(International Print/Online Journal)

SJIF IMPACT FACTOR: 5.565
PUBMED-National Library of Medicine ID-101739732

ISSN (Print): 2209-2870
ISSN (Online): 2209-2862

International Journal of Medical Science and Current Research (IJMSCR)
Available online at: www.ijmscr.com
Volume 6, Issue 1 , Page No: 204-207
January-February 2023

IJMSCR

Role of Low Dose Sodium Valproate for Migraine treatment in Non-Pregnant and Non-Lactating Females- A Placebo Control Study

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Type of Publication: Original Research Paper
Conflicts of Interest: Nil

Abstract

Aim and Objective: To see the efficacy of low dose sodium valproate as prophylactic agent in vascular headaches.

Materials and Methods: It was a prospective placebo control study**.**

Results and conclusion: Sodium valproate is safe and effective treatment in non-pregnant and non-lactating women for migraine prophylaxis even in low doses of 250 mg.

Keywords: Non pregnant, Low dose , Migraine , Valproate

Introduction

Chronic Migraine is a debilitative neurological condition affecting approximately 2 percent of world population.[1]The prevalence is double in women as compared to men especially in the productive years of their life.[2]Migraine is characterized by moderate to severe attacks of unilateral pulsating head pain, associated with photophobia, phonophobia, nausea and/or vomiting, typically lasting 4–72 hrs.[3] Classically, the migraine attack is comprised of three phases: a premonitory phase, the migraine headache itself, and a postdrome phase. The premonitory phase occurs 24–48 h prior to the headache phase and is typically characterized by symptoms such as mood alterations, fatigue and neck discomfort.[4] Approximately one third of the patient have aura comprised of transient focal neurological symptoms of visual, sensory or motor disturbances.

Previously pathophysiology of migraine was explained on the basis of popular vascular theory but now the theory is obsolete and it is believed that it is because of instability in central neurovascular control mechanism[5,6,7,8.] popularly known as cortical spreading depression (CSD) characterized by initial neuronal depolarization followed by spreading of the wave and subsequently decreased cortical activity and blood flow. There is significant increase in Calcitonin gene-related peptide (CGRP) a potent vasodilator levels during acute attack of migraine.[9,10]

Materials And Methods:

It was an observational study carried out over a period of six months and the diagnosis was made on the basis of clinical criterion only. A neuroimaging was done in patients with any atypical features and or any transient focal neuro-deficit. Total of fifty female patients in the age group of 20-40 years were enrolled for the study.

Females who were pregnant or were lactating were excluded from the study. An acute attack of Migraine was treated as per the protocol of the hospital and subsequently these patients were put on sodium valproate 250 mg prophylaxis and were followed fortnightly for next 12 weeks and the number of acute attacks over this period were noted and compared

with a placebo agent. Criterion used for the diagnosis is international classification of headache disorders 3(ICHD 3) which is as under.

1. At least 5 or more attacks in lifetime.

2. Headache attack lasting 4-72 hrs.

3. At least 2 out of 4 features (unilateral location, pulsating/throbbing quality, moderate-severe intensity, aggravation by/causing avoidance of routine physical activity).

4. At least 1 of the following features (nausea and/or vomiting, photophobia and phonophobia).

Results:

Table 1 Patient characteristics

Total Number of Patients	Male	Female	Mean age	Atypical Features	Pregnant	Lactating	Neuro-imaging Done
50	0	50	32	05	Nil	Nil	05

Table 2 Drugs Used In Acute Attacks

Severity of Attack	Paracetamol 500 mg	Naproxen 250 mg	Naproxen 500mg+Sumitriptan 85 mg
Mild	++		
Moderate		++	
Severe			++

Table 3 Comparison of Drug and placebo at 04 weeks

Group	Mild Acute Attacks 4 weeks	Moderate Acute Attacks 4 weeks	Severe Acute Attacks 4 weeks	P value <0.05	P value <0.05	P value <0.05
Drug	08	04	04	Significant	Significant	Significant
Placebo	16	08	08			

Table 4 Comparison of Drug and placebo at 08 weeks

	Mild	Moderate Acute Attacks	Severe Acute Attacks	P value	P value	P value
	Acute Attacks	8	8	<0.05	<0.05	<0.05

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	8 weeks	weeks	weeks			
Drug	12	6	6	Significant	Significant	Significant
Placebo	32	16	16			

Table 5 Comparison of Drug and placebo at 12 weeks

Group	Mild Acute Attacks 12 weeks	Moderate Acute Attacks 12 weeks	Severe Acute Attacks 12 weeks	P value <0.05	P value <0.05	P value <0.05
Drug	16	8	8	Significant	Significant	Significant
Placebo	48	24	24			

Discussion:

Valproic acid, a GABAergic drug, has been shown to be effective for migraine prophylaxis. Results from several dose- and serum level-adjusted studies have recommended valproic acid doses within a range of 500 to 1500 mg per day for migraine prophylaxis. Sodium valproate significantly reduced frequency, severity, and duration of migraine headaches. The medication was well tolerated and did not result in discontinuation.[11] In a study done by Sorenson [12] 22 patients with severe migraine resistant to previous prophylactic treatments participated in a prospective open trial of valproate in migraine prophylaxis; 17 had common and 5 classic migraine. Follow-up was from 3 to 12 months; 11 patients were free from migraine attacks, 6 had a significant reduction of the frequency so the effectiveness of drug was seen in 77 percent of the patients.

In our study 34 patients out of 50 had no moderate to severe attacks of acute headache at the end of 12 weeks of treatment amounting to 68 percent of response. Possible explanation to a little less response 77 versus 68 is possibly because of low dose of valproic acid used in our study.

Similar effects with low dose valproic acid were seen with kinze et[13] al in his study in which he has recommended 500 mg of valproic acid use.

Conclusion:

Sodium valproate is safe and effective treatment in non pregnant and non lactating women for migraine prophylaxis even in low doses of 250 mg and doses can be adjusted to clinical responses ranging from 500-1500 although low doses of 250 to 500 mg are relatively well tolerated.

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