Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/g6r32510

ROLE OF LACOSAMIDE IN DIABETIC NEUROPATHY: AN EXPERIENCE AT TERTIARY CARE HOSPITAL

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Abstract

Introduction: Diabetic neuropathy is a devastating complication that diabetic patients are bound to develop due to the long-term effect of this condition on the nerves, resulting in neuropathic pain. This lack results in many current treatments having either low effectiveness or best Side effects that are all altogether intolerable. A new AED that possesses a unique mechanism of stabilizing inactivated Nav1.7 sodium channels is Lacosamide which has also revealed promising results regarding neuropathic pain treatment.

Objectives: To assess lacosamide's effectiveness, safety, and tolerability over a six-month period in patients with diabetic neuropathy at a Pakistani tertiary care hospital.

Materials and Methods: A prospective observational research including 120 individuals with diabetic neuropathy was carried out between January and June of 2024. At baseline and during routine follow-ups, pain scores were evaluated, and negative effects were tracked.

Results: 78% of patients experienced at least a 50% reduction in neuropathic pain, with lacosamide significantly reducing it by 67%. There was no serious safety issues, and the side effects were minor and temporary.

Conclusion: Diabetic neuropathy can be effectively treated with lacosamide, which has few side effects and provides significant pain relief.

Keywords: Lacosamide, neuropathic pain, diabetic neuropathy, pain control, antiepileptic medications, and sodium channel modulation.

INTRODUCTION

Lacosamide is a new antiepileptic drug that has recently been considered a potential candidate for diabetic neuropathy treatment because of the high prevalence of the latter in diabetic patients. Diabetic neuropathy is a chronic disease that affects nerves in the body due to high blood sugar levels it affects the sensory nerves of the body and evokes pain and dysfunction of the autonomic nerves. Thus,

managing neuropathic pain is always a problem because existing treatments do not produce sufficient pain relief and have side effects. In this regard, lacosamide has been identified as a novel drug, the mechanism of action being the specific slow inactivation of voltage-gated sodium channels, which contributes to stabilizing neuronal hyperexcitability. A review of case reports from tertiary care hospitals has indicated that this drug may be useful in managing diabetic neuropathy pain with a relatively safe profile meaning that lacosamide should be considered a useful addition to pain management therapies (3).

It has been reported that lacosamide is a more effective antiseizure agent compared to other neuropathic pain medications such as pregabalin as well as gabapentin. A clinical study presented a head-to-head comparison of these agents revealed that lacosamide helped decrease the pain level in patients with diabetic neuropathy without the side effects associated with its usage like that of pregabalin (2). This is particularly desirable at this time to avoid the cognitive side effects that are prevalent in most neuropathy treatments currently. In addition, a placebo-controlled 'double-blind' clinical trial on the extent of efficacy of lacosamide in peripheral neuropathic disorders such as diabetic neuropathy revealed the effectiveness of the substance as it helped in decreasing the level of pain and in increasing the functional capacity of the patient (3). These findings offer additional information concerning the applicability of lacosamide in the estimation of neuropathic pain syndrome.

Lacosamide originally received approval for epilepsy therapy, but further research has evaluated its efficacy for usage in pain control. Researchers conducted on the cognitive impact of the drug in epilepsy patients particularly has given evidence about the safety level of the drug. It is different from other antiepileptic medications that have been documented to cause cognitive impairment, lacosamide does not seem to have a direct negative effect on cognition (4). This characteristic is especially useful in the management of diabetic neuropathy because most patients with this condition are elderly men and women with a history of cognitive dysfunction. Furthermore, there are published data concerning the effect of lacosamide in cryptogenic sensory polyneuropathy – the disease, whose pathophysiology is similar to the one observed in diabetic neuropathy – the data on efficacy and safety are positive.

The safety of lacosamide has been also investigated in different configurations of the clinical study. A number of observational studies have suggested that some patient may get symptoms like dizziness, and this may be followed by fatigue and several studies have recommended that these side effects are generally mild, and they do not warrants patient stopping her therapy. Moreover, lacosamide's pharmacokinetic profile is quite suitable for long term use due to the absence of major drug interaction and therefore useful for patients who take many other medications (7). Moreover, the research studies concerning its application in the treatment of refractory epilepsy have evidenced that it has the optimal dose-proportionality which makes it suitable in approaching neuropathic pain states including diabetic neuropathy.

The underlying basis of diabetic neuropathy is multifactorial and includes metabolic, inflammatory as well as vascular factors and their impact on nerves and perception of pain (9). Thus, Lacosamide shows great compatibility in its mechanism of action for neuropathic pain as it increases slow sodium channel inactivation. It works by adjusting the sodium channels to lower the excitability of injured nerves to bring down the pain and enhance the working of the nerves (10). This is different from the conventional treatments for neuropathic pain which normally rely on the modulation of calcium channels or the central nervous system where the side effects are usually sedation and dizziness.

However, potential drawbacks of lacosamide has been reported because of its impact on patients' cardiovascular systems. Literature which examined the effects of intravenous lacosamide on cardiac profile indicates that the drug only slightly increases PR interval and poses minimal risk to patients if they do not have cardiac disease (11). This information is very relevant in the epidemiology of diabetic neuropathy since the majority of patients with diabetes have cardiovascular complications. Consequently, when administering lacosamide to patients with these comorbidities, extra caution in patient selection and dose titration should be exercised. Other chronic pain disorders have also shown the wider use of lacosamide for neuropathic pain situations. The results of TMD clinical trials with a history of neuropathic pain treatment have stressed the possibility of lacosamide in the context of

chronic pain disorders, excluded from diabetic neuropathy (12). Further, we are also discussing non-gabapentinoid anticonvulsants and muscle relaxants to acknowledge the efficacy of lacosamide in the present management of acute pain control (13). This increases its value as neuropathic pain medication because of its probable efficacy in multiple pain remedies.

In addition, it is revealed that the efficacy of lacosamide in refractory status epilepticus has been established from hospital-based research and it is useful in other neurological disorders related to IGE and aberrant neuronal excitability (14). These observations further enhance the understanding of lacosamide as an agent with additional potential uses within the clinical practice. Further researches on back and neck pain also indicate that lacosamide could also be effective in the management of other types of chronic neuropathic pains besides diabetic neuropathy. Such evidence makes lacosamide an effective option in cases where a patient does not respond well to other drugs. Lastly, lacosamide is involved in the management of diabetic neuropathy has been proved by a growing study and more practical literature from tertiary care hospitals. This makes it suitable for patients with diabetic neuropathy due to its effectiveness in treating neuropathic pain, and good cerebral cardiac safety profile. However, large-scale, long-term studies should be done to explore the administration methods dose, and efficacy in high-risk persons or over the long term, body on ultra wave therapy and also in comparing the effectiveness of neuropathic pain treatments.

Objective: This study aims to assess the safety and effectiveness of lacosamide in treating pain associated with diabetic neuropathy to improve patient outcomes in a Pakistani tertiary care facility.

MATERIALS AND METHODS

Study Design: This prospective observational study was carried out at a tertiary care hospital to assess the safety and efficacy of lacosamide in patients with diabetic neuropathy.

Study setting: The study was conducted at the multiple centers includjing Department of Neurology, Bashir Hospital Sialkot, Pakistan and Sughra Shafi Medical Complex, Narowal, Pakistan.

Duration of the study: The study was conducted over six months, from January 2024 to June 2024.

Inclusion Criteria:

Patients who have clinical manifestations of diabetic neuropathy with relevant electrophysiological changes and are aged 18 years and above were included. Patients from 18 to 70 years of age with moderate to severe neuropathic pain for at least six months who have used other neuropathic pain treatments with suboptimal results were allowed. In the study, only patients who consented to participate and who also had a controlled blood sugar level for a period not less than three months were recruited. In the current study, only patients who were not on any contra-indications for the applied medication, and who agreed to complete follow-up assessments were recruited.

Exclusion Criteria

The excluded conditions included a history of epilepsy, severe renal or hepatic impairment, cardiac arrhythmias, or psychiatric disorders. The patients with a history of hypersensitivity to lacosamide and those receiving medications that may cause severe interaction with lacosamide were excluded from the study. Women currently or who plan to become pregnant, breastfeeding mothers, and patients with any of the malignant tumour diseases or major dysfunction of the central nervous system that could lead to noncompliance with the prescribed treatment regimens were not enrolled. In this study, it is also important not to include participants with bad diabetes control or other tertiary diseases that may affect the overall result of the study.

Methods

The participants were recruited from outpatient clinics by the inclusion criteria after receiving informed consent. For the cross-sectional assessment of the neuropathic pain intensity, a standardised NPS was employed and completed at baseline. Lacosamide was given once daily in a gradually increased dosage starting from 100 mg per day and up to 400 mg per day depending on the effectiveness and side effects reported by the subject. Every 2 weeks during the six months under study, the patients were followed up. This occurred until resolution of pain, functional improvement or onset of adverse effects unlikely to be related to the study intervention, whichever occurred first

was observed at each visit. Some of the other parameters included glycemic control medication compliance and possible drug interactions. The status of nerve function was assessed before the study and at the end of the study using electrophysiological tests. The patient self-reported outcomes based on the Oswestry Low Back Pain Disability Score, Pittsburgh Sleep Quality Index, and Euro Quality of Life Five-Dimension questionnaire. Specific safety measures consisted of checking for dizziness, cognitive impairment, and changes in cardiovascular rate. Data were analyzed using Statistical Package for Social Sciences (SPSS) version 26, any statistician value of less than 0.05 was considered statistically significant.

RESULTS

The study included 120 participants with a diagnosis of diabetic neuropathy. There were 42% female participants and 58% male participants, with an average age of 56.8 ± 9.5 years. On a 10-point scale, the Neuropathic Pain Scale (NPS), which measures the baseline level of neuropathic pain, ranged from 5 to 9. In the 6-month follow-up period, lacosamide medication led to a significant decrease in pain scores.

Table 1: Baseline Characteristics of Patients

Characteristic	Value (n = 120)
Mean Age (years)	56.8 ± 9.5
Gender (Male/Female)	58% / 42%
Mean Diabetes Duration (years)	12.3 ± 6.2
Baseline Pain Score (NPS)	7.5 ± 1.2
Comorbidities (Hypertension)	65%
Comorbidities (Cardiovascular Disease)	38%

Pain scores decreased by an average of 1.8 points at Week 4, and they improved much more in Weeks 8 and 12 (2.9 and 4.2 points, respectively). By the conclusion of Month 6, 78% of patients said their pain had decreased by at least 50%. Functional gains were also noted, with mobility scores and everyday activities showing notable improvements ($p < 0.05$) .

Table 2: Pain Reduction Over 6-Month Period

Timepoint	Mean Pain Score (NPS)	Percentage Reduction (%)
Baseline	7.5 ± 1.2	-
Week 4	5.7 ± 1.1	24%
Week 8	4.6 ± 1.0	39%
Week 12	3.3 ± 0.9	56%
Month 6	2.5 ± 0.8	67%

No serious side effects were recorded, although safety evaluations indicated minor nausea (8%), fatigue (10%), and dizziness (15%). Merely 5 patients (4.2%) stopped their medication because of adverse consequences. During the investigation, no notable cardiac abnormalities or cognitive deficits were observed.

Table 3: Adverse Effects of Lacosamide

Adverse Effect	Frequency (%)
Dizziness	15%
Fatigue	10%
Nausea	8%
Cognitive Issues	4%
Cardiac Issues	2%
Discontinuation Due to Side Effects	4.2%

In patients with diabetic neuropathy, lacosamide was generally well-tolerated and successful in lowering neuropathic pain and improving quality of life. Lacosamide is a viable therapy choice because most patients reported significant pain alleviation with few side effects.

DISCUSSION

Diabetic neuropathy is one of the complications of diabetes that affects a large population of patients with diabetes and is also a significant factor that reduces the quality of life of patients with this disease. Managing neuropathic pain is still a difficult task for clinicians and patients since to date neuropathic pain has a very complex character and current treatment possibilities are not effective. A newer antiepileptic drug, Lacosamide has good efficacy in various neuropathic pain states including diabetic neuropathy. This study assessed its efficacy and side effects in patients with diabetic neuropathies in a teaching hospital, in Pakistan which will prove beneficial in determining its role as a therapeutic agent. According to the findings of this study, lacosamide is effective in the management of diabetic neuropathy, by altering the intensity of neuropathic pain in the patients by 67 % after the six months of their treatment regimen. This finding supports other studies that have reported that lacosamide has a neuro-modulating action through the prolongation of the slow inactivated state of the voltage-gated sodium channels. In comparison with other neuropathic pain medications, including gabapentinoids or tricyclic antidepressants with widespread central nervous system activity, lacosamide's specific action reduces sedation and cognitive issue side effects, thus being more suitable for the long-term (1).

Several clinical trials, comparing lacosamide head to head to pregabalin have revealed a similar efficacy for this drug in managing neuropathic pain but with less side effects (2). In this study, moderate to good pain reduction was seen in 78% of patients and therefore the drug can be said to have good analgesic effects in diabetic neuropathy. Additionally, it has a positive effect on the functional status of patients, such as performing daily tasks and mobility, where notable improvements in physical functioning and sleep have been reported in a long time perspective. These changes has been seen in placebo-controlled studies, which strengthens the body of evidence showing that lacosamide can afford substantial pain reduction in people with diabetic neuropathy (3). One of the benefits of lacosamide witnessed in this study is that the medication was well tolerated. Most of the effects were mild and self-limiting, they included dizziness, occurring in 15% of the patients, fatigue in 10%, and nausea in 8%. However, in the present study, only 4.2% of patients gave up treatment because of adverse effects as compared to those who gave up treatment on other neuropathic pain medications commonly used in clinical practice. They mentioned safety profile was comparable with results from earlier studies, and lacosamide was generally well tolerated in different populations (4). The lack of significant hepatic metabolism and a more precisely defined dose-response relationship implies that the drug is appropriate for patients with multiple conditions and potential for drug-drug interaction (5).

Diabetic neuropathy and the subsequent changes in the perception of pain result from metabolic, vascular, and inflammation of nerves. Hyperglycemia is not only chronic but also induces oxidative stress and mitochondrial dysfunction that results in neuron death that manifests in burning pain, tingling, and numbness (6). Most of the available conventional treatments like tricyclic antidepressants or SSRIs and SNRIs act on the central pain pathways and they come along with side effects such as cognitive impairment, weight gain and cardiovascular complications which mask the use of these drugs in diabetic patients. On the other hand, lacosamide acts selectively on sodium channels which is different from other anti-epileptic drugs Painkillers in this class do not lead to many complications that are found in other pain relievers (7). The safety of lacosamide on cardiovascular has been a matter of concern especially so because many diabetic neuropathy patients have cardiovascular diseases. This effectiveness comes with relative safety though some research has indicated a small effect on PR interval prolongation thereby a concern regarding propellers of increased arrhythmias with this drug (8). Nonetheless, cardiac abnormalities were not detected in this study, while only two per cent of patients had minor cardiac issues that did not warrant stopping treatment. These results are consistent with other trials indicating though potentially having risks with

severe cardiovascular diseases, lacosamide is quite safe for most patients with diabetic neuropathy (9). The effect of the treatment on cognitive function is another significant consideration in neuropathic pain. Most patients with diabetes are already prone to cognitive impairment resulting from microvascular disease and chronic inflammation. First-generation antiepileptic drugs like valproate and carbamazepine has established side effects on cognitive function and therefore pose a significant challenge in the management of neuropathic pain condition. In contrast, lacosamide has a clinically insignificant effect on cognition which makes it suitable for elderly patients or patients with pre-existing cognitive disease(11). This is in line with the study since no Some of the manifested symptoms of cognitive impairments were noticeable during treatment in one or two sessions in the six months. Treatment of pain associated with diabetic neuropathy involves both medication and other techniques that may be used in combination or alone. Despite the impressive pain relief produced by lacosamide in this study, other treatments that may include physical therapy, glycemic control, and lifestyle changes must be applied to improve a patient's quality of life. Some authors has shown that lacosamide which when taken together with other neuropathic pain medications such as gabapentin or duloxetine will increase the analgesic effect and will also lower the dosage required per medication thus preventing side effects. It is possible then, for the next studies to build on the idea of combining treatments to fine-tune therapy for diabetic neuropathy. The results of the present study help to strengthen the list of literature evidence indicating the efficacy and safety of lacosamide in the treatment of diabetic neuropathy. Nevertheless, several limitations need to be mentioned. The study was carried out at one tertiary care hospital the number of patients recruited may be adequate for preliminary analysis but may not truly reflect the general diabetic population. However, the follow-up study lasted for only six months, and therefore, more extended studies are required to determine the effect and benefit of lacosamide in the long run. To overcome these limitations, future studies should include longer and more extensive follow-up and greater patient enrollment, possible in multi-centre studies (13).

Nevertheless, it is important to note that the findings of this study would be helpful towards understanding the effectiveness of lacosamide in managing diabetic neuropathy. A demonstrative safety profile with quantifiable and considerable pain relief and no apparent cognitive side effects support its use in neuropathic pain associated with diabetes. Subsequently, lacosamide may ensure its position within the group of first-line neuropathic drugs and is expected to become a standard treatment for patients who cannot tolerate traditional neuropathic pain treatments. Finally, this study possibly supports the use of lacosamide in diabetic neuropathy patients due to its efficient pain-relieving effects and functional enhancements without considerable side effects. Pharmacological details, side effects, and risks suggest that this drug may be more effective than typical neuropathic pain medicines. This study showed that although more investigations are needed to determine its effectiveness in the long run, Lacosamide has the potential to be the best solution to diabetic neuropathy for patients with chronic neuropathic pains.

CONCLUSION

The evidence in this present study supports the use of lacosamide for the treatment of diabetic neuropathy as it has strong efficacy and moderate tolerance in patients. During the study patients had a 67% reduction in the degree of pain and 78% of patients scored a 50% reduction in their pain level as a minimum. Mobility and daily activity performance were also reported to have significantly improved at the end of the study. Lacosamide was proven to be safe because it did not have severe side effects but just minor effects like dizziness and fatigue that lasted only for a few hours. However, a potential risk issue is that the study did not highlight any cardiovascular or cognitive side effects, which may suggest that the long-term use of the drug is safe for diabetic neuropathy patients. Thus, since lacosamide is a drug with a targeted mechanism of action, a low probability of interaction with other medications commonly used by patients, and good tolerability, it will be effective in treating patients suffering from neuropathic pain. However, to establish the drug's long-term use effects and the interaction of the drug with other drugs, more research should be conducted in the future.

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