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Original Article

Comparison between the Efficacy of Duloxetine and Amitriptyline in the Management of Painful Diabetic Peripheral Neuropathy: A Randomized Control Trial

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Abstract

Objective: To compare the efficacy of duloxetine and amitriptyline in reducing pain based on VAS in patients with diabetic distal painful neuropathy and to compare the safety profile in terms of fewer adverse effects.

Methods: This Randomized control trial was done at Mayo Hospital Lahore for a duration of 6 months following ethical approval. After obtaining IRB approval and meeting the inclusion criteria, 106 patients were selected and divided into two groups; A and B, and given duloxetine and amitriptyline respectively. Pain assessment was done in both groups using the VAS score system at 3, 6 and 12 weeks and adverse effects were documented based on subjective assessment by the patients.

Results: Duloxetine resulted in a reduced intensity from a mean of 3.91 ± 0.08 to 1.79 ± 0.06 while amitriptyline resulted in decrease in pain from 3.89 ± 0.06 to 2.45 ± 0.06 ($p<0.05$). Patients taking duloxetine reported fewer side effects as compared to amitriptyline.

Conclusion: Duloxetine has better efficacy in treating painful diabetic peripheral neuropathy both in terms of pain management and fewer side effects.

Keywords: Peripheral neuropathy, Duloxetine, Amitriptyline, Randomized Control Trial, Diabetes Mellitus, Efficacy, Safety Profile.

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Introduction

Peripheral neuropathy is a well-known complication of diabetes[1]. Among the neuropathies, Distal Symmetrical Peripheral Neuropathy [DSPN] is the most prevalent, followed by mono-neuropathies, radiculopathies and treatment induced neuropathies. It presents as burning, electric shock like, aching and lancinating pain starting distally from the feet and then progressing upwards to involve the upper limbs proximally in a glove and stocking pattern. In type 2 and type 1 diabetes, the occurrence of diabetic neuropathy varies ranging from 13% to 51% and 8% to 63% respectively. Overall, the prevalence of diabetic sensorimotor polyneuropathy ranges from 20% to 30%.[2]

While the complete etiology of diabetic sensorimotor polyneuropathy remains incompletely understood in the existing literature, several factors crucial to the pathogenesis have been identified. These factors encompass micro vascular insufficiency, advancing age, duration of diabetes, poorly controlled hypertension, oxidative stress and glycemic regulation.[3]

The pharmacologic therapies used for the treatment of DSPN include anticonvulsants, selective serotonin reuptake inhibitors, tricyclic antidepressants and norepinephrine reuptake inhibitors.[3] The first line drugs include pregabalin, duloxetine and amitriptyline.[4] Previous studies indicated that both duloxetine and amitriptyline are equally effective in treating DSPN.[5] However a study by Javeed et al., demonstrated that duloxetine is more effective as compared to amitriptyline.[6]

Despite the common use, there's a lack of direct comparative data between the medications. Understanding their relative efficacy can guide evidence-based treatment decisions and potentially improve patient outcome. Both duloxetine and amitriptyline have different mechanisms of actions, and elucidating their comparative efficacy may provide insights to their analgesic properties. Additionally, assessing adverse effects is crucial for informed treatment selection and patient adherence. Findings from this study can inform clinical practice guidelines and optimize personalized management strategies for patients with painful diabetic polyneuropathy, ultimately enhancing overall treatment outcomes and patient well-being.

Methods

After taking approval from the Institutional Review Board (IRB), a randomized control trial was conducted in Mayo Hospital, Lahore for a period of 6 months extending following ethical approval. A total of 106 patients between the ages of 25 and 65, from either gender, with any level of glycemic control and suffering from DSPN who were not taking any medi-cation previously were selected for the study. Pregnant patients, patients who were previously been taking duloxetine or amitriptyline for any cause within the last three months were excluded from the study. Also, patients diagnosed with IHD or arrhythmias and those having any identifiable causes of painful peripheral neuropathy were also excluded.

All participants were assigned to two groups either Group A or Group B by using lottery method in a ratio of 1:1. After taking written consent from each participant, detailed history and examination was conducted and a pretreatment assessment of the severity of pain was made using the VAS scale and confirmed by using conventional electrophysiological studies.

Group A was prescribed Duloxetine 20mg and was increased weekly till maximum tolerable dose of 120mg while Group B was started on Amitriptyline 25mg increasing weekly till maximum dose tolerable upto 75mg. The participants were advised to take the medication at bedtime and a diary was provided to each participant for maintaining record of drug intake and the incidence of side effects including constipation, nausea, somnolence, increased appetite, anorexia, dry mouth, dizziness and sweating. The participants were followed up at 3, 6 and 12 weeks.

Results

The overall demographics included 106 patients in age group with mean age of 55.65 ± 7 in group A and 53.88±6.44 in group B. Both groups included approximately equal gender distribution. Moreover, the BMI, Blood glucose level and serum HbA1c were also assessed and tabulated in Table 4.1 which showed that BMI, Fasting plasma glucose levels and HBA1C were not statistically different in both the groups.

Table 1: *Comparison of demographic characteristics*

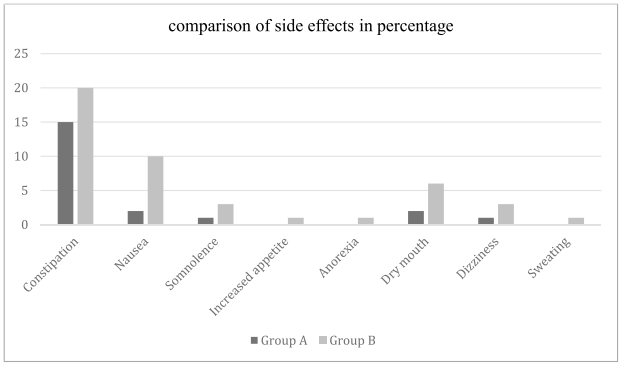
Characteristics	Group A (Duloxetine) Mean ± SD	Group B (Amitriptyline) Mean ± SD
Participants(n)	53	53
Age(years)	55.65 ± 7	53.88 ± 6.44
BMI(Kg/m^2)	24.66 ± 3.25	23.84 ± 3.40
Fasting plasma Glucose (mg %)	178.11 ± 33.82	176.46 ± 9.53
HbA1c	7.48 ± 1.78	7.09 ± 1.11

All the patients were studied for the presence of risk factors and related co–morbidities. There were 62.2% patients who were having hypertension and it was the most common risk factor found in our population and diabetes as the second most common risk factor in 44.4%. The results of the study indicate that the use of both drugs resulted in a significant decrease in pain from the baseline with a p-value of less than 0.05.

Table 2: *Comparison of VAS score for pain assessment*

Follow up	Group A	Group B
Baseline	3.91±0.08	3.89±0.06
Week 3	3.15±0.09	3.21±0.06
Week 6	2.45±0.12	2.84±0.01
Week 12	1.79±0.06	2.45±0.06

The results of the study show that Group A participants who were taking Duloxetine reported fewer side effects as compared to Group B participants taking Amitriptyline.



Discussion

Diabetes related peripheral neuropathy significantly impairs physical functioning rendering it a debilitating condition with widespread prevalence among its manifestations. Painful diabetic peripheral neuropathy stands

out as a challenging neuropathic pain syndrome.[7] Currently, only pain management and glucose control are effective treatments; nevertheless, they do not stop nerve degeneration.[8] The absence of a medication capable or universally eradicating pain or halting nerve degeneration underscores the multifaceted nature of neuropathic pain emergence and propagation.

High levels of evidence support the use of medications such as opioids, topical preparations, anticonvulsants and antidepressants for reducing pain in diabetic patients. Despite this, the FDA has sanctioned two medications, duloxetine and pregabalin, for addressing diabetic peripheral neuropathic pain.[9] In a study by Goldstein et al., a 12-week trial of duloxetine 60mg/d showed statistically significant higher improvement on the pain score compared with placebo. In the therapy of diabetic peripheral neuropathic pain, duloxetine at 60 and 120 mg/d was both safe and efficacious (Goldstein et al., 2005) which was consistent with the findings of our study.[10] In a study by Ramirez et al, Amitriptyline 50 mg/day may enhance motor and sensory nerve conduction velocity and subjective neuropathy symptoms, according to analysis of data from six clinical trials.[11] In a study performed by Kaur et al., comparing the therapeutic advantages of amitriptyline and duloxetine for patients with peripheral diabetic neuropathy results were consistent with our findings. Duloxetine showcased superior clinical outcome compared to amitriptyline coupled with fewer reported side effects.[12]

The most often reported side effects were dry mouth, fatigue, constipation and nausea. Because it alters the urethral striated sphincter muscle's resting tone and contraction, duloxetine is beneficial in treating stress incontinence. Urinary hesitancy has not been documented in studies or clinical trials of duloxetine for depression.[13] Another recent investigation affirms the efficacy of both antidepressants in managing fibromyalgia, albeit with variations depending on the individual patient's symptoms and characteristics.[14] Recent research has reinforced these findings, demonstrating a statistically significant contrast between the cohorts. Among Group A participants, 62% exhibited improvement following therapy, in contrast to Group B individuals, where the improvement rate stood at 35%.

Thus, Duloxetine is better as compared of Amitriptyline both, in terms of pain relief and fewer risk of side effects. However, the limitations of this study include small sample size and a single hospital setting. More studies need to be conducted to see the efficacy of drugs in patients having comorbidities and taking other medications to account for potential drug interactions.

Conclusion

The study highlights duloxetine as a more effective and tolerable treatment option compared to amitriptyline for managing diabetic neuropathy, offering superior pain reduction and fewer adverse effects, thereby advocating for its consideration as a primary therapeutic agent in clinical practice.

Ethical Approval: The IRB/EC approved this study via letter no. 324/RC/KEMU dated 18/05/2024.

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Authors' Contribution

GM: Conception
IA, MH: Design of the work
SB, MH: Data acquisition, analysis, or interpretation
GM, IA, MH: Draft the work
SB, MH: Review critically for important intellectual content
GM, IA, SB, MH, MH: Approve the version to be published
GM, IA, SB, MH, MH: Agree to be accountable for all aspects of the work

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