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ORIGINAL ARTICLE

Efficacy of Carbamazepine and Oxcarbazepine for Treating Trigeminal Neuralgia

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Abstract

Objective: To compare the efficacy of carbamazepine with oxcarbazepine for treating Trigeminal Neuralgia

Methodology: This was a randomized controlled trial conducted at Department of Oral Biology and Tooth Morphology, University Medical and Dental College (UMDC) Faisalabad, from October 2021 to April 2022. Total 56 patients (28 in each groups were randomized to revise carbamazepine and oxcarbazepine). Patient's selection was based on a predefined inclusion and exclusion criteria. In Group-A patients were given Carbamazepine (200mg twice a day upto1800mg) and in Group-B patients were given Ox-carbamazepine (200mg BD daily up-to 1200mg). Safety was measured in terms of side effects seen in patients after treatment allocation. The response of the patients to therapeutic effectiveness of drug was decided based on the frequency of attacks, i.e., good response: no attacks of pain; average response: two to three attacks of pain per day; and nonresponsive with no decrease in the frequency of attacks of pain.

Results: Results showed higher efficacy for oxcarbazepine when compared with carbamazepine. i.e. Complete response= Carbamazepine: 42.9% vs. Oxcarbazepine:67.9%, p-value=0.017 Mean pain score was significantly better with oxcarbazepine (2.82±0.77) when compared with carbamazepine (4.36±0.86). i.e. p-value<0.001. Safety profile was also better for oxcarbazepine as that of carbamazepine. Frequency of adverse effects was higher for carbamazepine as that of Oxcarbazepine. i.e. 35.7% vs. 14.3%, p-value=0.064

Conclusion: It is concluded that oxycarbazepine is more effective in terms of efficacy, side effects and pain control as that of carbamazepine in the management of Trigeminal neuralgia.

Key Words: Trigeminal neuralgia, Efficacy, carbamazepine, Oxycarbazepine. Mono therapy, Side effects

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Introduction

The International Association for the Study of Pain describes TN as "a sudden, usually unilateral, severe, brief stabbing, recurrent episodes of pain in the distribution of one or more branches of the trigeminal nerve."[1] The lifetime prevalence of TN is estimated to be 0.16%–0.3%,[2] It is more prevalent in women than in men (F:M ratio 3:2)[3] In adult series, the mean onset age is 53–57 years old, with a range of 24-93 years old.[3, 4]

TN is divided into idiopathic, classic, and secondary subtypes, each of which is associated with a different set of symptoms and potential causes. However, researchers have yet to identify a definitive cause for TN or identify its underlying processes. There is no known aetiology for the first kind, and roughly 10% of individuals with this condition still have no diagnosis despite undergoing diagnostic treatments including surgery or magnetic resonance imaging.(5) Several anticonvulsant medications are used in TN pharmacological treatment. Patients who

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have a poor to moderate response to carbamazepine or oxcarbazepine or who have adverse effects including drowsiness and dizziness may benefit from add-on medicines such as baclofen, lamotrigine, and pimozide.[6, 7] Carbamazepine was the first drug used for the treatment of TN as anticonvulsant in 1962-63 by Blom.

Their activity causes hyper-excited neuronal membranes to stabilize and repeated firing to be inhibited. Although CBZ and OXC are beneficial in the long-term treatment of trigeminal neuralgia, their tolerability remains a source of contention.[6, 8]

Oxcarbazepine is an analogue of carbamazepine, and its efficacy in the treatment of epilepsy is identical to that of carbamazepine. It is often used in acute orofacial pain episodes lasting seconds, as well as in the trigeminal nerve and its branches (ophthalmic, maxillary, and mandibular), referred to as trigeminal neuralgia (TN).[9] Because of its lesser negative effects than carbamazepine, oxcarbazepine is preferred by certain doctors and clinicians. Oxacarbazepine has advantages over carbamazepine since it has a smaller effect on the patient's haematological profile. Around one-third of patients with a history of carbamazepine hypersensitivity are also at risk of developing oxcarbazepine hypersensitivity.[9] Very few studies have compared both these drugs for treating trigeminal neuralgia. However, the effects of these drugs have been documented in the literature in comparison to other drugs or as a triple therapy combination. So, taking both drugs as mono therapy for treating Trigeminal neuralgia can lead us to conclude which drug is superior as a monotherapy so that in the future, combination therapies can also be derived on the efficacy of these drugs.

Material and Methods

This was a randomized controlled trial conducted at Department of Oral Biology and Tooth Morphology, University Medical and Dental College (UMDC) Faisalabad, in period of 10 months from October 2021 to April 2022. We included 56 patients (28 in each group) in this study as per predefined inclusion and exclusion criteria. Sample size calculation was done with online calculator open-epi (https://www.openepi.com/SampleSize/SSMean.htm). Sample size of 56 patients (28 in each group) in calculated with 95% confidence level, 90% power of study and by taking expected mean score for pain score with Carbamazepine and Ox-carbamazepine as 3.42±0.82 and 4.21±0.98 respectively.

Sample selection was done with the help of non-probability purposive sampling technique. Clinically diagnosed patients (as defined by the International Society of Headache Guidelines) in the age range of 20-50 years of either gender were included in the study. Patients taking any medication for the treatment of neuralgia, patients who had undergone surgical procedure for the treatment of trigeminal neuralgia, patients with renal and hepatic issue, patients with seizures, pregnant and lactating mothers, and patients with intolerance and allergic to both treatment drugs were excluded from the study. The patients were randomly divided into two groups. The institutional ethical review board committee. Carbamazepine (200 mg twice daily up to 1800 mg) was given to patients in Group A, while oxy-carbamazepine (200 mg BD daily up to 1200 mg) was given to patients in Group B. The efficacy of the treatment was determined by a reduction in pain score as measured by a visual analogue scale. Safety was measured in terms of side effects seen in patients after treatment allocation. The response of the patients to therapeutic effectiveness of the drug was decided based on the frequency of attacks, i.e., good response: no attacks of pain; average response: two to three attacks of pain per day; and nonresponsive with no decrease in the frequency of attacks of pain.

Data entry and analysis was carried out with Statistical Package for social sciences version-23. Quantitative variables were presented with mean±SD and qualitative variables were presented with frequency and percentage. Comparison of mean pain score between groups was carried out with the help of independent sample t-test. Response of treatment and side effects were compared in treatment groups with the help of chi square test. p-value $\leq$0.05 was considered statistically significant.

Results

Mean age of patients in Group-C and Group-OxC was 47.53±10.07 and 48.71±10.34 years. Age of patients in both groups ranges between 30-63 years. In Group-C 12(42.9%) patients were female and 16(57.1%) were male while in Group-OxC 14(50%) patients were male and 14(50%) were female. Mean duration of symptoms in Group-C and Group-OxC was 10.89±7.10 and 11.75±6.31 weeks respectively. In Group-C 6(21.4%) patients right side, 11(39.3%) patients left side and

11(39.3%) patients bilateral side was effected while in Group-OxC 13(46.4%) patients right side, 6(21.4%) patients left side and 9(32.1%) patients bilateral sides were effected. Mean pain score in Group-C and Group-OxC was 4.35±0.86 and 2.82±0.787 respectively.

Mean pain score was significantly higher in Group-C patients i.e. p-value<0.001. Treatment response was significantly better in Group-OxC patients as compared to Group-C i.e. p-value=0.017 In Group-OxC 19(67.9%) patients had complete treatment response, 6(21.4%) had nearly, 1(3.6%) patients had moderately and 2(7.1%) patients had partial treatment response. While in Group-C 12(42.9%) patients had complete, 3(10.7%) had nearly, 10(35.7%) had moderate and 3(10.7%) had partial treatment response. Adverse effects were higher in Group-C patients as compared to Group-OxC patients but the difference was not statistically significant i.e. Group-C: 35.7% vs. Group-OxC: 14.3%, p-value=0.064

Table I: Characteristics of Patients in study Groups. (n-56)

		Group-C (n=28)	Group-OxC (n=28)
Age		47.53±10.07	48.71±10.34
Gender	**Male**	16(57.1%)	14(50%)
	Female	12(42.9%)	14(50%)
Duration		10.89±7.10	11.75±6.31
Side	**Right**	6(21.4%)	13(46.4%)
	Left	11(39.3%)	6(21.4%)
	Bilaterla	11(39.3%)	9(32.1%)

Table II: Treatment response and Adverse effects in Treatment Groups. (n-56)

		Group-C (n=28)	Group-OxC (n=28)	p-value
Response	**Complete**	12 (42.9%)	19 (67.9%)	**0.017**
	Nearly	3 (10.7%)	6 (21.4%)	
	Moderately	10 (35.7%)	1 (3.6%)	
	Partial	3 (10.7%)	2 (7.1%)	
Side	**Yes**	10 (35.7%)	4 (14.3%)	**0.064**
	No	18 (64.3%)	24 (85.7%)	

Discussion

CTN may be treated in a variety of ways; however, it is usually advised to try medicinal methods first and only resort to surgery if they fail. Carbamazepine and oxcarbazepine, two types of anti-epileptic medicines (AEDs), make up the bulk of medical treatment.[10, 11]

In this study we compared carbamazepine with oxcarbazepine for treating Trigeminal Neuralgia. Results showed higher efficacy for oxcarbazepine when compared with carbamazepine i.e. Complete response= Carbamazepine 42.9% vs Oxcarbazepine 67.9%, p-value=0.017. Mean pain score was significantly better with oxcarbazepine (2.82±0.77) when compared with carbamazepine (4.36±0.86) i.e. p-value<0.001. Safety profile was also better for oxcarbazepine as that of carbamazepine. Frequency of adverse effects was higher for carbamazepine as that of Oxcarbazepine i.e. 35.7% vs. 14.3%, p-value=0.064

According to a locally published study from Faisalabad reported that Oxcarbazepine is more effective than carbamazepine for pain relieving in patients of Trigeminal Neuralgia. This finding support the results of this study showing higher efficacy of Oxcarbazepine for better pain control as compared to carbamazepine.[12] A recently published study from Italy compared both these drugs and reported higher side effects with carbamazepine (43.6%) as compared to oxcarbazepine (30.3%). (p-value<0.0001).[13] This finding is in line with the results of this study showing low frequency of side effects with oxcarbazepine but the difference for side effects between both drugs was not statistically significant in this study.

Contrary to the findings of this study, the following two studies reported the superior efficacy of carbamazepine as compared to Oxcarbazepine. A study conducted by Stefano et al reported the response rate of CMZ (600 mg dose, Dose range: 200-1220 mg and OXX (1200 mg dose, Dose range: 600-1800 mg as 98% and 94% respectively.[6] A randomised controlled trial study conducted by Besi et al reported response rate of 80% with CMZ at a dose range of (200-300 mg) and 68% with OXC at a dose ranging between 300-600 mg.[8] A recently published study from India reported that with carbamazepine as 73.07% of the patients had good response with an increased dose of 1200 mg per day.[14]

To that end, a good reaction to these medications may be considered an operant criteria of TN, even if it only requires a single administration of a low dosage. However, there aren't any agreed-upon standards for what constitutes adequate pain management (e.g., complete vs partial suppression of pain paroxysms). Also, individuals who have intolerable adverse effects from

carbamazepine or oxcarbazepine would not meet a treatment-related condition.[7] Some of Oxcarbazepine's benefits in treating neuropathy include: Reduced medication interactions, enhanced tolerability, and the elimination of the need to monitor hematologic markers. Dizziness, ataxia, sleepiness, and decreased alertness are some of the negative effects of carbamazepine, which seem to be exacerbated with constant dosing.[15,16] According to the results of local research, the use of Oxcarbazepine, Gabapentin, and Amitriptyline in combination treatment for persistent trigeminal neuralgia significantly reduces pain levels and improves quality of life.[17]

Carbamazepine's potential for metabolic interaction with other drugs is a concern, especially for the elderly and those with several medical conditions. Although oxcarbazepine is more likely to produce severe central nervous system depression or dose-related hyponatremia, it has fewer adverse effects than carbamazepine and is less prone to interact with other medications. Women have a far lower tolerance for each of these medicines than males do.[18]

Since the effectiveness of each medicine varies greatly depending on the person using it, if one doesn't work, the other may be attempted. 200 milligrammes of carbamazepine is equivalent to 300 milligrammes of oxcarbazepine if you're considering making the switch. Carbamazepine with a delayed release (retard) is most effective when patients have reached a stable condition.[18]

Carbamazepine remains the gold standard for the first therapy of TGN, despite the availability of other AEDs. Patients who are not surgical candidates may undergo add-on or switch treatment with second-line medicines. Montherapy or poly-therapy using many drugs of uncertain effectiveness for symptom relief may be attempted. When other treatments have failed, surgery may be considered.[19]

Additional therapy with gabapentin, pregabalin, lamotrigine, or baclofen, in addition to carbamazepine or oxcarbazepine, is helpful for many TN patients. When carbamazepine or oxcarbazepine cannot achieve maximum dose due to adverse effects, combination therapy should be explored. Although data is limited, it is possible that each of the aforementioned medications is effective when used alone as treatment.[17]

Conclusion

Based on the results of this study, it is concluded that oxycarbazepine is more effective in terms of efficacy, side effects, and pain control than carbamazepine in the management of trigeminal neuralgia. Further trials can be designed to see the efficacy of both of these drugs as monotherapy as well as triple therapy in combination with other drugs to treat trigeminal neuralgia more efficiently for patients with a good prognosis for this condition.

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