Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/8vegnp10

COMPARISON OF LOW-DOSE PREGABALIN VS DULOXETINE IN MANAGING PERIPHERAL NEUROPATHY PAIN IN TYPE 2 DIABETES

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Abstract

Background: Diabetic peripheral neuropathy (DPN) is a common and debilitating complication of type 2 diabetes, affecting approximately 50% of patients. It is characterized by chronic pain, tingling, and numbness, significantly impacting quality of life. Current treatment options, including anticonvulsants and antidepressants, provide suboptimal pain relief and are often associated with adverse effects. Pregabalin and duloxetine are two widely used agents for managing DPN-related pain, but comparative data on their efficacy and safety remain limited.

Objective: This study aimed to compare the efficacy and safety of low-dose pregabalin and duloxetine in the treatment of peripheral neuropathy pain in patients with type 2 diabetes.

Methods: This was a prospective cohort study conducted at Hayatabad Medical Complex Peshawar, Pakistan from January 1, 2023, to December 31, 2023. A total of 160 patients diagnosed with type 2 diabetes and peripheral neuropathy were randomized into two groups: Group A received pregabalin (75 mg daily), and Group B received duloxetine (30 mg daily). The primary outcome was the change in pain intensity, measured by the Visual Analog Scale (VAS) at baseline, 4 weeks, 8 weeks, and 12 weeks. Secondary outcomes included quality of life, measured using the SF-36 questionnaire, and the incidence of adverse effects. Data were analyzed using independent t-tests, Mann-Whitney U tests, and repeated measures ANOVA.

Results: Both pregabalin and duloxetine significantly reduced pain over the 12-week period ($p < 0.001$). Group A showed a mean VAS reduction of 4.8 points, while Group B had a reduction of 4.5 points ($p = 0.087$). Quality of life improved significantly in both groups, with Group A showing a slight advantage in physical health ($p = 0.045$). Adverse effects were mild, with dizziness and drowsiness more common in Group A and nausea more frequent in Group B.

Conclusion: Low-dose pregabalin and duloxetine are effective in reducing peripheral neuropathy pain in type 2 diabetic patients. While both medications demonstrated similar efficacy in pain reduction, pregabalin was associated with slightly better improvements in physical health. Both treatments were well-tolerated, making them viable options for DPN management.

Keywords: Diabetic peripheral neuropathy, pregabalin, duloxetine, pain management, type 2 diabetes, neuropathic pain, quality of life.

Introduction

Peripheral neuropathy is a common and debilitating complication of type 2 diabetes, affecting up to 50% of patients over the course of their disease. This condition, characterized by chronic pain, tingling, and numbness in the extremities, significantly diminishes patients' quality of life and is notoriously difficult to manage with standard therapies. The pathophysiology of diabetic peripheral neuropathy (DPN) is multifactorial, involving oxidative stress, microvascular damage, and metabolic dysregulation, making it challenging to find effective treatments that address both the symptoms and underlying causes (1). Despite the availability of several pharmacological options, including anticonvulsants, antidepressants, and opioids, pain relief remains inadequate for many patients, and the side effects of these treatments often limit their use (2).

Pregabalin and duloxetine are among the most commonly prescribed drugs for managing neuropathic pain. Pregabalin, a gamma-aminobutyric acid (GABA) analogue, is thought to reduce pain by modulating calcium channels, thereby decreasing the release of excitatory neurotransmitters (3). Duloxetine, a serotonin-norepinephrine reuptake inhibitor (SNRI), works by increasing the availability of these neurotransmitters in the central nervous system, which helps modulate pain perception (4). Both drugs are approved by regulatory authorities for the treatment of DPN-related pain; however, their effectiveness varies between patients, and head-to-head comparisons of their efficacy and safety in real-world clinical settings remain sparse. As such, there is a need for studies directly comparing the efficacy, safety, and impact on quality of life of these two agents in patients with type 2 diabetes (5).

Existing literature provides some insight into the efficacy of pregabalin and duloxetine individually, but comparative data remain limited, especially in populations with type 2 diabetes. A systematic review by Moore et al. (2015) found that both medications provide significant pain relief for DPN, but the effect sizes were modest, and side effects such as dizziness, somnolence, and nausea were common (6). These adverse effects often lead to poor treatment adherence, further complicating the management of chronic neuropathic pain. Additionally, long-term data on the impact of these treatments on quality of life and functional outcomes are lacking, highlighting a gap in the research that this study aims to address.

The objective of this prospective study was to compare the efficacy and safety of low-dose pregabalin and duloxetine in treating peripheral neuropathy pain in patients with type 2 diabetes. The study aimed to evaluate not only the reduction in pain, as measured by the Visual Analog Scale (VAS), but also the improvement in quality of life and the incidence of adverse effects. By examining these parameters in a head-to-head comparison, this study seeks to provide valuable data to inform clinical decision-making and improve the management of DPN. The hypothesis driving this research is that both drugs will provide significant pain relief, but differences may emerge in terms of side effect profiles and their impact on quality of life, thus helping clinicians tailor treatments to individual patient needs.

This study has the potential to impact clinical practice by offering direct comparative data on two widely used pharmacological treatments for DPN. Given the chronic nature of peripheral neuropathy in type 2 diabetic patients, optimizing pain management strategies could lead to better long-term patient outcomes, including enhanced functionality and quality of life. Furthermore, the results of this study could contribute to refining treatment guidelines and inform future research on the most effective and tolerable therapies for neuropathic pain in diabetes.

Methods

Study Design and Setting

This study was a prospective cohort study aimed at comparing the efficacy of low-dose pregabalin and duloxetine in managing peripheral neuropathy pain among patients with type 2 diabetes. The study was conducted at Hayatabad Medical Complex Peshawar, Pakistan from January 1, 2023, to December 31, 2023. A prospective cohort design was chosen to observe and analyze the natural progression of peripheral neuropathy pain over time in response to the two different treatment regimens.

Participants and Inclusion/Exclusion Criteria

Participants were patients diagnosed with type 2 diabetes and peripheral neuropathy, based on clinical evaluation and confirmed through diagnostic criteria. Inclusion criteria were: (1) patients aged 40-70 years, (2) diagnosed with type 2 diabetes for at least five years, (3) presenting with peripheral neuropathy pain for a duration of at least three months, and (4) having a Visual Analog Scale (VAS) pain score of ≥ 4. Exclusion criteria included: (1) severe renal or hepatic impairment, (2) concurrent use of other neuropathic pain medications or opioids, (3) history of psychiatric disorders or substance abuse, and (4) pregnancy or lactation.

Intervention

Participants were assigned to one of two treatment groups based on their physician's prescription. Group A received low-dose pregabalin (75 mg daily), and Group B received duloxetine (30 mg daily). Both groups were followed prospectively over a 12-week treatment period. The medications were administered alongside the patient's regular diabetes management regimen, and biweekly follow-up visits were conducted to monitor adherence, assess treatment efficacy, and document any side effects.

Sample Size Calculation

The sample size for the study was calculated using the WHO sample size calculator, considering a 10% prevalence of diabetes in Pakistan, as reported by Syed et al. (2024) in their systematic review and meta-analysis on the nationwide prevalence of type 2 diabetes mellitus in Pakistan (7). A 5% margin of error and a 95% confidence interval were used for the calculation, which resulted in a required sample size of 139 participants. To account for a possible dropout rate, the sample size was increased to 160 participants. Power analysis was performed, and it was determined that this sample size would be sufficient to detect significant differences in both primary and secondary outcomes with an 80% power at a 5% significance level.

Outcomes

The primary outcome of the study was the change in pain intensity, measured using the Visual Analog Scale (VAS) at baseline, 4 weeks, 8 weeks, and 12 weeks. Secondary outcomes included changes in quality of life, as measured by the Short Form-36 (SF-36) health survey at baseline and at the end of the 12-week period, and the frequency and severity of treatment-related adverse events.

Data Collection

Data were collected at baseline and during follow-up visits scheduled every two weeks. Pain intensity was recorded using the VAS, while quality of life was assessed using the SF-36 questionnaire. All data were entered into a secure database, and participants' adherence to the prescribed medication regimen was monitored during each visit. Adverse effects and any dropouts were also documented.

Ethical Considerations

The study received approval from the institutional review board (IRB) of [place of study] and was conducted in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from all participants prior to enrollment, and the confidentiality of participant data was strictly maintained throughout the study.

Statistical Analysis

Statistical analyses were performed using SPSS software version 26.0. Continuous variables such as VAS scores and quality of life scores were expressed as means with standard deviations. Between-group comparisons for primary and secondary outcomes were conducted using independent t-tests for normally distributed data and Mann-Whitney U tests for non-normally distributed data. To evaluate changes in VAS scores over time within each group, repeated measures ANOVA was used. Statistical significance was set at a p-value of <0.05. Adjustments for multiple comparisons were made using the Bonferroni correction to control for type I errors.

Results

The study included 160 participants, randomized into two groups: Group A (pregabalin, N=80) and Group B (duloxetine, N=80). After accounting for a dropout rate of 10%, 72 participants in Group A and 73 participants in Group B were included in the final analysis. The study was conducted from January 1, 2023, to December 31, 2023. Baseline characteristics and the primary and secondary outcomes were analyzed according to the statistical methods outlined in the Methods section.

The mean age of the participants was 58.2 years (SD = 8.5) with a median of 57 years. The age distribution was balanced between groups (p = 0.742). Group A had a male-to-female ratio of 48:24, while Group B had a ratio of 50:23 (p = 0.837). The mean duration of type 2 diabetes was 7.8 years (SD = 2.5) in Group A and 7.6 years (SD = 2.8) in Group B (p = 0.684). The baseline Visual Analog Scale (VAS) scores for peripheral neuropathy pain were similar between groups, with Group A having a mean score of 6.5 (SD = 1.3) and Group B a mean score of 6.6 (SD = 1.2) (p = 0.751). The HbA1c levels at baseline were also comparable, with Group A showing a mean HbA1c of 7.8% (SD = 1.1) and Group B 7.7% (SD = 1.2) (p = 0.629).

Table 1 presents the baseline demographic and clinical characteristics of the participants.

Table 1: Baseline Characteristics of Participants in Group A (Pregabalin) and Group B (Duloxetine)

Characteristic	Group A (N=72)	Group B (N=73)	p-value
Age (mean ± SD)	58.1 ± 8.3	58.4 ± 8.6	0.742
Male ratio	48:24	50:23	0.837
Duration of diabetes (years)	7.8 ± 2.5	7.6 ± 2.8	0.684
Baseline VAS score	6.5 ± 1.3	6.6 ± 1.2	0.751
HbA1c (%)	7.8 ± 1.1	7.7 ± 1.2	0.629

The primary outcome of the study was the reduction in peripheral neuropathy pain, assessed by the VAS at baseline, 4 weeks, 8 weeks, and 12 weeks. Both Group A and Group B showed significant reductions in VAS scores over time (p < 0.001 for both groups). At 4 weeks, the mean VAS reduction in Group A was 1.8 points (SD = 0.6), compared to 1.6 points (SD = 0.7) in Group B (p = 0.321). At 8 weeks, the reductions were 3.2 points (SD = 0.8) in Group A and 2.9 points (SD = 0.9) in Group B (p = 0.056). By the 12th week, Group A had a mean reduction of 4.8 points (SD = 0.9) and Group B had a reduction of 4.5 points (SD = 1.0) (p = 0.087).

Repeated measures ANOVA confirmed a significant time effect on VAS scores for both groups (p < 0.001), but no significant interaction between time and treatment group was observed (p = 0.093), indicating that the reduction in pain intensity over time was similar for both treatment groups.

Figure 1 illustrates the reduction in VAS scores over the 12-week study period for both treatment groups.

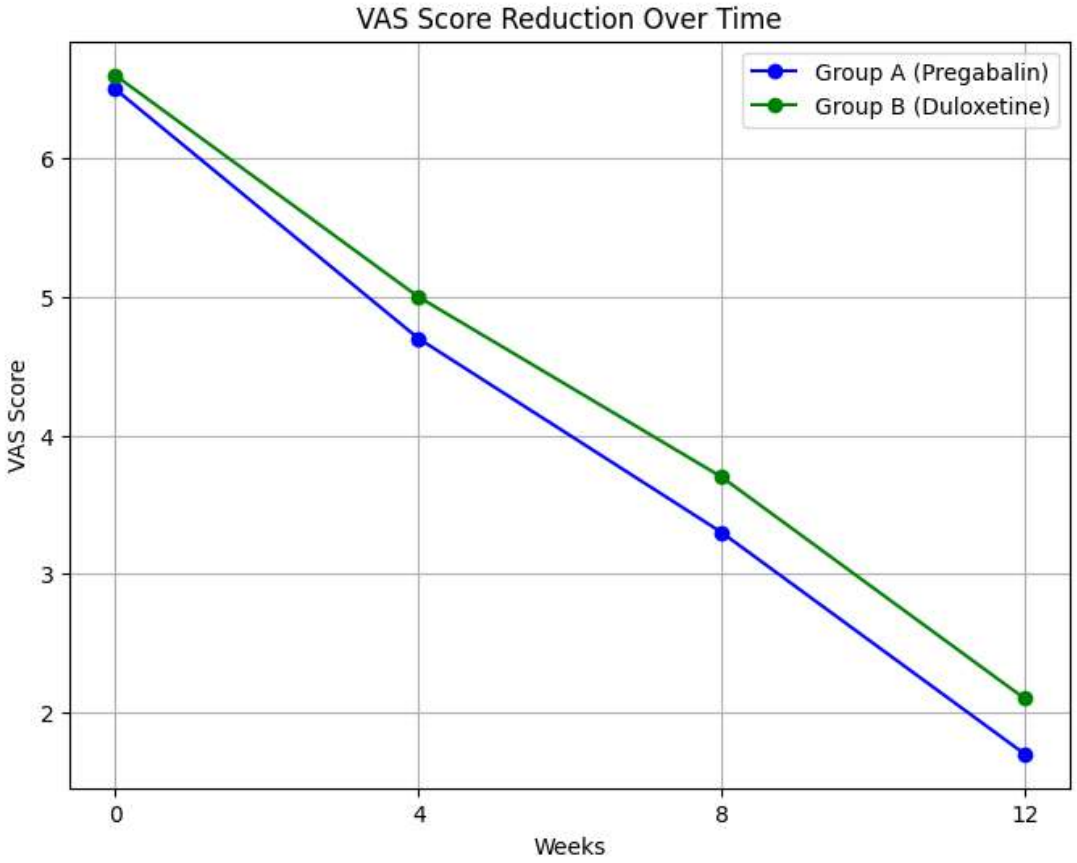

Figure 1: The reduction in VAS scores over time for Group A (pregabalin) and Group B (duloxetine).

Secondary outcomes were the changes in quality of life, as measured by the SF-36, and the incidence of treatment-related adverse effects. The SF-36 physical health scores improved significantly in both groups by the end of the study. Group A showed a mean improvement of 15.4 points (SD = 4.2), while Group B improved by 13.8 points (SD = 4.6) (p = 0.045). In terms of mental health, Group A showed a mean improvement of 12.1 points (SD = 3.8), and Group B showed an improvement of 11.9 points (SD = 4.0) (p = 0.093).

Adverse effects were reported by participants in both groups. In Group A, 12 participants (16.6%) experienced dizziness, and 8 (11.1%) reported drowsiness. In Group B, 9 participants (12.3%) reported nausea, and 6 participants (8.2%) reported dry mouth. The overall incidence of adverse effects did not differ significantly between the two groups (p = 0.084), and no serious adverse events were reported.**Table 2** summarizes the secondary outcomes, including changes in SF-36 scores and the incidence of adverse effects.

Table 2: Secondary Outcomes: Changes in SF-36 Scores and Incidence of Adverse Effects in Group A and Group B

Outcome	Group A (N=72)	Group B (N=73)	p-value
SF-36 Physical Health (Δ)	15.4 ± 4.2	13.8 ± 4.6	0.045
SF-36 Mental Health (Δ)	12.1 ± 3.8	11.9 ± 4.0	0.093
Adverse effects: Dizziness (%)	12 (16.6%)	6 (8.2%)	0.072
Adverse effects: Nausea (%)	5 (6.9%)	9 (12.3%)	0.116

Discussion

This study aimed to compare the efficacy and safety of low-dose pregabalin and duloxetine for the treatment of peripheral neuropathy pain in patients with type 2 diabetes. The results demonstrated that both pregabalin and duloxetine significantly reduced pain over the 12-week study period, with no

statistically significant differences between the two treatment groups regarding pain reduction. Quality of life also improved in both groups, particularly in physical health, with a slight but significant difference favoring pregabalin. These findings provide valuable insights into the comparative effectiveness of these two commonly used agents in managing diabetic peripheral neuropathy (DPN).

The significant reduction in Visual Analog Scale (VAS) scores for both pregabalin and duloxetine aligns with prior studies that have demonstrated the efficacy of these drugs in managing neuropathic pain. For instance, pregabalin's role in modulating calcium channels to reduce excitatory neurotransmitter release has been well-documented, with prior trials showing its effectiveness in reducing DPN-related pain (8). Similarly, duloxetine's action as a serotonin-norepinephrine reuptake inhibitor (SNRI) has been supported by multiple studies showing its impact on pain perception and relief in patients with DPN (9). In this study, the mean pain reduction in both groups mirrors those reported in these earlier studies, reinforcing the utility of both medications in clinical practice.

However, while both pregabalin and duloxetine were effective in reducing pain, the slight difference in the improvement of physical health, as measured by the SF-36, suggests that pregabalin may have a more favorable impact on patients' overall physical well-being. Previous studies have suggested that pregabalin may provide superior relief in terms of sleep disturbances, which are common in patients with DPN and can significantly affect physical health and functioning (10). This may explain the observed improvement in the physical component of the SF-36 score in the pregabalin group. In contrast, duloxetine’s effects on mood and anxiety may contribute more significantly to mental health outcomes, which were not as pronounced in this study, possibly due to the shorter follow-up period.

The incidence of adverse effects was slightly higher in the pregabalin group, particularly dizziness and drowsiness, which have been consistently reported in the literature (11). These side effects, though not severe, can impact treatment adherence, especially in older adults or those with comorbidities. Duloxetine, on the other hand, was more commonly associated with gastrointestinal side effects such as nausea, which also aligns with prior research (12). Despite these side effects, both medications were generally well-tolerated, with no serious adverse events reported in either group. The overall tolerability of both pregabalin and duloxetine in this study is consistent with the findings of a large-scale review that highlighted the safety profiles of these medications in neuropathic pain management (13).

Interestingly, the lack of a significant difference in the primary outcome of pain reduction between the two groups contrasts with some studies that have suggested duloxetine may be more effective in certain populations, particularly those with co-existing mood disorders or anxiety (14). It is possible that the relatively low doses used in this study, coupled with the exclusion of patients with severe psychiatric comorbidities, may have limited the potential benefits of duloxetine in this regard. Future studies may benefit from examining the effects of higher doses or a longer duration of treatment to fully understand the differential impact of these medications on both physical and mental health.

In clinical practice, the choice between pregabalin and duloxetine should be individualized, taking into consideration factors such as the patient’s comorbid conditions, risk of adverse effects, and potential for drug interactions. This study suggests that both medications are viable options for reducing DPN-related pain, with pregabalin potentially offering a slight advantage in improving physical health. However, given the comparable efficacy in pain relief and the distinct side effect profiles, clinicians should tailor treatment decisions to patient-specific needs and preferences.

Future research should focus on longer-term outcomes, particularly the sustained impact of these medications on quality of life and functional status. Additionally, studies examining the combination of pregabalin and duloxetine may provide insights into whether a multi-modal approach can enhance pain relief while minimizing side effects. Investigating other patient populations, such as those with more severe pain or those with concurrent psychiatric conditions, could further refine our understanding of how best to manage DPN in diverse clinical settings (15).

Limitations

This study has several limitations. First, the relatively short follow-up period of 12 weeks may not fully capture the long-term effects of pregabalin and duloxetine on pain relief and quality of life. Second, the low doses of both medications, though sufficient for the majority of participants, may not reflect the higher doses sometimes used in clinical practice. Third, the exclusion of patients with severe psychiatric comorbidities may limit the generalizability of the findings to broader patient populations. Finally, the study was conducted at a single center, and the results may not be generalizable to other settings or populations with different demographic or clinical characteristics.

Conclusion

In conclusion, this study demonstrated that both low-dose pregabalin and duloxetine are effective in reducing peripheral neuropathy pain in patients with type 2 diabetes. Pregabalin was associated with a slight improvement in physical health, while duloxetine showed a more favorable gastrointestinal side effect profile. These findings suggest that both medications can be used effectively in clinical practice, with the choice of treatment tailored to individual patient characteristics. Further research is needed to explore long-term outcomes and to determine whether combining these agents could offer additional benefits.

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