

COMPARISON OF EFFECTIVENESS OF CARBAMAZEPINE VERSUS TOPIRAMATE FOR THE MANAGEMENT OF TRIGEMINAL NEURALGIA

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ABSTRACT

Objective: To compare the effectiveness of Carbamazepine versus Topiramate for the management of trigeminal neuralgia.

Study Design: Comparative prospective study.

Place and Duration of Study: Oral and Maxillofacial Surgery department, Allied Hospital, Faisalabad Pakistan, from Nov 2017 to Nov 2018.

Methodology: A total of 60 patients (30 in each group) were included. Group A was treated with Carbamazepine 100mg TDS and group B with Topiramate 25mg TDS. Visual analogue scale was used to assess pain and was calculated at 1st visit (baseline), at 7th day, at 14th day and at 28th day.

Results: Out of 60 patients, mean of age was 54.78 ± 8.49 years. Right and left side of the face was involved in 41 (68.3%) and 19 (31.7%) patients respectively. Maxillary branch was involved in 24 (40%) and mandibular branch was involved in 36 (60%) patients. The mean of visual analogue scale after 7 days in group A was 4.53 ± 0.93 and in group B was 7.1 ± 1.07 , after 14 days mean of visual analogue scale in group A was 3.7 ± 1.02 and in group B was 4.03 ± 1.27 . Mean of visual analogue scale after 28 days in group A was 3.27 ± 1.01 3.93 ± 1.28 . The results were statistically significant with *p*-value of 0.03.

Conclusion: Topiramate has comparable efficacy as that of Carbamazepine at dose of 75-100mg with lesser side effects. So Topiramate can be used as first line of treatment in trigeminal neuralgia.

Keywords: Carbamazepine, Topiramate, Trigeminal neuralgia.

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INTRODUCTION

Trigeminal neuralgia (TN) also called as tic douloureux is defined as severe, sharp, sudden, and stabbing pain that is unilateral and occurs in one or more divisions of trigeminal nerve^{1,2}. Pain is triggered by non-noxious stimuli like yawning, washing of face, brushing teeth and eating or it may be spontaneous in nature with pain free intervals. TN is classified as classical, secondary and idiopathic³. Incidence of TN is 0.7-27 per 100,000 approximately⁴. Peak age of onset ranges from 35-72 years with female to male ratio of 3:2.3⁵. Mandibular division and right side of the face is more commonly affected³.

TN can be treated medically as well as surgically with medical management considered the primary treatment option. Carbamazepine (CBZ) is the first line of treatment for the management of TN². CBZ acts by keeping the voltage gated sodium channel in inactivated state. Reduction in pain is achieved within 24 hours⁶. CBZ is associated with side effects like drowsiness, dizziness, nausea, vomiting, hepatotoxicity, myelosuppression, aplastic anemia, hyponatremia, renal toxicity, constipation, urinary retention and cardiac dysfunction and decrease in efficacy after prolong use

due to auto-induction⁷. Other medical options include drugs like Oxcarbazepine, Lamotrigine, Topiramate, Gabapentin, Baclofen and Phenytoin⁸. Topiramate is found to be effective for the treatment of trigeminal neuralgia with lesser side effects. Topiramate is d-fructose derivative and acts by blocking sodium, calcium channels and GABA agonist⁹. Dizziness, ataxia, constipation, bad taste and paresthesia like side effects are reported at higher doses¹⁰.

The rationale of study was to compare the effectiveness of Topiramate with Carbamazepine for the treatment of TN, as CBZ is associated with more side effects and its efficacy decreases over time. So that an effective and safe alternate of CBZ will be introduced and prescribed to patients for the management of TN.

METHODOLOGY

A comparative prospective study was conducted in Oral and Maxillofacial Surgery department, Allied Hospital, Faisalabad Pakistan, from December 2017 to December 2018. Sample size was calculated using WHO calculator for two proportions: $P_1=75\%$, $P_2=25.7\%$, $n=5$ power of study= 90% , level of significance= 5% Sample size 60 (30 in each group). Consecutive non-probability was the sampling technique. This study was approved from Hospital ethics review committee (ltr no: 835/2017). Newly diagnosed cases with age between 35-70 years, irrespective of gender were

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included in the study. Patients allergic to Carbamazepine or Topiramate, with comorbidities, post-traumatic neuropathic pain were excluded from the study.

After taking informed consent from the patients, history, clinical examination was done. Detailed history about the nature of pain was taken and diagnosis of trigeminal neuralgia was made based on the typical characteristics of pain. OPG was done to rule out any dental cause of pain. Renal function test and liver function test were done. Patients allocated into group A and B using lottery method. Group A was treated with Carbamazepine 100mg TDS and group B was treated with Topiramate 25mg TDS. Visual analogue score (VAS) was used to assess the severity of pain. VAS was calculated at baseline (1st visit), after 7 days of start of drugs (2nd visit), after 14 days (3rd visit), after 21 days (4th visit). In case of relief of pain in both the groups same dose of the drugs were continued. Patients who did not show reduction in pain as well as no side effects, the dose of Carbamazepine was increased by 100mg up to maximum of 1200mg/day and the dose of Topiramate was increased by 25mg up to maximum of 400 mg/day. Patients who reported with side effects at any visit as well as no reduction in pain, drug was discontinued, results were recorded and alternative treatment option was advised.

Data was analyzed using SPSS-22. For qualitative variables like gender, side of the face, branch involved, frequencies and percentages were calculated. For quantitative variables like VAS, age mean and standard deviation were calculated. Independent sample t-test was applied and *p*-value <0.05 was considered statistically significant.

RESULTS

Among 60 patients (30 in each group), the age range was 38-70 years with mean of 54.78 ± 8.49 years. Mean of age in group A was 54.93 ± 8.01 years group B was 54.63 ± 9.09 years. Out of 60 patients, 21 (35%) were male and 39 (65%) were female with male to female ratio of 1:1.8. In group A, 12 (40%) were male and 18 (60%) were female. In group B, 9 (30%) patients were male and 21 (70%) were female. Right side of the face was involved in 41 (68.3%) and left side was involved in 19 (31.7%) patients (table-I).

Among 60 patients none of the patient reported with involvement of V1 division of trigeminal nerve. V2 was affected in 24 (40%) patients and V3 was affected in 36 (60%) patients (table-II). The mean of VAS at 1st visit (baseline) was 7.53 ± 0.50 in group A and 7.57

± 0.50 in group B. VAS after 7 days in group A was 4.53 ± 0.93 and in group B was 7.1 ± 1.07 , after 14 days mean of VAS in group A was 3.7 ± 1.02 and in group B was 4.03 ± 1.27 . Mean of VAS after 28 days in group A was 3.27 ± 1.01 and in group B was 3.93 ± 1.28 . *p*-value was 0.03 (table-III).

Table-I: Frequency of side of the face involved in trigeminal neuralgia.

Side of the face	Group A n (%)	Group B n (%)	<i>p</i> -value
Right	19 (63%)	22 (73%)	0.4
Left	11 (36%)	8 (26.6%)	

Table-II: Frequency of branch of trigeminal nerve involved in trigeminal neuralgia.

Branch of V nerve involved	Group A n (%)	Group B n (%)	<i>p</i> -value
V2	14 (46.6%)	10 (73.3%)	0.2
V3	16 (53.3%)	20 (26.6%)	

Table-III: Pain score in groups.

	Group A	Group B	<i>p</i> -value
Mean of pain score at 1 st visit	7.53 ± 0.507	7.57 ± 0.504	0.7
Mean of pain score 2 nd visit (after 7 days of start of medication)	4.53 ± 0.937	7.13 ± 1.07	0.00
Mean of pain score at 3 rd visit (after 14 days of start of medication)	3.70 ± 1.02	4.03 ± 1.27	0.2
Mean of pain score at 4 th visit (after 28 days of start of medication)	3.27 ± 1.01	3.93 ± 1.28	0.03

In group A, dizziness was reported in 12 patients, drowsiness was in 5 and ataxia was reported in 1 patient at first follow up visit. The dose of CBZ was decreased in patients who showed reduction in pain score along with side effects like dizziness and drowsiness. In group B, 29 patients at first follow up visit did not show any side effects and only 1 patient reported with dizziness. At 2nd follow up visit, 12 patients in group A reported with dizziness and 5 with drowsiness and in group B, 1 patient reported with nausea and 6 with numbness of extremities. The numbness was the only side effect in topiramate that disappeared with use of the medication without any intererention. At 3rd follow up visit 10 patients in group A complained of dizziness and 2 with drowsiness and in group B only 1 patient complained of dizziness (table-IV).

Table-IV: Frequency of complications at follow up visits.

Follow up Visit	Group	No Complication	Dizziness	Drowsiness	Nausea	Numbness of hands	Ataxia
1st follow up (after 7 days of start of medication)	Group A	12 (40%)	12 (40%)	5 (16%)	-	-	1 (3%)
	Group B	29 (96%)	1 (3%)	-	-	-	-
2nd follow up (after 14 days of start of medication)	Group A	13 (43%)	12 (40%)	5 (16.6%)	-	-	-
	Group B	21 (70%)	2 (6.6%)	-	1 (3%)	6 (20%)	-
3rd follow up (after 28 days of start of medication)	Group A	18 (60%)	10 (33%)	2 (6.6%)	-	-	-
	Group B	29 (96.6%)	1 (3%)	-	-	-	-

DISCUSSION

Trigeminal neuralgia is the most common and the most painful facial pain condition¹¹. Treatment of TN is challenging and is managed medically in most of the patients. Surgical management is advised to patients who cannot tolerate the side effects of the drugs or who become resistant to various pharmacological options¹².

Toledo *et al*¹³, Katheriya *et al*¹⁴, found that TN was more prevalent in fourth to eighth decades of life. Kalyanaraman *et al*¹⁵, and Katusic *et al*¹⁶, also reported that the peak age of onset of TN is between 5-8th decade of life. These results were in comparison to our study. The age range was 38-70 years with mean of 54.78 and SD of 8.49. Mean of age in group A was 54.93 ± 8.01 years group B was 54.63 ± 9.09 years.

In this study, out of 60 patients, 21 (35%) were male and 39 (65%) were female with male to female ratio of 1:1.8. Previous studies had also shown that females are predominately affected by Shah *et al*¹⁷, and Loh *et al*¹⁸, in their studies found female to male ratio of 2:1. Warraich *et al*, in their study found that 61% were female and 39% were male¹⁹.

Right side of the face was involved in 41 (68.3%) and left side was involved in 19 (31.7%) patients in our study. Neto *et al*, in their study also found right side was more commonly affected than the left side due to narrower foramen rotundum on right side of skull base²⁰. Siqueira *et al*, also found similar results²¹. In study conducted by Katheriya *et al*, right side was involved in 57.1% of cases and left side in 38.8% of cases¹⁴.

Among 60 patients in our study, V2 was affected in 24 (40%) patients and V3 was affected in 36 (60%) patients. No patient reported with V1 involvement. These results are in contrast to study conducted by Tine *et al*, who found that maxillary division was more commonly affected²². However, Loh *et al* found that mandibular division of trigeminal nerve was more commonly affected¹⁸. Katheriya *et al*, concluded that mandibular nerve was affected in 56.9%, and maxillary nerve in 42% of cases¹⁴,

Among 60 patients in our 2 patients were lost to follow up in group A and 1 patient was lost to follow up in group B. To complete the sample size 3 patients were added. In our study, VAS after 7 days in group A was 4.53 ± 0.93 and in group B was 7.1 ± 1.07, after 14 days mean of VAS in group A was 3.7 ± 1.02 and in group B was 4.03 ± 1.27. Mean of VAS after 28 days in group A was 3.27 ± 1.01 and in group B was 3.93 ± 1.28. This shows that CBZ is effective after 7 days with dose of 300mg/day than Topiramate with dose of 75mg/day. But at 3rd and 4th visit Topiramate was equally effective as CBZ. Wang *et al*, also found Topiramate to be equally effective as that of CBZ after 1 month of use⁹. Solaro *et al*, also showed in their study that Topiramate can be used effectively for the treatment of trigeminal neuralgia as an alternative to CBZ²³. Campbell *et al*, found effectiveness of CBZ was 70-80% for the management of TN. They also found that CBZ was initially efficacy of CBZ was 80% that declines to 50% due to auto-induction²⁴. Puri *et al*, described that CBZ was effective after 1 month of follow up in most of the patients but patients reported with side effects like nausea, drowsiness and vomiting⁸.

Wang *et al*, described that 15.8% of patients in their study using Topiramate showed side effects like dizziness, nausea, ataxia and confusion and 21.1% of patients with CBZ had side effects like dizziness, nausea, vomiting, fatigue and nystagmus. In comparison, in our study 40% patients with CBZ showed side effects and only 3.3% with Topiramate had side effects⁹.

LIMITATIONS OF STUDY

The major limitation with this study was small sample size i.e. 60 patients. This study should be conducted on a larger group of population. Secondly the patients were followed after one month only. CBZ showed resistance due to auto-induction and many side effects like hyponatremia, liver dysfunction and aplastic anemia after long term use. As the follow up time was only of one month, these results were not found. Hence studies with longer follow ups should be conducted.

CONCLUSION

Carbamazepine is more effective after one week but as the dose of Topiramate is increased to 75-100mg it is equally effective as that of Carbamazepine. However, Carbamazepine has more side effects than Topiramate. So Topiramate can be used for the treatment of trigeminal neuralgia with lesser side effects.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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