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COMPARATIVE STUDY OF EFFICIENCY OF DULOXETINE VERSUS PREGABALIN IN PATIENT OF DIABETIC NEUROPATHY.

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Abstract

Background: Diabetic peripheral neuropathy (DPN) is a common and painful complication of long-standing diabetes mellitus, significantly affecting patient quality of life and increasing the burden on healthcare systems. Duloxetine and Pregabalin are widely used pharmacological agents for managing painful diabetic neuropathy, but comparative studies are essential to guide optimal treatment selection.
Method: A prospective, observational, and analytical study was conducted at S.N. Medical College, Agra, involving 144 patients with clinically diagnosed DPN. Patients were randomly assigned into two groups: Group A received Duloxetine 20 mg daily, and Group B received Pregabalin 75 mg daily. Efficacy was assessed using clinical symptom evaluation and nerve conduction studies (NCV) of the common peroneal and median nerves. Follow-ups were conducted at 1, 3, and 6 months. Safety was evaluated through clinical observation and liver and kidney function tests.
Results: Both groups showed improvement in neuropathic symptoms no effect is seen in nerve conduction parameters over the study period. However, overall, there was no significant difference between the two drugs in terms of symptom relief or NCV improvement. Adverse effects were more frequently reported with Duloxetine (nausea, dry mouth), whereas Pregabalin was associated with dizziness and somnolence. A greater percentage of patients reported no side effects in the Pregabalin group (49%) compared to the Duloxetine group (45%).
Conclusion: Both Duloxetine and Pregabalin are effective and safe options for managing diabetic peripheral neuropathy. Pregabalin showed a slightly better safety profile and tolerability, while both drugs demonstrated comparable efficacy in symptom improvement and nerve conduction outcomes. Pregabalin may be preferred in patients prone to gastrointestinal side effects.

Keywords: Diabetic peripheral neuropathy, Duloxetine, Pregabalin, Nerve conduction study, Neuropathic pain, Safety profile, Efficacy comparison

Introduction

Diabetes mellitus (DM) is a chronic, progressive metabolic disorder characterized by persistent hyperglycemia resulting from impaired insulin secretion, insulin action, or both[1]. It has emerged as a global health crisis, with India ranking among the top countries in terms of diabetes burden. According to the International Diabetes Federation, approximately 40 million people in India are currently affected, with projections estimating this number to rise to 101 million by 2030 and 134 million by 2045[2]. The increasing prevalence is attributed to urbanization, sedentary lifestyles, unhealthy dietary habits, and genetic predisposition[3].

Diabetic neuropathy, particularly diabetic peripheral neuropathy (DPN), is one of the most prevalent and disabling chronic complications of diabetes, affecting nearly 50% of diabetic individuals[4]. A significant subset of these patients develop painful diabetic peripheral neuropathy (PDPN), characterized by burning, stabbing, or electric shock-like sensations, which severely impact functional ability, mental health, and overall quality of life[5]. The pathophysiology of PDPN involves oxidative stress, microvascular damage, and alterations in pain signaling pathways within the central and peripheral nervous systems[6]. As the global prevalence of diabetes continues to increase, the incidence of PDPN is also expected to rise, posing a considerable public health and socioeconomic burden[7].

Management of PDPN remains challenging, as conventional analgesics such as NSAIDs and opioids often fail to provide adequate relief[8]. The U.S. Food and Drug Administration (FDA) has approved a few pharmacologic agents specifically for the treatment of PDPN, including Pregabalin, Duloxetine, Tapentadol, and topical capsaicin[9]. Among these, Duloxetine and Pregabalin are the most widely prescribed first-line therapies due to their efficacy and tolerability[10].

Duloxetine is a serotonin-norepinephrine reuptake inhibitor (SNRI) that enhances descending inhibitory pain pathways by increasing the availability of serotonin and norepinephrine in the central nervous system. It also exhibits anti-inflammatory effects by inhibiting nuclear factor kappa B (NF-κB) and Toll-like receptor 4 (TLR4) signaling, thereby reducing neuroinflammation[11]. Pregabalin, on the other hand, is a gabapentinoid that binds to the α2δ subunit of voltage-gated calcium channels in the CNS, decreasing the release of excitatory neurotransmitters and reducing neuronal hyperexcitability[12]. Although both drugs are approved for PDPN treatment, their comparative efficacy, safety, and tolerability profiles remain subjects of ongoing investigation.

This study aims to conduct a direct comparison between Duloxetine and Pregabalin in patients with PDPN, evaluating their effectiveness through clinical symptom assessment and nerve conduction studies, and monitoring their safety through adverse event profiling and laboratory parameters.

Methods

Materials and Methods

This prospective, observational, and analytical study was conducted over 12 months in the Department of Pharmacology and Therapeutics, in collaboration with the Department of Medicine, at S.N. Medical College and Hospital, Agra, following approval from the Institutional Ethics Committee.

Inclusion Criteria:

Patients aged 18–60 years with a clinical diagnosis of diabetic peripheral neuropathy and a history of diabetes for more than six years.

Exclusion Criteria:

Patients with psychiatric disorders (e.g., bipolar disorder, OCD, PTSD), known hypersensitivity to the study drugs, pregnancy/lactation, substance abuse, or neuropathy due to other causes (e.g., fibromyalgia, leprosy, heavy metal exposure) were excluded. Patients with painful diabetic foot lesions, cognitive impairment, or those unwilling to give informed consent were also excluded.

Study Design and Participants:
A total of 144 eligible patients attending the Medicine OPD were alternately assigned to one of two groups:
Group A: Duloxetine 20 mg once daily
Group B: Pregabalin 75 mg once daily
Sample Size Calculation:
Using the formula $n = z^2pq/d^2$, with p = 10.6% (estimated prevalence), confidence level z = 1.96, and precision d = 5%, the required sample size was calculated as 144.

Baseline Evaluation and Follow-up:
All participants underwent baseline investigations including CBC, HbA1c, fasting and postprandial blood glucose, LFT, KFT, and nerve conduction velocity (NCV). Follow-up assessments were conducted at 1, 3, and 6 months to evaluate clinical symptoms (tendon reflexes, muscle strength, vibration, touch, and position sensation), biochemical markers, and NCV outcomes.

Statistical Analysis:
Data were analyzed using Microsoft Excel and EPI INFO. Paired T-test, +Chi squared Z-tests were used to compare continuous variables between groups. A p-value <0.05 was considered statistically significant.

Ethical Considerations:
The study received approval from the institutional Ethics committee (IEC) of S.N Medical College Agra. Written informed consent was obtained from all participants. Patients were advised to abstain from smoking and alcohol throughout the study.

Result:
A total of 144 patients diagnosed with diabetic peripheral neuropathy were enrolled and randomized into two groups: Group A (Duloxetine 20 mg/day) and Group B (Pregabalin 75 mg/day), with 72 patients in each group. The demographic and baseline clinical characteristics were comparable between the two groups.

1. Demographic Distribution
Gender: Group A comprised 45.83% males and 54.16% females, while Group B had 54.16% males and 59.72% females.

	Group A (Duloxetine)		Group B (Pregabalin)		Total No of patients
	No of patients (72)	Percentage	No of patients	Percentage	
Male	33	45.83%	29	54.16%	62 (43.05%)
Female	39	54.16%	43	59.72%	82 (56.94%)

Age: The mean age in Group A was 45.02 ± 0.94 years and 44.2 ± 0.84 years in Group B
Duration of Diabetes: The mean duration was 14.84 ± 4.26 years in Group A and 13.19 ± 4.14 years in Group B .
Nerve Conduction Study (NCV) Parameters Nerve conduction studies were performed on the common peroneal nerve (CPN) and the median nerve on both right and left limbs. Parameters assessed included nerve conduction velocity (m/s) and compound muscle action potential amplitude (mV) at baseline, 1 month, 3 months, and 6 months. Both groups showed improvement over time, but significant intergroup differences were observed at the 6-month follow-up, There we cant find any significant changes in either group

Table: Comparison of NCV Parameters Between Duloxetine and Pregabalin Groups

Nerve	Parameter	Time Point	Duloxetine (Mean ± SD)	Pregabalin (Mean ± SD)	p-value
Common Peroneal Nerve	Velocity (Rt) (m/s)	Baseline	42.04 ± 29.08	47.83 ± 29.42	0.237
		1 Month	57.11 ± 27.93	52.17 ± 31.09	0.317
		3 Months	45.82 ± 28.19	45.98 ± 27.19	0.972
		6 Months	43.38 ± 18.58	50.88 ± 21.65	0.279
	Velocity (Lt) (m/s)	Baseline	45.00 ± 24.32	46.22 ± 27.88	0.156
		1 Month	52.66 ± 27.36	51.61 ± 26.95	0.817
		3 Months	43.23 ± 25.20	45.02 ± 29.46	0.114
		6 Months	43.89 ± 12.32	49.44 ± 17.48	0.295
	Amplitude (Rt) (mV)	Baseline	6.79 ± 3.39	5.63 ± 2.72	0.152
		6 Months	5.23 ± 2.12	5.11 ± 2.43	0.740
	Amplitude (Lt) (mV)	Baseline	7.26 ± 3.65	6.77 ± 3.56	0.416
		6 Months	5.85 ± 2.37	6.21 ± 2.50	0.380
Median Nerve	Velocity (Rt) (m/s)	Baseline	49.07 ± 26.39	45.36 ± 24.03	0.379
		6 Months	50.43 ± 509.83	48.88 ± 16.74	0.331
	Velocity (Lt) (m/s)	Baseline	50.42 ± 24.93	46.31 ± 20.49	0.281
		6 Months	48.64 ± 21.09	47.48 ± 23.61	0.755
	Amplitude (Rt) (mV)	Baseline	6.20 ± 3.41	6.90 ± 24.93	0.060
		6 Months	4.97 ± 2.28	5.70 ± 2.38	0.062
	Amplitude (Lt) (mV)	Baseline	7.64 ± 3.97	7.67 ± 4.44	0.969
		6 Months	7.26 ± 2.31	7.06 ± 2.32	0.614

Common Peroneal Nerve (CPN)

Velocity (Right Side): At baseline, the mean conduction velocity was 42.04 ± 29.08 m/s in the Duloxetine group and 47.83 ± 29.42 m/s in the Pregabalin group ($p = 0.237$). After one month, a slight increase was observed in both groups, with mean values of 57.11 ± 27.93 m/s (Duloxetine) and 52.17 ± 31.09 m/s (Pregabalin) ($p = 0.317$). At three months, both groups showed similar values (45.82 ± 28.19 m/s vs. 45.98 ± 27.19 m/s; $p = 0.972$). By six months, Pregabalin demonstrated a higher mean velocity (50.88 ± 21.65 m/s) compared to Duloxetine (43.38 ± 18.58 m/s), though the difference remained statistically non-significant ($p = 0.279$).

Velocity (Left Side): Baseline values were 45.00 ± 24.32 m/s (Duloxetine) vs. 46.22 ± 27.88 m/s (Pregabalin) (p = 0.156). At one month, the groups showed comparable velocities (52.66 ± 27.36 vs. 51.61 ± 26.95; p = 0.817). No significant differences were observed at three months (43.23 ± 25.20 vs. 45.02 ± 29.46; p = 0.114) or six months (43.89 ± 12.32 vs. 49.44 ± 17.48; p = 0.295).

Amplitude (Right Side): At baseline, Duloxetine patients exhibited a slightly higher amplitude (6.79 ± 3.39 mV) compared to Pregabalin (5.63 ± 2.72 mV; p = 0.152). At six months, this declined to 5.23 ± 2.12 mV (Duloxetine) and 5.11 ± 2.43 mV (Pregabalin) (p = 0.740).

Amplitude (Left Side): Initial values were 7.26 ± 3.65 mV (Duloxetine) and 6.77 ± 3.56 mV (Pregabalin) (p = 0.416). At six months, values slightly reduced to 5.85 ± 2.37 and 6.21 ± 2.50 respectively (p = 0.380).

Median Nerve
Velocity (Right Side): Baseline values were 49.07 ± 26.39 m/s (Duloxetine) and 45.36 ± 24.03 m/s (Pregabalin) (p = 0.379). After six months, conduction velocities were similar (50.43 ± 509.83 vs. 48.88 ± 16.74; p = 0.331), though the unusually high standard deviation in the Duloxetine group suggests outlier data or a recording anomaly.
Velocity (Left Side): Initial mean velocities were 50.42 ± 24.93 m/s (Duloxetine) and 46.31 ± 20.49 m/s (Pregabalin) (p = 0.281). Six-month values remained comparable (48.64 ± 21.09 vs. 47.48 ± 23.61; p = 0.755).
Amplitude (Right Side): Duloxetine showed a baseline amplitude of 6.20 ± 3.41 mV versus 6.90 ± 24.93 mV in Pregabalin (p = 0.060), suggesting notable variability in the Pregabalin group. At six months, amplitude slightly favored Pregabalin (5.70 ± 2.38 mV) over Duloxetine (4.97 ± 2.28 mV; p = 0.062), though still not statistically significant.

Amplitude (Left Side): Baseline amplitudes were similar (7.64 ± 3.97 vs. 7.67 ± 4.44; p = 0.969), and after six months, both groups retained nearly identical values (7.26 ± 2.31 vs. 7.06 ± 2.32; p = 0.614).
Clinical Symptom Evaluation
A comprehensive evaluation of six key clinical symptoms—paresthesia, hypoesthesia, cramps/pain, muscle weakness, vibration sensation loss, and impaired position sense—was conducted at baseline and subsequently at 1-month, 3-month, and 6-month intervals for both treatment groups: Group A (Duloxetine) and Group B (Pregabalin).

Baseline Assessment

Comparative Analysis of Clinical Symptoms Between Group A (Duloxetine) and Group B (Pregabalin)

Symptom	Baseline Duloxetine Group A (%)	Baseline Pregabalin Group B (%)	1 Month Duloxetine Group A (%)	1 month Pregabalin Month Group B (%)	3 Months Duloxetine Group A (%)	3 Month Pregabalin Months Group B (%)	6 Months Duloxetine Group A (%)	6 Months Pregabalin Group B (%)
Paresthesia	48.6	45.8	48.6	48.6	51.4	48.6	45.8	44.4
Hypoesthesia	41.7	44.4	51.4	45.8	40.3	37.5	44.4	45.8
Cramps/Pain	48.6	48.6	58.3	54.2	61.1	55.6	52.8	55.6
Muscle Weakness	56.9	61.1	62.5	58.3	33.3	37.5	37.5	48.6
Vibration Sensation Loss	29.2	38.9	59.7	52.8	38.9	40.3	43.1	37.5
Position Sense Impairment	40.3	44.4	58.3	54.2	55.6	47.2	68.1	68.1

Paresthesia

At baseline, paresthesia was reported by 48.6% of patients in the Duloxetine group and 45.8% in the Pregabalin group. No change was observed at 1 month in either group (48.6%). At 3 months, the frequency slightly increased in Group A (51.4%) while remaining stable in Group B (48.6%). By 6 months, a reduction was noted in both groups (45.8% vs. 44.4%), indicating mild clinical improvement.

Hypoesthesia

The baseline prevalence of hypoesthesia was comparable between the groups (41.7% in Group A and 44.4% in Group B). After one month, Group A saw a rise to 51.4% while Group B decreased to 45.8%. At 3 months, frequencies dropped in both groups (40.3% and 37.5%, respectively) and remained similar at 6 months (44.4% and 45.8%).

Cramps and Pain

Cramps or pain were equally present at baseline (48.6% in both groups). By 1 month, a mild increase was observed in both: 58.3% (Group A) and 54.2% (Group B). This upward trend continued at 3 months (61.1% vs. 55.6%) but showed a slight reduction by 6 months (52.8% and 55.6%), though remaining higher than baseline levels.

Muscle Weakness

Muscle weakness was initially reported in 56.9% of Group A and 61.1% of Group B. At 1 month, both groups reported a slight increase (62.5% and 58.3%). By 3 months, there was a sharp decline in both groups (33.3% and 37.5%). At 6 months, Group A remained stable at 37.5%, while Group B rose to 48.6%, suggesting better sustained improvement in the Duloxetine group.

Vibration Sensation Loss

At baseline, vibration sensation loss was more frequent in Group B (38.9%) than in Group A (29.2%). After 1 month, prevalence peaked in both groups (59.7% and 52.8%, respectively), possibly due to increased reporting. Improvement was seen at 3 months (38.9% and 40.3%) and persisted at 6 months (43.1% vs. 37.5%).

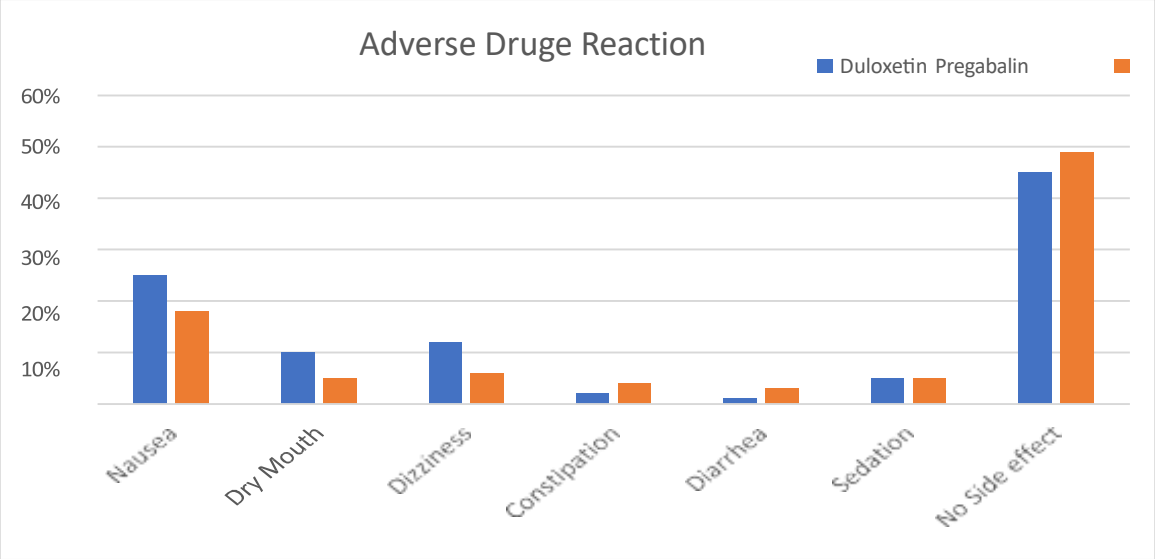
Position Sense Impairment

Position sense impairment was noted in 40.3% of Group A and 44.4% of Group B at baseline. Prevalence rose at 1 month (58.3% and 54.2%) and continued into the 3-month mark (55.6% vs. 47.2%). At the final 6-month evaluation, both groups recorded the same prevalence of 68.1%, indicating no differential improvement in this parameter.

4. Adverse Drug Reactions (ADRs)

Adverse events were closely monitored in both treatment arms—Duloxetine (Group A) and Pregabalin (Group B)—throughout the 6-month study period to assess the safety and tolerability of both medications in patients with diabetic peripheral neuropathy.

Comparison of Adverse Drug Reactions Between Duloxetine and Pregabalin



During the study, several common side effects were observed in both the Duloxetine and Pregabalin treatment groups. Nausea was the most reported side effect, affecting 25% of patients taking Duloxetine and 18% of those on Pregabalin. Similarly, dry mouth (10% vs. 5%) and dizziness (12% vs. 6%) were also more common with Duloxetine than Pregabalin.

On the other hand, constipation and diarrhea were slightly more frequent in the Pregabalin group, with 4% and 3% of patients affected, compared to 2% and 1% in the Duloxetine group. Sedation was reported equally in both groups at 5%.

It is worth noting that 45% of patients taking Duloxetine and 49% of those taking Pregabalin did not experience any side effects, indicating good overall tolerability for both drugs.

Safety Evaluation

Liver and kidney function tests (SGOT, SGPT, urea, creatinine) remained within normal limits in both groups throughout the study. No hepatotoxicity or nephrotoxicity was observed, confirming the hepatic and renal safety of both drugs over the 6-month period.

Conclusion

Common Peroneal Nerve (CPN):

Velocity (m/s): Both Duloxetine and Pregabalin groups showed fluctuating improvements over time, with Pregabalin demonstrating higher mean conduction velocities at most time points. However, the differences were not statistically significant at any point ($p > 0.05$). At 6 months, right CPN velocity was 50.88 ± 21.65 in the Pregabalin group vs. 43.38 ± 18.58 in the Duloxetine group; left CPN was 49.44 ± 17.48 vs. 43.89 ± 12.32, respectively.

Amplitude (mV): Minor improvements were observed in both groups without significant differences. Amplitude values declined slightly by 6 months in both groups. No statistically significant variation was noted across any time point ($p > 0.05$).

Median Nerve:

Velocity (m/s): Both groups showed stable conduction velocities throughout the study period. Although Pregabalin showed slightly higher values at several time points, all comparisons remained non-significant. Notably, at 6 months, right and left velocities were 48.88 ± 16.74 and 47.48 ± 23.61 in the Pregabalin group, compared to 50.43 ± 509.83 and 48.64 ± 21.09 in the Duloxetine group.

Amplitude (mV): Changes in amplitude were modest across both groups. Right and left amplitudes remained relatively stable, with no statistically significant differences at any follow-up interval.

Overall Interpretation:
However, no statistically significant intergroup differences were observed in either velocity or amplitude parameters across all nerves and time points.
Both medications showed a trend toward stabilization or mild improvement in nerve conduction over 6 months, with comparable electrophysiological outcomes.
At the outset of the study, both groups exhibited a comparable prevalence of neuropathic symptoms. Paresthesia was reported by 48.6% in both groups, while hypoesthesia was observed in 41.7% (Group A) and 44.4% (Group B). Cramps or pain were equally reported by 48.6% in both groups, and muscle weakness was slightly more prevalent in Group B (61.1%) compared to Group A (56.9%). Loss of vibration sensation and impairment of position sense were reported with moderate frequency but without significant differences. Statistical analysis using chi-square tests confirmed no significant intergroup differences in symptom prevalence at baseline ($p > 0.05$ for all parameters).

Symptom Progression Over Time
As treatment progressed, both groups demonstrated gradual and sustained clinical improvement across all evaluated parameters:
At 1 Month: Slight reductions in symptom prevalence were observed in both groups, though differences between the groups remained statistically insignificant.
At 3 Months: Clinical improvement continued steadily. Paresthesia and hypoesthesia reduced modestly, with mild improvements in cramps/pain and muscle strength. However, symptom prevalence remained statistically comparable between the two treatment arms ($p > 0.05$).
At 6 Months (Final Evaluation): Both groups showed a reduction in most symptom frequencies, reflecting the therapeutic impact of treatment:
Paresthesia: 45.8% (Group A) vs. 44.4% (Group B)
Hypoesthesia: 44.4% vs. 45.8%
Cramps/Pain: 52.8% vs. 55.6%
Muscle Weakness: 37.5% vs. 48.6%
Vibration Sensation Loss: 43.1% vs. 37.5%
Position Sense Impairment: 68.1% in both groups
Despite these observed reductions in symptom prevalence over the study period, none of the differences between groups at any time point reached statistical significance ($p > 0.05$), indicating that both Duloxetine and Pregabalin provided comparable efficacy in improving clinical symptoms of diabetic peripheral neuropathy.
These findings suggest that both treatments are effective in symptom management over a six-month course, without one being significantly superior to the other in terms of clinical symptom resolution.

Gastrointestinal Adverse Effects
Nausea and dry mouth were reported more frequently in the Duloxetine group, with nausea occurring in 25% of patients compared to 18% in the Pregabalin group. Similarly, dry mouth was twice as prevalent in the Duloxetine group (10% vs. 5%).
Constipation and diarrhea were more balanced between the groups, with Pregabalin showing slightly higher rates (4% vs. 2% for constipation and 3% vs. 1% for diarrhea), although these differences were minor and not clinically alarming.
Central Nervous System (CNS) Effects Dizziness was notably more frequent in Duloxetine users (12%) than Pregabalin users (6%), indicating a potential advantage of Pregabalin in terms of CNS tolerability. Sedation was reported equally in both groups (5%).

Overall Tolerability
A higher proportion of patients in the Pregabalin group (49%) reported no side effects compared to the Duloxetine group (45%), further supporting the favorable tolerability profile of Pregabalin.
Serious Adverse Events

Importantly, no serious adverse events or treatment discontinuations due to ADRs were observed in either group. Liver and renal function markers remained within normal limits, affirming the biochemical safety of both medications.

Although both Duloxetine and Pregabalin were generally well tolerated, Pregabalin exhibited a slightly superior safety profile, particularly with regard to gastrointestinal and CNS-related adverse effects. The higher incidence of nausea, dry mouth, and dizziness in the Duloxetine group may influence clinical decision-making, especially in patients who are sensitive to these side effects. Nevertheless, both medications remain viable options for managing diabetic peripheral neuropathy when tailored to individual patient tolerability.

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