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Original Article

# Comparison of Efficacy of Oral Lacosamide Versus Oral Topiramate in Young Adults with Chronic Migraine

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## ABSTRACT

***Objective:*** To compare the efficacy of the new anti-epileptic drug Lacosamide vs conventional treatment with Topiramate for the treatment of young adults presenting with chronic migraine.

***Study Design:*** Randomized controlled trial.

***Place and Duration of Study:*** Department of Anesthesia (Pain clinic) and Department of Medicine, Combined Military Hospital Rahim Yar Khan, Pakistan from Jan to Jun 2023.

***Methodology:*** The patients were divided into two groups, Group-T (n=145) and Group-L (n=145). Patients in Group-T received oral Topiramate at a dose of 50 mg twice a day while Group-L received oral Lacosamide at a dose of 100 mg twice a day. All the participants received the drug regime in both groups for a period of three months. Primary variables observed were improvement in the quality of life and migraine free days during therapy due to the disease according to the MIDAS (Migraine disability assessment) scoring system before and after 90 days of treatment.

***Results:*** While observing the primary variables, median MIDAS (Migraine Disability Assessment) scores before therapy were 11.00 (IQR=2.00) in Group-L versus 11.00 (IQR=3.00) in Group-T ($p$=0.743). The same median scores were 6.00 (IQR=1.00) in Group-L versus 8.00 (IQR=0.00) in Group-T ($p$<0.001). Mean days to an episode of migraine before start of therapy were 17.17±2.04 days in Group-L versus 17.06±1.99 days in Group-T ($p$=0.663). During therapy for 90 days, migraine free days following up to an episode of migraine were increased to 50.67±4.39 days in Group-L to 38.21±3.83 days in Group-T ($p$<0.001)

***Conclusion:*** Treatment with oral Lacosamide resulted increased migraine free days with a more conducive adverse effect profile.

**Keywords:** Chronic, Lacosamide, Migraine, Topiramate.

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## INTRODUCTION

Chronic migraine remains one of the most prevalent headache syndromes globally with an estimated prevalence of 1.1 billion people.[1] In Pakistan, the prevalence of migraine in the population varies around 22.5%. WHO labels migraine syndromes as the top 19th cause of diseases causing years lived with disability.[2] With such a high incidence of hinderance to the quality of life of people, it becomes imperative to develop new treatment regimens offering minimum side effects and improved efficacy for the disease.

With the increase in urbanization and long working hours especially in corporate setups, the incidence of migraine is increasing in the young adult demographic.[3] Various factors are attributable to this increase including stress, hectic academic routines, genetics as well as irregular sleep cycles.[4] The impact of these factors has increased the patient workload and young patients presenting with episodes of acute headaches, most of which convert into a chronic migraine requiring prolonged treatment and follow-ups.[5]

Topiramate belongs to the anti-epileptic class of drugs acting mainly on GABA receptors for their activation and inhibition of glutamate receptors for their activation resulting in controlled episodes of chronic migraine.[6] It is considered as one of the first line treatments for headache syndromes and has been extensively used in chronic migraine patients with an efficacy of decreasing migraine episodes in around 50% of patients.[7]

Lacosamide is a new class of anti-epileptics with major effect on the enhancement of slow voltage gated Na channel inactivation resulting in early ending of the action potential and relieving the increased brain activity associated with chronic migraine episodes.[8] It

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has recently been used as a trial drug showing promise of decreasing the episodes in patients with chronic migraine and offering better results than conventional treatment drug groups including beta blockers, Ca channel blockers, conventional anti-convulsant, TCAs and SNRIs.[9]

The objective of this study was to compare the efficacy of the new anti-epileptic drug Lacosamide with conventional treatment with Topiramate for the treatment of young adults presenting with chronic migraine.

## METHODOLOGY

This randomized controlled trial was carried out at the Department of Medicine and Pain clinic in Department of Anesthesia, Combined Military Hospital, Rahim Yar Khan, Pakistan from January to June 2023 after approval form the ethical review board (vide letter no: CMH-RYK-00100 dated 24 Dec 2022) and registered in the Iranian Trial Registry (irct.ir) with (trial ID IRCT20230809059091N1). A pilot study was carried out at the institute before the start of the trial with two groups of thirty patients each, one group to receive oral Lacosamide and the other to receive oral Topiramate. Mean difference of migraine free days with respect to control (patient when not on treatment) in both groups was 33.17±2.36 days for the Lacosamide and 24.66±2.39 days in the Topiramate group. Minimum sample size was then calculated using WHO calculator with these mean values keeping the confidence interval at 95%, power of test at 80% and population variance at 5000. Minimum sample size came out to be 72 for the Lacosamide and 130 for the Topiramate group. We analyzed 350 patients for randomization into the two groups and a total of 290 that fulfilled the inclusion criteria were divided into the Lacosamide (Group-L) (n=145) and Topiramate (Group-T) (n=145). Randomization was done into two groups and sampling technique was non-probability consecutive.

**Inclusion Criteria:** Young adult patients aged 18-30 years diagnosed with chronic migraine according to the standardized ICHD-310 (International classification of headache disorders) criteria presenting with an episode of acute migraine in the last one week, not on any consistent medication and only taking pain killers on SOS basis were included in the study.

**Exclusion Criteria:** Patients already on conventional treatment other than Topiramate and Lacosamide, patients with profound cardiac, renal, and liver disease, patients allergic to either Topiramate or Lacosamide, patients with co-morbidities including diabetes, hypertension, ischemic heart disease were excluded.

The patients were divided into two groups, Group-T (n=145) and Group-L (n=145) according to the inclusion criteria furnished after randomization as shown in Figure-1. Patients in Group-T received oral Topiramate at a dose of 50 mg twice a day while Group-L received oral Lacosamide at a dose of 100 mg twice a day. All the participants received the drug regime in both groups for a period of three months. Patients experiencing more than three acute episodes during the study period or MIDAS score of more than 20 were excluded from the study citing non-effectivity of the drug to patient condition.

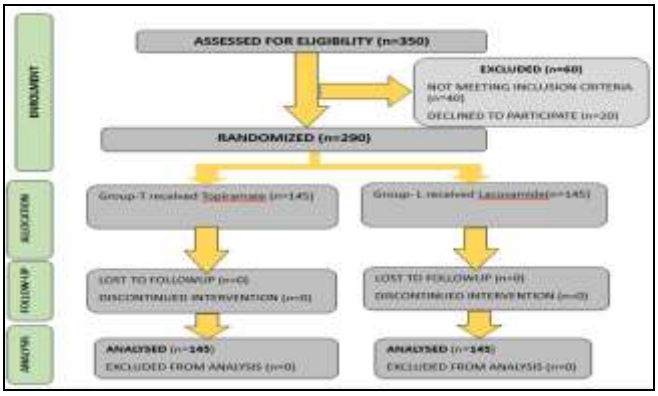


**Figure-1: Phases Of The Randomized Controlled Trial**

Primary variables observed was improvement in the quality of life and migraine free days during therapy due to the disease according to the MIDAS (Table-I) scoring system before and after 90 days of treatment.[11] The improvement was tabulated by a trainee medicine or trainee anesthesia with minimum 2 years of experience. The data was collected on a proforma with mild, moderate, severe disability according to the scoring done by using the standard questionnaire. All the patients were requested to follow up every two weeks or present if an episode occurred during the treatment period.

Demographic data were statistically described in terms of Mean±SD, frequencies, and percentages when appropriate. Independent samples t-test was used to compare statistically significant changes for primary and secondary endpoints. Median disability scores were compared using the Mann Whitney U test. A *p*-value of ≤0.05 was considered statistically significant.

All statistical calculations were performed using Statistical Package for the Social Sciences 26.0.

## RESULTS

A total of 290 patients were included in the study protocol after randomization into Group-L (n=145) receiving oral Lacosamide and Group-T (n=145) receiving oral Topiramate. Mean age of patients was 23.36±2.25 years in Group-L versus 23.57±2.30 years in Group-T ($p$=0.426). Mean weight was 65.28±4.32 kg in Group-L versus 65.49±4.13 kg in Group-T ($p$=0.667) (Table-II).

**Table-I: Midas (Migraine Disability Assessment) Scoring for Disability**

| MIDAS Grade | Definition | MIDAS Score |
|---|---|---|
| I | Little or No disability | 0-5 |
| II | Mild Disability | 6-10 |
| III | Moderate Disability | 11-20 |
| IV | Severe Disability | 21+ |

**Table-II Demographic Comparison among Groups (n=290)**

| Variable | Group-L (n=145) | Group-T (n=145) | $p$-value |
|---|---|---|---|
| Mean Age (Years) | 23.36±2.25 | 23.57±2.30 | 0.426 |
| Mean Weight (Kg) | 65.28±4.32 | 65.49±4.13 | 0.667 |

While observing the primary variables, median MIDAS (Migraine Disability Assessment) scores before therapy were 11.00 (IQR=2.00) in Group-L versus 11.00 (IQR=3.00) in Group-T ($p$=0.743). The same median scores were 6.00 (IQR=1.00) in Group-L versus 8.00 (IQR=0.00) in Group-T ($p$<0.001). Mean days to an episode of migraine before start of therapy were 17.17±2.04 days in Group-L versus 17.06±1.99 days in Group-T ($p$=0.663). During therapy for 90 days, migraine free days following up to an episode of migraine were increased to 50.67±4.39 days in Group-L to 38.21±3.83 days in Group-T ($p$<0.001) (Table-III).

**Table-III Comparison of Primary and Secondary Parameters Between Groups (n=290)**

| Variable | Group-L (n=145) | Group-T (n=145) | $p$-value |
|---|---|---|---|
| **Median Midas Scores** | | | |
| Before Starting Therapy | 11.00 (IQR=2.00) | 11.00 (IQR=3.00) | 0.743 |
| 90 Days Post-Therapy | 6.00 (IQR=1.00) | 8.00 (IQR=0.00) | <0.001 |
| Mean Migraine Free Days (Days to First Attack Before Therapy) | 17.17±2.04 | 17.06±1.99 | 0.663 |
| Mean Migraine Free Days (Days to First Attack During Therapy) | 50.67±4.39 | 38.21±3.83 | <0.001 |

Frequency of adverse effect profile showed that headache was observed in 11(7.6%) patients in Group-L versus 20(13.8%) patients in Group-T. Shaky movements of the body were reported by 06(4.1%) patients in Group-L versus 15(10.3%) patients in Group-T. Sedation was reported by 21(14.5%) patients in Group-L versus 22(15.2%) patients in Group-T (Table-IV).

**Table-IV Adverse Effect Profile (n=290)**

| Variable | Group-L (n=145) | Group-T (n=145) |
|---|---|---|
| Headache | 11(7.6%) | 20(13.8%) |
| Shaky Body Movements | 06(4.1%) | 15(10.3%) |
| Sedation | 21(14.5%) | 22(15.2%) |

## DISCUSSSION

Our study revealed that oral Lacosamide is as effective or better than oral Topiramate in younger patients where stress factors and migraine attacks are more frequent than the older population. The study was carried out in our demographic setup to look for alternatives to conventional therapy for treatment of migraine in the young adult patient demographic. Migraine has been associated with considerable morbidity in the younger population resulting in loss of school, college, and university days as well as loss of office hours. It is projected that the population prevalence in the younger demographic is around 22.5%.[12] The decreased functional capacity with multiple episodes and overall deterioration in the quality of life is a major problem for the younger demographic since the social and psychological trigger factors have been proposed to increase profoundly in the last three decades. The most common trigger factors proposed in this population are emotional stress, high caffeine intake, depression, sleep cycle disturbances and hormonal irregularities in females. These are especially concerning in the female demographic where migraine has been reported to result in adverse pregnancy outcomes.

Studies done on the international level for efficacy of Lacosamide for chronic migraine show that not only is it an anti-epileptic, but it also had non-nociceptive actions and prevents pain in a multitude of scenarios especially migraine.[13] Other studies conclude that treatment with Lacosamide resulted in effective prevention of migraine attacks and increasing the number of migraine free days from the start of therapy.[14] Another study also concluded that the pain free days were increased to a mean of 46 days which is in line with findings of our study as well.[15] Comparison with conventional therapy of Topiramate has been scarce but studies which have been done

prove that Lacosamide is a suitable alternative in preventing subsequent attacks as well as decreasing symptoms.[6] Various studies have also confirmed its role in preventing the aura as well as intensity of attacks associated with epilepsy.[16]

To our knowledge, there have not been any studies comparing the efficacy of these drugs in the younger demographic. However, their role in improving the headache and aura associated with migraine has been studied.[17] Lacosamide has proven to be better in controlling the aura, but the frequency of sedation as a side effect with both drugs has been comparable but not an indication to stop therapy.[18] However, in our study sedation was the most common side effect observed with patients asking to shift to alternate therapeutic regimens as the treatment affected their routine schedule in colleges, universities, and offices.

## LIMITATIONS OF STUDY

The limitations of this study are that of a single center. Multi-center study will cater more to our demographic area.

## RECOMMEDATIONS

Our study recommends the use of oral Lacosamide as a suitable alternative to oral Topiramate in young adults suffering from chronic migraine.

## CONCLUSION

Treatment with oral Lacosamide resulted in better quality of life, increased migraine free days with a more conducive adverse effect profile.

**Conflict of Interest:** None.

**Funding Souce:** None.

**Authors Contribution**

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

NTB & MU: Data acquisition, critical review, approval of the final version to be published.

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

RA & KRK: Data analysis, data interpretation, critical review, 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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