Original Article

Maxillofacial Surgery

Comparison of Analgesic Effects of Oral Carbamezapine with Pregablin in Idiopathic Trigeminal Neuralgia

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ABSTRACT

Introduction: Idiopathic trigeminal neuralgia, a form of neuropathic pain, caused by not well defined etiology, is a formidable therapeutic challenge to clinicians because it does not respond well to traditional drug therapies. Anticonvulsant drugs are regarded as useful treatment for neuropathic pain.

Carbamazepine, the first anticonvulsant studied in clinical trials, probably alleviates pain by decreasing conductance in Na^+ channels and inhibiting ectopic discharges. Pregabalin has the most clearly demonstrated analgesic effect for the treatment of neuropathic pain. . The role of anticonvulsant drugs in the treatment of Idiopathic trigeminal neuralgia is evolving and has been clearly demonstrated with Pregabalin and carbamazepine.

Objective: The aim of this study was to investigate.comparison of analgesic effects of oral carbamezapine with pregablin in idiopathic trigeminal neuralgia.

Study Design: interventional study.

Place and Duration of Study: Oral & Maxillofacial surgery department, LUMHS. Jan 2012 to DEC 2012 .

Materials and methods: 30 patients with well defined history and diagnostic clinical symptoms of idiopathic trigeminal neuralgia were selected, divided into two groups of 15 individuals with similar gender & age difference. Clinical trial were conducted with group 1 with carbamazepine and group 2 with Pregabalin for 4 weeks.

Subjective pain level of both groups was recorded before intervention (pre treatment recording) and after intervention ($1^{st,}$ 2^{nd}, 3^{rd} and 4^{th}) on weekly basis by using 0-10 visual analogue scale (zero represent no pain 10 represent pain that could not be worse).

Results: Following intervention, both groups were evaluated for pain score in 1^{st} and 2nd week, there was no significant difference observed between the two groups. (P value 0.44 and 0.456), but after 3^{RD} and 4^{TH} weeks it was observed that, there is significant difference, (p value 0.000 and 0.009) on visual analogue scale. It was observed that there was a significant difference between pretreatment and fourth week mean pain score in group 2, (8.9 and 1.07).

Similarly marginally significant difference with (r = .640) was seen in 1^{st} week of group 2 receiving Pregablin, the mean value was (2.53, 1.60) respectively.

Conclusion: Based on these results that are in line with the recommendations made by other studies, the 1^{st} line medical therapy is Carbamazepine but this should be changed to other drug therapy if there is no pain relief or adverse effect.

Key words: Trigeminal neuralgia, carbamazepine, pregabline.

INTRODUCTION

Idiopathic Trigeminal Neuralgia is characterized as a sudden sharp, shock like, or burning pain[1, 2]. but not every patient has these symptoms at the begin· a number of patients knowledge a dull, continuous, aching pain in the upper or lower jaw at the inception of their sickness, and only latter extend the characteristic paroxysmal pain, this has been described as prodromal pain or "Pre-trigeminal neuralgia"[4]. Similar prodromal feelings have also been reported in some cases of glossopharyngeal neuralgia.[5]

The occurrence of idiopathic trigeminal neuralgia is reported to be 3 - 5 per 100,000 with a female high proportion in an age-adjusted ratio of 1.74:1. It is the majority between ages of 50 to 69 years [1, 7] but young adult and children can also be affected.[6]

Clinically idiopathic trigeminal neuralgia can involve the distributions of one or more of the branches of the trigeminal nerve, which supplies sensation to the skin of the face and anterior half of the head. Trigeminal neuralgia is most commonly found in the maxillary and mandibular division or the maxillary branch alone.[1, 7-8] A small proportion of cases have an effect on the ophthalmic division alone and attacks are more commonly seen on the right side of the face.[1, 7] Attacks are usually triggered by non-painful stimuli such as touch, movement, wind exposure, eating, brushing teeth, shaving, washing, talking, or swallowing.[7, 9] The attacks can occur during the day or night but rarely

during sleep. The attacks come in multiple clusters of pain that last from a few seconds to several minutes.[9]

Carbamazepine is the chief agent for treatment of trigeminal pain. Most patients with neuralgia are benefited initially, but only 70% obtain continuing relief. no more than 5 to 20% of patients discontinue medication because of adverse effects.[7] Other drugs like, Gaba-pantene10, Phenytoin [11],Beclofen [12] and Pimozide[13], lamotrigine[14], tizanidine [15] are also used for the treatment of trigeminal neuralgia.

Pregabalin was invented by medicinal chemist Richard Bruce Silverman at Northwestern University in the United States [16] [17].Pregabalin has anticonvulsive and pain-relieving activity .It binds with high affinity to the alpha2-delta subunit protein of voltage-gated calcium channels [18]. The anxiolytic effects of pregabalin occur rapidly after administration, similar to the benzodiazepines which gives pregabalin an advantage over many anxiolytic medications.[19]

Pregabalin is also used off-label for the treatment of chronic pain neuropathic pain, perioperative pain, and migraine[20,21]. Pregabalin is indicated in the treatment of peripheral neurophatic pain.[22]

MATERIAL AND METHODS

This interventional research study was conducted in the Department of Oral & Maxillofacial surgery department, LUMHS from Jan 2012 to DEC 2012. 30 patients with well defined history and diagnostic clinical symptoms of idiopathic trigeminal neuralgia were selected.

Carbamazepine was used as control for comparative of pregablin for the relief of pain in trigeminal neuralgia. The inclusion criteria was patients aged 50 years or older who have experienced pain for at least 6 months and intensity score of at least 4 out of 10 on visual analogue scale. The patients were evaluated for a period of 4 weeks.

Group 1: group was given 400-milligram Carbamazepine daily in divided dosages alone and was continued throughout the study period.

Group 2 was given pregablin 100 mg bd during 1st week of study. In 2nd week the dose of pregablin was increased to 200 mg b.d. and in third and fourth week was continued in same manner up to 300mg bd .

Subjective pain level of both groups was recorded before intervention pre treatment recording and after intervention 1st, 2nd, 3rd and 4th on weekly basis by using 0-10 visual analogue scale zero represent no pain 10 represent pain that could not be worse.

RESULTS

In this study 30 patients were included comprising 15 in each group. Oral carbamazepine in one group and pregabline in other group was label as group 1 and group 2 respectively.

The demographic data of the two treatment group revealed that mean age in group 1 (50), and group 2 is (52) years with a P value of (<0.63) (table 2) which shows that there no significant difference with respect to age.

There were 5 male 10 female in group 1 while 4 male and 11 female in group 2 with male to female ratio in both groups was (1.75:1) respectively (chart 1).

Before the treatment started, ITN pain was evaluated using visual analogue scale in both groups and it was found that there was no statistically significant difference in pain score between both groups (p value < 0.285) (Table 2).

Table No.1; age distribution in patients of trigeminal neuralgia.

	Mean		95% CI		T. Statistic	P-value
	(group1 n=15)	(Group 2 n=15)	Lower	Upper		
Age	50 □ 6.3	52 □ 10.2	4.86	7.79	0.475	0.63

By T- test Values were preexisted by mean □ SD

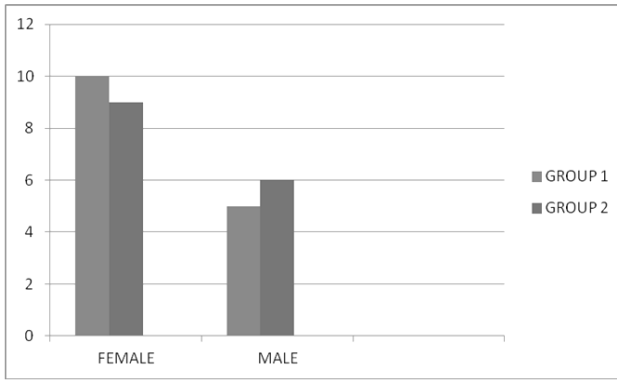

Figure No.1: Sex Distribution (Male to Female) n=30 *p* value □ 0.702

Site of Pain Distribution

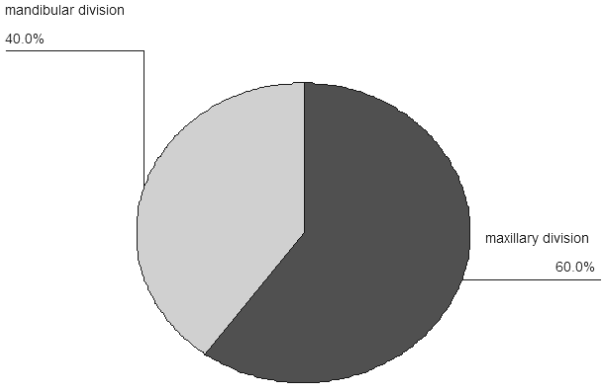

Figure No.2 Site of pain distribution (n=30)

Following intervention, both groups were evaluated for pain score in 1st and 2nd week, there was no significant difference observed between the two groups. (P value 0.44 and 0.456) (Table 2), but after 3RD and 4TH weeks it was observed that, there is significant difference, (p value 0.000 and 0.009) (Table 2) on visual analogue scale. It was observed that there was a significant

difference between pretreatment and fourth week mean pain score in group 2, (8.9 and 1.07) (Table 2).
Similarly marginally significant difference with (r = .640) (Table 3) was seen in 1st week of group 2 receiving Pregablin. (Table 4) the mean value was (2.53, 1.60) (Table 4) respectively.

Table No.2: Comparison of pain according to visual analogue scale between expose and non-expose. n=30

	Mean		95% CI		T Statistic	P-value
	(group 1) (n=15)	(group 2 n=15)	Lower	Upper		
Pre treat pain	8.9 □ 1.03	9.33 □ 0.97	-.352	1.152	1.090	0.285
After 1 week	0.80 □ 1.01	1.53 □ 1.21	-.989	0.456	-0.756	0.456
After 2 week	0.93 □ 1.03	1.72 □ 1.23	-0.451	1.25	0.963	0.344
After 3 week	1.73 □ 1.03	2.22□ 2.9	.625	3.90	2.828	0.009
After 4 week	1.07 □ 1.66	3.88□ 4.0	2.49	7.1	4.260	0.000

Values are preexisted by mean □ SD

Table No.3: Comparison of pain according to visual analogue scale for pre and first week treatment of exposed group. (n=15)

Correlation	Mean	Std deviation	r=
Pre Treatment	9.33	0.97	
First week	0.53	0.91	

DISCUSSION

The aim of our study is to see the analgesic effects of pregabline in idiopathic trigeminal neuralgia and established a comparison between pregabline and carbamezapine, Carbamazepine is considered as the drug of choice in medical therapy of Trigeminal Neuralgia. A number of authors have reported the use of Carbamazepine in the management of Trigeminal Neuralgia with better pain control but its adverse side effects and toxicity limits its continuation. There are some studies compared the efficacy of pregabline and Carbamazepine,[23.24,25] some studies have reported the use of pregabline for the treatment of Neuropathic pain.[26]
In this study we evaluate pain scoring before and after intervention. Before intervention there was no significant difference in pain scores between the two groups, but pain score was reduced significantly in-group 1 at the end of 3rd and 4th week. Although the difference was observed in pain scores in the two groups during first and second week but they were insignificant.
Carbamazepine and pregabline causes reduction in pain due to its Central effects .Our results reflect that following intervention in 3rd week exposed group showed decrease in pain relief, as the dosage of Carbamazepine was being tapered from 400 mg to complete withdrawal at the end of 3rd week. (P value 0.009). While second group was kept on Pregablin during treatment while group1 was still receiving Carbamazepine with dosage adjusted according to the symptoms. There was statistically significant difference seen between two groups (P value 0.00) shown better pain Control with group1.
So we reported that Carbamazepine is still the drug of choice in the management of Trigeminal neuralgia where as Pregablin does not provide effective pain control. This observation of pain control with group1 receiving Carbamazepine showed significant value during 1st, 2nd, 3rd 4th week.

CONCLUSION

Based on these results that are in line with the recommendations made by other studies, the 1st line medical therapy is Carbamazepine but this should be changed to other drug therapy if there is no pain relief or adverse effect. Patients with idiopathic trigeminal neuralgia, shows poor efficacy and tolerability of these drugs, Further research to understand the pathogenesis of idiopathic trigeminal neuralgia and well-designed clinical trials should further the opportunities to establish the role of anticonvulsants in the treatment modalities.

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