Research Article

A comparative study of pregabalin and gabapentin combinations in type 2 diabetic neuropathy patients

A. Vidhya, Muddala Vara Prasanna Rao*, P. Geetha

ABSTRACT

Introduction: Diabetes is a metabolic disorder; most of the patients are affected with nerve pain called neuropathic pain, which is acomplication that arises from diabetes called diabetic neuropathy. Diabetic Neuropathy Patients (DNP) results if the diabetic patient has high blood sugar levels for a long period. These high sugar level can damage the vessels that supplies blood to the nerve. **Aim and Objective:** To evaluatethe effectiveness of drug in Diabetic Neuropathic Patients (DNP). **Materials and Methods:** The study was carried out at general medicine department as a prospective study for 6 months using data entry form and pain rating scale form. **Results:** In this study,150patients with diabetic neuropathic pain were included and out of this 75 patients were given with Pregabalin + Alpha lipoic acid and remaining 75 were given with Gabapentin + Methylcobalamine therapy and the patients were selected based on the inclusion and exclusion criteria and the statistical analysis was done by Microsoft excel. **Conclusion:** From the present study we concluded that monotherapy with Pregabalin+Alphalipoic acid or Gabapentin+ Methylcobalamine produces clinically meaningful pain relief in patients with painful diabetic neuropathy and pain reduction was superior with Gabapentin+ Methylcobalamine compared to Pregabalin+Alphalipoic acid.

KEY WORDS: Anticonvulsants, Diabetes, Gabapentin, Neuropathic pain, Pregabalin

INTRODUCTION

A serious and the most common complications seen in type 1 and type 2 diabetes are diabetic neuropathy. When the sugar level of the diabetic patients found to be uncontrolled, there occurs the nerve damage. At the initial stage, there will not be any symptoms. This condition develops slowly and sometimes it may occur over the course of several decades. According to the International Diabetes Federation, 382 million people worldwide were affected by diabetes,[1] which is found to be one of the leading causes of neuropathy.[2] The distal symmetrical polyneuropathy (DSPN) is the most common clinical form of diabetic neuropathy which affects more than 90% of the patients worldwide.[3] Conventionally, DSPN affects the toes and distal foot and slowly progresses nearly to involve the feet and legs in the stocking distribution. It may also characterize the progressive loss of many nerve fibers that are affecting both the autonomic and somatic divisions, and thereby, diabetic retinopathy and nephropathy can also occur.[3] Foot ulceration and painful neuropathy are the two main clinical consequences of DSPN that is linked with higher morbidity and also mortality.[4] Frequently, patients may look for medical assistance only when they inquire pain,[5] which is a symptom that affects nearly 10%–26% of population.[6,7] Peripheral diabetic neuropathy is associated with increased biochemical markersof both inflammation and endothelial dysfunction. In this study three groups were used which measured the foot skin endothelium-dependent and independent vasodilation, nerve axon reflex - related vasodilation (NARV), inflammatory cytokines and biochemical markers of endothelial function.[8] sulodexide has protective effects on peripheral nerve damage which is caused by microvascular dysfunction. Thus, sulodexide is suggested to be a potential mew therapeutic agent for diabetic peripheral neuropathy.[9] Cardiovascular autonomic neuropathy (CAN) is studied in type - 1 - diabetic patients and it is found to have

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complications associated with it. They are associated with retinopathy with poor glycemic control. Patients with positive evaluation includes ewing tests, heart rate variability, spontaneous baroreflex slope and logistic regression.[10] A common complication of diabetes is painful neuropathy. It is characterised by burning feet, hyperalgesia to heat, mechancal stimuli. Diabetes was induced by Streptozotocin, further its induction process, calcitonin gene related peptide, substance P, prostaglandin E2 were released from the isolated skin and sciatic nerve which were assessed by immunoassays enzyme.[11]

MATERIALS AND METHODS

The study was carried out at corporate hospital, general medicine department Ayanavaram, Chennai. This study was a prospective study for 6 months using data entry form and pain rating scale form.

Phase I

Consent from hospital authority

It was a custom that every project work carried out in the hospital by Pharm D has to be approved by the dean and should be informed to all physicians, surgeons, and other health-care professionals of the hospital. Hence, a protocol of the study which includes the objectives and methodology was submitted to the dean of the study hospital.

The study was conducted with the expert guidance of senior and junior physicians of the hospital.

Design of patient information forum

A patient information forum has been prepared to inform the patient of the caregivers about the purpose and necessity of the study. The patient information forum assures that the confidentiality will be strictly maintained and also the study will help the betterment of patient health.

Data entry form

The format contains the details such as name, age, weight, IP/OP number, DOA, DOD, patient medical and medication history, family and personal history, vital signs, and visual analog scale (VAS) score.

Phase II

Inclusion criteria

The following criteria were included in the study:

- Males or females 18–75 years of age, diabetes mellitus (type II)
- Ange in medications for reducing blood sugar within 4 weeks before screening
- Experiencing daily pain due to diabetic neuropathy for at least 6 months but not more than 5 years
- Neuropathic pain must begin in the feet, with relatively symmetrical onset.

Exclusion criteria

The following criteria were excluded from the study:

- Untreated hypothyroidism
- Amputations due to diabetes mellitus (with the exception of toes)
- High risk of hepatitis B or C infection
- High risk of HIV, seizure disorder, and anticipated surgery.

Ward round participation

During data collection, patients were informed about the study using patient information format. A regular ward round in the study department was carried out.

Phase III

Data collection continued

The collection of data was continued in this place also in the same way as explained in Phase II.

Data analysis

The obtained data were analyzed and were categorized based on its treatment.

The statistical method was done using unpaired "*t*"-test using GraphPad Prism analysis software.

RESULTS

This study was designed to find out the safety of pregabalin+alpha-lipoic acid and gabapentin+methylcobalamin therapy in diabetic neuropathic pain.

In this study, patients with diabetic neuropathic pain were included and out of this 75 patients were given pregabalin+alpha-lipoic acid and remaining 75 were given gabapentin+methylcobalamin therapy and the patients were selected based on the inclusion and exclusion criteria and the statistical studies have been analyzed.

Among the study population of 150, 100 (66.67%) were male and 50 (33.33%) were female [Figure 1, Table 1].

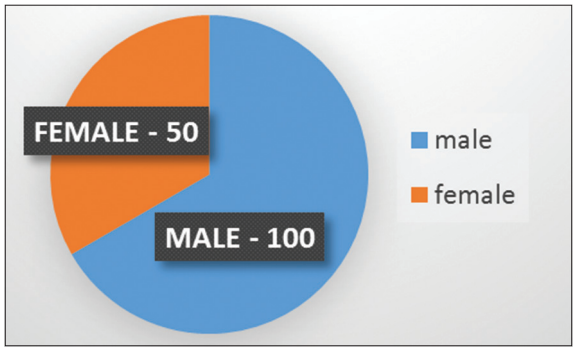

Figure 1: Gender-wise distribution

Among the study population of 150, 91 patients were in the age group 18–30 years, 19 patients were in the age group of 31–49 years, 29 patients were in the age group of 50–69 years, and 11 were in the age group of above 70 [Figure 2, Table 2].

The intensity of the pain relief was 8.9 on day 0, 6.9 on day 3, and 4 on day 7 for pregabalin+alpha-lipoic acid and 8.7 on day 0, 5.9 on day 3, and 2.9 on day 7 for gabapentin+methylcobalamin [Figure 3, Table 3].

Out of 150 patients, 11 had no change, 9 of them had poor, 30 of them had moderate, 10 of them had good, and 7 of them had excellent efficacy for pregabalin+alpha-lipoic acid therapy and 6 of them had no change, 7 of them had poor, 35 of them had moderate, 25 of them had good, and 10 had excellent efficacy on combination of gabapentin+methylcobalamin [Figure 4, Table 4].

Table 1: Gender-based distribution of the study population

Gender	Number of patients (%)
Males	100 (66.67)
Females	50 (33.33)

Table 2: Age distribution of the study populations

Age distribution	Number of patients (%)
18–30	91 (60.66)
31–49	19 (12.67)
50–69	29 (19.33)
Above 70	11 (7.33)

- Group A – pregabalin+alpha-lipoic acid
- Group B – gabapentin+methylcobalamin.

Score of pain at admission assessed by VAS decreased significantly as compared to baseline score

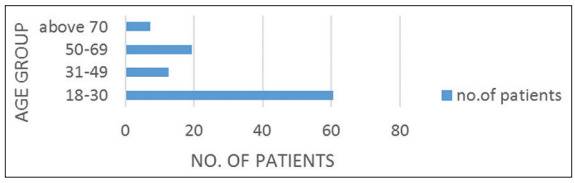

Figure 2: Age-based distribution versus study populations

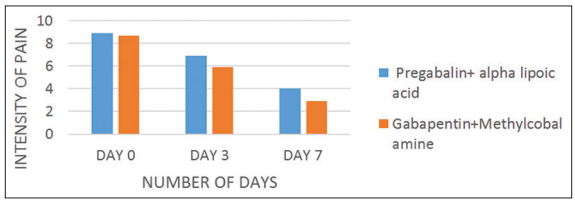

Figure 3: Intensity of pain relief

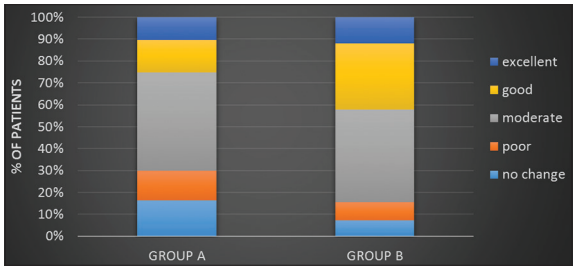

Figure 4: Overall efficacy assessments

Table 3: Intensity of pain relief as per visual analog scale

Days	Pregabalin+alpha-lipoic acid	Gabapentin+methylcobalamin
0	8.9	8.7
3	6.9	5.9
7	4	2.9

Table 4: Overall efficacy assessments

Groups	No change	Poor	Moderate	Good	Excellent
Pregabalin+alpha lipoic acid	11	9	30	10	7
Gabapentin+methylcobalamin	6	7	35	25	10

Table 5: Efficacy assessment of pregabalin+alpha-lipoic acid and gabapentin+methylcobalamin using VAS

Efficacy assessments of pregabalin+alpha-lipoic acid and gabapentin+methylcobalamin using VAS severity of pain based on VAS							
Pregabalin+alpha-lipoic acid				Gabapentin + methylcobalamin			
Mean scores of pain for 75 patients		Difference in mean scores at admission and at discharge	*P*-value	Mean scores of pain for 75 patients		Difference in mean scores at admission and at discharge	*P*-value
During admission	At discharge			During admission	At discharge		
5.15	1.12	4.12	<0.05	5.25	0.55	4.38	<0.05

VAS: Visual analog scale

within both groups, i.e., group of patients receiving gabapentin+methylcobalamin and patients receiving pregabalin+alpha-lipoic acid. However, decrease in severity of pain at discharge assessed by VAS was more pronounced within patients receiving gabapentin+methylcobalamin as compared to patients receiving pregabalin+alpha-lipoic acid [Figure 5, Table 5].

Among 150 patients, 110 (73.33%) of them were doing physical exercise along with medications and 40 (26.67%) of them were taking drugs alone. Decrease in pain severity was pronounced to be more in management with medications with physical exercise than medications alone [Figure 6, Table 6].

DISCUSSION

Neuropathic pain carries a disease burden for patients and is also associated with a significant and economic burden. Both the drugs were administered for 6 weeks and their major effects on pain and other parameters such as itching and numbness were evaluated. Pain intensity was evaluated using VAS scores.

Table 6: Impact of drugs versus physical exercise on diabetic neuropathic pain

Management	Number of patients, *n* (%)
Medications alone	40 (26.67)
Medications+physical exercise	110 (73.33)

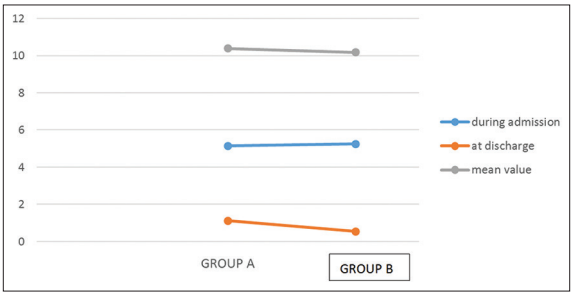

Figure 5: Efficacy assessment using visual analog scale

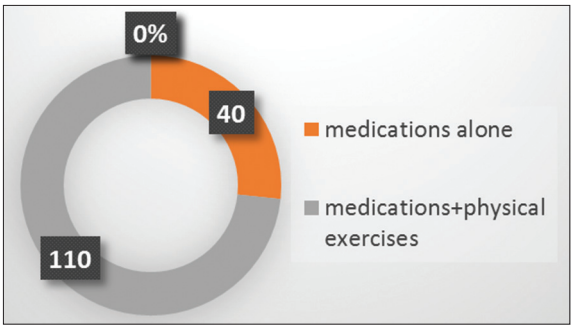

Figure 6: Impact of drugs versus physical exercise on diabetic neuropathic pain

Effect on Burning Sensation

At the end of 6 weeks treatment, more patients in the Pregabalin+Alpha lipoic acid group recovered from itching sensation as compared to the Gabapentin+Methylcobalamine group.

Effect on Pain

Gabapentin+Methylcobalamine was found to be superior to Pregabalin+Alpha lipoic acid in providing relief from pain.

Effect on Numbness

Gabapentin+Methylcobalamine was also found to be more effective than Pregabalin+Alpha lipoic acid in reducing numbness.

Effect on VAS Scores

VAS score was measured for all the patients in both the groups (pregabalin+alpha-lipoic acid and gabapentin+methylcobalamin) at baseline and there was no significant difference ($P > 0.05$) in the mean value of VAS score at baseline in the two study groups. At the end of 6 weeks, both the groups demonstrated a decrease in the VAS scores; however, there was a significant difference ($P < 0.05$) in the mean value of VAS score in the two study groups. The improvement in VAS score was significantly ($P < 0.01$) more in the pregabalin+alpha-lipoic acid group as compared to the gabapentin+methylcobalamin group. Thus, both drugs showed an improvement in VAS score which suggests that both drugs are effective in painful diabetic neuropathy. But, in comparison to Pregabalin, Gabapentin resulted in more improvement in the VAS score.

CONCLUSION

Diabetic neuropathy develops in poorly controlled diabetic patients as a late complication. The treatment of diabetic neuropathy may include symptomatic relief of complications besides good glycemic control. In the present study, both pregabalin+alpha-lipoic acid and gabapentin+methylcobalamin showed an improvement in VAS score, but the improvement was significantly more with Gabapentin+Methylcobalamine than Pregabalin+Alpha lipoic acid. In this study, Gabapentin+Methylcobalamine was clearly ahead of Pregabalin+Alpha lipoic acid in efficacy parameters like improvement in pain, itching and numbness.

So, from the present study we conclude that monotherapy with Pregabalin+Alphalipoic acid or Gabapentin+ Methylcobalamine produces clinically meaningful pain relief in patients with painful diabetic neuropathy and pain reduction is superior with Pregabalin+Alphalipoic acid compared to Gabapentin+Methylcobalamine. Therefore, it is suggested that these findings should be considered

in the decision-making process when choosing the therapeutic option for the treatment of diabetic neuropathic pain. However, further more studies showed that larger number of patients and patients with longer duration are necessary to confirm the benefits of both Pregabalin+Alpha lipoic acid over Gabapentin+Methylcobalamine in patients with Diabetic neuropathic pain.

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