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Comparison of Carbamazepine Alone and in Combination with Gabapentin as Medical Therapy to Control Pain Associated with Trigeminal Neuralgia

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ABSTRACT

Objective: To investigate mean pain scores in patients of trigeminal neuralgia treated with Carbamazepine alone and in patients given combination therapy of Carbamazepine with Gabapentin after 4 weeks of starting therapy.

Materials and Methods: A prospective clinical study was undertaken at the Department of Oral and Maxillofacial Surgery, Armed Forces Institute of Dentistry, Rawalpindi from July 2019 to March 2020. The first group received 100 mg of Carbamazepine twice daily and the second group received 100mg of Carbamazepine along with 300mg of Gabapentin twice daily. The patient was instructed to grade the intensity of pain on the Visual Analogue Scale (VAS) every week for four weeks after initiation of therapy. Mean pain scores for the week were calculated and compared.

Results: A total of 80 respondents were recruited with a mean age and standard deviation was 48.69 ± 11.8 years. A comparison of the mean VAS score of 3rd week in both groups revealed that there was a significant difference (p<0.001). Similarly, by week four, the difference between VAS scores of Groups A and B differed significantly (p=0.007). Age and gender did not significantly impact the postoperative VAS pain score at four weeks of follow-up.

Conclusion: The combination of Carbamazepine with Gabapentin resulted in better pain control in patients with trigeminal neuralgia as compared to Carbamazepine. Mean VAS score after 4th week in both groups Group A (Carbamazepine alone), and Group B (Carbamazepine plus Gabapentin), it was found that there was a significant difference between both groups and a significantly lower mean pain score was found in Group B as compared to Group A.

Keywords: Carbamazepine, Gabapentin, Trigeminal Neuralgia

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INTRODUCTION

Trigeminal neuralgia is a condition known for causing severe neuropathic pain. The disease's ability to cause such severe pain leads to a halt in everyday activities like talking, eating, drinking and touching the face. It also affects the psychological, social and physical needs of the individual.[1] Trigeminal neuralgia not only affects life on a social level, but it also produces serious mental health effects. As highlighted by an epidemiological study, the mental health effects of the condition include increased mood swings, depression and inadequate sleep.[2] The disease's nature is such that it is manageable by surgical, medical and dental healthcare professionals, hence there are different variations in its treatments which eventually leads to a delay in the access of specialist care.[3] Therefore, prompt and accurate treatment is required to curb the intense pain caused by the condition.

At present, drugs can be used for nerve block, and then, neurotomy, microvascular decompression, or radiofrequency thermocoagulation can be used for treatment, but available treatments are still far from the ideal effect and pain tends to recur.[4,5] Carbamazepine is the first choice for the treatment of primary trigeminal neuralgia, and it is effective for most patients, but it has many adverse reactions; blood routine, electrolytes, and liver and kidney functions should be monitored during medication.[6]

Gabapentin has been used in clinics for more than 10 years as a new type of anti-epileptic drug. Its good curative effect for neuropathic pain has been reported in many literature studies.[7,8] Primary trigeminal neuralgia is also a neuropathic pain in mechanisms. At present, many randomized controlled trials (RCTs) comparing the safety and efficacy of gabapentin and carbamazepine for primary trigeminal neuralgia have been carried out. Whether carbamazepine alone or in combination with gabapentin can be used as a medical therapy for pain associated with trigeminal neuralgia has not been verified by evidence-based research. This study aimed to assess the effect of these two drugs alone or in combination for the management of TN, to provide evidence-based medicine for medical practice.

MATERIALS AND METHODS

This prospective clinical study was undertaken at the Department of Oral and Maxillofacial Surgery, Armed Forces Institute of Dentistry, Rawalpindi from July 2019 to January 2020. Permission was taken and already submitted by the Ethical Committee of the Armed Forces Institute of Dentistry for the study.

A consecutive sampling technique was used for the recruitment of patients. With the help of the WHO sample size calculator following are the calculations; Power: 80% Alpha: 0.05 Group I mean and standard deviation: 2.67 ± 0.95 Group II mean: 2.40 ± 0.86 Sample size: n: 80 (40 each group).

All patients who were recently diagnosed with trigeminal neuralgia who had not received any medical therapy for the disease were included irrespective of gender aged between 30 to 70 years. Pregnant women, nursing mothers and those with long-term history of trigeminal neuralgia which was refractory to treatment or those with compromised medical status were excluded from the study.

An informed written consent of the patients was obtained on consent forms after explaining the significance of the study. Demographic details (including name, age, gender, and contact) were obtained and recorded on specific Data Collection Forms. The patients were selected according to inclusion criteria and studied using a random controlled design and were randomly allocated as patients with odd registration numbers were assigned to the first group receiving 100 mg of Carbamazepine twice daily and patients with even registration numbers were assigned to the second group receiving 100 mg of Carbamazepine along with 300mg of Gabapentin twice daily irrespective of the gender and age. The patient was instructed to grade the intensity of pain on the Visual Analogue Scale (VAS) as 1 – No pain; 2 – Just notable pain; 3 – Weak pain; 4 – Moderate pain; 5 – Severe pain every week for four weeks after initiation of therapy. The mean of pain scores for all the whole week was calculated and compared.

Data was analyzed using statistical software SPSS version 25. Descriptive statistics were used to analyze Qualitative and Quantitative variables. Quantitative variables like age and pain score of 4 postoperative weeks were measured as mean ± Standard deviation (SD). Qualitative variables like Gender were measured as frequency and percentage. Independent sample t-test (Student t-test) was applied to compare quantitative variables like age and pain score of 4 postoperative

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weeks between 2 groups. *P* value ≤ 0.05 was significant. Stratification was done to control effect modifiers like age and gender. Post-stratification independent sample t-test was applied for quantitative variables like age and pain score of 4 postoperative weeks. *P* value ≤ 0.05 was significant.

RESULTS

A total of 80 respondents were recruited with a mean age and standard deviation was 48.69 ± 11.802 years. Males were 42/80 (52.5%) while females were 38/80 (47.5%) as shown in Table 1.

Table 1. Demographics and VAS Pain Score of the Participants

Age	48.69 ± 11.8
Age groups	
<50 years	46 (57.5%)
>50 years	34 (42.5%)
Gender	
Male	42 (52.5%)
Female	38 (47.5%)
VAS Pain score	
1st week	3.84 ± 0.88
2nd week	2.83 ± 0.81
3rd week	2.43 ± 0.84
4th week	1.86 ± 0.88

A comparison of the mean VAS score of 3rd week in both groups revealed that there was a significant difference (p<0.001). Similarly, by week four, the difference between VAS scores of Groups A and B differed significantly (p=0.007) as shown in Table 2.

The minimum mean VAS Pain score after 1st week was 2 and the maximum was 5 with mean and standard deviation as 3.84 ± 0. 878. The minimum VAS Pain score after 2nd week was 2 and the maximum was 4 with mean and standard deviation as 2.83 ± 0.808. The minimum VAS Pain score after 3rd week was 1 and the maximum VAS Pain score after 3 weeks was 4, with mean and standard deviation as 2.43 ± 0.839. The minimum VAS Pain score after 4th week was 1 and the maximum was 4 with mean and standard deviation as 1.86 ± 0.882 (Figure 1).

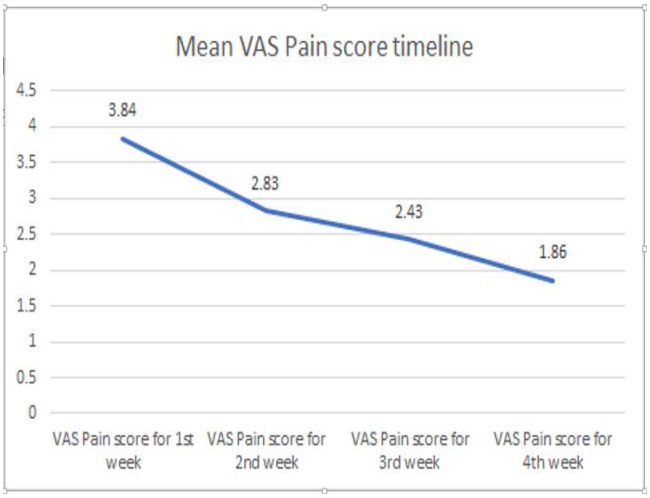

Figure 1: Mean VAS Pain Score

As shown in Table 3, age and gender did not significantly impact the postoperative VAS pain score at four weeks of follow-up.

Table 2: Comparison of mean VAS in both groups

VAS Pain Score	Group A (n=40)	Group B (n=40)	*p*-value
VAS Pain score for 1st week	3.85 ± 0.893	3.83 ± 0.874	0.9
VAS Pain score for 2nd week	2.93 ± 0.859	2.73 ± 0.751	0.271
VAS Pain score for 3rd week	2.75 ± 0.840	2.10 ± 0.709	0.001
VAS Pain score for 4th week	2.13 ± 0.992	1.60 ± 0.672	0.007

Table 3: Association of VAS pain scores at 4th week with age and gender

Parameter	Group A	Group B	*p*-value
Age			
< 50 years	2.13 ± 1.058	1.52 ± 0.730	0.082
> 50 years	2.12 ± 0.928	1.71 ± 0.588	0.132
Gender			
Male	1.96 ± 0.976	1.42 ± 0.507	0.073
Female	2.35 ± 0.996	1.76 ± 0.768	0.064

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DISCUSSION

The objective of the present study was to investigate mean pain scores in patients of trigeminal neuralgia treated with Carbamazepine alone and in patients given combination therapy of Carbamazepine with Gabapentin after 4 weeks of starting therapy.

It was found that there was a significant difference between the two therapeutic groups with respect to VAS score at 3rd and 4th week of treatment. Age and gender did not significantly affect the efficacy of the treatment.

Killian et al (1968) reported the effect of carbamazepine on 24 patients randomized in two groups. One group of patients were given carbamazepine titrated to a sufficient dose (maximum dose not stated) and the other group had a placebo.[9] A definite response (eg, disappearance or decrease of pain) was found in patients who took carbamazepine, whereas minimal to no response was reported in patients who took a placebo.

Yuan et al (2016) reported the effect of carbamazepine gabapentin in a meta-analysis of 14 RCTs including 1156 patients, one group of patients was administered gabapentin up to 3600 mg and the other group was given carbamazepine up to 2400 mg.[10] It was noted that patients of both groups responded similarly to both gabapentin and carbamazepine (odds ratio 1·6 [95% CI 1·2 to –2·2], p=0·002). A total of 170 (26%) patients in the gabapentin group and 306 (48%) patients in the carbamazepine group had similar side-effects, namely vertigo, somnolence, nausea, and fatigue.

Hercules S et al reported that the management of trigeminal neuralgia with pharmacotherapy was instituted for all patients with this disorder before any interventional therapy was attempted for pain relief.[11] Carbamazepine, an antiepileptic, was a well-established drug in the treatment of Trigeminal neuralgia. Various studies and authors have reported variable benefit and relapse rates in patients with Trigeminal neuralgia with carbamazepine. There was evidence that pregabalin and gabapentin were effective in neuralgic pain.[12,13]

Carbamazepine treats seizures and the symptoms of trigeminal neuralgia by inhibiting sodium channels. In bipolar 1 disorder, carbamazepine has been found to decrease mania symptoms in a clinically significant manner according to the Young Mania Rating Scale (YMRS).[14-16] Carbamazepine has a narrow therapeutic index. In studies of Han Chinese ancestry patients, a pronounced association between the HLA-B*1502 genotype and Steven Johnson syndrome and/or toxic epidermal necrolysis (SJS/TEN) resulting from carbamazepine use was observed.[17]

This study has certain limitations. For instance, since it only had 80 patients from a single centre, the findings of our study cannot be generalized to a larger population. A further large-scale study with a diverse population is required to find out the efficacy of both treatment regimes.

CONCLUSION

A combination of Carbamazepine with Gabapentin resulted in better pain control in patients with trigeminal neuralgia as compared to Carbamazepine. VAS score after 4th week in both groups (Group A (Carbamazepine alone), Group B (Carbamazepine plus Gabapentin), it was found that there was a significant difference score found in between both groups and significantly lower Group B as compared to Group A.

DISCLAIMER

None to declare.

CONFLICT OF INTEREST

There is no conflict of interest among the authors.

ETHICAL STATEMENT

Ethical approval was provided by the Institutional Review Board and Ethical Review Committee at Armed Forced Institute of Dentistry, Rawalpindi, Pakistan.

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AUTHORS CONTRIBUTION

Conception and design of the study: A. Mariam, N. Khan

Acquisition of data: A. Mariam

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Drafting of the manuscript: N. Tahir, N. Rashid, S. Fazal, R. Naseer

Critical review of the manuscript: A. Mariam, N. Khan

Approval of the final version of the manuscript to be published: A. Mariam, N. Khan, N. Tahir, N. Rashid, S. Fazal, R. Naseer

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