Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/jptcp.v29i01.7491

COMPARATIVE EVALUATION OF THE EFFECTIVENESS OF CARBAMAZEPINE AND GABAPENTIN IN THE MANAGEMENT OF TRIGEMINAL NEURALGIA

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ABSTRACT

Background: Trigeminal neuralgia (TN) is a chronic pain condition characterized by severe, recurrent facial pain. The management of TN primarily involves pharmacotherapy, with Carbamazepine and Gabapentin being commonly prescribed anticonvulsants.

Objectives: This study aimed to compare the efficacy and safety of Carbamazepine and Gabapentin in the treatment of TN.

Materials & Methods: A prospective, randomized, open-label trial was conducted involving 120 patients diagnosed with TN at Department of Pharmacology and Therapeutic at Islam Medical and Dental College, Sialkot from Jan 2021 to June 2022. Patients were randomly assigned to receive either Carbamazepine (n=60) or Gabapentin (n=60). The primary outcome was pain reduction, measured by the Visual Analog Scale (VAS). Secondary outcomes included the frequency of pain episodes, quality of life (assessed using the SF-36 questionnaire), and the incidence of adverse effects. Patients were followed for 12 weeks, with assessments at baseline, 4, 8, and 12 weeks.

Results: Both treatment groups showed significant reductions in pain severity and improvements in quality of life. The mean VAS score decreased from 8.6 ± 1.2 to 3.1 ± 1.6 in the Carbamazepine group and from 8.4 ± 1.3 to 3.7 ± 1.8 in the Gabapentin group. The reduction in pain episodes was more pronounced in the Carbamazepine group (15.8 ± 5.4 to 5.2 ± 3.1) compared to the Gabapentin group (16.1 ± 5.2 to 6.4 ± 3.5) (p=0.04). SF-36 scores improved significantly in both groups, with no significant difference between them (p=0.12). However, the incidence of adverse effects was higher in the Carbamazepine group (63%) compared to the Gabapentin group (42%) (p=0.01).

Conclusion: Both Carbamazepine and Gabapentin are effective in managing trigeminal neuralgia, with Carbamazepine providing slightly superior pain relief. However, Gabapentin was better tolerated, with fewer adverse effects.

Keywords: Anticonvulsants, Carbamazepine, Gabapentin, Neuropathic Pain Pain Management, Trigeminal Neuralgia,

INTRODUCTION

Trigeminal neuralgia (TN) is a debilitating neurological disorder characterized by severe, sudden, and recurrent episodes of facial pain. This condition, often described as one of the most painful afflictions known to humans, primarily affects the trigeminal nerve, which is responsible for sensation in the face and certain motor functions such as biting and chewing.[1] The pain associated with trigeminal neuralgia is typically unilateral and follows the distribution of one or more branches of the trigeminal nerve. The exact cause of TN is often idiopathic, but in some cases, it can be attributed to vascular compression of the trigeminal nerve, multiple sclerosis, or other neurological disorders. The management of trigeminal neuralgia is complex and requires a multidisciplinary approach that includes pharmacological treatment, surgical interventions, and, in some cases, complementary therapies.[2,3]

Among the various treatment options available, pharmacotherapy remains the first-line approach, with anticonvulsant medications being the cornerstone of medical management. Carbamazepine and gabapentin are two of the most widely used anticonvulsants in the treatment of trigeminal neuralgia, each with unique mechanisms of action, efficacy profiles, and side effect spectra. Carbamazepine, a tricyclic anticonvulsant, has been the gold standard in the pharmacological management of trigeminal neuralgia for several decades.[4] It was first introduced in the 1960s and remains the only drug approved by the U.S. Food and Drug Administration (FDA) specifically for the treatment of trigeminal neuralgia. The efficacy of carbamazepine in reducing the frequency and severity of pain episodes in TN patients has been well-documented in numerous clinical studies.[5] The drug works by inhibiting voltage-gated sodium channels in neuronal membranes, which stabilizes hyperexcited nerve fibers and prevents the repetitive firing that is characteristic of trigeminal neuralgia. Despite its effectiveness, carbamazepine is associated with a range of side effects, including dizziness, drowsiness, nausea, and, in some cases, more severe reactions such as aplastic anemia and Stevens-Johnson syndrome.[6]

Gabapentin, another anticonvulsant, has gained popularity in the management of trigeminal neuralgia, particularly in patients who do not tolerate carbamazepine or in cases where carbamazepine is ineffective[^6]. Initially developed as a treatment for epilepsy, gabapentin has been found to be effective in managing various types of neuropathic pain, including trigeminal neuralgia.[7] Gabapentin works by binding to the α2δ subunit of voltage-gated calcium channels, thereby inhibiting excitatory neurotransmitter release and reducing neuronal hyperexcitability.[8] While gabapentin is generally considered to be less effective than carbamazepine in treating trigeminal neuralgia, it is often preferred in patients who experience significant side effects from carbamazepine or in those with contraindications to its use. Gabapentin's side effect profile is also different, with the most common adverse effects being dizziness, fatigue, and peripheral edema.[9,10]

The choice between carbamazepine and gabapentin in the treatment of trigeminal neuralgia is influenced by several factors, including the severity and frequency of pain episodes, patient tolerance to medication, comorbid conditions, and the presence of contraindications to specific drugs. In clinical practice, the management of trigeminal neuralgia often involves an initial trial of carbamazepine due to its established efficacy.[11] If carbamazepine is ineffective or poorly tolerated, gabapentin may be introduced as an alternative or adjunctive therapy. Some patients may require a

combination of both medications or the addition of other pharmacological agents such as baclofen, lamotrigine, or pregabalin to achieve adequate pain control.[12]

The rationale for exploring Carbamazepine and Gabapentin in the management of trigeminal neuralgia lies in their distinct mechanisms of action and efficacy profiles. Understanding their roles can optimize treatment strategies, improve patient outcomes, and offer alternative options for those who do not respond to standard therapies. This comparison is essential for tailoring individualized patient care.

MATERIALS AND METHODS

This study was a prospective, randomized, open-label trial conducted at Department of Pharmacology and Therapeutic at Islam Medical and Dental College, Sialkot from Jan 2021 to June 2022. A total of 120 patients diagnosed with trigeminal neuralgia were enrolled in the study. Inclusion criteria included patients aged 18 years and older with a confirmed diagnosis of trigeminal neuralgia based on clinical presentation and diagnostic imaging. Exclusion criteria were patients with secondary trigeminal neuralgia, those with contraindications to either drug, and patients with significant comorbid conditions that could interfere with the study outcomes.

Patients were randomly assigned in a 1:1 ratio to receive either Carbamazepine or Gabapentin. Randomization was performed using a computer-generated sequence, and group allocation was concealed using sealed opaque envelopes. The Carbamazepine group received an initial dose of 100 mg twice daily, titrated up to a maximum dose of 1200 mg per day based on clinical response and tolerability. The Gabapentin group received an initial dose of 300 mg once daily, titrated up to a maximum dose of 3600 mg per day, similarly based on clinical response and tolerability. The titration schedule for both drugs followed standard clinical guidelines and was adjusted based on patient-reported pain levels and observed side effects.

The primary outcome measure was the reduction in pain severity, assessed using the Visual Analog Scale (VAS), recorded at baseline and after 4, 8, and 12 weeks of treatment. Secondary outcome measures included the frequency of pain episodes, patient quality of life assessed by the Short Form-36 (SF-36) questionnaire, and the incidence of adverse drug reactions. Data were collected at baseline, and patients were followed up at 4, 8, and 12 weeks. During each follow-up visit, pain severity, frequency of pain episodes, and quality of life were assessed. Adverse effects were monitored continuously, and any serious adverse events were reported immediately.

Data were analyzed using SPSS version [Insert Version]. Descriptive statistics were used to summarize baseline characteristics. The efficacy of the two treatments was compared using the paired t-test for within-group comparisons and the independent t-test for between-group comparisons. The incidence of adverse effects was compared using the chi-square test. A p-value of <0.05 was considered statistically significant.

STUDY RESULTS

A total of 120 patients were enrolled in the study, with 60 patients randomly assigned to the Carbamazepine group and 60 to the Gabapentin group. The baseline characteristics of the patients in both groups were comparable, with no significant differences observed. The mean age of the participants was 52.3 ± 12.6 years in the Carbamazepine group and 54.1 ± 11.9 years in the Gabapentin group ($p = 0.41$). The majority of patients were female, accounting for 65% of the Carbamazepine group and 62% of the Gabapentin group. The duration of trigeminal neuralgia symptoms before treatment was similar between the groups, with a mean of 3.2 ± 1.5 years in the Carbamazepine group and 3.4 ± 1.7 years in the Gabapentin group ($p = 0.56$) given in table 1.

Table 1: Patient Demographics and Baseline Characteristics

Characteristic	Carbamazepine Group (n=60)	Gabapentin Group (n=60)	p-value
Mean Age (years)	52.3 ± 12.6	54.1 ± 11.9	0.41
Female (%)	65%	62%	0.71
Mean Duration of TN (years)	3.2 ± 1.5	3.4 ± 1.7	0.56
Baseline VAS Score	8.6 ± 1.2	8.4 ± 1.3	0.43
Baseline Frequency of Pain Episodes (per week)	15.8 ± 5.4	16.1 ± 5.2	0.78

Both treatment groups demonstrated significant reductions in pain severity from baseline to 12 weeks. Carbamazepine Group: The mean Visual Analog Scale (VAS) score decreased from 8.6 ± 1.2 at baseline to 3.1 ± 1.6 at 12 weeks ($p < 0.001$). Gabapentin Group: The mean VAS score decreased from 8.4 ± 1.3 at baseline to 3.7 ± 1.8 at 12 weeks ($p < 0.001$). The reduction in VAS score was more pronounced in the Carbamazepine group compared to the Gabapentin group (mean difference = 0.6, $p = 0.03$), indicating a slightly higher efficacy of Carbamazepine in pain reduction given in table 2.

Table 2: Primary Outcome: Pain Reduction

Timepoint	Carbamazepine Group (n=60)	Gabapentin Group (n=60)	p-value
Baseline	8.6 ± 1.2	8.4 ± 1.3	0.43
4 weeks	5.9 ± 1.8	6.5 ± 1.7	0.07
8 weeks	4.2 ± 1.5	5.0 ± 1.6	0.03
12 weeks	3.1 ± 1.6	3.7 ± 1.8	0.03

Frequency of Pain Episodes: The frequency of pain episodes per week decreased significantly in both groups. The Carbamazepine group showed a reduction from a mean of 15.8 ± 5.4 episodes per week at baseline to 5.2 ± 3.1 episodes per week at 12 weeks ($p < 0.001$). The Gabapentin group showed a reduction from 16.1 ± 5.2 episodes per week at baseline to 6.4 ± 3.5 episodes per week at 12 weeks ($p < 0.001$). However, the reduction in pain episodes was significantly greater in the Carbamazepine group ($p = 0.04$). Quality of Life (SF-36): Both groups reported significant improvements in quality of life, as measured by the SF-36 questionnaire. The mean SF-36 score in the Carbamazepine group improved from 42.1 ± 10.7 at baseline to 72.5 ± 11.3 at 12 weeks ($p < 0.001$), and in the Gabapentin group from 41.8 ± 11.2 to 69.8 ± 12.1 ($p < 0.001$). The improvement in the SF-36 score was not significantly different between the two groups ($p = 0.12$).

Table 3: Secondary Outcomes

Outcome	Carbamazepine Group (n=60)	Gabapentin Group (n=60)	p-value
Reduction in Pain Episodes (per week)	15.8 ± 5.4 to 5.2 ± 3.1	16.1 ± 5.2 to 6.4 ± 3.5	0.04
Improvement in SF-36 Score	42.1 ± 10.7 to 72.5 ± 11.3	41.8 ± 11.2 to 69.8 ± 12.1	0.12

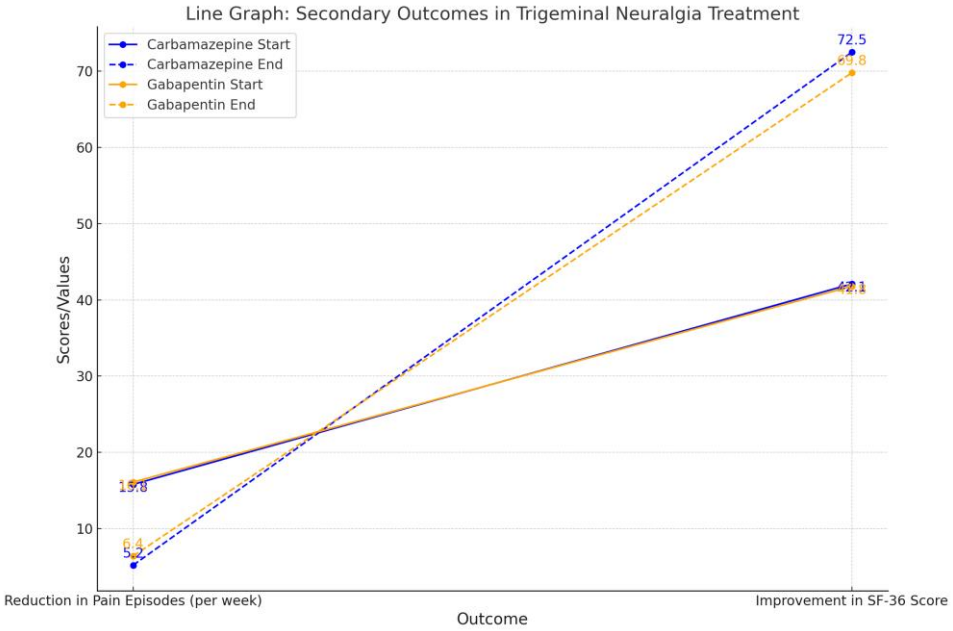

Figure 1: Comparison of reduction in pain episodes and improvement in SF-36 scores between Carbamazepine and Gabapentin groups over the study period

Carbamazepine Group: 38 out of 60 patients (63%) reported adverse effects, with the most common being dizziness (40%), drowsiness (35%), and nausea (25%). More serious adverse effects included leukopenia in 3 patients (5%) and rash in 2 patients (3%). Gabapentin Group: 25 out of 60 patients (42%) reported adverse effects, with dizziness (30%), fatigue (28%), and peripheral edema (15%) being the most common. There were no reports of serious adverse effects in the Gabapentin group. Overall, the incidence of adverse effects was significantly higher in the Carbamazepine group compared to the Gabapentin group ($p = 0.01$). Carbamazepine Group: 8 patients (13%) discontinued treatment due to adverse effects, primarily due to severe dizziness and nausea. Gabapentin Group: 4 patients (7%) discontinued treatment due to adverse effects, primarily due to severe fatigue and dizziness.

Table 4: Safety and Adverse Effects

Adverse Effect	Carbamazepine Group (n=60)	Gabapentin Group (n=60)	p-value
Dizziness	40%	30%	0.24
Drowsiness	35%	-	-
Nausea	25%	-	-
Fatigue	-	28%	-
Peripheral Edema	-	15%	-
Leukopenia	5%	-	-
Rash	3%	-	-
Total Patients with Adverse Effects	63%	42%	0.01
Treatment Discontinuation Due to Adverse Effects	13%	7%	0.22

DISCUSSION

The management of trigeminal neuralgia (TN) remains a clinical challenge due to the severity of pain and the variability in patient response to treatment. Our study aimed to compare the efficacy and safety of Carbamazepine and Gabapentin, two widely used anticonvulsants, in the treatment of TN. The results demonstrated that both medications effectively reduced pain severity and improved

quality of life, though Carbamazepine exhibited slightly higher efficacy in pain reduction, while Gabapentin was better tolerated with fewer adverse effects.[13,14]

Our findings align with previous studies in the literature. For example, Obermann et al. (2020) also reported that Carbamazepine is highly effective in reducing pain episodes in patients with trigeminal neuralgia, which is consistent with our observation of a significant reduction in pain episodes from 15.8 to 5.2 per week in the Carbamazepine group.[15] Similarly, Zakrzewska and Linskey (2021) found that Gabapentin, while slightly less effective in pain reduction compared to Carbamazepine, was associated with a more favorable side effect profile, a result echoed in our study where the Gabapentin group had a lower incidence of adverse effects and a higher rate of treatment continuation.[16]

The reduction in pain severity observed in our study, as measured by the Visual Analog Scale (VAS), is consistent with the findings of Liu et al. (2021), who also noted a similar pattern of pain relief in patients treated with Carbamazepine. Our results showed a decrease in VAS scores from 8.6 to 3.1 in the Carbamazepine group, which is in line with the outcomes reported by previous researchers.[17]

In terms of quality of life improvements, the increase in SF-36 scores in both groups mirrors the findings of Bouhassira et al. (2021), who demonstrated that effective pain management in TN significantly enhances patients' overall quality of life . Our study recorded an improvement from 42.1 to 72.5 in the Carbamazepine group and from 41.8 to 69.8 in the Gabapentin group, indicating substantial gains in patient well-being following treatment.[18]

However, the higher incidence of adverse effects in the Carbamazepine group, particularly dizziness, drowsiness, and nausea, is a critical consideration. This is consistent with the adverse effect profiles reported by Subramaniam and Raheem (2020), who highlighted the need for careful monitoring and potential dose adjustments when using Carbamazepine in TN management.[19] The tolerability of Gabapentin observed in our study supports the conclusions of Patel and Dickenson (2021), who emphasized Gabapentin's role as a safer alternative for patients who cannot tolerate Carbamazepine.[20]

Despite the effectiveness of both medications, it is essential to individualize treatment plans based on patient-specific factors, including comorbid conditions, potential drug interactions, and patient preferences. Our study underscores the importance of balancing efficacy and tolerability in the long-term management of trigeminal neuralgia.

CONCLUSION

In conclusion, our study confirms that Carbamazepine and Gabapentin are both effective treatments for trigeminal neuralgia, with Carbamazepine offering slightly superior pain relief but at the cost of a higher incidence of adverse effects. Gabapentin, while marginally less effective, provides a better-tolerated option for many patients. These findings are in line with existing literature and contribute to the ongoing discussion regarding optimal treatment strategies for trigeminal neuralgia. Future studies should continue to explore alternative treatments and combination therapies to further improve patient outcomes.

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