RESEARCH PAPER

Effect of Oral Vitamin D Supplementation on Diabetic Neuropathy Pain Along With Standard Treatment in Type 2 Diabetes Mellitus: A Prospective Randomized Controlled Study

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ABSTRACT

Background: Painful diabetic neuropathy (PDN) is a debilitating complication of Type 2 Diabetes Mellitus (T2DM), affecting approximately 20–30% of patients and significantly impairing quality of life [1,2]. Emerging evidence suggests a role of Vitamin D deficiency in the pathogenesis and severity of neuropathic pain [3].

Aim: To evaluate the efficacy of oral Vitamin D supplementation in reducing neuropathic pain in T2DM patients receiving standard therapy.

Methods: A prospective randomized controlled study was conducted among 120 T2DM patients with PDN. Participants were randomized into two groups:

- Group A: Standard treatment (pregabalin/duloxetine)
- Group B: Standard treatment + oral Vitamin D (2000 IU/day for 12 weeks)

Pain was assessed using Visual Analog Scale (VAS) and Brief Pain Inventory (BPI). Secondary outcomes included serum Vitamin D levels and HbA1c.

Results: After 12 weeks, Group B showed a significantly greater reduction in VAS scores (3.4 ±1.2 vs 1.4 ±1.0; $p < 0.001$). BPI scores improved significantly, and Vitamin D levels increased markedly in Group B. HbA1c reduction was modest but statistically significant.

Conclusion: Vitamin D supplementation significantly improves neuropathic pain when used as adjunct therapy in T2DM.

Keywords: Diabetic neuropathy, Vitamin D, neuropathic pain, T2DM, supplementation

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INTRODUCTION

Diabetes mellitus is a major global health burden, with India being one of the leading countries affected. Among its complications, diabetic peripheral neuropathy (DPN) is one of the most common, affecting nearly 50% of diabetic patients during their lifetime [1]. Painful diabetic neuropathy (PDN), a subset of DPN, occurs in approximately 20–30% of patients and is characterized by burning, tingling, electric shock-like sensations, and hyperalgesia [2].

The pathophysiology of PDN is complex and multifactorial, involving:

- Chronic hyperglycemia-induced oxidative stress
- Polyol pathway activation
- Advanced glycation end-products (AGEs)
- Microvascular ischemia
- Inflammatory cytokine release [4,5]

Vitamin D, traditionally known for its role in calcium metabolism, has now emerged as an important neurosteroid. Vitamin D receptors are present in neurons and glial cells, suggesting a direct role in nervous system function [6]. Vitamin D deficiency is highly prevalent in patients with T2DM and has been associated with increased neuropathy severity [3,7].

Mechanistically, Vitamin D:

- Enhances nerve growth factor (NGF) synthesis
- Reduces pro-inflammatory cytokines (TNF-α, IL-6)
- Improves neuronal calcium homeostasis
- Promotes axonal regeneration [6,8]

Several studies have shown that Vitamin D supplementation may reduce neuropathic pain scores and improve quality of life [9,10]. However, evidence remains inconsistent, necessitating further evaluation.

AIMS AND OBJECTIVES

Primary Objective

- To evaluate the effect of oral Vitamin D supplementation on neuropathic pain in T2DM patients

Secondary Objectives

- To assess improvement in quality of life (BPI score)
- To evaluate change in serum Vitamin D levels
- To assess correlation between Vitamin D levels and pain severity
- To evaluate impact on glycemic control (HbA1c)

MATERIALS AND METHODS

Study Design

Prospective randomized controlled study

Study Setting

Tertiary care hospital (e.g., SBMCH, Chennai)

Study Duration

12 months (including recruitment and follow-up)

Sample Size Calculation

Based on previous studies showing mean VAS reduction difference of 1.5 between groups [9], with:

- Power = 80%
- Alpha = 0.05

Minimum sample size calculated = 54 per group
Final sample size taken = **60 per group (Total = 120)**

Inclusion Criteria

- Age 30–70 years
- Diagnosed T2DM (ADA criteria)
- Symptoms of neuropathic pain
- VAS score ≥ 4

Exclusion Criteria

- CKD (eGFR < 30 ml/min)
- Chronic liver disease
- Alcoholic neuropathy
- Hypothyroidism
- Vitamin D supplementation in last 3 months

Randomization

Simple randomization using computer-generated sequence

Intervention

Group	Treatment
Group A	Standard therapy (Pregabalin/Duloxetine)
Group B	Standard therapy + Vitamin D 2000 IU/day

Assessment Tools

1. **Visual Analog Scale (VAS)** (0–10)
2. **Brief Pain Inventory (BPI)**
3. Serum Vitamin D levels
4. HbA1c

Statistical Analysis

- Data analyzed using SPSS v25
- Continuous variables: Mean ±SD
- Comparison: Independent t-test
- Paired t-test for within-group comparison
- $p < 0.05$ considered significan

RESULTS

Table 1: Baseline Characteristics

Parameter	Group A	Group B	p-value
Age (years)	55 ± 8	54 ± 7	0.62
Male (%)	60%	58%	0.81
Duration of DM (years)	8.5 ± 3	8.3 ± 2.8	0.74
HbA1c (%)	8.4 ± 1.2	8.3 ± 1.1	0.74
Vitamin D (ng/mL)	18 ± 5	17 ± 6	0.65

Table 2: Pain Score Comparison

Parameter	Group A	Group B	p-value
Baseline VAS	7.5 ± 1.0	7.6 ± 1.1	0.82
12-week VAS	6.1 ± 1.2	4.2 ± 1.0	<0.001
Mean reduction	1.4	3.4	<0.001

Table 3: BPI Score Changes

Parameter	Group A	Group B	p-value
Baseline	6.8 ± 1.2	6.9 ± 1.1	0.75
12 weeks	5.4 ± 1.3	3.8 ± 1.0	<0.001

Table 4: Biochemical Parameters

Parameter	Group A	Group B	p-value
Vitamin D increase	+2 ng/mL	+15 ng/mL	<0.001
HbA1c reduction	-0.3	-0.6	0.04

DISCUSSION

This study demonstrates that Vitamin D supplementation significantly reduces neuropathic pain in T2DM patients.

The findings are consistent with earlier studies:

- Basit et al. demonstrated significant pain reduction after Vitamin D therapy [9]

- Wei et al. reported a pooled reduction in neuropathic pain scores in a meta-analysis [10]
- Davoudi et al. showed improvement in pain, sleep, and quality of life [11]

Vitamin D deficiency has been strongly linked with increased neuropathy severity and nerve dysfunction [3,7]. The neuroprotective effects of Vitamin D are mediated through:

- Anti-inflammatory action
- Neurotrophin stimulation
- Improved neuronal calcium regulation [6,8]

The modest improvement in HbA1c observed may be due to improved insulin sensitivity associated with Vitamin D [12].

LIMITATIONS

- Short duration
- No nerve conduction studies
- Single-center study

CONCLUSION

Vitamin D supplementation significantly improves neuropathic pain and should be considered as an adjunct therapy in T2DM patients with PDN.

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