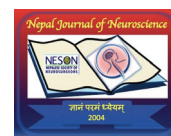


A comparative analysis of amitriptyline, flunarizine and topiramate in the treatment of primary headache



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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.

In Nepal 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. We conducted this study 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 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 142 patient data was analyzed. The most common age group were between 20 to 39 years (56.34%) followed by 40 to 59 years (33.80%). Females were predominant in the group 124 (87.32%). 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: All three drugs namely amitriptyline, flunarizine and topiramate, are significantly 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.

Key words: Headache impact test, Primary Headache.

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Introduction

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 (GBD2015) 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 In Nepal according to Manandhar et al out of 2100 participants, 1794 reported headache during the preceding year.⁶

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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.⁷ 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 was a retrospective data analysis of the patient who attended neuroscience OPD for the treatment of primary headache during February 2019 and February 2020. The diagnostic criteria used for the diagnosis of different type of headache are International Headache Society (IHS) criteria.⁸

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 14-70 years old, primary headache as per IHS criteria and patients under prophylactic therapy either amitriptyline, topiramate or flunarizine.

The exclusion criteria were children (<14 years) and elderly (>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. Female, obese and child bearing age patients were counseled not to be pregnant while on Topiramate.

The Headache Impact Test-6 (HIT-6) contains six factors to be monitored that could be altered due to headache as pain, social functioning, role functioning, vitality, cognitive functioning, and psychological distress.⁹

The monitoring is based on answers which were responded to by the patients in terms of “never”, “rarely”, “sometimes”, “very often”, or “always”. The total score of the questionnaire ranges from 36 to 78, where higher score indicates a greater impact of headache on the daily life of the respondent. Score were interpreted using four groupings that indicate the severity of impact of headache on the patient’s daily life.¹⁰

Patients were evaluated on their first OPD visit and HIT 6 scoring was calculated. The pre-treatment HIT 6 score signified the status of the patient before the initiation of the treatment for primary headache. They were prescribed either amitriptyline, flunarizine or topiramate depending on the clinical ground. Patients with TTH and/ or with sleep related problems were prescribed amitriptyline. Those who were obese and had completed their family were prescribed topiramate and those who did not have sleep related issues were prescribed flunarizine. The patients were followed on 1st month and 3rd month and again HIT 6 score was calculated respectively on each subsequent OPD visit. The retrospective data were retrieved from the file.

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

Demographic profiles of patients

Among 512 patients visiting OPD with headache, excluding those not fitting the criteria and those who lost follow up at 1st and 3rd month, we remained with 142 patients. Most patients were between 20 to 39 years of age (56.34%) followed by 40-59 years of age (33.80%) with minimum age of 14 years and maximum age of 64 years respectively. Among the patients in the study group, the majority were female (87%).

Medication

As shown in the Table 1, 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.

| Drug Category | HIT6 score (Mean ± S.D.) | | | P-value (Paired sample T-test) |
|---------------|--------------------------|----------------|----------------|--------------------------------|
| | Pre-treatment | Post-treatment | Change | |
| Amitriptyline | 67.98 ± 4.543 | 50.75 ± 5.448 | -17.23 ± 6.643 | <0.001 |
| Flunarizine | 63.57 ± 4.758 | 49.51 ± 7.990 | -14.06 ± 7.155 | <0.001 |
| Topiramate | 67.49 ± 5.472 | 51.67 ± 7.031 | -15.82 ± 5.907 | <0.001 |

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

A comparative analysis of amitriptyline, flunarizine and topiramate in the treatment of primary headache

| Drug Category | Change in HIT6 score (Mean ± S.D.) | P-value |
|---------------|------------------------------------|--|
| Amitriptyline | -17.23 ± 6.643 | 0.063 ^a , 0.076 ^b , 0.056 ^c |
| Flunarizine | -14.06 ± 7.155 | |
| Topiramate | -15.82 ± 5.907 | |

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

Discussion

We reviewed retrospective data in the treatment of primary headache disorder except

cluster headache for the period of one year. The criteria set by International headache society for primary headache has many points for considering the diagnosis which may be clumsiness in the article setting. The medication used was different for different patients depending upon the clinical ground. The total number of patients was 142. The pretreatment Headache Impact Test was tested in each patient which was significant for all the groups; Amitriptyline (67.98 ± 4.543), Flunarizine (63.57 ± 4.758), Topiramate (67.49 ± 5.472). Therefore, these groups of patients were comparable.

In this analysis maximum number of patients were between 20 to 39 years (56.34 %) followed by 40 to 59 years (33.80%). The migraine was common between the age group of 20 to 50 years and more common in females (87 %) than males. This may be

probably due to the hormonal changes and other stressors of life. Similar findings are reported in other studies.¹¹

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 17.23 ± 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 %.¹²

Flunarizine is a calcium channel blocker that reduces smooth muscle spasm. In this study, flunarizine was able to reduce HIT6 score significantly 14.06 ± 7.155 (p<0.001). In a study by Gracia-Naya flunarizine was more effective than topiramate in the treatment of chronic migraine.¹³

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 15.82 ± 5.907 (p<0.001). A study in Arch Neurol. 2004 stated that topiramate in dosage of 100 to 200 mg /day was effective as a preventive therapy for patients with

migraine.¹⁴ Out of 39 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.¹⁵

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 (17.23 ± 6.643) than Flunarizine and Topiramate. In view of availability and cost amitriptyline are easily available and cheaper than other.¹⁶ The limitations of this study were shorter duration of follow up for 3months, small sample size and single center 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 age 20 -59 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.

Conflict of Interest: None

Source(s) of support: None

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