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Original Article

Efficacy of Pregabalin with Methylcobalamin in Neuropathic Pain: A study in the Nepalese Population of Eastern Region

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Abstract

Background

Neuropathic pain is a severe condition that is challenging to treat. The objective of this study was to determine the efficacy of a fixed-dose combination of sustained-release pregabalin and methylcobalamin in reducing neuropathic pain in Nepalese patients.

Materials and Methods

This was a prospective, hospital based, observational study. Patients received fixed dose combination of 75 mg sustained-release pregabalin combined with 1500 mcg immediate release methylcobalamin. Data was collected at prefixed interval for pain reduction and associated comorbidities. Pain intensity was measured on a ten-point visual analog scale and sleep quality was measured by Sleep Quality Scale. Data was analysed using appropriate statistical methods.

Results

Out of the total patients, 52% belonged to the age group 39-59 years, with females more than males. Age and gender difference were statistically significant with neuropathic pain. The study also revealed that radiculopathy and diabetic neuropathy were significantly associated with specific age groups. Patients in severe and distressful pain in day 1 have significantly improved to mild (70%) and tolerable (24%) pain by day 14. The mean VAS score showed an overall reduction of 58.75% over 14 days. The comorbidities observed with neuropathy, were diabetes mellitus (42%), hypertension (22%), alcoholism (18%), and smokers (6%). By day 14, 85% and 11% patients reported to have good and excellent sleep quality, respectively, compared to the poor and fair sleep quality assessed on day 1 and day 7.

Conclusion

There was significant improvement in pain and sleep quality with the use of 75 mg pregabalin and 1500 mcg methylcobalamin in patients with neuropathic pain.

Keywords: *Age group, Efficacy, Methylcobalamin, Nepal, Neuropathic Pain, Pregabalin*

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Introduction

Neuropathic pain is caused by dysfunction in the somatosensory nervous system and is characterized by symptoms such as burning, tingling, or shooting pain. It is a significant global health concern, affecting approximately 7–10% of the general population but is expected to increase with aging and survival rates from diseases like diabetes and cancer. The diverse nature of neuropathic pain, affecting both peripheral and central pathways, makes diagnosis and epidemiology challenging. This condition greatly impacts patients' quality of life, causing mobility issues, financial burdens, and emotional distress [1, 2, 4].

The standard analgesics are frequently insufficient, adjuvant medicines such antidepressants and antiepileptics are used. Pregabalin is a well-established antiepileptic medication that reduces neurotransmitter release and modulates calcium channels to reduce pain. By promoting the production of myelin sheaths, methylcobalamin, an active form of vitamin B12, aids in nerve regeneration. Research suggests that they work well together, but there is limited data to support this theory, especially in country like Nepal [3, 4,19].

This study aims to evaluate the efficacy of combining pregabalin and methylcobalamin in managing neuropathic pain in the Nepalese population. It seeks to address gaps in current treatment strategies, providing insights to optimize therapy for better patient outcomes.

Material and Methods

This hospital-based observational prospective study was conducted to evaluate the analgesic efficacy of pregabalin with methylcobalamin in relieving neuropathic pain among outpatients visiting the Department of Orthopaedics at Nobel Medical College and Teaching Hospital, Biratnagar, Nepal. The study took place over six months, from October 2016 to April 2017. Data collection was performed on the 1st, 7th, and 14th days following drug treatment. Ethical approval was obtained from the institutional ethical committee (IRC-NMCTH 27/2016), and informed written consent was secured from each participant before enrolment in the study.

The study included patients diagnosed with neuropathic pain, aged 18 years or older, willing to participate, and able to report pain intensity using the Visual Analog Scale (VAS) [5], and quality of sleep using the Sleep Quality Scale [6,7]. Patients were excluded if they had allergies to pregabalin or methylcobalamin, were pregnant, had a history of drug addiction or abuse, or had significant cardiac, hepatic, or renal insufficiency. Patients unwilling to participate were also excluded.

The sample size for this study was determined using Cochran's formula [25], which considers

$n_o = Z^2 * p * q / e^2$ where,

n_o = sample size,

Z^2 = area under the acceptance region in a normal distribution $(1 - \alpha)$,

e = preferred level of precision,

p = estimated proportion of an attribute that is present in the population [19],

and q = 1- p

Now, n_o =Sample size, Z=1.96, e=0.05, p=0.723 and q =0.277

Since the total population was finite, the sample size was further adjusted using the Modified Cochran Formula for Small Populations.

$n = n_o / [1+\{(n_o-1)/N\}]$

Where n is the sample size and N =150 is the population size.

Based on these calculations, 100 patients of either sex, aged over 18 years and experiencing neuropathic pain from any cause, who visited the Department of Orthopaedics at Nobel Medical College and Teaching Hospital, were selected for this study.

Patients were monitored for two weeks to assess pain severity using the Visual Analogue Scale (VAS) [5], and sleep quality using the Sleep Quality Scale [6,7]. The VAS is a 10 cm scale where pain intensity ranges from 0 (no pain) to 10 (totally disabling pain) as '0' (0-no pain, 2-mild pain, 4-tolerable pain, 6-distressfull pain, 8-severe pain, 10-totally disabling pain). The Sleep Quality Scale is assessed to report their quality of their sleep over the past 24 hours on a 10-point numeric rating scale ranging from 0 ("terrible sleep") to 10 ("excellent sleep"). Socio-demographic data, medical history, and clinical assessments were documented using a structured questionnaire. Primary efficacy outcome measures were pain intensity differences (PID) assessed on VAS at different time point intervals and from the quality of sleep every night using a 10-point numeric rating Sleep Quality Scale started from the day of drug administration with an effective dose. Data was recorded on predesigned proforma, and statistical analysis was performed using SPSS Version 20, with data were expressed as mean, standard deviation (SD), and percentage. The p-value of less than 0.05 was considered statistically significant,

ensuring the reliability of the findings.

Results

Table 1: Demographic Characteristics (N=100)

Patients factors	%	Mean ± Std.	Kolmogorov-Smirnov (Lilliefors Corr.), p value
Age		2.02 ± 0.7	0.26, <.001
18-38	23		
39-59	52		
60-80	25		
Gender		1.44 ± 0.5	0.37, <.001
Male	44		
Female	56		

Table 1 shows that frequent number of patients were diagnosis neuropathy pain found in 39-59 age group (52%) and more predominant gender was female (56%). The chi-square analysis shown that age and gender were statistically significant with diagnosis of neuropathy pain.

Table 2: Diagnosis of Neuropathy pain associate with age group (N=100)

Diagnosis of Neuropathy	Age group 18-38(%)	39-59(%)	<60(%)	p value
Radiculopathy	17%	19%	4%	<.001
Carpel tunnel syndrome	4%	4%	0%	0.085
Diabetic neuropathy	2%	20%	20%	<.001
Herpetic neuralgia	0%	9%	1%	0.036
Total	23%	52%	25%	

Table 2 shows that number of patients with diagnosis of neuropathy pain more in 39-59 age group (52%) and less frequent in 18-38 age group was only 23%. The chi-square analysis shows that radiculopathy and diabetic neuropathy were statistically significant with diagnosis neuropathy pain.

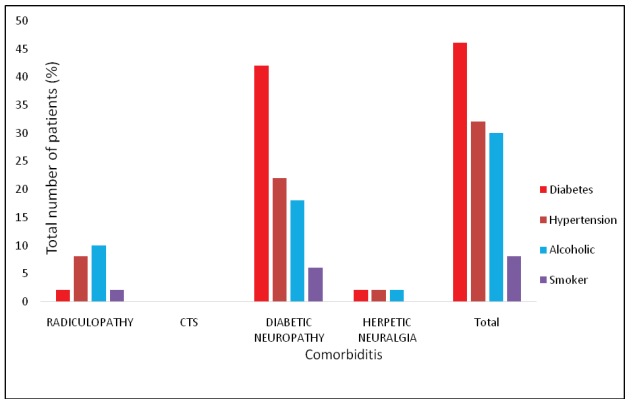

Figure 1: Distribution of comorbidities in various neuropathic pains

Figure 1 shows that a greater number of patients had comorbidities in diabetic neuropathy such as 42% diabetes mellitus, 22% hypertensive, 18% alcoholic and 6% smoking.

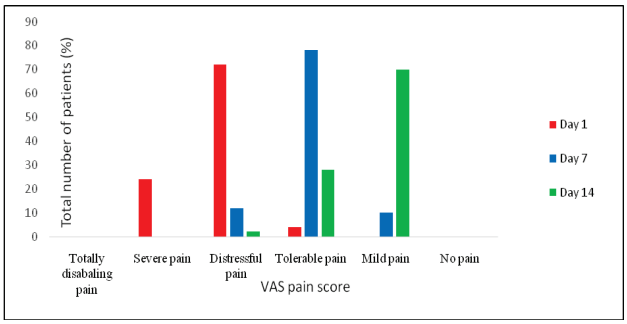

Figure 2: Distribution of pain intensity in two weeks

Figure 2. shows that changes in pain intensity on day 1, day 7 and day 14 where patients in severe and distressful pain in day 1 have significantly improved to mild (70%) and tolerable (24%) pain by day 14 after treatment with the combination of pregabalin along with methylcobalamin.

Table 3: Improvement in pain score over the treatment, compared with baseline

Evaluation day	Total number of patients	Pain score on VAS (Mean ± Std.)	% change
Day 1	100	64 ± 9.85	0
Day 7	100	40.4 ± 9.42	36.87%
Day 14	100	26.4 ± 10.2	58.75%

Table 3 shows that changes in mean VAS pain score at day 1, day 7 and day 14 after treatment with combination of pregabalin along with methylcobalamin. The overall change in pain score was 58.75%.

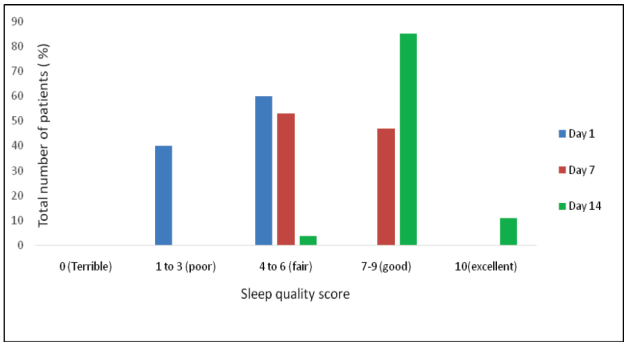

Figure 3: Distribution of sleep quality scores in days

Figure 3 indicates that 85% of patients reported good sleep quality and 11% reported excellent sleep quality by day 14 of treatment, a significant improvement compared to poor and fair sleep quality reported on days 1 and 7.

Discussion

According to number of earlier research, NSAIDs and opioid analgesics don't work well for the majority of neuropathic pain. Chronic use of opioid analgesics carries a long-term risk of habituation. Tricyclic antidepressants (TCAs) frequently result in autonomic side effects such as dry mouth, impaired vision, constipation, and urine retention, as well as problematic cardiovascular side effects like arrhythmias and postural hypotension [8]. The combination of pregabalin and methylcobalamin is important in managing neuropathic pain because it addresses both symptomatic relief and the underlying causes of nerve damage. Pregabalin, via modulating calcium channels in nerve cells, reduces the release of excitatory neurotransmitters like glutamate and substance P. This helps in quick and effective symptomatic relief by decreasing nerve hyperactivity and pain perception. Methylcobalamin is a bioactive form of vitamin B12 that supports nerve repair and regeneration by enhancing myelin sheath production, which is crucial for protecting and repairing damaged nerves. Together, these mechanisms address both immediate pain relief and long-term nerve recovery [9,19]. Studies suggest that combining pregabalin with methylcobalamin results in better pain relief and functional recovery compared to using either drug alone. Methylcobalamin complements pregabalin by not only managing pain but also targeting the underlying neuropathy, making the combination especially effective in conditions like diabetic neuropathy or post-herpetic neuralgia [9-11]. Neuropathic pain often affects daily activities, sleep, and mental health. The combination therapy improves overall quality of life by addressing pain and nerve health, leading to better functional outcomes. When used together, pregabalin and methylcobalamin show a synergistic effect, meaning their combined efficacy is greater than the sum of their individual effects. This synergy is particularly beneficial in chronic conditions where prolonged pain relief and nerve healing are critical. The addition of methylcobalamin may allow for lower doses of pregabalin, reducing the risk of side effects like dizziness, drowsiness, and peripheral edema, while maintaining efficacy. The combination of pregabalin with methylcobalamin is important because it not only offers comprehensive pain relief but also promotes nerve health, making it a superior choice for managing neuropathic pain. By addressing both symptoms and aetiology, it ensures better long-term outcomes for patients [9-13]. In this research, the majority of patients diagnosed as neuropathy pain found in 39-59 age group (52%) and more predominant gender was female (56%). The chi-square analysis shown that age and gender were statistically significant with diagnosis of neuropathy pain.

In previous studies reported that middle-aged individuals (39-59 years) are a significant group affected by neuropathic pain due to lifestyle factors, chronic conditions, and occupational strains. Studies highlight those patients involved in heavy manual work, even within the home, may develop conditions like lumbar neuropathy due to prolonged poor posture or repetitive tasks [14, 4].

In our research, the number of patients with diagnosis of neuropathy pain falls more in 39-59 age group 52% and less frequent in 18-38 age group 23%. The chi-square analysis shows radiculopathy and diabetic neuropathy were statistically significant with diagnosis neuropathy pain. This collaborates with the findings of the earlier research works. These conditions represent common and well-documented causes of neuropathic pain, each with distinct pathophysiological mechanisms [15].

Radiculopathy is a frequent contributor to neuropathic pain, often resulting from nerve root compression or inflammation due to conditions such as herniated discs or spinal stenosis. A study using chi-square analysis showed a significant association between radiculopathy and symptoms of neuropathic pain, such as burning sensations, numbness, and radiating pain [15,16]. Diabetic neuropathy is one of the most common forms of neuropathic pain, affecting up to 50% of individuals with diabetes. Chi-square statistical testing has been utilized to link diabetic neuropathy strongly with neuropathic pain diagnoses, particularly in middle-aged and elderly populations. This relationship is attributed to hyperglycaemia-induced nerve damage, which leads to oxidative stress and reduced nerve repair mechanisms [15,16].

In our study, a greater number of patients had comorbidities in diabetic neuropathy such as 42% diabetes mellitus, 22% hypertensive, 18% alcoholic and 6% smoking. Previous study revealed that over 40% of individuals with diabetic neuropathy are often reported to have poorly managed diabetes as a primary contributor. The duration of diabetes and uncontrolled blood sugar levels is central risk factors. Around 20-30% of diabetic neuropathy patients have concurrent hypertension. Hypertension exacerbates nerve damage due to vascular complications, further aggravating neuropathy. Alcohol use is

associated with an increased risk of neuropathy. A reported prevalence of 15-20% among individuals with diabetic neuropathy suggests that chronic alcohol intake may amplify nerve damage through toxic effects. Smoking is linked to microvascular complications, which increase the risk of neuropathy. Research has shown smoking prevalence rates among neuropathy patients between 5-10% depending on the population and other risk factors [17,18]. In this study after two weeks of treatment with a combination of pregabalin and methylcobalamin, patients in severe and distressful pain in day 1 have significantly improved to mild (70%) and tolerable (24%) pain by day 14, The previous study reported that a significant reduction in mean Visual Analog Scale (VAS) scores by 72.3% over 14 days, with improvements noted as early as the first week. Additionally, both positive and negative symptoms of peripheral neuropathy improved significantly in over 50% of patients within the two-week period. Common adverse effects included giddiness (4.7%), sedation (3.6%), dizziness (2.9%), drowsiness (2.3%), and nausea (2.3%). Overall, the combination therapy was well-tolerated, with more than 95% of investigators and patients rating its efficacy and tolerability as good to excellent [19]. Present and earlier studies suggest that the combination of pregabalin and methylcobalamin is effective in reducing neuropathic pain and improving associated symptoms over a two-week treatment period [20].

In our study, the changes in the mean VAS pain score were observed at day 1, day 7, and day 14 following treatment with a combination of pregabalin and methylcobalamin, resulting in an overall reduction of 58.75% in pain scores. Previous studies reported on neuropathic pain treatments (including pregabalin and methylcobalamin) have consistently shown that pain relief tends to improve progressively over a few weeks. Initial pain relief is often limited, with significant reductions occurring after 7 to 14 days of treatment. Similarly, research involving diabetic neuropathy and post-herpetic neuralgia patients also reported that pain intensity was often most reduced at two weeks, but initial pain reduction was moderate in the first seven days [15, 16, 21]. Dongre et al. noted a significant reduction in neuropathic pain after 14 days in patients treated with a combination of pregabalin and methylcobalamin, similar to our results. By day 7, pain reduction was already noticeable but modest, while at day 14, the pain relief was more pronounced [15, 16, 19, 21, 22].

In a previous study on neuropathic pain management conducted by Prabhoo R et al. results revealed that initial pain intensity was significantly reduced by week 2, reflecting the progressive improvement observed in our data [11].

By day 14 of our study, 85% patients reported good sleep quality and 11% reported excellent sleep quality, compared to the poor and fair sleep quality observed on day 1 and day 7. Previous studies have reported that effective management of diabetic neuropathy significantly improves sleep quality over time, particularly by addressing management of pain and related symptoms, which gradually improves with continued therapy [23, 24].

Conclusion

Our findings indicate that neuropathic pain primarily affects middle-aged people, with women accounting for a statistically significant higher proportion of cases than men. Multiple comorbidities were common in patients with diabetic neuropathy. By the fourteenth day of treatment, combined medication therapy showed exceptional effectiveness in reducing pain and enhancing the quality of sleep. Among the therapeutic options, the combination of pregabalin and methylcobalamin was especially effective in managing neuropathic pain and enhancing patients' overall quality of life.

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Conflict of interest: None

Reference:

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