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Comparative Analysis of Topiramate with Amitriptyline in Prophylaxis of Migraine without Aura Among Outpatients Visiting Tertiary Care Hospital

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ABSTRACT

Objective: To ascertain the better drug between Topiramate and Amitriptyline for the prevention of migraines without aura among patients of the adult age group visiting the tertiary care hospital.

Study Design: Comparative cross-sectional study.

Place and Duration of Study: Combined Military Hospital, Malir Cantt Pakistan, from May to Oct 2022.

Methodology: Two hundred seventy individuals visiting the Outpatient Department of the tertiary care hospital were included in the study who were suffering from migraines without aura. They were randomly assigned to groups of 135 each, which were to receive Topiramate and Amitriptyline, respectively. After informed consent, their treatment was started with monthly follow-ups. Data was collected in the form of a questionnaire derived from the Migraine Disability Assessment Questionnaire (MIDAS), Headache Impact Test (HIT-6) and Migraine Specific Quality of Life Questionnaire (MSQ 2.1), both at the start of treatment and later at the end of the study.

Results: Two hundred seventy individuals were included in the study. It comprised 162(60%) females and 108(40%) males. Their mean age was 36.51±9.77 years. There was a significant improvement in migraine symptoms among topiramate and amitriptyline groups (p-value<0.001). There was no significant difference in the efficacy of Topiramate and Amitriptyline (p-value=0.411)

Conclusion: There was no significant difference in the efficacy of Topiramate and Amitriptyline in the prevention therapy of migraine.

Keywords: Amitriptyline, Headache, Migraine, prophylaxis, Pulsatile headache, Topiramate.

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INTRODUCTION

Migraine is an episodic neurological disorder characterized by moderate to severe headaches associated with nausea, vomiting and/or increased sensitivity to light, sound or both.[1] The pathophysiology of migraine has been studied for a long time in order to understand the cause of migraine.[2] Initially, it was theorized that migrainous headaches occurred due to dilatation of blood vessels while the aura which occurs during these episodes is a result of vasoconstriction.[3,4] However, later, it was found that this was not the case, and if vasodilation occurred at all, it was just a secondary symptom.[5,6] One year Prevalence of migraine in Pakistan is 22.5%, more common in younger age groups and females.[7]

The acute attacks of migraine are treated by NSAIDs with parenteral antiemetics and triptans. If attacks are frequent (>4 per month) or long-lasting (≥12 hours duration), then their prophylactic treatment is indicated. The choices include Anti-epileptic drugs, Calcium Channel blockers, Beta Blockers and Antidepressant medication.[8] Topiramate is an anti-epileptic drug approved by the FDA for migraine prophylaxis. Its starting dose is 25 mg daily, which can be titrated up to 100 mg/day in divided doses. However, it causes sedation, cognitive dysfunction, paresthesias and psychiatric disturbances.[9] Amitriptyline is another drug used in migraine prophylaxis, which is an antidepressant and can be given up to a maximum of 100 mg per day. It is recommended in the American Academy of Neurology guidelines as well.[10] The objective of this study is to compare the efficacy of Topiramate and Amitriptyline in reducing the mean monthly number of migrainous headaches from the previous baseline. This study highlights the importance of considering both efficacy and tolerability when selecting a prophylactic medication for migraine prevention. The choice between the two medications should be based on carefully evaluating the patients' needs and preferences, considering both efficacy and tolerability.

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METHODOLOGY

The comparative cross sectional study was conducted at Combined Military Hospital Malir Cantt Pakistan from May to October 2022 after approval was taken from the Ethical Committee of the Institute (Reference Number 82/2021/Trg/ERC). The sample size calculated using OpenEpi Online software based on a 22.5% prevalence of migraine.[11]

Inclusion Criteria: Patients of either gender, aged 12 or older diagnosed with common migraine disorder as per ICHD-3 criteria were included.

Exclusion Criteria: Patients with diagnosed Clinical Depression or any other psychiatric illness, diagnosed epilepsy, trigeminal neuralgia, cluster headache or any other type of headache; patients with radiological evidence of other causes of headache, tumours, stroke, vasculitis and infections; and patients with a history of dementia, stroke or any neuropsychiatric illness other than migraine were excluded.

Patients were then randomized into two groups through the lottery method. One Group received Topiramate, and the other group subjects received Amitriptyline for migraine prophylaxis. They were then presented with a questionnaire, which was carefully developed using previously recognized questionnaires, the Migraine Disability Assessment Questionnaire (MIDAS), Headache Impact Test (HIT-6) and Migraine Specific Quality of Life Questionnaire (MSQ 2.1) as guiding tools. Patients were then prescribed prophylactic medicines according to their respective groups and were called for regular follow-ups. The study was done over six months, and factors like frequency and severity of headaches, their impact on daily activities and overall functionality were assessed. These parameters, which included headache frequency, severity, use of abortive therapy during acute episodes, any symptoms compelling withdrawal from prophylactic therapy, etc, were given scores from 0 to 2, with a total score of 8 for each individual. The data was recorded and then compared with the baseline frequency and severity of headaches the patients had at the start of the study, both within groups and between the groups.

Statistical Package for Social Sciences (SPSS) version 26.0 was used for the data analysis. As the normality assumptions were unmet, all the quantitative variables were explored using the median and interquartile range, whereas frequencies and percentages were calculated for qualitative variables. Inferential statistics were explored using Wilcoxon signed rank test. The *p*-value of 0.05 or less was taken as significant.

RESULTS

A total of 270 subjects were included in the study and were randomized into Topiramate and Amitriptyline groups of 135 each. The mean age of patients included in the study was 36.51±9.77 years. It comprised 108(40%) males and 162(60%) females. Comparison of headache parameters before and after the treatment of migraine preventive therapy are shown in the Table-I. There was a significant improvement in migraine symptoms among topiramate & amitriptyline groups (*p*-value<0.001). There was no significant difference in the efficacy of Topiramate and Amitriptyline (*p*-value=0.411) (Table-II).

Table-I: Comparison of Parameters Before and After the Treatment of Migraine Preventive Therapy (n=270)

Parameters	Before treatment (n=135)		After Treatment (n=135)	
	Median	IQR	Median	IQR
Topiramate-Group				
Average monthly Frequency of headache(no. of episodes per month)	2	0	1	0
Average Headache intensity scale (from 0 to 2)	1	0	1	1
Average Quality of life score (from 0 to 2)	1	0	1	1
Monthly use of Abortive therapy for acute migraine (Number of times per month)	1	0	0	1
Average score (out of 8)	5	0	3	2
Amitriptyline-Group				
Average monthly Frequency of headache(no. of episodes per month)	2	0	1	1
Average Headache intensity scale(from 0 to 2)	1	0	1	1
Average Quality of life score(from 0 to 2)	1	0	1	1
Monthly use of Abortive therapy for acute migraine(Number of times per month)	1	0	0	0
Average score (out of 8)	3	2	2	2

Table-II: Comparison of Effectiveness of Migraine Preventive Therapy Between two drugs (n=270)

Average Reduction in Scores	Values		*p*-value (Wilcoxon Test)
	Median	IQR	
Topiramate Group	2	2	0.411
Amitriptyline Group	2	2	

DISCUSSION

Our study showed that Topiramate and Amitriptyline hold equal efficacy in preventing further episodes of migraine. This study shed light on the fact that migraine was more common in females than their male counterparts. This female dominance was appreciable in one study.[12] Another study showed that the prevalence of migraine was higher in females (23.83%) as compared to males (23.83% and 15.50%).[13] Topiramate was given at around 100 mg /day as a single dose or divided doses in one group assigned through randomization. It showed a significant decline in the severity and frequency of headaches as well as an improvement in the quality of life. A similar result was found in a study where Topiramate showed a significant decline in the frequency and severity of headaches compared to its placebo group (*p*-value 0.025).[14] However another study showed a comparison between Botox and Topiramate for chronic migraine prophylaxis, her research results revealed that Topiramate showed improvement in the quality of life of the users as depicted by the Migraine Disability Assessment (MIDAS) score.[15] Amitriptyline was started and titrated per patient response up to 100 mg daily as a single or divided dose. The study showed that it also showed significant improvement in the migraine symptoms and the resolution of acute episodes as well.[16]

One previous study depicted the positive impact of Amitriptyline, which not only bettered the severity of the disorder under discussion but also improved the quality of life of its users, which was previously compromised due to the primary illness.[17] The degree of improvement in headache parameters was compared between groups receiving Topiramate and Amitriptyline, respectively, and it was found that neither drug was superior to the other one in providing a better relief of symptoms (*p*-value=0.363). This finding is in concordance with the another study that showed treatment models of Topiramate and Amitriptyline to be equally effective in preventing headache disorders with no superiority over others.[18] Research work of Kothiyal *et al*. displayed similar results showing similar efficacy of both drugs in reducing migraine occurances.[19] Our study did not take into account the side effects of the drugs for which further studies are required in order to ascertain the risk benefits & patient suitability while selecting the drug for prophylaxis.

CONCLUSION

Migraine is one of the most debilitating illnesses that can affect young adults' quality of life badly. For this purpose, prophylactic agents are required if headaches are frequent and severe. Among these, Topiramate and Amitriptyline hold equal efficacy in preventing further episodes of migraine.

Conflict of Interest: None.

Author's Contribution

Following authors have made substantial contributions to the manuscript as under:

WUHK: & UZF: Conception, study design, drafting the manuscript, approval of the final version to be published.

HH: & UN: Data acquisition, data analysis, data interpretation, critical review, approval of the final version to be published.

AG: & KA: Critical review, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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