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VITAMIN D SUPPLEMENTATION IN PATIENTS WITH CHRONIC LOW BACK PAIN: AN OPEN LABEL, SINGLE ARM CLINICAL TRIAL

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ABSTRACT **Background:** Vitamin-D deficiency may possibly be related to chronic low back pain (CLBP). **Objective:** The study is aimed to assess the impact of vitamin-D supplementation on pain intensity, functional disability, and vitamin-D levels in patients with CLBP. **Methods:** Sixty-eight eligible patients (CLBP for ≥ 3 months, pain score ≥ 50 on visual analogue scale (VAS) and plasma 25-Hydroxyvitamin D3 levels < 30 ng/mL) were enrolled. Patients were supplemented with 60,000 IU of oral vitamin-D3 given every week for 8 weeks. Efficacy parameters included pain intensity and functional disability measured by VAS and modified Oswestry disability questionnaire (MODQ) scores at baseline, 2, 3, and 6-months post-supplementation. Plasma 25(OH) D3 levels were measured at baseline and 8 weeks. **Results:** Baseline mean (SD) vitamin-D levels were 12.8 (5.73) ng/mL and increased to 36.07 (12.51) post supplementation ($P < 0.01$). Forty-five (66%) patients attained normal levels (> 29 ng/mL) post supplementation. Significant reduction in VAS was observed at 2, 3, and 6 months [61 (19), 45(19), 36 (18)] as compared to 81 (19) at baseline ($P \leq 0.001$ at all-time intervals). A significant improvement in the functional ability was also observed at 2, 3, and 6 months [36 (12), 31 (13), and 26 (10)] as compared to baseline 45 (16) ($P \leq 0.001$ at all-time intervals).

KEYWORDS :

INTRODUCTION:

Back pain is the most common pain complaints second only to headache [(1)]. Chronic low back pain (CLBP) is often progressive and the cause may be difficult to ascertain. Despite the availability of many pharmacological and invasive methods of treatment, many patients still suffer from considerable morbidity [(1)]. Vitamin-D deficiency has been correlated with chronic musculoskeletal pain including low back pain (LBP) [(1-4)]. A high prevalence of vitamin-D deficiency (up to 83%) has been reported in patients with CLBP in comparison to the general population [(1-4)]. The mechanisms underlying these associations remain unclear [(5,6)].

Theoretically, 2 possible links have been postulated. Firstly, the diffuse pain in bones and muscles, weakness, and paresthesia may be caused by hypovitaminosis D. Secondly, hypovitaminosis D could play a role in the development of modic changes via the increased susceptibility to inflammation in the vertebral end plates [(7)]. The prevalence of vitamin-D deficiency is found to be 50% – 90% on the Indian subcontinent and is at tributed to low dietary intake along with skin color and changing lifestyle despite the availability of ample sun light [(8)]. Evidence on the efficacy of vitamin-D supple mentation in symptom improvement in chronic pain including CLBP is conflicting. A randomized clinical trial conducted in an Iranian population reported inefficacy of vitamin-D supplementation in non-specific LBP patients [(9)]. The present study is performed with an aim to assess the efficacy and safety of vitamin-D3 supplementation in improving pain and other outcomes in CLBP patients having below normal vitamin-D levels.

METHODS:

Study Design And Population:

This single arm, open label study was conducted in our hospital OPD. Every year, the clinic provides a comprehensive diagnostic evaluation for approximately 1000 new patients with various pain conditions.

Inclusion Criteria:

Patients of either gender, aged 18 – 75 years with CLBP for ≥ 3 months with or without leg pain not responding to medications and physical therapies, having low plasma 25- Hydroxyvitamin D3 levels (< 30 ng/mL) were eligible for study recruitment. The diagnosis of CLBP was established based on signs and symptoms and investigations like magnetic resonance imaging (MRI). Patients were required to have a stable pain score for 3 months before recruitment and could be on any oral analgesic therapy.

The questionnaires included VAS to measure CLBP intensity, functional disability using Modified Oswestry disability questionnaire (MODQ), work status, and the prior use ofmedications.

Exclusion Criteria:

Patients were excluded if they had evidence of other causes of neuropathy or painful conditions like diabetes mellitus, rheumatoid arthritis, and symptomatic osteoarthritis of the hip, knee, and ankle. Patients diagnosed with epilepsy, metabolic bone disease (hypo- or hyperparathyroidism), chronic renal disease, and medical or surgical disorders affecting vitamin-D metabolism (gastric surgery, chronic liver disease, renal failure, intestinal malabsorption, systemic infection, cancers, etc.) were also excluded. Patients consuming drugs altering bone metabolism like corticosteroids or bisphosphonates, pregnant and lactating mothers, and women intending to be pregnant were also excluded. Patients taking vitamin-D supplements during the past 3 months were also excluded from the present study.

Measurement Of Plasma Vitamin – D Levels [25- Hydroxyvitamin -d (25(oh)d3)]:

After an overnight fasting, a blood sample was taken. Plasma 25(OH) D3 levels were measured by electrochemiluminescence immunoassay (ECLIA). This technique provides a broad measuring range and high precision at the low end of detection to aid in the assessment of deficient patients. All the blood samples were collected between 9:00 AM and 10:00 AM to prevent any circadian variation.

Study Procedure:

All new patients referred to the pain clinic during the data collection period were screened for eligibility criteria including fasting plasma 25(OH) D3 levels. Eligible patients providing written informed consent were enrolled. All the information was recorded in a structured case record form. Baseline evaluation included sociodemographic characteristics including age, gender, education, smoking, and alcoholic status as assessed through a direct patient interview. Height and weight were measured to calculate body mass index (BMI), and categorized as < 18.4, 18.5 to 24.99, 25 to 29.99, and ≥ 30 kg/m^2, which are the cut-off points for underweight, normal, overweight, and obesity [(12)] (Table 1).

Table No. 1

PARAMETER		VALUE
AGE (YR)	MEAN (SD)	44 (12)
MALE	N (%)	37 (55)
BMI*	MEAN (SD)	25.8 (3.7)
SMOKING	N (%)	12 (18)
ALCOHOL	N (%)	8 (12)
DURATION OF LOW BACK PAIN (MONTHS)	MEDIAN (IQR)	36 (13-96)

Bmi- Basal Metabolic Index

Treatment Regimen:

Induction Phase:

Active vitamin-D3 sachet in a dose of 60,000 IU every week orally for a period of 8 weeks was given to the enrolled patients. Patients having serum vitamin-D level < 5 ng/mL were given 60,000 IU daily orally for the initial 5 days and then 60,000 IU every week for the next 8 weeks. The vitamin-D level was repeated at the end of induction therapy. If the vitamin-D level remained low < 29 ng/mL at this point, then the similar treatment regimen was repeated as mentioned above.

Maintenance Phase:

The patients achieving normal levels of vitamin D after induction therapy were put on maintenance therapy. This consists of 60,000 IU orally every month given for the next 6 months. Treatment was stopped for the patients who achieved serum vitamin-D level > 60 ng/mL.

Mode Of Supplementation:

Patients were advised to take the active vitamin-D3 sachet containing 60,000 IU orally by mixing in a glass of milk early morning every week.

Efficacy Endpoints:

Study endpoints included plasma 25(OH) D3 levels after completion of 8 weeks of the induction phase of vitamin-D supplementation, change in pain score from baseline as measured by VAS, disability as measured by MODQ, and drug tolerability. Proportion of patients achieving effective pain relief (EPR), defined as ≥ 50% reduction in pain score from baseline as assessed on VAS at 3 months, was also calculated. Patient characteristics and outcome measures were collected at baseline, 2, 3, and 6 months post supplementation.

Statistical Analysis:

Patient characteristics and baseline and follow-up parameters were expressed in mean and standard deviation (SD), numbers and percentage (%), and median and interquartile range (IQR). Baseline and follow-up VAS, MODQ, and plasma 25 OH D were analyzed using paired student t-test. Proportion of patients achieving plasma 25 OH D level normalization after supplementation therapy was analyzed using chi square test. All statistical tests were performed by using the SPSS 15.0 version. A *P* value of < 0.05 was accepted as significant.

RESULTS:

A total of 180 potentially eligible patients were screened for study participation. Thirty-two (18%) patients were ineligible due to normal vitamin-D levels. Of 148 (82%) deficient patients, 80 were excluded (18 refused to participate and 62 did not complete follow up). Hence, 68 CLBP patients were included in the final analysis. The average (SD) age of patients was 44 (12) with 37 (55%) being men. The mean (SD) BMI of study patients was 25.8 (3.7). Prior to inclusion into this study the participants' median (IQR) duration of CLBP was 36 (13 – 96) months and mean (SD) VAS and MODQ was found to be 81 (19) and 45 (16) showing the majority had severe pain and disability at study inclusion (Table 1).

Vitamin – D Levels:

Baseline mean (SD) vitamin-D levels were found to be 12.8 (5.73) ng/mL. Sixty-one (90%) patients were found to be vitamin-D deficient and 7 (10%) had insufficient levels. Serum vitamin-D levels increased significantly to 36.07 (12.51) post-supplementation (*P* < 0.01). Forty-five (66%) patients attained normal vitamin-D levels (> 29 ng/mL) after the vitamin-D supplementation induction phase while 18 (27%) and 5 (7%) remained insufficient and deficient, respectively (Tables 2).

Table 2. Vitamin D Status At Baseline.

	SUFFICIENT N (%)	INSUFFICIENT N (%)	DEFICIENT N (%)	P VALUE
TOTAL	-	7 (10)	61 (90)	-
MEN	-	-	37 (100)	
WOMEN	-	7 (23)	24 (77)	
TOTAL	45 (66)	18 (27)	5 (7)	0.45
MEN	26 (70)	9 (24)	2 (6)	
WOMEN	19 (61)	9 (29)	3 (10)	

Clinical Efficacy:

Significant reduction in pain score was observed post supplementation. Mean (SD) VAS scores were 61 (19), 45 (19), and 36 (18) at 2, 3, and 6 months, respectively, as compared to 81 (19) at baseline ($P \leq 0.001$ at all-time intervals as compared to baseline).

EPR was achieved in 36 (53%) and 43 (63.2%) patients at 3 and 6 months, respectively. Significant improvement in functional disability was also observed post supplementation. Mean (SD) MODQ scores were 36 (12), 31 (13), and 26 (10) at 2, 3, and 6 months, respectively, as compared to baseline 45[16] ($P < 0.001$ at all-time intervals). No adverse drug reactions were observed with oral vitamin-D supplementation in the study.

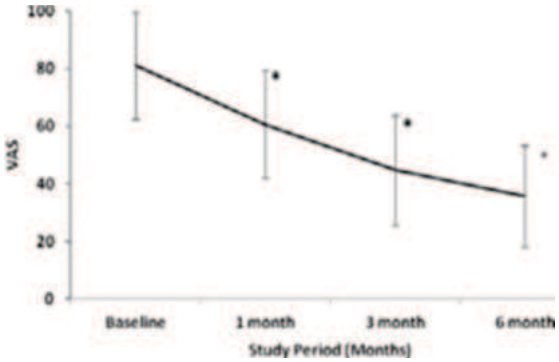

Figure 1:

Limitations:

The results of the present study can be confounded with the effects of concomitant medications. This is a major limitation of the present as there is insufficient data regarding concomitant analgesic medications. Another major limitation is the lack of comparator as we planned this study with the observation that our regular clinic patients seem to be more deficient in vitamin D3. In addition, the regular analgesic therapy was not altered, but patients receiving epidural injections were not recruited in the study. After the induction phase, the majority reported good pain relief and the co-medications were reduced accordingly. Finally, we did not document patients having radicular and axial pain specifically, which can also confound the results.

CONCLUSION:

The present study shows that vitamin-D supplementation can improve the pain and disability in patients with CLBP. The study results should be carefully interpreted as it is a single arm, open label study and concomitant medication usage was not assessed. Altogether, intense research is needed to establish the effect of vitamin- D on CLBP. RCTs with longer duration, large sample size, and different outcome assessment in different age groups are recommended.

No conflict of interest.

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