

RESEARCH ARTICLE

Efficacy of enalapril in the treatment of migraine prophylaxis – A clinical study

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Received: January 11, 2020; **Accepted:** April 21, 2020

ABSTRACT

Background: Migraine is the most common problem in the world and few angiotensin-converting enzyme (ACE) inhibitors have previously been shown to be effective in migraine prophylaxis. **Aim and Objective:** This research aimed to determine the efficacy of enalapril in migraine prophylaxis. **Materials and Methods:** A hospital-based observational study of 6 months carried out at outpatient department. A total of 50 patients with migraine attacks of more than 5 in a month were selected and were subjected to complete physical examination, particularly neurological examination. The Headache Impact Test-6 was used to measure the patient's headaches in terms of mean severity, duration, and frequency within 1 month. A record of each headache attack was maintained by rating on the visual analog scale from 1 to 10 depending on the severity of each attack. Patients were prescribed enalapril 10 mg daily with a dose divided into 5 mg twice daily for 2 months of the study duration. **Results:** Headache severity before treatment was 8.33 ± 0.39 and it significantly reduced to 4.65 ± 0.30 in the 1st month and in the 2nd month, it reduced to 4.07 ± 0.50 . The mean head ache duration before treatment was 15.94 ± 3.30 and with treatment with enalapril it reduced to 6.79 ± 0.74 in the 1st month and 5.84 ± 0.74 in the 2nd month. The mean headache frequency before the treatment was 14.10 ± 3.00 and by treating with enalapril, it significantly reduced in the 1st month to 9.80 ± 1.79 and 8.76 ± 1.53 in the 2nd month. **Conclusion:** Enalapril can be beneficial as it decreases the incidence, intensity and duration of the headaches in migraine prophylaxis. The results of our study support the use of ACE inhibitors in the migraine prophylaxis.


KEY WORDS: Migraine; Enalapril; Angiotensin-Converting Enzyme Inhibitors; Angiotensin

INTRODUCTION

Migraine is the most common headache disorder occurring in humans,^[1] affecting young adults, especially women.^[2] Migraine is an episodic, persistent neurological condition. The incidence of migraine is strongly linked to significant pain, handicap, and

reduced quality of life. It is a key health issue and migraine management is required. Management of migraines specializes of preventing causes, behavioral adjustments, lifestyle modifications, non-pharmacology, and drug treatments. Due to its high incidence and possible relationship with serious disorders like stroke in the general population,^[3,4] discovering medications for its prophylaxis seem to be significant.

About 240 million people worldwide experience around 1.4 billion migraine attacks annually. Severe migraines are on the World Health Organization international illness burden index, and they are a serious health problem both for people and for society since they have a direct impact on their quality of life.^[5] This disorder is a serious problem.^[6]

Access this article online	
Website: www.njppp.com	Quick Response code
DOI: 10.5455/njppp.2020.10.01006202021042020	

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Effective management of migraine depends on accurate diagnosis ruling out other causes for headache.

In 1988, the International Headache Society published criteria for the diagnosis of a number of different headache types.^[7] Those for migraine headaches with or without aura are reproduced below:

ICH Diagnostic Criteria for Migraine

Migraine without aura (MO) – five headache attacks lasting 4–72 h (untreated or unsuccessfully treated), which has at least two of the four following characteristics: Unilateral location, pulsating quality, moderate or severe intensity (inhibits or prohibits daily activities), aggravated by walking stairs, or similar routine physical activity. During headache, at least one of the two following symptoms occurs: Phonophobia and photophobia, nausea and/or vomiting.

Migraine with aura (MA) – at least two attacks occur fulfilling with at least three of the following: One or more fully reversible aura symptoms indicating focal cerebral cortical and/or brain stem functions, at least one aura symptom develops gradually over more than 4 min, or two or more symptoms occur in succession.

No aura symptom lasts more than 60 min; if more than 1 aura symptom is present, accepted duration is proportionally increased. Headache follows aura with free interval of at least 60 min (it may also simultaneously begin with the aura). Migraine with typical aura is diagnosed when there is homonymous visual disturbance, unilateral paresthesias, and/or numbness, unilateral weakness, and aphasia or unclassifiable speech difficulty.

Traditional drug therapy is divided into two, i.e. acute or symptomatic treatment and preventive or prophylaxis. Many patients with migraine can only be treated with acute treatment. Long-term preventive therapy is needed for severe or frequent migraine patients.

Enalapril (C₂₀H₂₈N₂O₅): Enalapril, the first dicarboxylate-containing angiotensin-converting enzyme (ACE) inhibitor. It is administered orally as the monoethyl enalapril, which serves as a prodrug.^[4] Enalapril, after hydrolysis to enalaprilat, inhibits ACE which results in decreased plasma angiotensin II, leading to decreased vasopressor activity aldosterone secretion. Thus, enalapril blocks the conversion of angiotensin I to angiotensin II, decreasing blood pressure, decreasing aldosterone secretion, slightly increasing serum potassium levels, and causing sodium and fluid loss; increased prostaglandin synthesis also may be involved in the antihypertensive action. The purpose of this study was to determine enalapril's potential role in reducing migraine headaches.

MATERIALS AND METHODS

Site of Study

The study was conducted at the Outpatient Department of Osmania General Hospital.

Type of Study

It is a retrospective observational study.

Sample Collection

Sample size: Fifty patients.

Sampling Methods

This was a consecutive sampling method.

Inclusion Criteria

Patients who had more than 5 migraine attacks per month were included in the study.

Exclusion Criteria

Patients with ACEI hypersensitivity, pregnancy, lactation, and enalapril intolerance, asthma, diabetes mellitus, coronary artery disease, documented liver or kidney diseases, morbid obesity (body mass index >35 kg/m²), active cigarette smoking, alcohol or other substance abuse, sinusitis, tension-type headaches greater than 5 days a month, and <4 migraine attacks a month were excluded from our study.

Statistical Analysis

Data were presented in the form of statistical tables and charts. SPSS software version 20 was used for statistical analysis.

Ethical Approval

Approval was taken from the Institutional Ethics Committee before commencement of the study.

A total of 50 patients with migraines attacks of more than 5 in a month were selected and were subjected to complete physical examination, particularly neurological examination. The Headache Impact Test-6 was used to measure the patient's headaches in terms of mean severity, duration, and frequency within 1 month. A record of each headache attack was maintained by rating on the visual analog scale from 1 to 10 depending on the severity of each attack.

Patients were prescribed enalapril 10 mg daily with a dose divided into 5 mg twice daily for 2 months of the study duration.

RESULTS

A total of 50 patients with migraine were selected for the study. Majority of the patients belonged to the age group of 21–30 years around 56% followed by the age group of 31–40 years with 30%, followed by 11–20 years with 8%, 41–50 years age group with 4%, and the least being 2% belonged to the age group of 51–60 years [Table 1].

The prevalence of migraine was more in females compared to males with females accounting for 78% and males accounting for 22%. Headache severity before treatment was 8.33 ± 0.39 and it significantly reduced to 4.65 ± 0.30 in the 1st month and in the 2nd month, it reduced to 4.07 ± 0.50 . The mean headache duration before treatment was 15.94 ± 3.30 and with treatment with enalapril, it reduced to 6.79 ± 0.74 in the 1st month and 5.84 ± 0.74 in the 2nd month. The mean headache frequency before the treatment was 14.10 ± 3.00 and by treating with enalapril, it significantly reduced in the 1st month to 9.80 ± 1.79 and 8.76 ± 1.53 in the 2nd month [Table 2].

Table 1: Demographic data of the patients with respect to age and gender

Age group (in years)	Number of patients	Percentage
11–20	4	8
21–30	28	56
31–40	15	30
41–50	2	4
51–60	1	2
Gender		
Male	11	22
Female	39	78

DISCUSSION

Migraine remains as one of the highly prevalent disorders of humankind. It is associated with poor quality of life and high levels of disability. Optimal management of migraine requires an amalgamation of pharmacological and non-pharmacological measures. The pharmacological methods are essential for trigger identification and avoidance and behavioral and lifestyle modifications. The current study investigated the effectiveness of enalapril treatment in improving the quality of life, reducing disability, decreasing pain intensity, attack frequency, and duration of migraine attack among migraineurs.

The majority of patient were in the age group of 21–30 years, approximately 56% of them followed by 31–40 years of age with 30%, 11–20 years with 8%, 41–50 years with 4%, and <2% with 51–60 years of age. This shows middle-aged people; generally, teenagers are more susceptible to migraine due to various underlying causes. The prevalence of migraine in females was much higher than compared to males, i.e. 78% of females and 22% of males. Headache severity before treatment was 8.33 ± 0.39 and it significantly reduced to 4.65 ± 0.30 in the 1st month and in the 2nd month, it reduced to 4.07 ± 0.50 .

The mean headache duration before treatment was 15.94 ± 3.30 and with treatment with enalapril, it reduced to 6.79 ± 0.74 in the 1st month and 5.84 ± 0.74 in the 2nd month. The mean headache frequency before the treatment was 14.10 ± 3.00 and by treating with enalapril it significantly reduced in the 1st month to 9.80 ± 1.79 and 8.76 ± 1.53 in the 2nd month. There was a significant reduction in the headache severity, duration, and frequency before treatment and during the course of treatment in the 1st and 2nd months, respectively. This data outcome shows that enalapril in very effective in

Table 2: The mean of headache severity, headache duration, and headache frequency measured before treatment and during the 1st and 2nd months of the treatment with enalapril

Mean	Before treatment	At the 1 st month with enalapril	At the 2 nd month with enalapril	P-value*
Headache severity (1–10)	8.33 ± 0.39	4.65 ± 0.30	4.07 ± 0.50	0.000
Headache duration (hours)	15.94 ± 3.30	6.79 ± 0.74	5.84 ± 0.74	0.001
Headache frequency (attacks per month)	14.10 ± 3.00	9.80 ± 1.79	8.76 ± 1.53	0.001

Table 3: Description of research on the treatment of headache associated substances involving the rennin–angiotensin mechanism

Study	Drug	Duration	Number of patients	Type of study	Year	Efficacy outcome	Type of headache population
Bender ^[8]	Lisinopril Enalapril	3 months–3 years	17	Open study	1995	Frequency of headache	Migraine headache
Onder <i>et al.</i> ^[9]	ACE inhibitor (enalapril, captopril, lisinopril, and ramipril)	12 weeks	762	Open study	2003	Headache frequency	Hypertensive patients
Camarda <i>et al.</i> ^[10]	Enalapril	12 months	1	Case report	2003	Headache frequency	Migraine headache

ACE: Angiotensin-converting enzyme

treating migraines significantly was positive reduction of headaches severity, frequency, and duration.

In 1995, a small open study by Bender^[8] explored the use of the ACE-Is enalapril (most) or lisinopril (some) in 17 patients with migraine [Table 3]. The medication was given once daily in doses from 10 to 25 mg for a period of 3 months–3 years. Ten patients reported a marked effect on their headache, in six, the effect was moderate, and in one, there was only a slight effect.

CONCLUSION

The study provides evidence to support the enalapril treatment as an appropriate and effective one to bring about positive changes in clinical outcomes of migraineurs. The outcomes of the study reinforce the importance of a comprehensive management of migraine headaches and generate evidence that inform clinical practice regarding the management of migraine. We conclude that enalapril can be a good option as it reduces the headache parameters such as frequency, duration, and severity.

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How to cite this article: Bindu EH, Raghuv eer B. Efficacy of enalapril in the treatment of migraine prophylaxis – A clinical study. *Natl J Physiol Pharm Pharmacol* 2020;10(07):533-536.

Source of Support: Nil, **Conflicts of Interest:** None declared.