International Journal of Health Sciences and Research
www.ijhsr.org ISSN: 2249-9571

Original Research Article

Evaluation of Efficacy and Safety of Pregabalin as an Add on Therapy to Carbamazepine in Patients of Trigeminal Neuralgia

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ABSTRACT

Introduction: Pain and fear of pain continue to be the commonest and strongest motivation for the people to seek facial pain treatment. Pain is a personal experience of the sufferer that cannot be shared and wholly belongs to the sufferer. Trigeminal neuralgia (TN) is a notable facial pain disorder resulting in periodic severe pain that produces one of the most severe kinds of pain known to mankind. Treatment of this debilitating condition may be varied, ranging from medical to surgical interventions. However antiepileptic drugs are commonly used for its treatment. This study was done with an aim to evaluate the efficacy and safety of pregabalin as an add on therapy to carbamazepine in patients of trigeminal neuralgia.

Materials and Methods: This was a prospective, open label, randomized, comparative clinical study conducted on 50 patients. The patients were randomly divided in two groups of 25 patients to receive following two treatments. Group I (n=25) received tablet carbamazepine as a monotherapy *initially* 200 mg daily per orally in divided doses and gradually built up as per clinical response with maximum titrated dose upto 1000mg/day. Group II (n=25) received capsule pregabalin 75 mg OD and tablet carbamazepine 200 mg daily per orally in divided doses and dose gradually built up as per clinical response with maximum titrated dose upto 300mg/day for pregabalin for a period of 12 weeks. Efficacy assessment was done by Visual analogue scale (VAS), Verbal rating scale (VRS) and safety was assessed by monitoring of adverse drug reactions. The patients were assessed at the end of 4^{th}, 8^{th} and 12^{th} weeks.

Results: There was statistically significant reduction in mean pain score at 4^{th}, 8^{th} and 12 week, in both the groups when compared to the baseline i.e both carbamazepine and pregabalin as an add on therapy to carbamazepine were effective in reducing the pain. However on intergroup comparison, pregabalin as an add on drug to carbamazepine(Group II) produced better response with earlier onset of pain relief with statistically significant reduction in mean pain score at 8^{th} and 12^{th} weeks when compared to carbamazepine alone (Group I). There were no serious adverse effects in either of treatment group. Common adverse effects in group I were drowsiness, nausea and vomiting while in group II, drowsiness and dry mouth were commonly noticed

Conclusion: The present study suggested that pregabalin as an add on therapy to carbamazepine was found to cause significant reduction in pain scoring at 8^{th} & 12 weeks and could be a promising drug in patients of trigeminal neuralgia when therapeutic options are limited.

Key Words: carbamazepine, pregabalin, trigeminal neuralgia, visual analogue scale, verbal rating scale

INTRODUCTION

Trigeminal neuralgia (TN) which is also known as Fothergill disease or Tic douloureux disease is a form of neuropathic pain characterized by the occurrence of abrupt pain which is generally one-sided,

severe, brief, sharp and recurrent in the distribution area of one or several branches of the V^{th} nerve. [1] Pain is commonly evoked by trivial stimuli including washing, shaving, smoking, talking and brushing the teeth but may also occur spontaneously. [2] The International Headache Society (IHS) in year 2013 defined strict clinical criteria for trigeminal neuralgia diagnosis. [2] According to these criteria a diagnosis can be made when there is at least three attacks of unilateral facial pain i.e occurring in one or more division of the trigeminal nerve with no radiation beyond the trigeminal distribution. Pain with at least three of the following four characteristics i.e. recurring in paroxysmal attacks lasting from a fraction of a second to two minutes, severe intensity, electric shock-like shooting, stabbing pain, precipitated by innocuous stimuli to the affected side of face. Trigeminal neuralgia is further divided as typical and atypical. [3] In Typical type there is an idiopathic episodic pain lasting for several seconds, with pain-free intervals between the attacks whereas in atypical type there is continuous or repeated pain between transient paroxysms. [3] The prevalence of trigeminal neuralgia in the general population is 0.015% [4] and overall incidence ranges from 12.6 to 27 per 100,000/year [5] which increases with the advancing age. Middle aged and elderly persons are primarily affected, higher incidence is seen in women with 5.9 cases per 100,000 in females as compared with men with 3.5 cases per 100,000 in males. The diagnosis of trigeminal neuralgia is purely clinical and is made on the basis of characteristic pain in the trigeminal nerve distribution. Patients with trigeminal neuralgia suffer pain episode for months or years before the condition is finally diagnosed and unfortunately episodes of TN have a devastating impact on patient's Quality of life.

The first-line of treatment is always medical therapy. Of the drugs currently used to treat trigeminal neuralgia, most of them are anticonvulsants. Additionally only a handful of these drugs have been investigated in small randomized control trials for the treatment of trigeminal neuralgia and many of these trials have methodological flaws and are outdated. [6] Carbamazepine is the most studied medication for treatment of trigeminal neuralgia and is therefore the drug of choice. It is a sodium channel blocker and promotes the inactivated state of voltage activated sodium ion channels.

Pregabalin is a calcium channel blocker which shows specific affinity for the alpha2delta (α2δ) auxiliary subunits of voltage dependent calcium channels. The pregabalin exhibits analgesic, anxiolytic and anticonvulsant properties. It is structurally related to gabapentin and absorbed orally. It is not bound to plasma protein and is excreted unchanged mainly in urine without undergoing metabolism, its half life is approximately 6 hour. In randomized, placebo-controlled clinical trials pregabalin has demonstrated efficacy in reducing pain in patients with diabetic neuropathy and post herpetic neuralgia thereby significantly improving affective symptoms, sleep and quality of life. [7] Furthermore the pharmacokinetic profile of pregabalin allows for easy management and rapid dose escalation to therapeutic dosages.

Presently, surgical treatment options for trigeminal neuralgia are generally explored only when patients are refractory to medical management. A patient is said to be refractory when he/she cannot bear the adverse effects of the medication, experience breakthrough pain or cannot take the medications because he/she are medically complex patients with polypharmacy for other conditions. [8]

The present study has been planned in the view of the fact that, trigeminal neuralgia is common neuropathic pain disorder. Also it has a potential risk for causing depression and poor quality of life if left untreated. Despite the fact that many standard drugs such carbamazepine and other anticonvulsants are available for treatment of trigeminal neuralgia, but still

there is a search for an ideal analgesic with minimal side effects, maximal analgesia and improved patient compliance. Pregabalin is a commonly used therapy currently recommended as first line treatment for a number of neuropathic pain conditions such as diabetic peripheral neuropathy, postherpetic neuralgia, spinal cord injury etc. Pregabalin has been used as an add-on therapy along with NSAIDS, opioids, antiepileptic drugs and antidepressants drugs in uncontrolled neuropathic pain and its administration resulted in significant reduction in pain and improvement in the psychological well-being. So a comparative study was planned where combination of carbamazepine and pregabalin was compared with carbamazepine as a standard line of drug.

MATERIALS AND METHODS

This was a prospective, open label, randomized, comparative clinical study conducted by the Department of Pharmacology in collaboration with the Department of Neurology at Pt. B.D. Sharma PGIMS, Rohtak. In present study patients of either sex of more than 18 yrs of age attending the OPD in Neurology department with facial pain of trigeminal neuralgia were selected. The study was conducted over a period of 1 year and 50 patients were included. The Study was in accordance with the principles of good clinical practice (ICH-GCP) and declaration of Helsinki. The study was conducted after obtaining ethical clearance from institutional ethical committee (IEC). An informed consent was obtained from all the patients enrolled in this study.

The eligible patients were randomly divided into two study groups i.e. Group I and Group II with the help of computer generated random numbers. Each study group had 25 patients and were found to be comparable at the time of their initial visit with regard to demographic parameters such as age, gender, side involved and other parameters (as shown in table 1). Patients were allocated to receive one of the 2 different treatments in an open fashion. Group I (n=25) received tablet carbamazepine as a monotherapy initially 200 mg daily per orally in divided doses and gradually built up as per clinical response with maximum titrated dose upto 1000mg/day. Group II (n=25) received capsule pregabalin 75 mg OD and tablet carbamazepine 200 mg daily per orally in divided doses and dose gradually built up as per clinical response with maximum titrated dose upto 300mg/day for pregabalin for a period of 12 weeks and subjected to clinical assessment for safety and efficacy of drug. During the study, patients were not permitted to take any non-study drugs. Inclusion criteria were diagnosed cases of trigeminal neuralgia, patients of either gender of more than 18 years of age, patients who are ready to give written informed consent. Exclusion criteria were patients with history of psychiatric illness, patients with severe hepatic and renal disorders and other co-morbid conditions, pregnant and lactating women, history of known hypersensitivity to pregabalin and carbamazepine, patients who refused to give informed consent.

Efficacy assessment was determined by visual analogue scale (VAS) which is 100-mm vertical / horizontal line with no pain at one end and worst imaginable pain at other end. Subjects respond to the VAS by placing a mark through the line at a position which best represents their current perception of a given phenomenon between the labelled extremes and by verbal rating scale (VRS) on this scale, pain intensity was determined by severity of pain as: 0= none,1=mild, 2= moderate 3= severe and 4= very severe. Scoring was done pretreatment and at 4^{th}, 8^{th} and 12^{th} week (post-treatment). Patients were assessed after carbamazepine and pregabalin treatment to observe the presence of any adverse effects probably related to drugs. Any other unusual adverse events reported by the patients were also recorded. Patients having major toxicity to pregabalin and carbamazepine necessitating discontinuation

of treatment were withdrawn from the study and appropriate treatment was given

DATA ANALYSIS: Data was expressed as Mean ± SEM. Both intragroup and intergroup statistical analysis was done. Intragroup analysis was done by using ANOVA. Intergroup analysis was done by using unpaired 't' test. A p-value of less than 0.05 was considered as statistically significant.

RESULTS

TABLE-1: DEMOGRAPHIC PROFILE OF STUDY PARTICIPANTS IN BOTH THE GROUPS [N= 25 IN EACH GROUP]

Demographic Profile	Group I (n=25)	Group II (n= 25)
Age in years	52.9 ±3.59	51.3 ±3.33
Gender		
Male	19 (76%)	18 (72%)
Female	06 (24)	07 (28%)
Side of face involved		
Right side	16 (64%)	18 (72%)
Left side	09 (36%)	07 (28%)
Vascular loop around Trigeminal nerve	4 (16%)	6 (24%)
Drug allergy	NO	NO

Age is expressed as Mean ± SEM (standard error of mean) while categorical values are expressed as actual number of patients and their percentage.

EFFICACY ASSESSMENT

The assessment of efficacy was done at baseline, 4th, 8th and 12th weeks by using Visual analogue scale and Verbal rating scale

A) *Visual analogue scale (VAS):*

The visual analogue scale scoring for facial pain was calculated in all the patients of either group before drug administration (baseline) and at the end of 4th, 8th and 12th week after starting the treatment.

VAS SCORING IN GROUP I:

Intragroup analysis (Figure 1): At baseline mean VAS score was 82.08 ± 1.01. There was statistically significant reduction in mean pain score at week 4th (69.28 ± 1.01), 8 (66.08± 1.05) and 12 (64.40 ± 1.09), as compared to baseline.

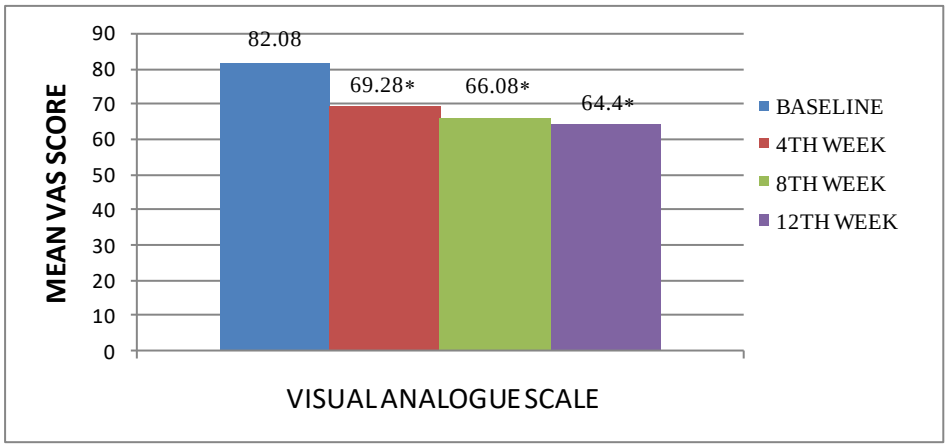

FIGURE 1: VAS SCORING IN GROUP I

* p < 0.05, indicates significant value noted at 4,8 and 12 weeks.
All values are expressed as Mean ± SEM

VAS SCORING IN GROUP II:

Intragroup analysis (Depicted in Figure 2):

At baseline mean VAS score was 82.48 ± 0.79. There was statistically significant reduction in mean pain score at 4th week (66.16 ± 1.22), 8th (60.96± 1.34) and 12th week (55.84 ± 1.54), as compared to baseline.

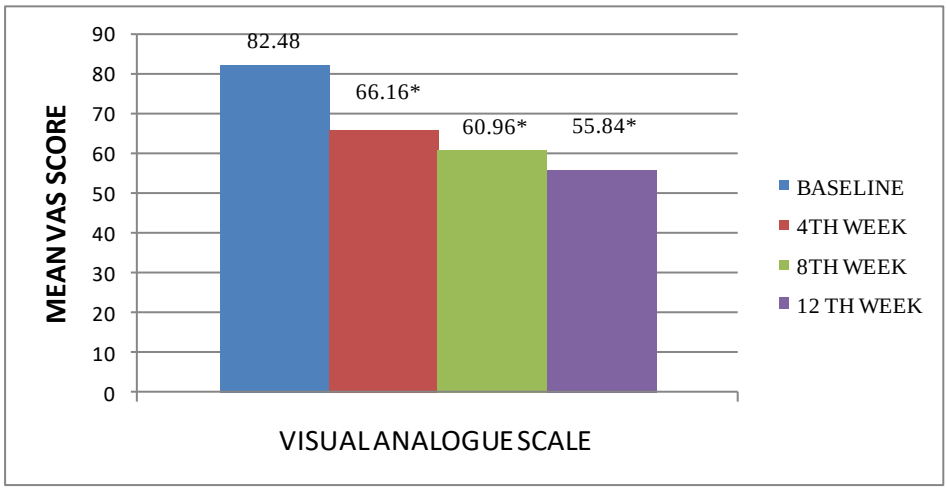

FIGURE 2: VAS SCORING IN GROUP II
* p < 0.05, indicates significant value noted at 4,8 and 12 weeks.
All values are expressed as Mean ± SEM

VAS Intergroup analysis (Table 2 Figure 3):

At the end of 4 weeks, pain reduction on visual analogue scale was 12.8 and 16.32 points which was not significant (p >0.05). But at the end of 8 weeks better response was seen in group B with more reduction in pain score values (21.52) as compared (16) in group A which was statistically significant reduction (p<0.05). Also at the end of 12 weeks better response was seen in group B with more reduction in pain score values (26.64) as compared to (17.68) in group A which was statistically significant (p<0.05).

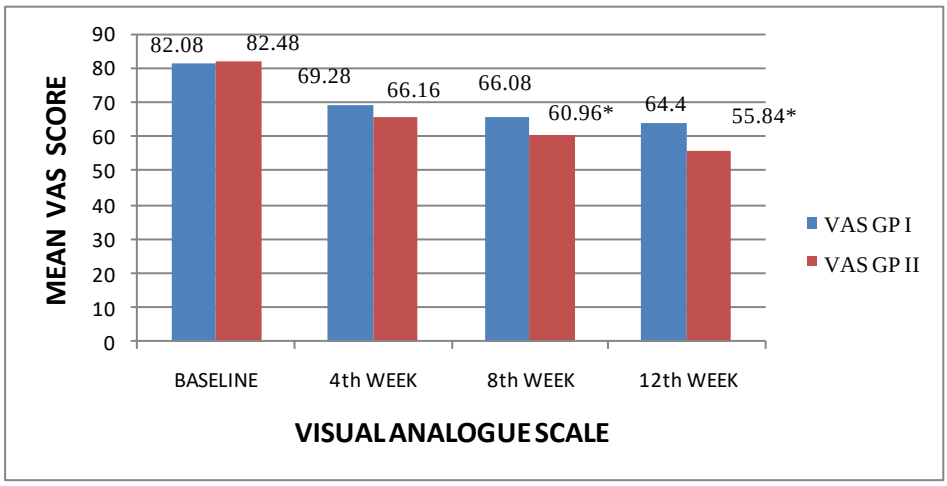

FIGURE 3: INTERGROUP COMPARISON OF VAS SCORING IN GROUP I Vs GROUP II
# p <0.05 indicate significant values at 8th and 12th week.
All values are expressed as Mean ± SEM

TABLE 2: INTERGROUP COMPARISION OF VAS SCORES BETWEEN BOTH THE GROUPS AT BASELINE, 4, 8 AND 12 WEEKS

Time interval	Group 1	Group II	p value
Baseline	82.08 ± 1.01	82.48± 0.79	0.97
4nd week	69.28 ± 1.01	66.16 ± 1.22	0.09
8th week	66.08± 1.05#	60.96± 1.34#	< 0.05
12th week	64.40 ± 1.09#	55.84 ± 1.54#	< 0.05

# p <0.05 indicate significant values at 8th and 12th week.
All values are expressed as Mean ± SEM

B) Verbal rating scale (VRS):

On this scale, pain intensity was determined by severity of pain as: 0= none, 1=mild, 2= moderate, 3= severe and 4= very severe.

VRS SCORING IN GP I: Intragroup analysis (Figure 4):

At baseline mean VRS score was 3.12 ± 0.08. There was statistically significant reduction in mean pain score at 4th week (2.20 ± 0.10), 8th (2.16± 0.95) and 12th week (2.16 ± 0.75), as compared to baseline.

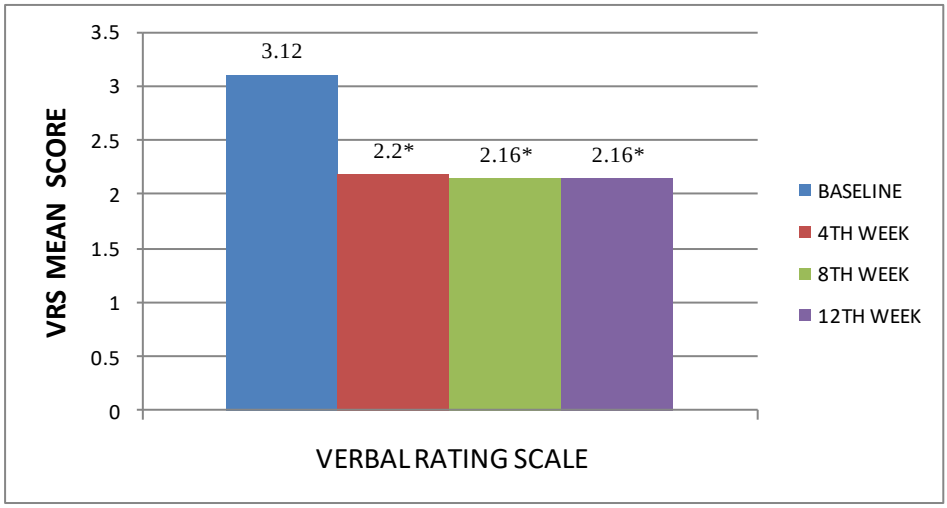

FIGURE 4: VRS SCORING IN GROUP I
* p < 0.05 indicates significant values at 4th,8th and 12th week.
All values are expressed as Mean ± SEM

VRS SCORING IN GP II: Intragroup analysis (Figure 5):

At baseline mean VRS score was 3.16 ± 0.07. There was statistically significant reduction in mean pain score at 4th week (2.0 ± 0.0), 8th (1.84± 0.07) and 12th weeks (1.72 ± 0.09), as compared to baseline.

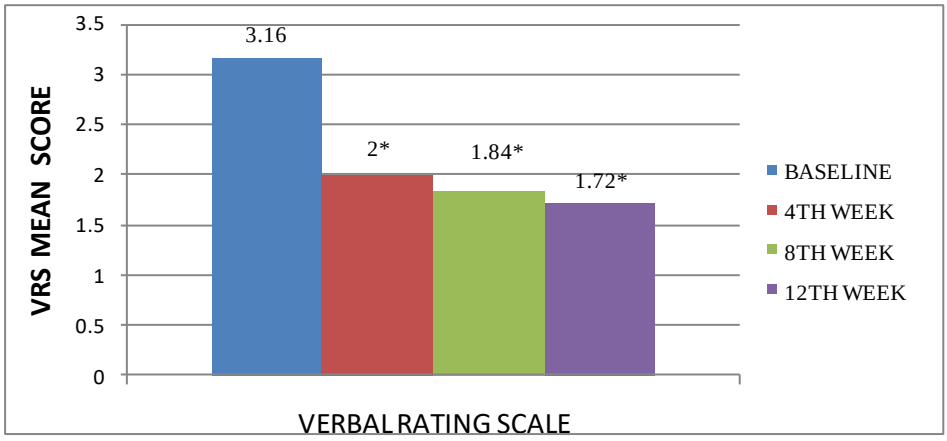

FIGURE 5: VRS SCORING IN GROUP II
* p < 0.05 indicates significant values at 4th,8th and 12th week.
All values are expressed as Mean ± SEM

VRS Intergroup analysis (Table 3; Figure 6):

At the end of 4 weeks pain reduction on verbal rating scale value was 0.92 and 1.16 which was not significant (p >0.05). But at the end of 8 weeks better response was seen in group B with more reduction in pain score value by (1.32) as compared to (0.96) in group A which was statistically significant (p<0.05). Also at the end of 12 weeks better response was seen in group B with more reduction in pain score value by (1.44) as compared to (0.96) in group A which was statistically significant (p<0.05).

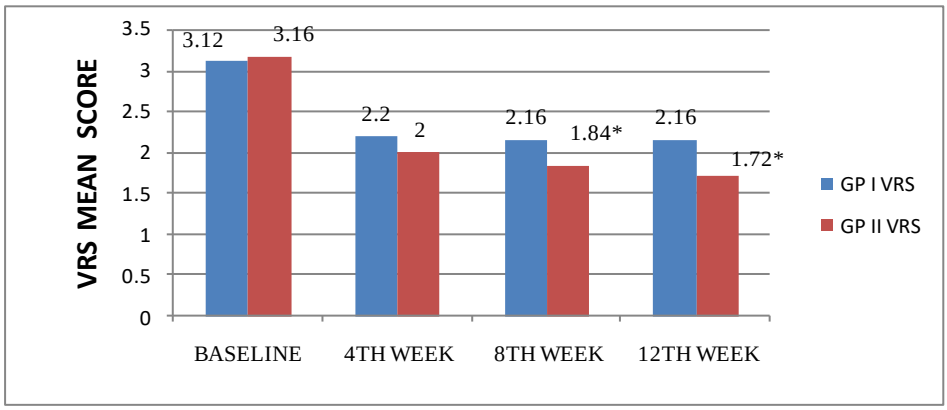

FIGURE 6: INTERGROUP COMPARISON OF VRS SCORING IN GROUP I Vs GROUP II

TABLE 3: INTERGROUP COMPARISION OF VRS SCORES BETWEEN BOTH THE GROUPS AT BASELINE, 4th, 8th AND 12th WEEKS

Time interval	Group 1	Group II	P value
Baseline	3.12 ± 0.08	3.16± 0.07	0.91
4nd week	2.20 ± 0.10	2.0 ± 0.00	0.07
8th week	2.16± 0.95#	1.84± 0.07#	<0.05
12th week	2.16. ± 0.75#	1.72 ± 0.09#	<0.05

# p <0.05 indicates significant values at 8th and 12th week.
All values are expressed as Mean ± SEM

SAFETY ASSESSMENT [Table 4, Figure 7,8]:

During the entire study period all patients were closely monitored for any adverse effect both according to the adverse effect check list and by voluntary reporting by the patients. Table 4, shows adverse drug reactions observed in both the groups - I and II. Side-effects were mild and there were no serious adverse effects (SAE) reported in either of the treatments groups. In group I out of 25 patients, total 8 patients (32%) had side-effects whereas in group II out of 25 patients, 12 patients (48%) reported adverse effects. In group I, 3 patients (12%) had complained of drowsiness, which was noticed within few days of treatment and recovered at the end of 8 weeks. 3 patients (12%) complained of nausea and vomiting, which developed with initiation of treatment and recovered at the end of 8 weeks 1 patient (4%) complained of skin rashes after 2-3 days of treatment and recovered after reducing the dose. One patient (4%) complained of headache at the end of 8th week which was recovered at the end of 12th weeks. However, none of the patients were withdrawn from the study due to any adverse effects.

In group II, 4 patients (16%) complained of drowsiness, within few days after initiation of treatment and recovered at the end of 8th week. 3 patients (12%) complained of dry mouth, in which 2 patients recovered and 1 patient still complained of dry mouth at the end of 12 weeks. 2 patients (8%) complained of nausea and vomiting, with initiation of treatment and recovered at the end of 8th weeks. 2 patients (8%) complained of weight gain at the end of 12 weeks and 1 patient (4%) complained of peripheral oedema at the end of 12 weeks. Also in this group none of the patients were withdrawn from the study due to any adverse effects.

On laboratory investigations in group I, 3 Patients (12%) had raised liver enzymes (SGPT/SGOT levels > than 40 U/L), 3 patients (12%) developed leucopenia (TLC count < 4000/mm^3) and 2 patients (8%) had increased blood urea/ serum creatinine levels [(>50mg/dL)/(>1.1mg/dL)] observed at the end of 12 weeks. While in group II, 2 patients (8%) had raised liver enzymes (SGOT/SGPT levels > than 40 U/L), 2 patients (8%) developed leucopenia (TLC count < 4000/mm^3) and 1 patient (4%) had increased blood urea/ serum cretinine levels [(>50mg/dL)/(>1.1mg/dL)] observed at the end of 12 weeks

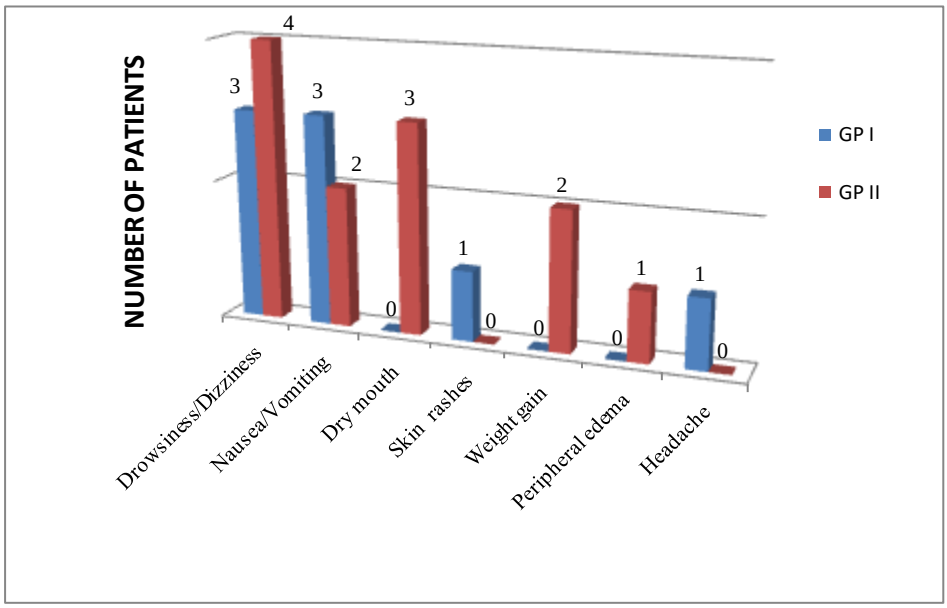

FIGURE 7: COMPARISON OF ADVERSE DRUG REACTIONS OBSERVED IN GROUP I AND GROUP II

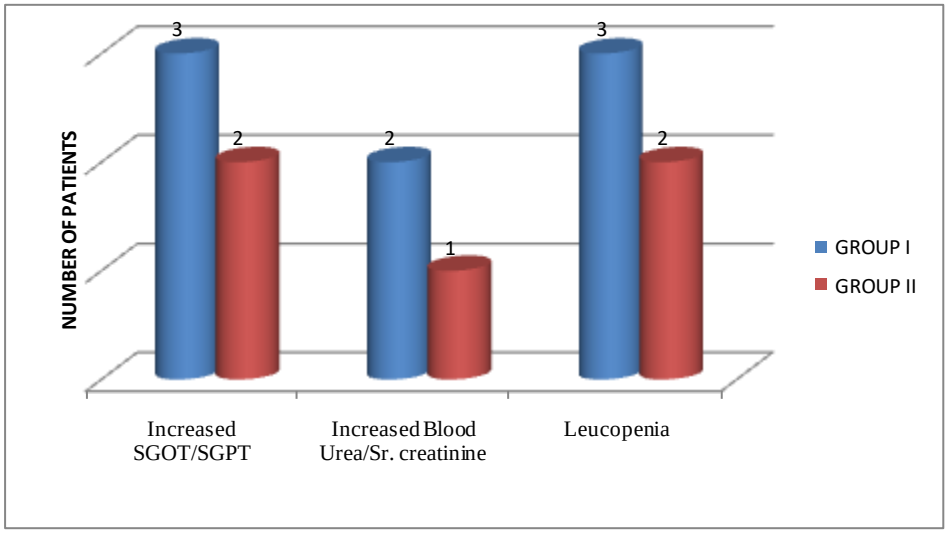

FIGURE 8: LAB INVESTIGATIONS IN BOTH THE GROUPS

TABLE 4: COMPARISON OF ADVERSE DRUG REACTIONS OBSERVED IN GROUP I AND GROUP II

Adverse drug reactions	Group I (n=25) (No. of patients)	Group II (n=25) (No. of patients)
Drowsiness / Dizziness	3 (12%)	4(16%)
Nausea / Vomiting	3 (12%)	2(8%)
Skin rashes	1(4%)	0(0%)
Dry mouth	0(0%)	3(12%)
Weight gain	0(0%)	2(8%)
Peripheral edema	0 (0%)	1 (4%)
Headache	1 (4%)	0 (0%)
Lab Investigation		
Raised Liver enzymes levels (SGOT / SGPT >40 U/L)	↑ in 3 (12%)	↑ in 2 (8%)
Raised Blood urea (>50mg/dL)/ Serum creatinine levels (>1.1mg/dL)	↑ in 2 (8%)	↑ in 1(4%)
Leukopenia (TLC count < 4000/mm^3)	3 (12%)	2 (8 %))

DISCUSSION

The International Association for the Study of Pain (IASP) has defined pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage". [9] Trigeminal neuralgia (TN) is a notable facial pain disorder characterized by sudden, severe,

brief, stabbing or lancinating recurrent episodes of pain in the distribution of one or more branches of the trigeminal nerve. It is one of the classical neuropathic pain conditions that have been known for centuries. In our study the patients who received tablet carbamazepine showed significant reduction in mean pain score on VAS and VRS scoring across the time. These findings are in concordance with previous study done by Campbell et al, in which carbamazepine has been shown to be much more effective than a placebo in the treatment of trigeminal neuralgia. [10] In this study, 70 patients were selected for the study between 20 to 84 years of age and were divided into two treatment groups i.e one group received carbamazepine and other group received placebo and further cross-over of the treatments was done. All patients included in the trial were suffering from facial pain at the time of enrollment. Two groups were compared for efficacy in relieving pain and this trial lasted for eight weeks, i.e the subjects passed two periods of alternate fortnights on each drug. The results were assessed as regards severity of the pain, number of paroxysms daily and it was noted that the group who received carbamazepine showed 58% improvement while those who were on placebo showed only 41% improvement. In this controlled trial, carbamazepine has been shown to be more effective than placebo in treatment of trigeminal neuralgia where pain evaluation was confirmed by similar well established pain evaluation scores.

Similar results like our study was found in study conducted by Tomson et al [11] which demonstrated the interrelationship between dose and serum concentrations of carbamazepine and carbamazepine-10,11-epoxide and showed clinical efficacy in 7 patients with trigeminal neuralgia. Carbamazepine is highly specific in relieving the pain of trigeminal neuralgia. It has therefore been suggested that carbamazepine response can be used as a diagnostic indicator.

De la calle J.L, [12] conducted a study to investigate the impact of pregabalin on neuropathic pain and patients with uncontrolled pain who have been referred to pain clinics. In this study adult patients with uncontrolled pain who had a score of >4 in the DN4 questionnaire were evaluated at baseline, 3rd and 6th month. Evaluations included pain levels using a visual analog (VAS) scale as well as anxiety, depression, sleep, disability, and treatment satisfaction employing validated tools. Sample comprised 413 patients who met the selection criteria, had not received pregabalin previously, and were prescribed pregabalin at the study initiation, mainly as add-on therapy. Overall, patients had a statistically significant reduction in VAS pain score of 41 points (54 % reduction, $p<0.001$), varying from 64 % reduction (oncological pain) to 31 % reduction (central neuropathic pain. The result of the study suggested that in patients with uncontrolled neuropathic pain of various origins who were treated at pain clinics, the addition of pregabalin to a pharmacological treatment regimen was associated with a clinically significantly improvement of pain and psychological well-being and a reduction in the impact of neuropathic pain on daily activities. Add-on treatment with pregabalin was well tolerated. Similar results were observed in our study where patients receiving pregabalin as an add on therapy to carbamazepine showed significant reduction in mean pain score from 82.48±0.79 to 55.84±1.54, with overall reduction by 26.640±.75 observed at the end of 12th week. Additional benefit of our study was that we also assessed the analgesic activity of drug in two groups by VRS scoring which also showed significant reduction in the mean pain scoring at the end of 12th week.

Gilron I [13] showed in randomized, placebo-controlled clinical trial that pregabalin demonstrated efficacy for pain relief in patients with diabetic neuropathy and peripheral post herpetic neuralgia, significantly improving affective symptoms,

sleep and quality of life. Our study has an additional benefit that it was a randomized, active comparator controlled study. Pérez C et al. studied the effects of pregabalin (PGB) on patient-reported health outcomes in 65 PGB-naive subjects with trigeminal neuralgia refractory to previous analgesic therapy in a prospective, multicentre observational study carried out in primary care. 12 weeks monotherapy with PGB (n = 36) or add-on (n = 29), reduced baseline intensity of pain by a mean ± S.D. of -40.0 ± 22.1 mm [-55.4%, effect size (ES) 2.32; P < 0.0001] with 59.4% of responders (pain reduction ± 50%), and produced 34.6±29.3 additional days with no/mild pain.

Obermann M et al [14] conducted a prospective, open label study aimed to evaluate the efficacy of pregabalin in 53 patients suffering from trigeminal neuralgia with and without concomitant facial pain where patients received pregabalin (PGB) 150-600 mg daily and were prospectively followed for 1 year. The primary outcome was number of patient's pain free interval or with reduction of pain intensity by > 50% and of attack frequency by > 50% after 8th week. Secondary outcome was sustained pain relief after 1 year. Thirty-nine patients (74%) improved after 8 weeks with a mean dose of 269.8 mg/day. In PGB group 13 patients (25%) experienced complete pain relief and 26 patients (49%) reported pain reduction > 50%, whereas 14 patients (26%) did not improved. Patients without concomitant facial pain showed better response rates (32 of 39, 82%) compared with patients with concomitant chronic facial pain (7 of 14, 50%, P = 0.020). Concomitant chronic facial pain appears to be a clinical predictor of poor treatment outcome. PGB appeared to be effective in the treatment of trigeminal neuralgia. Similar to above study, we also observed in our study that pregabalin showed better analgesic activity when used as an add on therapy to carbamazepine in patients of trigeminal neuralgia

There is paucity of data with head to head parallel comparison between carbamazepine and pregabalin in India till date. In one similar study done by Rustagi R et al [15] 22 patients with diagnosis of refractory TN were enrolled and randomly allotted into 2 groups of 11 each. Each group was subjected to a crossover analysis using LTG and PGB together with CBZ, for a period of 6 weeks. Patients maintained a pain diary, the scores of which, along with global evaluation scores, determined the primary outcome. Re-evaluation of symptoms after 6 months was done to assess long term efficacy with study drugs. Both LTG and PGB were more efficacious than CBZ alone ($p<0.05$). Unlike LTG, side effects like nausea, insomnia and concentration loss were minimal with PGB thus exhibiting greater patient compliance. Secondary analysis showed complete relief in 4 patients on PGB while 6 patients had partial relief. Our study showed significant reduction in mean pain score between the two groups. At the end of study, pregabalin as an add on therapy significantly reduced pain at the end of 8th and 12th week ($p<0.05$) on VAS and VRS scale

Crawford M et al [16] provided evidence regarding the real-life efficacy of pregabalin in the treatment of peripheral neuropathic pain (NeP) in Denmark. In this prospective, observational, non interventional study, pregabalin was prescribed and compared with baseline. The primary study end points after 3 months of observation were changes in the average level of pain during the past week, the worst level of pain during the past week, and the least level of pain during the past week. The Wilcoxon signed-rank test was used to perform paired analyses, and a multivariate regression analysis investigated factors driving change in pain. A total of 86 of the 128 patients included were regarded as efficacy evaluable (those completing 3 months of pregabalin treatment). Patients were long-time sufferers of peripheral NeP, and 38% of them had comorbidities. The average dose of pregabalin was 81.5 mg/d at baseline and 240 mg/d after 3 months. A clinically and statistically significant

improvement of 2.2 points in the average level of pain intensity was found after 3 months. Positive results were also found for pain-related sleep interference, patients' global impression of change, quality of life and work and productivity impairment. So this real-life study indicates that for some patients (two-thirds), addition of pregabalin for peripheral NeP helps to reduce their pain intensity and improves quality of life significantly. Our study also showed that there was significant change in quality of life in both the groups. Both treatment drugs were well tolerated. No unusual or severe adverse effect occurred during the treatment in our study. Adverse effect profile in the study was consistent with previous studies. Kalapos [17] in his study reported common adverse effects of carbamazepine that include dizziness, nausea, drowsiness, blurred vision. Freynhagen R et al [18] showed through a trial that the most common adverse event occurred with pregabalin treatment were dizziness (24.3%) and somnolence(15%). Other side-effects were dry mouth, peripheral edema, constipation, blurred vision and weight gain.

CONCLUSION

There was statistically significant reduction in mean pain score and improvement in quality of life at 4th, 8th and 12 week, in both the groups when compared to the baseline i.e. both carbamazepine and pregabalin as an add on therapy to carbamazepine were effective in reducing the pain. However on intergroup comparison, pregabalin as an add on drug to carbamazepine(Group II) produced better response with earlier onset of pain relief with statistically significant reduction in mean pain score at 8th and 12th weeks when compared to carbamazepine alone (Group I). There were no serious adverse effects in either of treatment group. Common adverse effects in group I were drowsiness, nausea and vomiting while in group II, drowsiness and dry mouth were commonly noticed. The present study suggested that pregabalin as an add on therapy to carbamazepine was found to cause significant reduction in pain scoring and could be a promising drug in patients of trigeminal neuralgia when therapeutic options are limited.

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How to cite this article: Narwat A, Sharma V, Kiran Bala K. Evaluation of efficacy and safety of pregabalin as an add on therapy to carbamazepine in patients of trigeminal neuralgia. Int J Health Sci Res. 2018; 8(3):78-89.

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