

Comparative evaluation of crestal bone level in patients having low level of Vitamin D treated with dental implant with or without Vitamin D3 supplements

ABSTRACT

Introduction: Vitamin D has been shown to play a vital role in bone mineral homeostasis by stimulating the intestinal absorption of calcium and phosphate. The critical role of Vitamin D in bone metabolism triggered the need to evaluate the effect of Vitamin D deficiency and hence replacement of the same on osseointegration of dental implants. This prospective study evaluated the crestal bone level in patients having low level of Vitamin D treated with dental implant with or without Vitamin D3 supplements.

Materials and Methods: A prospective clinical study was conducted on 32 patients based on the inclusion and exclusion criteria. Patients were divided into two groups on the basis of Vitamin D level < 30 ng/ml (Group I: patients receiving Vitamin D3 supplements, i.e., cholecalciferol 1 g sachet 60,000 IU/month) or <30 ng/ml (Group II: not receiving Vitamin D3 supplements). The crestal bone level measurements were made with the help of Digimizer Image Analysis, MedCalc software.

Results: All implants showed clinically acceptable crestal bone level at interval of 1 week (baseline), 3 months, and 6 months. There was a statistically nonsignificant difference seen for the values between the groups ($P > 0.05$) for all other values at various time intervals. However, there was a statistically significant/highly significant difference seen for the values between the groups ($P < 0.01, 0.05$) for 3 months distal with higher values for Group I as compared to Group II.

Conclusion: From the study, it can be concluded that cholecalciferol has systemic effects on accelerating bone formation around titanium implant.

Keywords: Cholecalciferol, MedCalc software, osseointegration, Vitamin D

INTRODUCTION

Tooth loss is a common phenomenon and can occur because of trauma, caries, or periodontal disease. Dental implants are now a reliable solution for the functional and esthetic rehabilitation of partially and completely edentulous patients.^[1-3]

Factors improving osseointegration consist of implant-related factors, use of adjuvant treatment methods such as bone grafting, osteogenic biological coatings, and biophysical stimulation as well as pharmacological agents.^[4] Supplementation with cholecalciferol (Vitamin D3) is reported to show favorable impacts on bone mineral density.^[5,6]

Vitamin D is a fat-soluble biomolecule, which is obtained through Vitamin D-rich diet or is generated in the skin on

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ultraviolet light exposure.^[6-8] Vitamin D-binding protein is responsible for transporting Vitamin D from the skin or intestine to the liver, where it is metabolized and yields 25-hydroxyvitamin D, or 25(OH)2D. Next, 25(OH)2D will produce the active form of Vitamin D in the kidneys: 1,25-dihydroxyvitamin D, also known as 1,25(OH)2D or calcitriol, which is responsible for binding to Vitamin D receptor (VDR).^[9] The VDR is a ligand-dependent transcription factor of the nuclear receptor superfamily. VDR belongs to the NR11 subfamily along with other nuclear receptors involved in xenobiotic metabolism, such as pregnane X receptor.^[10]

Vitamin D deficiency has become increasingly common and can result from inadequate dietary intake together with insufficient exposure to sunlight.^[11] Vitamin D has been shown to play a vital role in bone mineral homeostasis^[12] by stimulating intestinal absorption of calcium and phosphate.

Serum levels of Vitamin D in the 25(OH) D form are the most accurate way of determining Vitamin D status: A patient with <10 ng/mL is considered to be Vitamin D deficient; one with 10–30 ng/mL is considered to have low levels of Vitamin D. The optimal blood level of Vitamin D is a value >30 ng/mL.^[13]

Vitamin D deficiency likewise negatively influences bone regeneration, including fracture healing^[14] and also osseointegration of implants.^[15] A genome-wide screening additionally suggested that Vitamin D deficiency influences the osseointegration of dental implants by regulating the circadian rhythm system and the cartilage extracellular matrix.^[16] Hence, Vitamin D supplementation is an effective treatment for reduced peri-implant bone formation because it directly counteracts the catabolic mechanisms of Vitamin D deficiency.^[17] Hence, the aim of our study was to evaluate the crestal bone level in patients having low Vitamin D level treated with dental implant with or without Vitamin D3 supplements.

MATERIALS AND METHODS

A prospective, randomized clinical trial was conducted involving total of 32 patients aged between 20 and 40 years. The patients were assessed based on chief complaints needing replacement of missing mandibular posterior teeth. Ethical clearance no. PGIDS/IEC/17/13 was obtained from the Institutional Ethical Committee of PGIDS, Rohtak. After explaining the proposed study criteria including alternative treatment options, potential risks, and benefits, a signed informed consent was obtained from all patients.

Inclusion criteria

1. Patients who consented to participate in the study and will also be available for follow-up
2. Patients with maintainable oral hygiene and nonsmokers
3. Patients having adequate quality and quantity of bone at the placement site
4. Patients who were having Vitamin D level <30 ng/ml.

Exclusion criteria

1. Patients with the presence of infection around site of implant placement
2. Patients with a history of bleeding disorder or on anticoagulant drugs
3. Patients with immunocompromised state or debilitating disease and recent history of myocardial infarction
4. Patients on Vitamin D3 supplements.

Grouping of subjects

A total of 32 implants were placed (16 implants in Group I and 16 implants in Group II) in patients requiring restoration of mandibular posterior teeth. Patients were divided into the following groups on the basis of Vitamin D level.

- Group I: Patients having Vitamin D <30 ng/ml, treated with dental implant and received Vitamin D3 supplements (cholecalciferol sachet 60000 IU/month) for 3 months and continued for 6 months depending on level of Vitamin D
- Group II: Patients having Vitamin D <30 ng/ml, treated with dental implant and not received Vitamin D3 supplements.

Pre-surgical assessment

1. An informed consent was obtained and history was recorded
2. Preoperative radiographic assessment: Intraoral periapical (IOPA) X-ray and orthopantomograph were done for the evaluation of bone
3. Investigations such as complete hemogram (Hb, bleeding time, and closure time) and all vitals were recorded (blood pressure, pulse, and heart rate) to evaluate patient's fitness for implant placement
4. Clinical photographs were taken.

Estimation of Vitamin D levels

Sample collection

Five milliliters of blood sample was collected in a sterile plain vacutainer under all aseptic conditions from all the patients at the time of diagnosis. Blood samples were processed and serum was separated by centrifugation at 2000 rpm × 10 min after clotting. Samples were stored at –20°C in separate aliquots for estimation of Vitamin D in batches subsequently.

The subsequent blood samples were taken at 3-month and 6-month follow-up period from Group I patients receiving Vitamin D supplements.

Method

Serum 25OH Vitamin D was estimated by radioimmunoassay (RIA) method on fully automated RIA Analyzer SR300 by STRATEC Biomedical AG, Germany, using Beckman Coulter 25OH Vitamin D total RIA kit.

Implant surgery planning and procedure

Diagnostic records

The diagnostic impression was made and diagnostic cast was prepared and mounted on mean value articulator.

Intraoral periapical radiograph

This involved:

- a. Fabrication of the vinyl polysiloxane putty jig

A vinyl polysiloxane putty jig was made to standardize the radiographic film holder (Rinn XCP) for each and every patient in terms of angulation and also position of the film relative to the X-ray beam. Vinyl polysiloxane putty was mixed and attached to bite plane of the film holder. The film holder was placed into the patient's mouth at a proper angulation, and the patient was instructed to bite on putty to obtain the indentation of maxillary teeth. The periapical radiographs were taken using the long-cone paralleling technique with radiographic film holders (Rinn XCP) making the use of customized putty. The occlusal jig was stored separately for each patient and used for taking radiographs at subsequent visits.

Surgical procedures

Implants were placed in a conventional manner under aseptic conditions.

Postoperative instructions were provided to the patient regarding diet, oro-dental hygiene and medications, which were prescribed.

Patients were recalled after 24 h for review and after 7 days for suture removal and radiographic and crestal bone level evaluation at baseline, 3 months, and 6 months postoperatively.

Radiographic evaluation of crestal bone level

All implants were evaluated radiographically at baseline (within 1 week after implant placement), 3 months, and 6 months after implant placement [Figures 1-6].

The intraoral periapical radiographs were obtained using a paralleling technique and were digitalized. The first thread

of implant was taken as a reference line because it was static, permanently visible, and easy to locate on all radiographs. The point of bone-to-dental implant contact was selected as the bone level. The measurements were obtained using Digimizer Image Analysis, Medcalc software, version 4.3.5.0 (Medcalc software Ltd, Ostend, Belgium). Before analysis, the images were calibrated geometrically to record the radiographic dental implant length. Measurements were made at baseline, 3 months, and 6 months at the mesial and distal aspects of implants by dropping perpendiculars from the reference line to the bone level.

Statistical procedures

Information obtained was compiled on a MS Office Excel Sheet (v 2010, Microsoft Redmond Campus, Redmond, Washington, United States).

Data went through statistical analysis utilizing the Statistical Package for the Social Sciences (SPSS v 21.0, SPSS Inc. Chicago, Illinois, U.S.A).

Descriptive statistics such as frequencies and percentage for categorical data and mean and standard deviation for numerical data have been depicted.

Normality of numerical data was checked using Kolmogorov–Smirnov and Shapiro–Wilk tests and was found that the data did not follow a normal curve; hence, nonparametric tests have been used for comparisons.

- Intergroup comparison (two groups) was done using Mann–Whitney U-test
- Intragroup comparison was done using Friedman's test (for >2 observations), followed by pairwise comparison using Wilcoxon signed-rank test.

For all the statistical tests, $P < 0.05$ was considered to be statistically significant, keeping α error at 5% and β error at 20%, thus giving a power to the study as 80%.

The results of our study showed that there was a statistically significant/highly significant difference seen for the values between the groups ($P < 0.01, 0.05$) for 3 months distal with higher values for group I as compared to group II [Graph 2]. While there was a statistically non-significant difference seen for the values between the groups ($P > 0.05$) for all other values at various time intervals [Graphs 1 and 2].

DISCUSSION

Dental implant has become a treatment of choice in most of the situations of missing teeth. To be specific, failure to osseointegrate and peri-implantitis are the most frequent

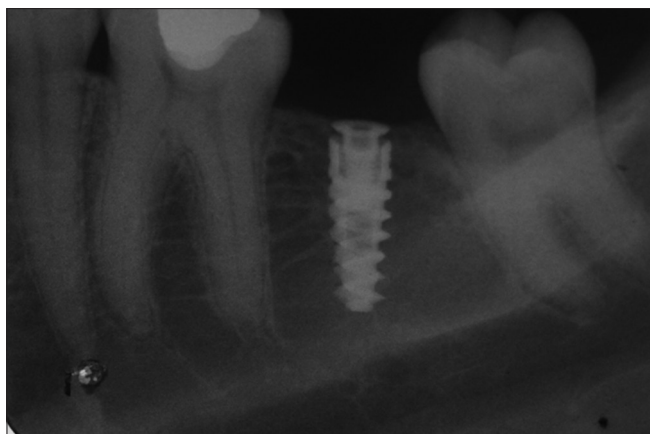


Figure 1: Intraoral periapical 1 week after implant placement (Group I)



Figure 2: Intraoral periapical 3 months after implant placement (Group I)



Figure 3: Intraoral periapical 6 months after implant placement (Group I)



Figure 4: Intraoral periapical 1 week after implant placement (Group II)



Figure 5: Intraoral periapical 3 months after implant placement (Group II)

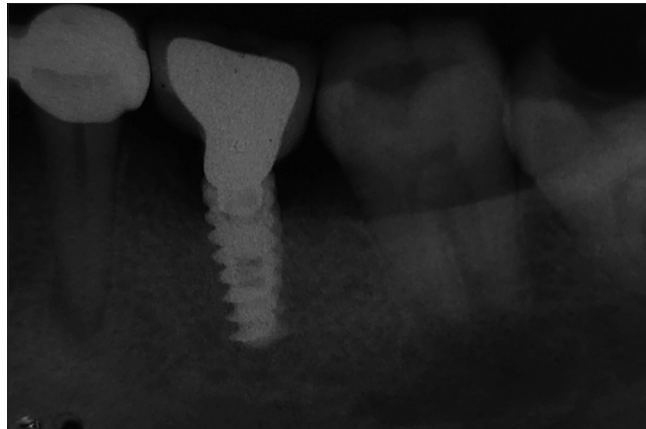


Figure 6: Intraoral periapical 6 months after implant placement (Group II)

causes of early implant failure.^[3,18,19] To date, only a few clinical studies in the dental literature have investigated the effects of Vitamin D deficiency on osseointegration and on bone regeneration.^[7,20,21] Most of these are experimental animal studies, and only a few of them are clinical research in humans.

Vitamin D plays a fundamental role in bone metabolism.^[13,18] It regulates calcium and phosphate homeostasis in the tissues, and it is a fundamental element in the mineralization

of bones and teeth.^[13,18] In dental implantology, Vitamin D has actually been investigated nearly exclusively as an influencing factor of the BIC (bone-to-implant contact) and implant stability.^[22] Vitamin D demonstrates several effects on bone metabolism: It upregulates the gene expression of osteocalcin, osteopontin, and 24-hydroxylase, increases extracellular matrix protein formation by osteoblasts, and stimulates osteoclast activity.^[20]

The long-term survival of implants is assessed by the amount of marginal bone loss around the dental implant. The quantity of bone loss anticipated from dental implant during the 1st year must be <2 mm, apical to implant-abutment junction. After the 1st year, it is expected that bone loss will be 0.2 mm annually.^[23] Hence, our study aimed to evaluate the crestal bone level in patients having low and normal levels of Vitamin D treated with dental implant with or without Vitamin D supplements. Follow-up period was of 6 months.

Table 1 shows the crestal bone level (mm) on mesial and distal sides of dental implant utilizing IOPA radiograph at baseline, at 3 months, and 6 months after implant placement in Group I. Table 2 shows the crestal bone level (mm) on mesial and distal sides of dental implant utilizing IOPA radiograph at baseline, at 3 months, and 6 months after implant placement in Group II. Table 3 shows the mean percentage difference between both the groups.

Graph 1 shows a comparison of bone level on mesial aspect of implant between Groups I and II at different time intervals. Graph 2 shows a comparison of bone level on distal aspect of implant between Groups I and II at different time intervals.

In the present study, we evaluated the mesial and distal crestal bone levels in patients of both the groups. It was observed that there is definitely better osseointegration of implants in patients supplemented with Vitamin D. There was lesser bone loss in patients with low Vitamin D level who were supplemented with Vitamin D. This can be attributed to role of Vitamin D in induction of anti-inflammatory cytokines and a reduction in level of pro-inflammatory cytokines, thus decreasing the body's response to surgical intervention.

Calcitriol plays a immunomodulatory role stimulating both the acquired and innate responses.^[24]

There was an increase in serum Vitamin D levels (up to 45 ng/ml) in Group I patients who were supplemented with Vitamin D. The normal range of Vitamin D level is 30–100 ng/ml. The second reason is role of Vitamin D in calcium metabolism because Vitamin D supplementation may increase calcium availability, which may promote the mineralization at the rate at which new bone is mineralized.^[25] Furthermore, Vitamin D is known to stimulate osteocalcin and alkaline phosphatase production in the osteoblasts which may counteract the effect of lowering turnover.^[25]

The results of our study are in accordance with a study conducted by Javed *et al.*, who concluded that Vitamin D supplementation could stimulate bone formation and, as a result, augment the contact between the surface of titanium implants and bone.^[22] Similar results were reported by Zhou *et al.*, who found an increase in osseointegration in osteoporotic rats given Vitamin D supplements,^[26] and Wu *et al.*, who demonstrated an increase in the percentage of contact between bone and implant in diabetic rats given Vitamin D supplements.^[27] The results of these studies also support our study because Vitamin D activates osteoblasts and increases the production of extracellular matrix proteins by osteoblasts.

In the present study, the difference in mesial and distal crestal bone levels between various time intervals was found to be nonsignificant in Group I [Graphs 1 and 2]. This is because of Vitamin D supplementation that crestal bone loss was less. However, there was a statistically significant difference seen in Group II for values between all the time pairs ($P < 0.01, 0.05$) except 3 months to 6 months distal where there was

Table 1: Measurements of crestal bone level (in mm) on mesial and distal sides of implant in Group I

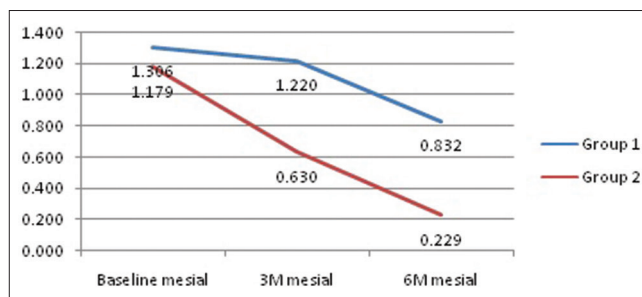
S.No.	Baseline		3 month		3 month	
	Mesial	Distal	Mesial	Distal	Mesial	Distal
1.	1.07	0.623	1.553	1.339	1.358	0
2.	1.622	2.189	1.888	2.579	1.422	2.064
3.	1.569	1.366	1.222	0.698	1.814	1.256
4.	1.009	1.021	0.789	0.868	1.331	1.409
5.	0.953	1.053	0.789	1.213	1.724	1.149
6.	0.9	0.876	1.333	1.63	1.077	1.928
7.	1.495	1.762	2.138	2.614	0	0.215
8.	1.197	0.884	0.892	0.701	1.015	0.95
9.	3.727	3.408	3.249	2.999	2.396	2.675
10.	0.481	0	1.791	1.271	0.855	1.006
11.	0.725	1.245	0.894	1.947	0.95	1.23
12.	2.885	2.885	1.734	1.8	1.548	1.481
13.	1.047	0	1.007	0	1.05	0.051
14.	1.055	1.055	0.987	0.88	1.092	1.058
15.	1.147	1.095	-1.108	1.034	-0.475	0.238
16.	0	1.16	0.849	1.12	-1.679	0.845

Table 2: Measurements of crestal bone level (in mm) on mesial and distal sides of implant in Group II

S.No.	Baseline		3 month		6 month	
	Mesial	Distal	Mesial	Distal	Mesial	Distal
1.	1.859	0.165	1.478	0	0	-0.529
2.	0	-0.882	0	0	0	0.325
3.	0	-0.514	-1.637	-0.98	-0.773	-0.822
4.	1.207	1.169	0.959	0.532	-0.7	0.6
5.	0.894	1.022	1.081	1.032	1.676	0.905
6.	1.282	1.165	0.938	1.536	-1.438	-1.741
7.	0.969	1.099	0.881	0	0.761	1.012
8.	0	0.961	0	0.961	0	0.815
9.	2.004	1.728	1.617	1.671	1.524	1.631
10.	1.111	1.304	0	0.582	-0.767	0
11.	1.987	2.5	1.852	2.1	1.95	2.012
12.	1.458	1.185	0	-0.678	-0.12	-0.57
13.	2.767	2.57	2.127	2.061	1.39	1.341
14.	1.453	1.13	-0.772	-0.647	-1.18	-2.491
15.	1.256	1.491	1.005	1.571	0.888	1.571
16.	0.617	0.947	0.558	0.558	0.452	0.497

Table 3: Mean percentage difference between groups

Group I			
	B to 3M Mesial	B to 6M Mesial	3M to 6M Mesial
Mesial	6.9230	36.15	31.40
	B to 3M Distal	B to 6M Distal	3M to 6M Distal
Distal	8.45	16.92	23.94
Group II			
	B to 3M Mesial	B to 6M Mesial	3M to 6M Mesial
Mesial	46.15	81.19	65.07
	B to 3M Distal	B to 6M Distal	3M to 6M Distal
Distal	39.33	73.58	56.25



Graph 1: Intergroup comparison of mesial bone level at various time intervals

nonsignificant difference seen ($P > 0.05$) [Graphs 1 and 2]. This is attributed to the crestal bone loss which occurs during the 1st year after implant placement. There is nonsignificant difference from 3 months to 6 months because, after loading of implant, remodeling of bone occurs which maintains the crestal bone levels.

Finally, Gaber *et al.*^[28] evaluated the effect of cholecalciferol on dental implant osseointegration in dogs. They concluded that Vitamin D3 had systemic effects on increasing bone formation around dental titanium implant. This also supports our study that Vitamin D supplementation promotes the osseointegration of implants.

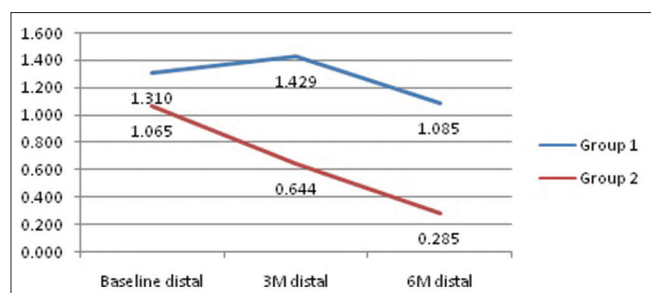
Vitamin D3 has been extensively studied for its dual action of promoting bone remodeling.^[27] Supplementation is an effective means of improving Vitamin D status.^[29] As osseointegration of dental implants also relies on bone metabolism, there is the possibility that decreased blood levels of Vitamin D can negatively influence healing processes and new bone formation on the implant surface.^[30]

Vitamin D insufficiency might similarly reduce bone remodeling activities around dental implants and potentially extend the healing time for osseointegration to occur.^[31] Hence, based on the results of our study, we can conclude that the establishment of osseointegration during early periods may require Vitamin D-dependent regulatory mechanisms.

Hence, within the results of our study, we can conclude that Vitamin D supplementation is an effective approach to improve the osseointegration of dental implants.

The merits of study are:

1. This is a prospective study design
2. Only same type of Vitamin D supplement (cholecalciferol 60000 IU 1 g sachet) was given to all patients in the study group
3. Optimization of Vitamin D status may also have additional general health benefits
4. Since half-life of 25(OH)D is a month or longer, so daily dosing is not necessary
5. IOPA X-rays were obtained using paralleling technique to minimize distortion



Graph 2: Intergroup comparison of distal bone level at various time intervals

- A single implant system was used throughout the study
- In the present study, all patients participated until the end of the study.

Limitations of our study

The limitations were small sample size and brief follow-up time period.

CONCLUSION

The connection between serum levels of Vitamin D and osseointegration of dental implants has been evaluated in very few studies, the majority of them in animals.

In the present study, it was observed that there is definitely much better osseointegration of implants in individuals supplemented with Vitamin D. In cases where a link between reduced serum levels of Vitamin D and enhanced risk of dental implant failure is shown, the clinician may provide a dose of Vitamin D in the weeks before surgery. By doing this way, the clinician might regulate the serum levels and help enhance the healing process.

Obviously, even more prospective clinical research studies as well as randomized controlled trials are needed to show a significant correlation between decreased serum levels of Vitamin D and increased risk of dental implant failure and hence prove that Vitamin D supplementation can promote the osseointegration of dental implants.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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