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Efficacy of Gabapentin vs Oxcarbazepine in terms of pain, sleep and quality of life in patients with diabetic peripheral neuropathy

Wadha Nawal Zaffer[1], Faiz Unnisa[1], Farath Unnisa[1], Ayesha Tahoora Fatima[1], Azmath Unnisa Begum[1], Mohammed Zoheb[2]

[1]Department of Pharmacy practice, Deccan School of Pharmacy, India
[2]Department of Neurology, Owaisi Hospital and Research Centre, Deccan College of Medical Sciences, India

ABSTRACT

Background. The treatment of peripheral diabetic neuropathy is difficult to treat considering the pain is severe, long-lasting and does not respond to analgesics. Gabapentin has been recommended as the first line treatment for DPN but owing to cognitive dysfunction and other side effects the drug is discontinued. Recent studies suggest that oxcarbazepine; an antiepileptic drug has good-efficacy in management of DPN. This prospective, observational and comparative study was done to compare gabapentin and oxcarbazepine monotherapy in patient of DPN.

Objectives. We assessed the efficacy of Oxcarbazepine monotherapy in terms of pain score, sleep score and quality of life and compared with gabapentin monotherapy.

Methods. 100 patients with DPN or examinations suggesting DPN were divided into 2 groups to receive gabapentin 300-1200 mg/day or Oxcarbazepine 300-600mg/day. Assessment of pain scores, sleep score and quality of life were done at different duration during the course of therapy.

Results. Out of total subject selected, the maximum (46%) subjects were between age group 60-90 years and the least effected were (24%) between age group 50-59 years. Male were more prevalent with 57% when compared to females with 43%. Improvement in Sleep was seen on using Group II with p value (0.0005). However, the correlation of Pain and Quality of life with the treatment shows p –value 0.24, 0.31 and 0.27 respectively showing non-significance.

Conclusion. The sleep improved statistically correlated in patients with DPN, but not with quality of life and pain as the calculated p value was (p= 0.24, 0.31 and 0.27) respectively. Findings of this study suggest that oxcarbazepine can be used as an alternative treatment owing to its similar analgesic efficacy and improvement in sleep.

Keywords: diabetic peripheral neuropathy, Gabapentin, Oxcarbazepine, sleep score, pain score, quality of life

INTRODUCTION

Diabetic Peripheral Neuropathy, a Diabetic complication is characterised by peripheral nerve dysfunction. It is a disabling condition which has a wide spectrum of symptoms such as sensation of needles, pins, aching, tightness and burning sensations, sometimes electric or stabbing sensations [1]. Pain or disorders in the primary functions of the nervous system start with diabetic neuropathic changes [2]. At night, the neuropathic pain intensifies which likely causes sleep disorders and affects the patient's quality of life as well as worsens glycemic level [3].

Of all the risk factors for diabetic neuropathy, chronic hyperglycaemia seems to have the most definitive association. The other predisposing factors may include duration of diabetesmellitus, increased age, genetic susceptibility, lipotoxicityand glucotoxicity, inflammation, and oxidative stress [4].

The main aim for the management of DPN patients is stable and optimum glycemic control, but relief from neuropathic pain forms an essential part of a better quality of life [5].

Treatment of DPN is challenging as the pain seems to be severe and long lasting and does not respond to simple analgesics.

Corresponding author:
Mohammed Zoheb
E-mail: zoheb.mohammed@gmail.com

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Gabapentin as an anticonvulsant medication is commonly used for the treatment of DPN [6, 7] but it produces significant motor and cognitive deficits even at or near the lowest effective doses [8].

Whereas Oxcarbazepine which is a 2nd generation antiepileptic drug showed significantly higher reduction in pain scores in patients of DPN treated with oxcarbazepine when compared to those treated with placebo [9].

This study was designed to compare Gabapentin Monotherapy and Oxcarbazepine Monotherapy in terms of Pain, Sleep and overall Quality of life in patients with DPN.

METHODOLOGY

Materials and methods

This study is Prospective, Observational and Comparative study with a sample size of 100 patients which have been done in the duration of 1 year at Neurology and General medicine out-patient Department in Owaisi hospital and research centre.

Study Site - Ethical Approval: Approved by Institutional Review Board on 09/02/2021 at Deccan College of Medical Sciences and allied Hospital, Hyderabad, Telangana.

Study criteria

A. Inclusion Criteria:

- Adults >18 years of age in both sex
- Individuals diagnosed as Diabetes mellitus
- Clinical Diagnosis of Peripheral neuropathy

B. Exclusion Criteria:

- Pregnant and lactating women
- Infants and babies
- Patients with Renal failure
- Patients with heart failure
- Patients with coexisting diseases
- Patients with Autoimmune diseases
- Peripheral neuropathy due to other aetiologies

Study procedure

100 patients with DPN were enrolled, with 50 patients on gabapentin in the group I, the rest 50 on oxcarbazepine in group II in Owaisi hospital and research centre from October 2020 to October 2021. The subjects were aged above 18 of either gender.

During the titration period of 1 week, Gabapentin 150 mg a day and oxcarbazepine 150 mg a day were slowly escalated to 300 mg/day (150 mg twice a day) in group I and group II. No change in drug dosages was allowed during the 12 weeks of maintenance period.

The average pain score, Sleep score and quality of life was measured before the start of the therapy and later it was assessed at 2nd,4th and 12th week using Numeric Pain Rating Scale(NPRS) ,Visual Analogue Scale(VAS), Medical Outcome Sleep Study Scale (MOS) and SF-12 questionnaire respectively.

1. COMPARISON OF PAIN SCORE

NPRS

TABLE 1. Comparison of NPRS before and after Treatment in Group I

Variable	Review				P value
	Baseline	2 Weeks	4 Weeks	12 Weeks	
Minimum	4	3	1	1	<0.0001
Maximum	10	9	8	7	
Median	6.5	5	4	3	
Mean± SEM	6.80± 0.23	5.54± 0.21	4.02± 0.26	3.02± 0.22	

Significant difference was found before and after treatment

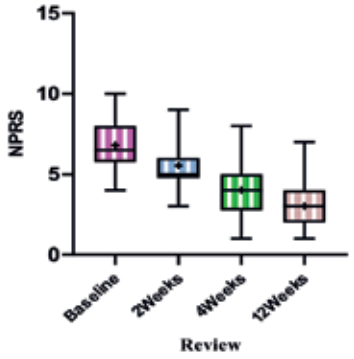

FIGURE 1. Comparison of NPRS before and after Treatment in Group I

TABLE 2. Comparison of NPRS before and after Treatment in Group II

Variable	Review				P value
	Baseline	2 Weeks	4 Weeks	12 Weeks	
Minimum	4	2	1	1	<0.0001
Maximum	10	9	7	6	
Median	7	5.5	4	2	
Mean± SEM	7.02± 0.16	5.44± 0.21	3.76± 0.24	2.50± 0.20	

Significant difference was found before and after treatment

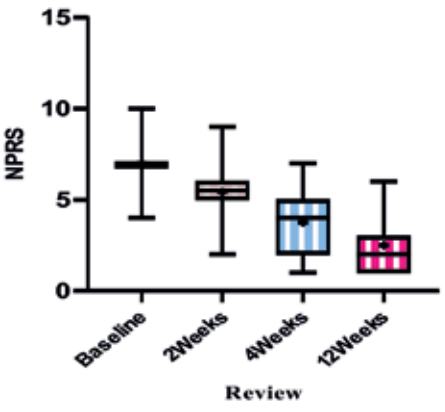

FIGURE 2. Comparison of NPRS before and after Treatment in Group II

VAS

TABLE 3. Comparison of VAS before and after Treatment in Group I

Variable	Review				P value
	Baseline	2 Weeks	4 Weeks	12 Weeks	
Minimum	48	32	16	11	<0.0001
Maximum	98	91	86	73	
Median	69	53	43	30	
Mean± SEM	71.78± 2.20	58.30± 2.19	42.98± 2.69	32.64± 2.31	

Significant difference was found before and after treatment

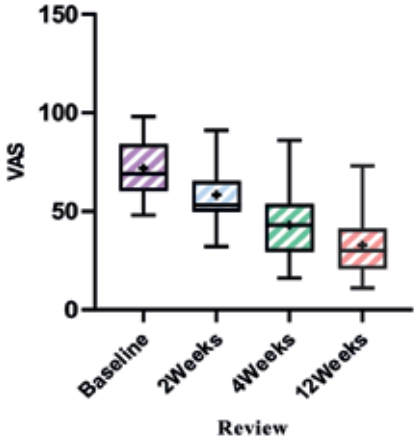

FIGURE 3. Comparison of VAS before and after Treatment in Group I

TABLE 4. Comparison of VAS before and after Treatment in Group II

Variable	Review				P value
	Baseline	2 Weeks	4 Weeks	12 Weeks	
Minimum	47	23	15	10	<0.0001
Maximum	100	94	76	65	
Median	72	59.50	42	22.50	
Mean± SEM	73.54± 1.52	58.28± 2.17	41.88± 2.26	27.78± 2.09	

Statistically significant difference was found before and after treatment

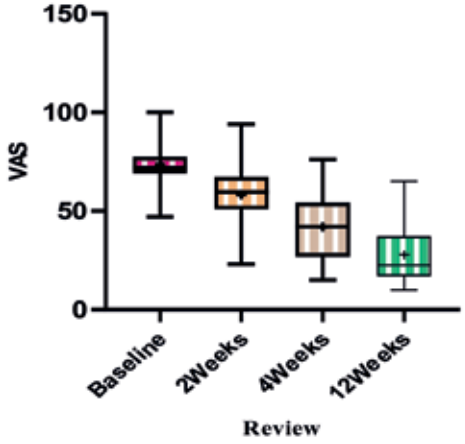

FIGURE 4. Comparison of VAS before and after Treatment in Group II

2. COMPARISON OF SLEEP SCORE

TABLE 5. Comparison of Sleep Score before and after Treatment in Group I

Variable	Review				P value
	Baseline	2 Weeks	4 Weeks	12 Weeks	
Minimum	0	0	0	0	<0.0001
Maximum	1	1	1	1	
Median	0	0	0	1	
Mean± SEM	0.12± 0.04	0.30± 0.06	0.40± 0.06	0.72± 0.06	

Statistically significant difference was found before and after treatment

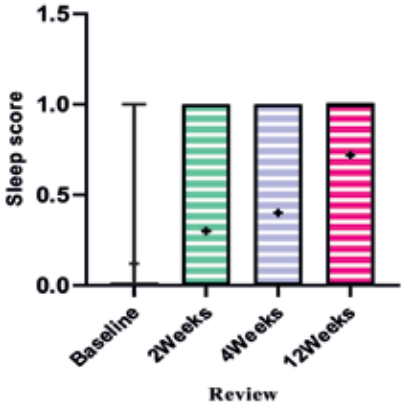

FIGURE 5. Comparison of Sleep Score before and after Treatment in Group I

TABLE 6. Comparison of Sleep Score before and after Treatment in Group II

Variable	Review				P value
	Baseline	2 Weeks	4 Weeks	12 Weeks	
Minimum	0	0	0	0	<0.0001
Maximum	1	1	1	1	
Median	0	0	1	1	
Mean ± SEM	0.36± 0.06	0.48± 0.07	0.64± 0.06	0.92± 0.03	

Statistically significant difference was found before and after treatment

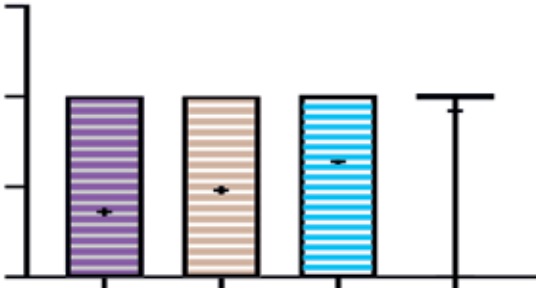

FIGURE 6. Comparison of Sleep Score before and after Treatment in Group II

3. COMPARISON OF QOL SCORE

TABLE 7. Comparison of QOL Score before and after Treatment in Group I

Variable	Review				P value
	Baseline	2 Weeks	4 Weeks	12 Weeks	
Minimum	45.90	56.80	64.10	71.50	<0.0001
Maximum	86.70	84.20	91.30	99.40	
Median	68.50	76.65	86.45	93.30	
Mean± SEM	68.24± 1.47	75.63± 0.89	84.14± 1.00	90.14± 1.05	

Statistically significant difference was found before and after treatment

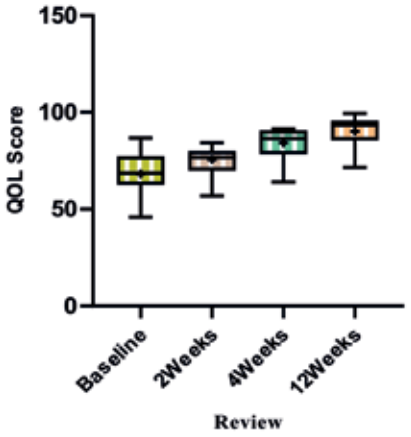

FIGURE 7. Comparison of QOL Score before and after Treatment in Group I

TABLE 8. Comparison of QOL Score before and after Treatment in Group II

Variable	Review				P value
	Baseline	2 Weeks	4 Weeks	12 Weeks	
Minimum	54.20	59.10	63.60	72.40	<0.0001
Maximum	85.50	91.30	97.50	99.90	
Median	74.90	82.35	89.15	94.10	
Mean± SEM	74.06± 0.98	81.19± 1.00	87.67± 1.04	92.68± 0.91	

Statistically significant difference was found before and after treatment

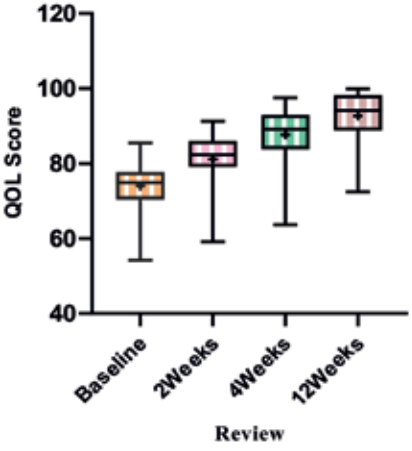

FIGURE 8. Comparison of QOL Score before and after Treatment in Group II

TABLE 9. Comparison of Efficacy of Treatment From baseline to 12 weeks (%)

Scale	Group		P value
	I	II	
NPRS (Reduction)	56	64	0.2482
VAS (Reduction)	55	62	0.3151
Sleep score (Improvement)	83	61	0.0005*
QOL score (Improvement)	32	25	0.2729

Though both the drugs gabapentin and oxcarbazepine were effective but statistically significant difference was not found in the efficacy between Group I and II except sleep score.

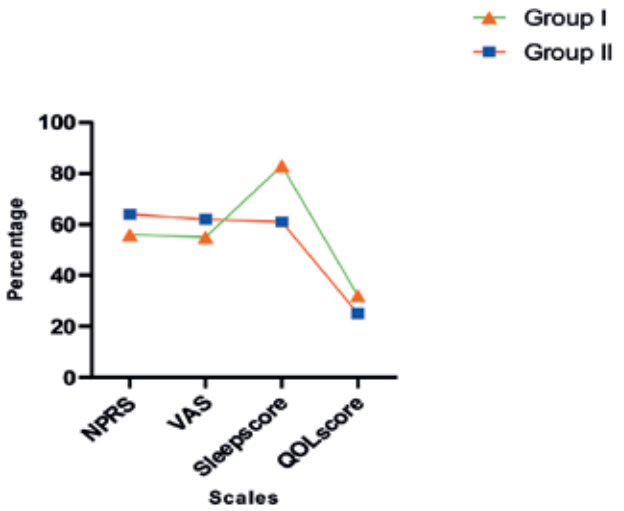

FIGURE 9. Comparison of Efficacy of Treatment

DISCUSSION

Peripheral neuropathy is one of the Micro-vascular complication of Diabetes mellitus. The prevalence of neuropathy in diabetic patients varies from 6% to 51% depending on various factors like Age, Glycemic status, Duration of diabetes and demographics [10].The symptoms vary from mild parasthesias to extreme burning, distal weakness and autonomic dysfunction. It is the sensory symptoms and its complications which are extremely debilitating for the patients. These sensory symptoms not only affect the quality of life but also have significant psycho-social consequences. Treatment of DPN has come a long way in the past decade or two, however patient satisfaction remains a challenge. The treatment of peripheral diabetic neuropathy is difficult to treat considering the pain is severe, long-lasting and does not respond to analgesics. Gabapentin has been recommended as the first line treatment for DPN. It provides good level of symptomatic relief, but the required dose for such a relief is quiet high recommended between 1800-3600mg/day. At such high doses various cognitive effects are noted, restricting its utility. Common Side effects of gabapentin are somnolence, dizziness, ataxia, nausea, fatigability and weight gain [11].

Oxcarbazepine, known for its good anti-seizure efficacy, is considered in management of DPN. A recent Cochrane review of 3 multicentre randomised trial evaluating the efficacy of oxcarbazepine in individuals with DPN and found that it was considerably more effective than placebo as there was significant reduction in pain scores; however, this result was based on data only from the trial conducted by Beydoun et al. because data from other two trials were not included in meta-analysis [9]. Studies have shown that the side effects of oxcarbazepine have been relatively more prominent in the female population, with the most common being Tiredness, sleepiness, difficulty concentrating and skin rashes [12].

In this study 110 DPN patients were enrolled in the study during the duration of 1 year from October 2020 to October 2021 were assessed out of which 6 did not meet the inclusion criteria and 4 discontinued the treatment. Hence 100 patients met the inclusion criteria and were included in the study.

The Pain score, Sleep score and Quality of life score was assessed and compared for groups of gabapentin and oxcarbazepine. The comparison was done statistically by t -test, chi-square test and one-way ANOVA test using SPSS software vr.20.

There was significant reduction in the pain in both the groups (P 0.248 Vs P 0.3151); however there was no superiority of one group over the other. There are no head to head studies comparing the outcome of both the drugs with respect to sensory symptoms. Studies have shown that the most important indicator for quality of life in patients with DPN is management of sensory symptoms like pain, parasthesia and calf cramps {13}

The correlation of Sleep using MOS scale between Gabapentin and Oxcarbazepine was estimated using the t test method and P value calculated as 0.0005, as the value is less than 0.05 it shows that both arestatistically correlated. The day time somnolent effect was not noted in Oxcarbazepine group and tolerability was relatively better in comparison to Gabapentine group.

The comparison of QOL showed non-statistical significance of both groups with p-value 0.2729.

Our study shows that oxcarbezepine can be an equally potential drug in comparison to gabapentine for treatment of DPN. In patient sub group who do not tolerate gabapentine it can be a better alternative. Dose escalation is relatively well tolerated with Oxcarbazepine when compared to Gabapentine.

Major limitations of this study were short-term follow-up of only 12 weeks and a smaller sample size. Potential side- effects that were not apparent due to the short-term study period could have been observed in long-term follow-up.

CONCLUSION

Findings of this study suggest that oxcarbazepine can be used as an alternative treatment owing to its similar analgesic efficacy and improvement in sleep. However further large, Multicentre studies are needed to establish its efficacy in DPN population.

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