

ORIGINAL ARTICLE

Management of Diabetic Neuropathy: A Comparison of Duloxetine with Amitriptyline

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ABSTRACT

Objective: To evaluate the pain-relieving effects of duloxetine vs those of amitriptyline in the treatment of diabetic neuropathy.**Methodology:** In this randomized trial control, 150 cases of diabetic neuropathy by using convenient sampling technique from Medical Department of Madinah Teaching Hospital, Faisalabad were enrolled and divided in 2 equal groups randomly. Group A was assigned to (Duloxetine) and B assigned to (Amitriptyline). Patients received the trial drug in the morning with water for 6 weeks. Group A got 60 mg of Duloxetine and Group B 75 mg of amitriptyline. VAS pain rating. Patient consultations included a diary card. Patients recorded daily improvements on a visual analogue scale for the first three weeks. We administered three weeks of medicine and arranged an examination in week 6. When pain levels were 50% lower than baseline, we rated them as reduced. Patients were phoned.**Results:** The mean age was 46.19±6.39 years. 41(54.67%) of Group-A and 39(52%) of Group-B were male, whereas 34(45.33%) and 36(48%) were female. Both groups' mean VAS pain ratings were 1.48±0.50; $p = 0.746$ shows no difference. Group-A (0.48±0.50) and Group-B (0.92±0.69) vary significantly ($p=0.0001$). Group-A (52%) and Group-B (28%) were effectively treated after 6 weeks, $p=0.002$.**Conclusion:** Our research shows that duloxetine is superior to amitriptyline for the management of diabetic neuropathy, especially in terms of minimising the frequency with which patients report experiencing pain.**Keywords:** Diabetic neuropathy, management, duloxetine, amitriptyline, efficacy

INTRODUCTION

The prevalence of type 2 diabetes mellitus (DM) is staggering; it is a worldwide epidemic.¹ Both financial security and quality of life are significantly impacted by diabetes and its complications.² As the disease progresses, it can cause issues in a wide variety of organs, which doctors classify as either macrovascular or microvascular.

Commonly associated with diabetes is a condition known as diabetic peripheral neuropathy (DPN). As defined by the American Diabetes Association, DPN occurs "after other causes of peripheral nerve injury in diabetic individuals have been excluded."³ Diabetic complications may include heart disease and stroke (CVD). One study found that diabetics had a twofold higher chance of developing cardiovascular disease, particularly ACS and heart failure (HF).⁴

The prevalence of DPN has presented significant challenges for global health budgets. The significant health costs caused by DPN are a global problem that must be effectively managed. Amputations are more likely to become necessary because of neuropathy-related foot ulcers and infections. People with diabetes have an increased risk of amputation.⁵ Diabetic neuropathy can progress slowly over time, and there is a weak correlation between the severity of the underlying pathology and the emergence of clinical symptoms. It has been suggested that primary care settings become more involved in the prevention and early diagnosis of DPN as the prevalence of type 2 diabetes mellitus continues to rise.⁶

Antiglycemic medications and dietary management both play a crucial part in the preventive and management measures for DPN, which generally centre on glycemic control as the primary focus. The development of DPN can be delayed with the proper control of risk factors such as hypertension, hypercholesterolemia, and hyperglycemia.⁷ Despite this, even with adequate treatment of these risk variables, approximately forty percent of individuals still develop DPN.⁸⁻⁹

There are a number of treatments available to alleviate the symptoms of DPN; however, there is no treatment plan that can be identified as stopping or slowing the progression of the disease. The treatment choices include into two major categories: those that include the use of pharmaceuticals and those that involve the use of non-pharmacological or topical techniques. Antidepressants and

gabapentinoid antiepileptics are examples of the former category of medications. These medications have been well researched, and their effectiveness in reducing symptoms has been demonstrated. Numerous nutritional supplements, such as benfotiamine and alpha-lipoic acid, topical therapies (capsaicin, lidocaine patch) and neuromodulation treatments are examples of non-pharmacological or topical therapeutic approaches. The therapies that fall within this varied category are not properly researched or shown no significant effectiveness, and due to this reason having a low rate of clinical adoption. There have been a number of studies conducted on various treatment methods, and the results have indicated that they have the potential to lessen the severity of DPN.¹⁰

It has been suggested that tricyclic antidepressants (TCAs) such as amitriptyline be used initially in the treatment of neuropathic pain. It is theorised that they exert their effects by blocking the reuptake of norepinephrine and/or serotonin in the brain. While alpha-adrenergic blockade and sodium channel effect are two putative mechanisms of action, antagonism of the NMDA-receptor is another.¹¹

Both duloxetine hydrochloride (duloxetine) and pregabalin are presently approved by the FDA for the management of chronic peripheral neuropathic pain.¹² Its function is to regulate the blocking of reuptake of serotonin and norepinephrine.¹³

Antidepressants like duloxetine and amitriptyline are often prescribed to patients suffering from fibromyalgia. There is no consensus among the published systematic reviews on which medication is more efficient while also being safer.

In this study, a comparison will be made between the clinical benefits of duloxetine for patients with DPN and the benefits of amitriptyline for these patients. Because of this, we will be able to adapt the treatment for this prevalent condition, which will ultimately result in improved patient care.

METHODOLOGY

In this randomized trial control, 150 cases of diabetic neuropathy by using convenient sampling technique from Medical Department of Madinah Teaching Hospital, Faisalabad were enrolled and divided in 2 equal groups randomly. Group A and B. Patients received the trial drug in the morning with water for 6 weeks. In group A cases got 60 mg of Duloxetine and group B 75 mg of

amitriptyline. Baseline VAS pain rating was recorded. Patient consultations included a diary card and advised to recorded daily improvements on a visual analogue scale for the first three weeks. We administered three weeks of medicine and arranged an examination. When pain levels were 50% lower than baseline, we rated them as reduced (efficacy). Patients were followed up through phone call and instructed to take the medication once daily, routine walk, with a full glass of water for up to 6 weeks. A VAS pain rating after 6 weeks was obtained. Each client was handed a diary card to keep track of their thoughts and feelings throughout the followup including symptoms, any improvements in symptom severity as measured by a visual analogue scale. After the first three weeks, we prescribed another three weeks' duration and advised to come back for another examination in week 6. The pain scores were recorded and recorded efficacy i.e. decrease in pain by 50% from their baseline. Telephone interactions with patients were maintained for the purpose of following up with them. Age, as well as the VAS score at both baseline and 6 weeks, were used to determine means and standard deviations. Gender and effectiveness frequencies and percentages were computed. Effectiveness between the two groups was compared using the Chi-Square test. The cutoff for significance was set at a p value of less than 0.05. The 20th edition of SPSS was used for all the statistical processing here.

RESULTS

In this sample, we found that the average age was 46.19 ± 6.39 years. According to the gender breakdown of the patients, there were 41 men (54.67%) in Group-A and 39 females (52.6%) in Group-B. Of the female patients, there were 34 (45.33%) in Group-A and 36 (48.33%) in Group-B.

There was no statistically significant difference between the two groups, with the mean pain score on the VAS being 1.48 ± 0.50 in Group-A and 1.51 ± 0.52 in Group-B ($p=0.746$). There was a statistically significant difference between the two groups after 6 weeks of therapy, with the mean pain score being 0.48 ± 0.50 in Group-A and 0.92 ± 0.69 in Group-B ($p0.0001$). (Table 1)

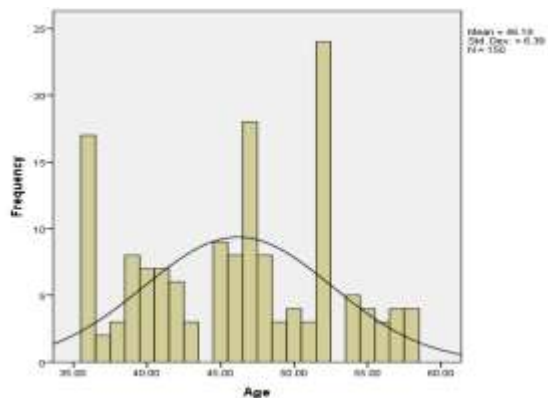


Fig. 1: Distribution of cases according to age

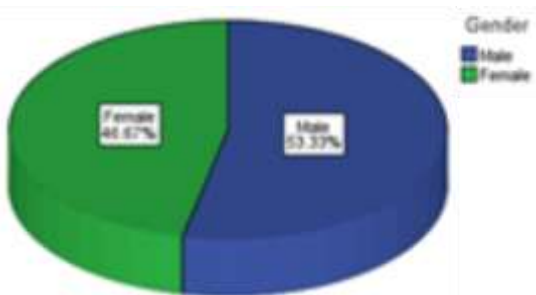


Fig. 2: Distribution of cases according to gender

Table 1: Comparison of Mean Pain Score in both Groups (n=150)

VAS	Group-A (n=75)	Group-B (n=75)	P value
At baseline	1.48±0.50	1.51±0.52	0.746
After 6 weeks of treatment	0.48±0.50	0.92±0.69	0.0001

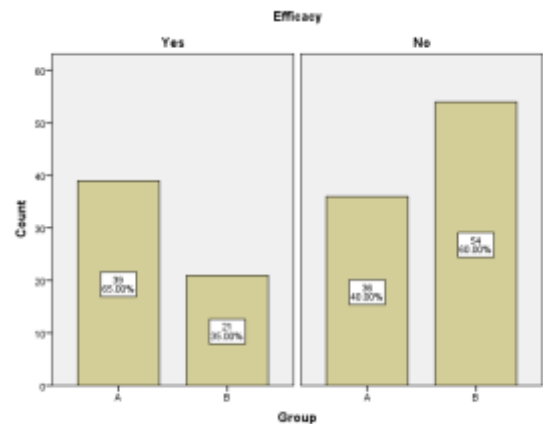


Fig. 3: Comparison of efficacy in both groups

DISCUSSION

Examples of neuropathic pain resulting from central nervous system or peripheral nervous system injury include painful diabetic neuropathy (PDN), postherpetic neuralgia (PHN), and surgery. In short, it wreaks havoc on people's daily lives.¹⁴ Some persons with neuropathic pain clearly respond to treatment, while others do not.¹⁵ Medication options for neuropathic pain include antidepressants (such as SSRIs or SNRIs), antiepileptics (such as valproate, carbamazepine, gabapentin, pregabalin), opioids (such as morphine or codeine), various analgesics, a topical lidocaine patch, and topical capsaicin. There has been a lot of study done to evaluate the validity of these claims.⁶

In this study, a comparison was made between the clinical benefits of duloxetine for patients with DPN and the benefits of amitriptyline for these patients. Because of this, we may be able to adapt the treatment for this prevalent condition, which may ultimately result in improved patient care.

In a prior trial with comparable results, we found that 59% of patients treated with duloxetine had pain relief.¹⁷ In yet another research investigation, 41.4% of amitriptyline-treated individuals had pain relief.¹⁸

There were fewer withdrawals from prior trials due to adverse events while using 60 mg of duloxetine compared to 120 mg. The most often reported unwanted effects included nausea, tiredness, constipation, weight loss, and dry mouth. Duloxetine is effective in treating stress incontinence because it modifies the resting tone and contraction of the urethral striated sphincter muscle. Research and clinical trials of duloxetine for depression did not report any cases of urinary hesitancy.¹⁹⁻²⁰

Another recent study confirms that both antidepressants, though to varying degrees depending on the patient's symptoms and profile, are useful in treating fibromyalgia.²¹ A recent research corroborated these findings by revealing a statistically significant difference between the two groups, with 62% (n=62) of Group-A patients improving after treatment compared to 35% (n=35) of Group-B patients improving. The pain-relieving effects of duloxetine were found to be significantly greater than those of amitriptyline in individuals with diabetic neuropathy.²²

CONCLUSION

In the treatment of diabetic neuropathy, we observed that duloxetine is more effective than amitriptyline, specifically in reducing the number of times patients suffer discomfort.

REFERENCES

1. The country report, the IDF Atlas 2015 - Saudi Arabia. International Diabetes Federation. Accessed: December 13, 2016: <http://reports.instantatlas.com/report/view/846e76122b5f476fa6ef09471965aedd>
2. Prajapati A, Kothari N, Ganguly B: Economic burden of diabetes mellitus in western India- a hospital-based study. *Int J Basic Clin Pharmacology* 2016;21:2572-80.
3. Diabetes country profile. Saudi Arabia. WHO. (2016):. http://www.who.int/diabetes/country-profiles/sau_en.pdf?ua=1.
4. Thompson A, Di Angelantonio E, Gao P, Sarwar N: Diabetes mellitus, fasting glucose, and risk of causespecific death. *N Engl J Med* 2011;13:829-841.
5. Begum S, Venkatesan M, Ganapathy K. Foot care practices, its barriers and risk for peripheral neuropathy among diabetic patients attending medical college in rural Puducherry. *Int J Community Med Public Health* 2018;6:203-7.
6. Mathiyalagen P, Kanagasabapathy S, Kadar Z. Prevalence and Determinants of Peripheral Neuropathy Among Adult Type II Diabetes Mellitus Patients Attending a Non-communicable Disease Clinic in Rural South India. *Cureus* 2021;13(6): e15493.
7. Miranda-Massari JR, Gonzalez MJ, Jimenez FJ, Allende-Vigo MZ, Duconge J: Metabolic correction in the management of diabetic peripheral neuropathy: improving clinical results beyond symptom control. *Curr Clin Pharmacol* 2011;6:260-73.
8. Callaghan B, Feldman E: The metabolic syndrome and neuropathy: therapeutic challenges and opportunities. *Ann Neurol*. 2013;74:397-403.
9. Juster-Switlyk K, Smith AG: Updates in diabetic peripheral neuropathy. *F1000 Research* 2016;5:738.
10. Zaheer A, Zaheer F, Saeed H. A Review of Alternative Treatment Options in Diabetic Polyneuropathy. *Cureus* 2021;13(4): e14600.
11. Zillox L, Russell JW. Treatment of diabetic sensory polyneuropathy. *Curr Treat Options Neurol* 2011;13:143-59.
12. Zillox L, Russel JW. Maintaining efficacy in the treatment of diabetic peripheral neuropathic pain: role of duloxetine. *Diabetes Metab Syndde Obes*. 2010;3:7-17
13. Wright A, Luedtke KE, Van DenBerg C. Duloxetine in the treatment of chronic pain due to fibromyalgia and diabetic neuropathy. *J Pain Res*. 2011;4:1-10
14. Jensen MP, Chodroff MJ, Dworkin RH. The impact of neuropathic pain on health-related quality of life: review and implications. *Neurology* 2007;68:1178-82.
15. McQuay HJ, Tramer M, Nye BA, Carroll D, Wiffen PJ, Moore RA: A systematic review of antidepressants in neuropathic pain. *Pain* 1996;68:217-27.
16. Khaliq W, Alam S, Puri N. Topical lidocaine for the treatment of postherpetic neuralgia. *Cochrane Database Syst Rev* 2007; 2:CD004846.
17. Kour H. Hota D, Bhansali A, Dutta P, Bansal D, Chakrabarti A. A comparative evaluation of amitriptyline and duloxetine in painful diabetic neuropathy. *Diabetes Care* 2011;34:818-22.
18. Shabir B, Shafi F, Mahboob F. Amitriptyline Vs pregabalin in painful diabetic neuropathy: a randomized placebo-based study. *Pak J Med Health Sci[Internet]*.2011 Oct-Dec [cited 2011];5(4):(about 4p)
19. Ramsey SD, Newton K, Blough D. Incidence, outcomes and cost of foot ulcers in patients with diabetes. *Diabetes Care* 1999;22:382-7.
20. Moulik PK, Mtonga R, Gill GV. Amputation and mortality in new onset diabetic foot ulcers stratified by etiology. *Diabetes Care* 2003;26:491-4.
21. de Farias ÁD, Eberle L, Amador TA, da Silva Dal Pizzol T. Comparing the efficacy and safety of duloxetine and amitriptyline in the treatment of fibromyalgia: overview of systematic reviews. *Adv Rheumatol*. 2020 Jul 8;60(1):35.
22. Javed MA, Alam MA, Maqsood A, Azher A, Arif M, Qayyum A. Comparison of efficacy of duloxetine with amitriptyline in terms of reduction in frequencyof pain in the patients of diabetic neuropathy. *Professional Med J* 2020;27(9):1891-4.