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Original Research Article

A Randomized Double-Blind Study Comparing the Efficacy and Safety of Duloxetine vs. Gabapentin in Diabetic Polyneuropathy Patients

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Conflict of interest: Nil

Abstract:

Introduction: Diabetic peripheral neuropathy denotes the manifestation of symptoms and indications of peripheral nerve impairment in individuals with diabetes, following the exclusion of other potential etiologies. Among the myriad long-term complications of diabetes, diabetic neuropathies stand as a prevalent occur-rence, affecting approximately 60% of diabetic patients. The objective of this investigation is to evaluate the effectiveness and safety profiles of tablet duloxetine 60 mg and tablet gabapentin 300 mg in patients presenting with diabetic polyneuropathy.

Materials and Methods: This investigation comprised a randomized, comparative, double-blind parallel group study conducted on 78 patients experiencing diabetic polyneuropathic pain who were randomly assigned to two distinct groups. One group received duloxetine 60 mg while the other received gabapentin 300 mg. The evaluation of efficacy encompassed the utilization of the visual analog scale (VAS), the abbreviated version of the McGill pain questionnaire, and the patients' global impression of change score. Safety assessment was conducted through the scrutiny of adverse drug reaction profiles.

Results: Within the duloxetine group, the mean VAS score diminished significantly at the 3-month mark. Similarly, within the gabapentin group, the mean score diminished significantly at the 3-month mark. Noteworthy statistical significance was observed in the disparity between baseline and 3-month mean McGill scores in both groups.

Conclusions: Duloxetine 60 mg once daily emerges as more effective than gabapentin 300 mg once daily in alleviating diabetic neuropathic pain. Furthermore, both pharmaceutical agents demonstrate favorable tolerability, albeit with gabapentin exhibiting superior tolerability compared to duloxetine.

Keywords: Duloxetine, Gabapentin, Visual Analog Scale, McGill Pain Questionnaire.

Introduction

Diabetic peripheral neuropathy, denoted by the presence of symptoms and signs of peripheral nerve damage in individuals with diabetes, sub-sequent to excluding other potential causes, stands as one of the most prevalent long-term complications of the condition. It encompasses polyneuropathy, mononeuropathy, and autonomic neuropathy, with distal symmetric poly-neuropathy being the most common manifestation.

Symptoms such as numbness, tingling, sharp or burning sensations in the feet, often worsening at night, and occasionally accompanied by allodynia, hyperalgesia, and paresthesia, typify diabetic neuropathic pain [1-3]. Risk factors for diabetic neuropathy include the duration of diabetes, poor glycemic control, in-creased body mass index, smoking, hypertension, and hypertriglyceridemia. Although pain tends to subside with disease progression, sensory deficits persist. Approximately 60% of diabetic patients experience neuropathy, making it a leading cause of lower limb amputations in both the USA (50–75%) and India (76–78%) [1]. Neurological complications affect both Type 1 and Type 2 diabetes patients, with neuropathic pain reported in 11–32% of those with polyneuropathy [4].

The incidence of diabetic neuropathy in Type 2 diabetes patients in South India is reported to be

19.1% [5]. It is associated with increased physician visits and work disability due to physical limitations. While no cure exists, treatment primarily focuses on controlling risk factors. However, symptomatic treatment with drugs such as amitriptyline, duloxetine, gabapentin, or pregabalin is often necessary. Combination therapy may be required if mono-therapy fails, although it has not shown superiority over monotherapy.

Duloxetine (60–120 mg/day) and gabapentin are FDA-approved for neuropathic pain. Duloxetine inhibits serotonin and norepinephrine reuptake stimulating their activity in pain inhibition pathways. Gabapentin acts on central and peripheral regions, likely targeting the α2 delta-1 subunit of voltage-gated N-type calcium channels, among other mechanisms. This study aims to compare the efficacy and safety of duloxetine 60 mg and gabapentin 300 mg tablets in diabetic polyneuropathy treatment [6].

Materials and Methods

This study was a randomized, comparative, double-blind parallel-group study involving patients of both sexes aged above 20 years. Patients with Type 2 diabetes mellitus responding to oral anti-diabetic drugs and those exhibiting symptoms of diabetic polyneuropathy with duration of less than one week were eligible for inclusion. Exclusion criteria comprised patients with Type 1 diabetes mellitus, other types of neuropathy or neurological disorders, current medication for diabetic polyneuropathy, renal, hepatic, or cardiac diseases, pregnancy or lactation, and positive HIV or HBs Ag status.

Participants who provided written informed consent were assigned a patient code and enrolled in the study, totaling 78 patients. They were randomly assigned to two groups using computer-generated randomization. One group received duloxetine 60 mg, while the other received gabapentin 300 mg.

Patients were instructed to take the medication orally daily after breakfast. The tablets were labeled as A or B and administered by nursing staff, ensuring blinding. Follow-up assessments were conducted at 0, 1, 2, and 3 months, with investigations including hemogram, serum creatinine, fasting and postprandial blood sugar, and liver enzymes, performed at recruitment and study completion (3 months). Each patient received their assigned drug for 1 month, with instructions for once-daily administration after breakfast. Follow-up evaluations occurred at the 1st and 3rd months, during which Visual Analog Scale (VAS) scores, the short form of the McGill Pain Questionnaire, and the Patient Global Impression of Change score were recorded. Adverse events were also documented. Treatment continued until the end of the study or until the next follow-up appointment.

Efficacy was evaluated using VAS, the short form of the McGill Pain Questionnaire, and the Patient Global Impression of Change score, while safety was assessed based on adverse drug reaction profiles [7-9].

Results

Table 1 illustrates that the age and sex distribution were comparable across both groups, indicating their similarity.

As depicted in Table 2, the comparability between the groups is evident, as there were no statistically significant differences in baseline parameters.

Table 3 highlights the evaluation of intervention efficacy, focusing on the reduction in VAS scores from baseline to the study's conclusion. In both the duloxetine and gabapentin groups, the mean reduction in VAS scores from baseline to 3 months exhibited statistical significance. Moreover, the disparity between baseline and 3-month mean McGill scores in both groups was statistically significant.

The reduction in VAS scores for the gabapentin group decreased by approximately 26.15%, 42.5%, and 51.21% at 1 month, 2 months, and 3 months, respectively. Conversely, the duloxetine group experienced a decrease of around 34.39%, 53.45%, and 65.12% in VAS scores at 1 month, 2 months, and 3 months, respectively (refer to Table 4).

Table 5 indicates that both drugs demonstrated comparability concerning adverse events. Furthermore, no significant alterations were observed in laboratory investigations conducted at baseline and at the study's conclusion between both groups.

Table 1: Socio-demographic characteristics of study participants

Parameter	Duloxetine group		Gabapentin group		Total		p Value
	n	%	n	%	n	%	
Gender							
Male	17	21.79	18	23.08	35	44.87	0.78
Female	22	28.21	21	26.92	43	55.13	
Age groups (years)							
30–40	9	11.54	11	14.10	20	25.64	0.71
41–50	12	15.38	14	17.95	26	33.33	
51–65	18	23.08	14	17.95	32	41.03	

Table 2: Baseline parameters in study participants

Parameter	Duloxetine group	Gabapentin group	p Value
Age	47.90±7.50	48.20±7.70	0.618
Duration of diabetes	11.10±3.75	10.80±3.60	0.701
FBS	142.80±38.80	145.20±34.30	0.872
PP2BS	233.20±66.80	231.40±58.20	0.803
VAS	55.30±6.60	53.10±8.00	0.429
McGill Score	11.70±2.40	12.10±2.50	0.942

Table 3: Intragroup comparison of efficacy variables

Parameter	Duloxetine group			Gabapentin group		
	Baseline	Next f.up	p Value	Baseline	Next f.up	p Value
VAS baseline vs 1st month	55.30±6.60	35.80±4.30	<0.05	53.10±8.00	39.90±6.30	<0.05
VAS baseline vs 2nd month	55.30±6.60	27.20±4.60	<0.05	53.10±8.00	31.20±5.00	<0.05
VAS baseline vs 3rd month	55.30±6.60	20.90±5.10	<0.05	53.10±8.00	27.40±4.70	<0.05
McGill score baseline vs 3rd month	11.70±2.40	5.10±1.60	<0.05	12.10±2.50	6.40±1.60	<0.05

Table 4: Intergroup comparison of efficacy variables

Parameter	Duloxetine group	Gabapentin group	p Value
VAS 1st month	35.80±4.30	39.90±6.30	<0.05
VAS 2nd month	27.20±4.60	31.20±5.00	<0.05
VAS 3rd month	20.90±5.10	27.40±4.70	<0.05
McGill score 3rd month	5.10±1.60	6.40±1.60	<0.05
PGI score at the end of the study	5.46±0.76	4.09±0.79	1.31

Table 5:

Parameter	Duloxetine group		Gabapentin group		Total	
	n	%	n	%	n	%
Loss of Appetite	1	1.28	0	0.00	1	1.28
Loose stools	3	3.85	0	0.00	3	3.85
Dizziness	1	1.28	4	5.13	5	6.41
Tiredness	0	0.00	1	1.28	1	1.28
Headache	3	3.85	1	1.28	4	5.13
Excessive sweating	0	0.00	3	3.85	3	3.85
Nausea	8	10.26	1	1.28	9	11.54
Sleepiness	4	5.13	4	5.13	8	10.26

Discussion

The present study aimed to examine and compare the efficacy and safety of duloxetine 60 mg tablets versus gabapentin 300 mg tablets among patients with diabetic polyneuropathy [10]. Baseline characteristics were similar between the two groups. At the end of the 3-month study period, there was a statistically significant difference between the two groups in terms of efficacy scores, including VAS, McGill, and PGI scores, indicating that duloxetine 60 mg once daily was more efficacious than gabapentin 300 mg in patients with diabetic polyneuropathic pain. Both medications were well tolerated. Reference to the Oregon Evidence-Based Practice Center's final report on drugs for neuropathic pain in 2007 highlighted the lack of head-to-head comparison data between drugs for this condition [10]. Adjusted indirect comparisons using the method described by Bucher et al. suggested no significant differences in efficacy between duloxetine and other medications (gabapentin, pregabalin, and venlafaxine) for neuropathic pain [11]. However, this contradicts the findings of the current study. While safety analyses showed no discernible differences between duloxetine and other medications, this aligns with the present study. Contrasting results were noted in a study by Devi et al., where both duloxetine and gabapentin were equally effective, showing no statistically significant difference [12].

Discrepancies in the findings could be attributed to methodological variations, including patient inclusion criteria; the last observation carried forward method, and baseline values of VAS

scores. The present study, being double-blinded, aims to mitigate biases, unlike the open-labeled trial conducted by Devi et al. A German-based observational study by Happich et al. indicated that duloxetine was more efficacious than gabapentin and pregabalin in treating diabetic polyneuropathy, supporting the current study's findings [13]. Similarly, a multinational, randomized, double-blind, parallel-group study by Tesfaye et al. comparing duloxetine with pregabalin found duloxetine to be superior in terms of efficacy [14]. In a study by Kaur et al., duloxetine and amitriptyline were found to be similarly efficacious and safe in painful diabetic neuropathic pain [15]. However, the mechanism of action of amitriptyline differs from gabapentin, the latter being the focus of the current study. Quilici et al.'s meta-analysis comparing duloxetine, pregabalin, and gabapentin in diabetic peripheral neuropathic pain suggested no significant differences in terms of efficacy and safety among the three drugs [16]. Rudroju et al.'s network meta-analysis concluded that gabapentin was the most effective, while amitriptyline was the least safe among five medications [17,18]. It's important to note that the present study has limitations, including being a single-center study with a smaller sample size and a 12-week study period. Replication and extension of the findings are warranted for a more comprehensive understanding of their specificity.

Conclusion

In our investigation, we observed that both duloxetine 60 mg once daily and gabapentin 300 mg once daily effectively alleviate diabetic polyneuropathic pain. However, duloxetine at this dosage demonstrates greater efficacy compared to gabapentin for managing diabetic neuropathic pain. Additionally, both medications exhibit good tolerability, with gabapentin showing superior tolerance in comparison to duloxetine. We assessed patients using available assessment scales, which could be further refined with more precise measurement tools. Nevertheless, comprehensive multicentric studies with larger sample sizes and longer durations, exploring various drug combinations, are essential to yield accurate, authentic, and conclusive results.

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