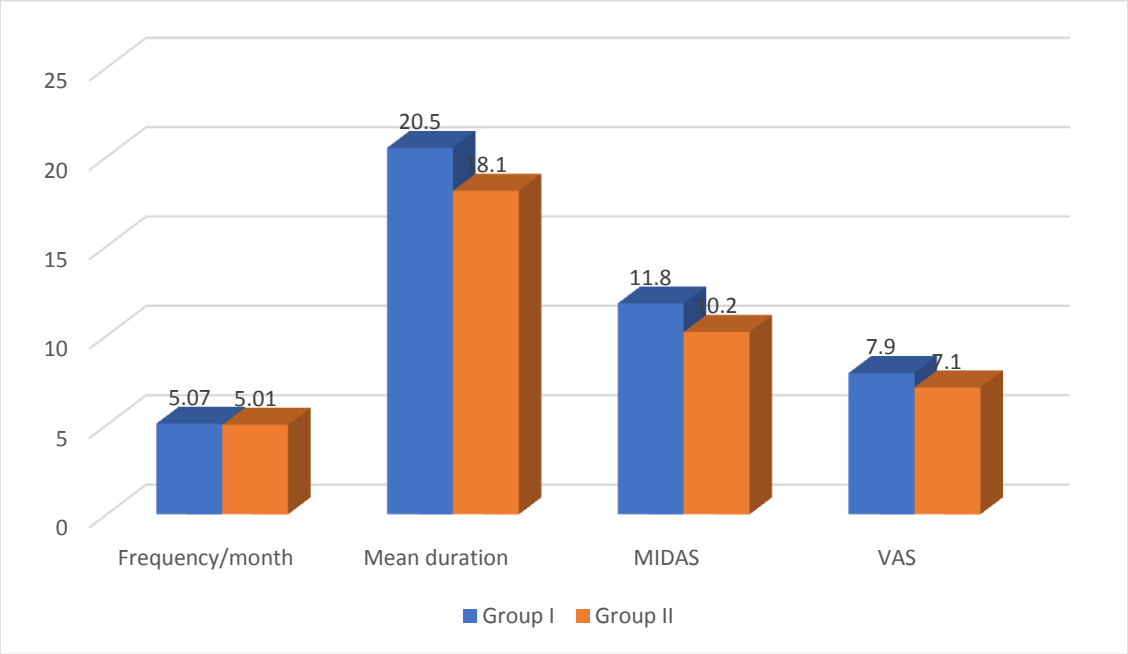
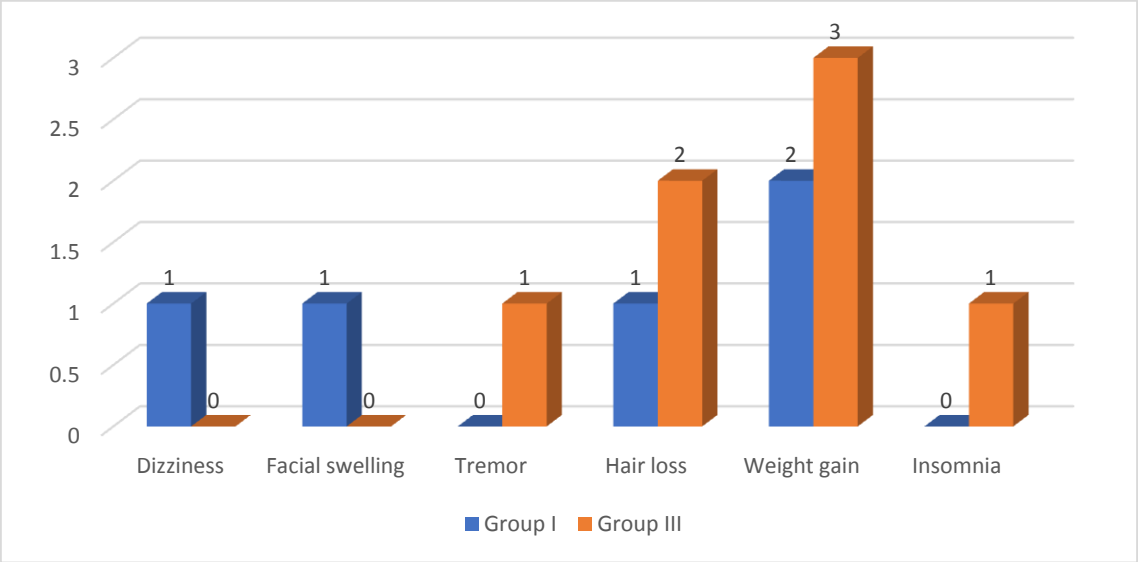


Table III Comparison of adverse effects

Adverse effects	Group I	Group III	P value
Dizziness	1	0	0.25
Facial swelling	1	0	0.17
Tremor	0	1	0.11
Hair loss	1	2	0.91
Weight gain	2	3	0.72
Insomnia	0	1	0.15

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

Graph II Comparison of adverse effects



DISCUSSION

Migraine headaches are common, with a worldwide prevalence ranging between 8 and 18%. Migraines cause significant disability, even during periods between attacks and are responsible for $1 billion in medical costs and $16 billion in lost productivity per year in the US alone.[7] The diagnostic criteria for migraine headaches have evolved over time.[8] Currently, the International Headache Society (IHS) diagnostic criteria for migraine includes having at least 5 attacks that last 4–72 hours, that are unilateral, pulsating, moderate or severe in intensity and aggravated by or cause avoidance of routine physical activity and are also accompanied by nausea and/or vomiting, photophobia or phonophobia.[9] IHS further classifies migraine as with or without an aura and as episodic or chronic. Chronic migraine is defined as more than 15 migraine headaches per month for more than 3 months.[10] 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. We focus on prophylactic migraine headache treatment in this manuscript.[11] 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). Two emerging prophylactic candidates are angiotensin converting enzymes (ACE) and angiotensin receptor antagonists (ARB).[12] The present study compared propranolol and divalproex sodium in prophylaxis of migraine.

We found that there were 18 males and 10 females in group I and group II had 12 males and 16 females in group II. Bhat et al[13] found that patients between 18 to 65 years, with history of 3 to 12 migraines a month (IHS) for six months were included. Patients 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. No significant differences were found between the groups with regards to mean age or other baseline migraine features. All the drugs significantly decreased the frequency, duration and severity of migraine (P<0.001). There is no statistically significant difference between propranolol, flunarizine and divalproex sodium for any of the efficacy parameters. All the three treatments were well-tolerated and safe.

We found that mean frequency/month of migraine was 5.07 in group I and 5.01 in group II. The mean duration of migraine was 20.5 in group I and 18.1 in group II, MIDAS was 11.8 in group I and 10.2 in group II and VAS was 7.9 in group I and 7.1 in group II. Jackson et al[14] conducted a controlled trials of adults with migraine headaches of at least 4 weeks in duration. Placebo controlled trials included alpha blockers (n = 9), angiotensin converting enzyme inhibitors (n = 3), angiotensin receptor blockers (n = 3), anticonvulsants (n = 32), beta-blockers (n = 39), calcium channel blockers (n = 12), flunarizine (n = 7), serotonin reuptake inhibitors (n = 6), serotonin norepinephrine reuptake inhibitors (n = 1) serotonin agonists (n = 9) and tricyclic antidepressants (n = 11). In addition, there were 53 trials comparing different drugs. Drugs with at least 3 trials that were more effective than placebo for episodic migraines included amitriptyline, -flunarizine (-1.1 headaches/month (ha/month), fluoxetin, metoprolol, pizotifen, propranolol, topiramate and valproate. Several effective drugs with less than 3 trials included: 3 ace inhibitors (enalapril, lisinopril, captopril), two angiotensin receptor blockers (candesartan, telmisartan), two anticonvulsants (lamotrigine,

levetiracetam), and several beta-blockers (atenolol, bisoprolol, timolol). Network meta-analysis found amitriptyline to be better than several other medications including candesartan, fluoxetine, propranolol, topiramate and valproate and no different than atenolol, flunarizine, clomipramine or metoprolol.

CONCLUSION

Authors found that both drugs found to be equally effective in management of migraine patients.

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