



Comparative Effectiveness of Drugs in the Treatment of Primary Headache

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Abstract: **Introduction:** Primary headache disorder, characterized by recurrent headache is the most prevalent disease leading to widespread ill health and impaired quality of life. Headache is one of the most common cause of patient attending neurology clinic. Amitriptyline, flunarizine and topiramate are common drugs in the treatment of primary headache. **Objective:** To compare the efficacy of drugs namely Amitriptyline, flunarizine and topiramate in the treatment of primary headache. **Methods and Materials:** This is the retrospective data analysis study was conducted at Dept. Of Neurology, Enam Medical College Hospital, Savar, Dhaka, Bangladesh from March to June 2022. Data analysis of primary headache patients treated with amitriptyline, flunarizine and topiramate. On their first, second and third subsequent visits, Headache Impact Test 6 Scoring was done by a medical person. Patients were treated clinically. After the third follow up data were analyzed using SPSS version 20.0. Categorical variables were compared by chi-square test, paired sample t-test, ANOVA test and Welch test. **Results:** A total of 121 patient data was analyzed. Most patients were between 16 to 40 years of age (54.34%) followed by 41-60 years of age (33.80%) with minimum age of 16 years and maximum age of 60 years respectively. Among the patients in the study group, the majority were female (85%). All three medications: amitriptyline, flunarizine and topiramate were able to significantly lower Headache impact test -17.23 ± 6.643 , -14.06 ± 7.155 , -15.82 ± 5.907 respectively ($P < 0.001$). Amitriptyline was found to be better than other two drugs in reducing Headache Impact Test. **Conclusion:** Primary headache is a common presentation in neurological OPD. Female between ages 16-60 years had more primary headache. Amitriptyline, flunarizine and topiramate all are effective in the treatment of primary headache. Though tension type of headache is the most common type of headache, amitriptyline seems to be equally effective in treatment with other primary headaches.

Keywords: Headache impact test, Primary Headache.

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INTRODUCTION

The primary headaches are composed of multiple entities that cause episodic and chronic

head pain in the absence of an underlying pathologic process, disease, or traumatic injury. The most common of these are migraine, tension-type

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headache, and the trigeminal autonomic cephalgia. Primary headache disorder, characterized by recurrent headache is the most prevalent disease leading to widespread ill health and impaired quality of life [1, 2]. It is among the most common disorder of the nervous system that has been underestimated, under-recognized and under-treated throughout the world. Global Burden of Disease Study 2015 (GBD-2015) found neurological disorders ranked as second leading cause of death (16.8% of global deaths) to which tension-type headache (1337.3 to 1681.6 million cases), migraine (872.1 to 1055.6 million) and medication overuse headache (50.8 to 67.4 million) contributed topmost followed by Alzheimer’s disease and other dementias (40.2 to 52.7 million) [3]. Migraine and other primary headaches are chronic common disorders affecting around 1/2 to 3/4 of the adult population [4]. The number of patients who requires prophylaxis is approximately 15% [5]. Another review analyzed focused only on dichotomous outcomes among patients with episodic migraines and found no difference in likelihood of experiencing at least 50% improvement in headaches between different classes of oral medications. Many drugs are being used for the prophylaxis of migraine and tension type headache. The common drugs used for the prophylaxis are beta blockers, topiramate, tricyclic antidepressants especially amitriptyline, calcium channel blockers- flunarizine and divalproate sodium [6]. We compared the efficacy and tolerability of amitriptyline, flunarizine and topiramate in the prophylaxis of migraine, chronic migraine headache and tension type headache.

METHODS AND MATERIALS

This is the retrospective data analysis study was contacted at Dept. Of Neurology, Enam Medical College Hospital, Savar, Dhaka, Bangladesh from March to June 2022. 121 patients included in our study. Primary headache patients treated with amitriptyline, flunarizine and topiramate. On their first, second and third subsequent visits, Headache Impact Test 6 Scoring was done by a medical person. Patients were treated clinically. They were

prescribed amitriptyline, flunarizine or topiramate depending on the clinical ground. Patients with TTH and/ or with sleep related problems were prescribed amitriptyline. The diagnostic criteria used for the diagnosis of different type of headache are International Headache Society (IHS) criteria [7]. Informed consent was taken from all the patients diagnosed to have primary headache as per IHS criteria and underwent complete physical examination by the neurologist. Inclusion criteria included patients of age 16-60 years old, primary headache as per IHS criteria and patients under prophylactic therapy either amitriptyline, topiramate or flunarizine. The exclusion criteria were children (70 years). Patients with mental illness and those with the diagnosis other than primary headache and those on multiple medications were also excluded. They were treated on personal basis considering sex, weight and other medical condition. Those who were obese and had completed their family were prescribed topiramate and those who did not have sleep related issues were prescribed flunarizine. Obtained data were analyzed using SPSS version 20.0. Categorical variables were compared by chi-square test, paired sample t-test, ANOVA test and Welch test. Brown Forsythe test were used to compare the numeric variables among drug groups and within each group, respectively. Significance level was set at 0.05.

RESULTS

A total of 121 patient data was analyzed. Most patients were between 16 to 40 years of age (54.34%) followed by 41-60 years of age (33.80%) with minimum age of 16 years and maximum age of 60 years respectively. Among the patients in the study group, the majority were female (85%). Table 1 show that compared with pre-treatment, post treatment medications were significantly effective in reducing HIT 6 score. All the group patient had significant decrease in the HIT 6 score with non-significant Superiority of one over another (p >0.001). However, amitriptyline was slightly more effective in reducing HIT 6 score which is shown in Table 2.

Table 1: Pre and Post treatment HIT 6 score comparison (Paired sample t-test).

Drug Category	HIT6 score (Mean ± S.D.)			P-value (Paired sample T-test)
	Pre-treatment	Post-treatment	Change	
Amitriptyline	68.98 ± 4.543	51.75 ± 5.448	-18.23 ± 6.643	<0.001
Flunarizine	64.57 ± 4.758	48.51 ± 7.990	-15.06 ± 7.155	<0.001
Topiramate	67.49 ± 5.472	52.67 ± 7.031	-16.82 ± 5.907	<0.001

Table 2: Comparison of change in HIT 6 of different medication groups a=ANOVA test b=Welch test c=Brown-Forsythe test

Drug Category	Change in HIT6 score (Mean ± S.D.)	P-value
Amitriptyline	-18.23 ± 6.643	0.063a, 0.076b, 0.056c
Flunarizine	-15.06 ± 7.155	
Topiramate	-16.82 ± 5.907	

DISCUSSION

The medication used was different for different patients depending upon the clinical ground. The total number of patients was 121. The pretreatment Headache Impact Test was tested in each patient which was significant for all the groups; Amitriptyline (68.98±4.543), Flunarizine (64.57±4.758), Topiramate (67.49±5.472). Therefore, these groups of patients were comparable. In this analysis Most patients were between 16 to 40 years of age (54.34%) followed by 41-60 years of age (33.80%) with minimum age of 16 years and maximum age of 60 years respectively. Among the patients in the study group, the majority were female (85%). This may be probably due to the hormonal changes and other stressors of life. Similar findings are reported in other studies [8]. The next step we wanted to know was about the effectiveness of individual drugs in the treatment of primary headache. Amitriptyline is a tricyclic antidepressant that is often prescribed for prevention of migraine. In this study amitriptyline was able to reduce the HIT 6 score by 18.23 ± 6.643 (p<0.001). In a study, amitriptyline was able to reduce headache in four weeks-time by more than 55.3% comparing placebo 34 % [9]. Flunarizine is a calcium channel blocker that reduces smooth muscle spasm. In this study, flunarizine was able to reduce HIT6 score significantly 15.06 ±7.155 (p<0.001). In a study by Gracia Naya flunarizine was more effective than topiramate in the treatment of chronic migrane [10]. However, in our study topiramate was slightly more effective which may be non-significant. Most patients responded well with treatment. Topiramate is an anti-epileptic drug that has been proven to be effective in the treatments of migraine. In this study Topiramate was able to reduce HIT 6 score by 16.82 ± 5.907 (p<0.001). A study in Arch Neurol *et al*, stated that topiramate in dosage of 100 to 200 mg /day was effective as a preventive therapy for patients with migraine [11]. Out of 34 patients in the treatment group of topiramate develop eye problem and had to be referred to the ophthalmologist. In study by Dodick, topiramate is non-inferior to amitriptyline which is against findings of ours [12]. All medication was able to reduce HIT6 score significantly with p value<0.001. They were equally effective. In comparison to individual drugs amitriptyline was slightly more effective

(18.23±6.643) than Flunarizine and Topiramate. In view of availability and cost amitriptyline are easily available and cheaper than other [7]. The limitations of this study were shorter duration of follow up for 3months, small sample size and single centre study. We were unable to categorize the different subgroups of primary headache. This study has given insight for conducting better studies in the neurological field in the future.

CONCLUSION

Primary headache is a common presentation in neurological OPD. Female between ages 16-60 years had more primary headache. Amitriptyline, flunarizine and topiramate all are effective in the treatment of primary headache. Though tension type of headache is the most common type of headache, amitriptyline seems to be equally effective in treatment with other primary headaches.

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