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"Effect of oral systemic administration of vitamin D on the rate of maxillary canine retraction: A randomized controlled trial"

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ABSTRACT

Objective: The trial was conducted to determine the effects of systemically delivered Vitamin D (1,25 dihydroxycholecalciferol) on the rate of maxillary canine retraction till the space closure and on the root resorption.
Materials and methods: A two-arm parallel randomized controlled trial was conducted in patients with Angle's Class I bimaxillary protrusion requiring at least upper first premolars extraction and distal movement of canine for malocclusion correction. The enrolled patients were randomized and allocated to the experimental group (Oral Vitamin D = 0.25 μg given) and control group (Placebo given). The canine retraction was initiated using nickel-titanium (NiTi) closed coil springs delivering a force of 100 gm per side and Vitamin D levels were monitored at monthly intervals. The patients' casts were digitally scanned and examined for differences in the rate of canine retraction at initial (T0), 4 weeks (T1), 8 weeks (T2), 12 weeks (T3), 16 weeks (T4) and 20 weeks (T5) intervals were calculated. The volumetric root resorption was done on CBCT of the area of interest at T0 and after completion of retraction. Descriptive statistics and paired *t*-test were used to determine any differences.
Results: 32 patients (18–24 years) were randomized in the experimental group (n = 16) and control group (n = 16) and no dropout was noted till the end of the study. The results showed a statistically significant increase in the rate of canine retraction in the experimental group as compared to the control group at different time intervals. The differences in the mean canine retraction between group 1 and group 2 at T1-T0, T2-T1, T3-T2, T4-T3, and T4-T0 were 0.28 ± 0.12, 0.29 ± 0.10, 0.31 ± 0.08, 0.37 ± 0.06 and 1.18 ± 0.10 mm respectively. The total mean canine retraction for group 1 was achieved at T4 time interval while it was achieved at T5 interval for group 2. The intergroup comparison of maxillary canine roots showed no statistically significant difference in volumetric root resorption.
Conclusion: The active form of vitamin D can be an effective agent to accelerate orthodontic tooth movement (OTM).

1. Introduction

Orthodontic tooth movement occurs as a result of application of mechanical forces which transfer to the various cell signaling pathways of the periodontal ligament resulting the localized bone resorption and deposition. Alteration in the normal functions of bone metabolism can be undertaken to affect the rate of orthodontic tooth movement.[1] The process of increasing the rate of orthodontic tooth movement translates into the terminology called "Accelerated Orthodontics" which is synonymous with the decrease in orthodontic treatment duration.[2] Various studies and systematic reviews have been conducted to assess the effects of various modalities to accelerate the rate of tooth movement and decrease the orthodontic treatment duration.[3–6] These approaches to 'accelerated orthodontics' can be broadly divided into biological, physical, and surgical approaches. The biological approach includes local or systemic administration of biological factors such as prostaglandins, vitamin D_3, parathyroid and relaxin hormone, etc.[1]

Vitamin D_3 is mentioned in the literature as the most important

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biomodulator of bone tissue which justifies our study to assess its role on the rate of orthodontic tooth movement. $1,25(OH)_2D_3$ greatly stimulates the differentiation and activation of mononuclear phagocytes.[7] The experimental study of Suda et al.[8] revealed that the differentiation of mononuclear phagocytes into osteoclasts is strictly regulated by osteoblastic cells, the process of which is also stimulated by vitamin D_3. In the differentiation of mononuclear phagocytes into osteoclasts, the target cells for $1\alpha,25(OH)_2D_3$ appear to be osteoblastic stromal cells. Osteoblastic cells produce several proteins such as BGP, MGP, osteopontin, and the third component of complement (C3) in response to the vitamin. They appear to be somehow involved in osteoclast differentiation and functions. Thus, Vitamin D plays an important role in bone resorption.[9] The target production of 1,25 DHCC is in the order of 25–100 μg and optimal values of reference of serum vitamin D level in adults are 30–100 ng/ml and values of 21–29 ng/ml are insufficient whereas <20 ng/ml is deficient.[10] The studies in animals done by Yamamoto et al.,[11] and Kale et al.[12] showed an increase in tooth movement rate upon local administration of vitamin D_3. The recent systematic reviews of human trials also concluded that local administration of Vitamin D enhances the OTM (Orthodontic Tooth Movement), but hasn't reported any study conducted related to the oral administration of Vitamin D and its effects on tooth movement.[7,13] Studies in humans done by Blanco et al. showed positive outcomes upon systemic administration of vitamin D in humans.[14] To the best of our knowledge, there was only one study conducted in humans involving oral systemic administration of vitamin D with positive results however there was no mention of the CONSORT statement guidelines of randomized controlled trial, no power of the study, and no method of randomization. Also, the effect of vitamin D administration on root resorption was not assessed. Hence, this randomized controlled trial was planned to determine the effects of oral systemic administration of vitamin D on the rate of orthodontic tooth movement and root resorption in patients undergoing fixed orthodontic treatment requiring upper first premolars extraction.

2. Materials and methods

2.1. Trial design

This study was a single centre, two-arm randomized controlled clinical trial conducted in the Department of Orthodontics and Dentofacial Orthopaedics in collaboration with the Department of Biochemistry, Pt. B. D. Sharma University of Health Sciences, Rohtak after obtaining approval from the institutional ethical committee (PGIDS/IEC/2019/20). The trial was registered prospectively in Clinical Trials Registry (NCT05202496) and was conducted according to the CONSORT statement (Fig. 1) and the CONSORT Statement: Application within and adaptations for orthodontic trials.[15]

2.2. Participants, eligibility criteria, and settings

The study sample was selected from subjects reporting to the outpatient department of the institute requiring fixed orthodontic treatment. A total of 94 patients were examined for the study from January 2021 to September 2023 and 32 patients (18–24 years)

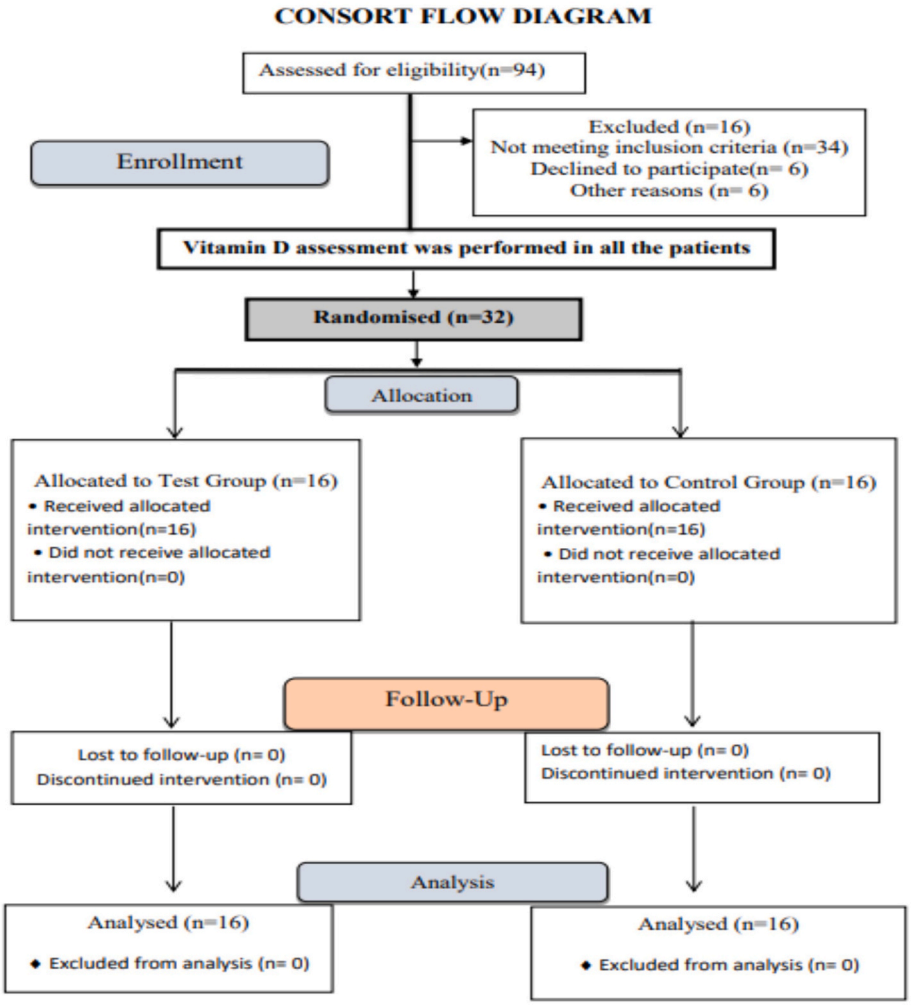

Fig. 1. CONSORT flow diagram.

fulfilling the inclusion criteria were selected. The included patients fulfilled the criteria of having Angle's Class I malocclusion requiring at least extraction of upper first premolars and normal Vitamin D level before randomization. The patients having any systemic/bone/metabolic/hormonal disease illness known to affect the outcome of orthodontic therapy or requiring administration of vitamins, any kind of prolonged drug administration (chronic drug intake) or significant medical history (including drug allergy), pregnant or lactating women and hypersensitivity to Vitamin D or its analogues/derivatives were excluded from the study. Patients were informed of all the theoretical risks and benefits of the interventions under test. A valid, informed written consent from the patient and an agreement to be randomized was obtained before registering for this clinical study.

2.3. Interventions

The patients were randomly divided into the following two groups based on the type of intervention.

Group 1 (Experimental Group) = Vitamin D supplementation in the form of capsules was given before the initiation of canine retraction
Group 2 (Control group) = Placebo tablets with no medicinal content were given

All the patients of both groups had received a detailed orthodontic and periodontal evaluation (clinical and paraclinical examinations) and pre-treatment orthodontic records including CBCT and Vitamin D levels were recorded. Before alignment and leveling patients were randomly divided into Group 1 and Group 2. Preadjusted edgewise 0.022″ slot MBT brackets (Ortho Organizers, Carlsbad, CA) were bonded by a single investigator (R. M.) after the therapeutic extraction of the first premolars performed by single oral surgeon (R.S.). All patients received instructions regarding good oral hygiene. Also, it was prohibited to take drugs during the follow-up period and in case of pain associated with dental movement, only the administration of paracetamol was allowed as it had been proven that it has no role in affecting the tooth movement.[16] After alignment and levelling of the arch and passive ligation of 0.019 X 0.025" stainless steel archwire, individual canine retraction was started with a nickel-titanium closed-coil spring (Ortho-organiser, Carlsbad, CA) stretched to generate a force of 100 gm on each side measured with dontrix gauge (Fig. 2). The 16 patients in group 1 were instructed to have 0.25 μg of Vitamin D capsules every day during the phase of space closure and were asked to report any unwanted effects or problems after taking the capsules. In group 2, 16 patients received placebo tablets every day during the phase of space closure. Pre-treatment and subsequent vitamin D levels at four monthly intervals were checked in the study group and control group in the Department of Biochemistry of the institute.

2.4. Primary outcome

Alginate impressions of all the patients were taken and study models were scanned using the model scanner (Up3D, Shenzhen, China) to produce the digital model. The STL file generated from the scanner software was uploaded in the MeshLab software (Version 2022.02, ISTI-CNR, Pisa, Italy). The digital models were superimposed at the third rugae of the maxilla and the linear measurements were calculated from the canine cusp tips of the models at various time intervals (Fig. 3). The rate of canine retraction was measured at T0 - before starting of retraction i.e. zero for both the groups, T1 - after 4 weeks of retraction, T2 - after 8 weeks of retraction, T3 - after 12 weeks of retraction, T4 - after 16 weeks of retraction, T5 - after 20 weeks of retraction/till the completion of canine retraction.

2.5. Secondary outcome

The determination of root resorption was done with CBCT scans of the area of interest obtained using Carestream CS-9300 3D digital imaging system just before the start of retraction and after completion of retraction. Volumes were reconstructed using a 180 μm voxel; tube voltage 85 kVp; current measured 5–8 mA; and exposure time 20 s (field of view: 5 × 10 cm). 3D volume rendering of the DICOM data of the CBCT scans was performed with 3D slicer software (version 4.11.20210226; www.slicer.org) on Microsoft Windows 10. Upon volume rendering, the regions of the scan outside the region of interest (ROI) were sculpted manually and removed with step-by-step segmentation and careful recapitulation from all the aspects of the volume rendered view. Thereafter, the tooth of interest was isolated in the volume-rendered view and volume of the ROI was calculated with the

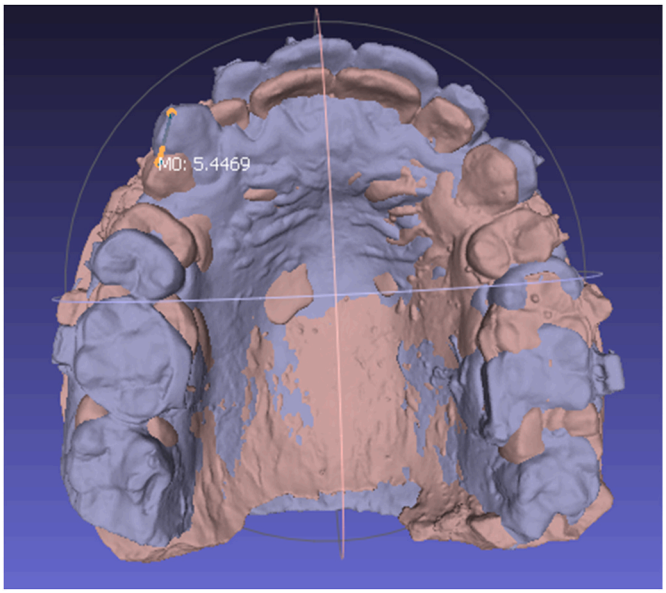

Fig. 3. Assessment of canine retraction (in mm) after superimposition of 3D models.

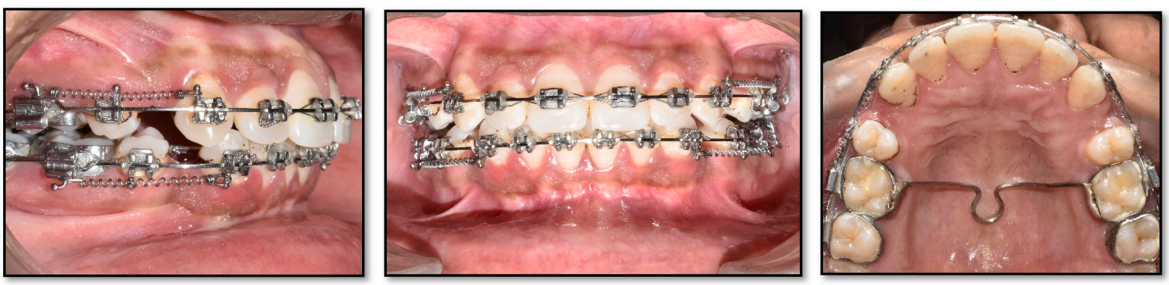

Fig. 2. Representative case of the study.

help of volume determination tool of the segment statistics. The difference in the volumetric measurement was calculated with the formula used as follows: 13RR = 13R0 - 13R1 where, 13R0 = pre-treatment volumetric measurement of the root of right canine, 13R1 = post-alignment volumetric measurement of the root of right canine, 13RR= Amount of root resorption of right canine. Similarly, the volumetric root resorption was calculated for the left canine (Fig. 4).

All the measurements were performed by the other author (D.K.) of the study who is calibrated to perform the measurements and is not involved in taking the records of the patients. The measurements were repeated on 10 % of the sample randomly selected by the author (R.S.) after 3 weeks of the first measurements and also this author was not involved in any clinical measurements. The intraobserver reliability was assessed with the intraclass correlation coefficient and showed a good correlation (r = 0.90) for the repeated measurements.

2.6. Sample size estimation

The sample size was calculated from a previous human study[14] with effect size being the mean difference in tooth movement between two groups and an average of standard deviation of two groups. G power software was used for determining sample size with a power of 95 % and alpha significance level at 0.05, and accounting for a dropout of 20 %, a total of 16 patients were kept in each group.

2.7. Randomization and allocation concealment

The patients meeting the inclusion and exclusion criteria were allocated to the two groups using block randomization with a block size of four each kept with the author not associated with clinical treatment (R. S.). Computer software-generated randomization codes were used (www.randomizer.org). The opaque sealed envelopes with sequential numbers were used for allocation concealment. The patients and evaluator for analysis were blinded to the nature of the intervention. The data was coded and presented to the blinded evaluator for analysis.

2.8. Statistical analysis

Statistical analysis was done with Statistical Package for Social Sciences (SPSS, version 23.0, Chicago, USA). The normality of data was assessed with the Shapiro-Wilk normality test. The data was normally distributed and parametric tests were used for statistical analysis. Descriptive statistics, including mean, standard deviation, and minimum and maximum values were calculated. Unpaired *t*-test was used to compare inter-groups means. Paired *t*-test was used for the intra-group comparison of means. For all the statistical tests, $p \leq 0.05$ was considered to be statistically significant.

3. Results

The demographic and clinical characteristics of the sample i.e. age, gender, and serum vitamin D level were matched for control and experimental group (Table 1). Fig. 1 shows the CONSORT diagram of the patients included in the randomized clinical trial. The study consisted of 16 males and 16 females with a mean age of 22.38 ± 2.01 years (mean age of 22.13 ± 1.99 years of the experimental group and 22.63 ± 2.03 years of the control group). The mean serum vitamin D levels of the control and experimental groups were 31.4 ± 0.03 ng/ml and 31.2 ± 0.04 ng/ml respectively at the start of treatment (Table 2). The statistical comparison of the baseline data between the two groups did not reveal any significant differences. No patient dropout was noted in the study and the canine retraction was successfully completed in both the groups. There was rise in serum vitamin D levels in the experimental group at the end of 30 days, 60 days, 90 days, and 120 days with values of 33.3 ± 0.07 ng/ml, 37.8 ± 0.08 ng/ml, 40.5 ± 0.07, 43.6 ± 0.06 in the experimental group and 31.2 ± 0.06 ng/ml, 30.8 ± 0.08 ng/ml, 31.3 ± 0.06 ng/ml and 31.4 ± 0.08 ng/ml in the control group respectively (Table 2). It was statistically significant at the end of 60, 90, and 120 days and the levels were within the lower range of serum vitamin D and no side effects were reported by the patients during the trial.

Table 3 shows the intergroup comparison of canine retraction. The

Table 1
Demographics and clinical characteristics of sample.

	Males	Females	Age (in years) (Mean ± SD)	Serum Vitamin D level (ng/ml) (Pretreatment)
Group 1 (n = 16)	9	7	22.13 ± 1.99	31.2 ± 0.04
Group 2 (n = 16)	7	9	22.63 ± 2.03	31.4 ± 0.03
Total (n = 32)	16	16	22.38 ± 2.01	31.4 ± 0.80

Group 1 = Vitamin D supplementation given.
Group 2 = Control group.

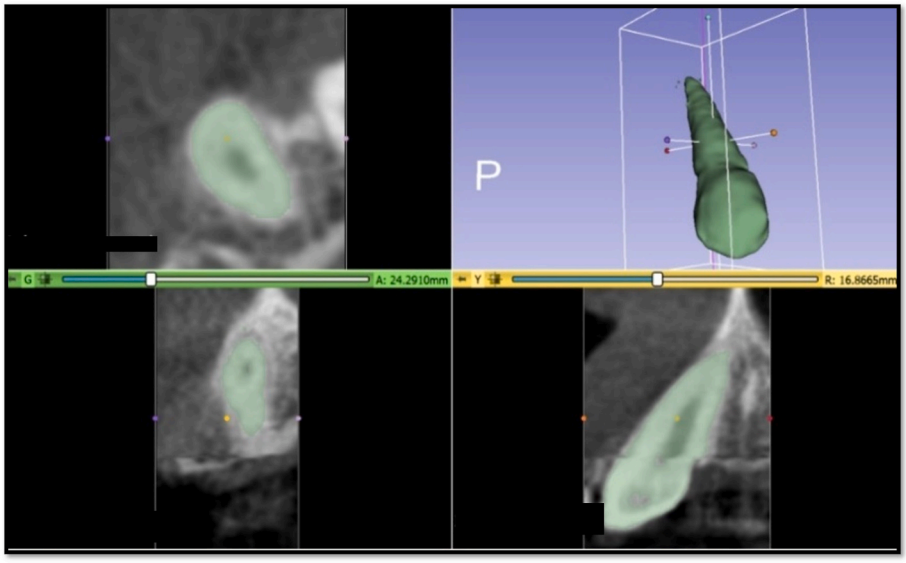

Fig. 4. Calculation of volumetric root resorption (in mm^3) with Slicer software.

Table 2
Serum vitamin D levels (ng/ml) at monthly intervals in group 1 and group 2.

Serum Vitamin D level (ng/ml)	Pretreatment	P value	At the end of 30 days	P value	At the end of 60 days	P value	At the end of 90 days	P value	At the end of 120 days	P value
Group 1	31.2 ± 0.04	0.59	33.3 ± 0.07	0.46	37.8 ± 0.08	0.04*	40.5 ± 0.07	0.03*	43.6 ± 0.06	0.03*
Group 2	31.4 ± 0.03	(NS)	31.2 ± 0.06	(NS)	30.8 ± 0.08		31.3 ± 0.06		31.4 ± 0.08	

*P ≤ 0.05 = Statistically significant NS = Non-significant.
Group 1 = Vitamin D supplementation given.
Group 2 = Control group.

Table 3
Intergroup comparison of rate of canine retraction between the experimental and control group patients during various time intervals.

Time Intervals	Group 1 (Mean ± SD) (Right Side)	Group 1 (Mean ± SD) (Left Side)	Group 1 (Mean ± SD)	95 % CI	Group 2 (Mean ± SD) (Right Side)	Group 2 (Mean ± SD) (Left Side)	Group 2 (Mean ± SD)	95 % CI	Mean Difference (Group 1 vs Group 2)	Percentage Change	P value (Group 1 vs Group 2)
T1-T0	1.32 ± 0.04	1.32 ± 0.03	1.32 ± 0.03	1.30–1.33	1.05 ± 0.15	1.02 ± 0.18	1.04 ± 0.16	0.96–1.12	0.28 ± 0.12	21.4	0.001*
T2-T1	1.34 ± 0.04	1.34 ± 0.03	1.34 ± 0.03	1.32–1.35	1.03 ± 0.13	1.08 ± 0.13	1.05 ± 0.13	0.99–1.11	0.29 ± 0.10	21.7	0.001*
T3-T2	1.36 ± 0.04	1.37 ± 0.03	1.37 ± 0.03	1.35–1.38	1.07 ± 0.12	1.05 ± 0.09	1.06 ± 0.11	1.01–1.11	0.31 ± 0.08	23.3	0.001*
T4-T3	1.41 ± 0.04	1.42 ± 0.05	1.41 ± 0.05	1.38–1.43	1.01 ± 0.11	1.07 ± 0.09	1.04 ± 0.10	0.99–1.09	0.37 ± 0.06	28.1	0.001*
T5-T4	0	0	0	0	1.07 ± 0.08	1.07 ± 0.09	1.07 ± 0.08	1.03–1.11			
T4-T0	5.42 ± 0.15	5.46 ± 0.11	5.44 ± 0.13	5.37–5.50	4.22 ± 0.22	4.29 ± 0.25	4.26 ± 0.23	4.15–4.37	1.18 ± 0.10	23.6	0.001*
T5-T0	0	0	0	0	5.29 ± 0.23	5.36 ± 0.26	5.33 ± 0.24	5.21–5.45			

*P ≤ 0.05 = Statistically significant.
Group 1 = Vitamin D supplementation given.
Group 2 = Control group.
T0 = before starting of retraction, T1 = after 4 weeks of retraction, T2 = after 8 weeks of retraction, T3 = after 12 weeks of retraction.
T4 = after 16 weeks of retraction, T5 = after 20 weeks of retraction/till the completion of canine retraction.

mean canine retraction in experimental and control groups from T0 to T5 was 5.44 ± 0.13 mm and 5.33 ± 0.24 mm respectively and was similar for both groups. There were statistically significant differences between the groups at various time intervals. The differences in the mean canine retraction between group 1 and group 2 at T1-T0, T2-T1, T3-T2, T4-T3, and T4-T0 were 0.28 ± 0.12, 0.29 ± 0.10, 0.31 ± 0.08, 0.37 ± 0.06 and 1.18 ± 0.10 mm respectively. The total mean canine retraction for group 1 was achieved at T4 time interval while it was achieved at T5 interval for group 2. A mean of approximately 23 % increase in the rate of canine movement was noted in the experimental group. The intergroup comparison of maxillary canines **(13, 23)** showed no statistically significant difference (P ≥ 0.05) in volumetric root resorption between experimental and control groups (Table 4).

Table 4
Volumetric changes (mm^3) in the retracted canine roots between group1 and group 2 from pretreatment (T0) to postretraction (T4/T5).

	Group 1		Group 2		P Value
	13	23	13	23	Group 1 vs Group 2
Mean pretreatment volume	679.34 ± 6.46	682.45 ± 6.35	681.45 ± 6.69	678.67 ± 6.38	0.33 (for 13) (NS) 0.43 (for 23) (NS)
Mean posttreatment volume	634.23 ± 7.46	641.37 ± 8.35	653.18 ± 7.68	645.36 ± 7.89	
Mean loss	45.13 ± 8.56	41.11 ± 6.63	27.17 ± 6.67	33.29 ± 6.80	
Percentage change	6.83	6.23	4.18	4.96	

Group 1 = Vitamin D supplementation given.
Group 2 = Control group.
13 = Maxillary right canine 23 = Maxillary left canine.

4. Discussion

Orthodontic treatment time involving extraction of premolars generally requires 18–24 months of treatment. Any procedure that helps in reducing this treatment duration can be attributed to the terminology of acceleration in tooth movement.[17] This acceleration in orthodontic tooth movement can be carried out with the help of various methods involving both surgical and non-surgical approaches. Surgical methods reported in the literature consist of corticotomy, microsteoperforations, piezocision, etc. while non-surgical methods comprised of vibration, low-intensity pulsed ultrasound, and biological methods.[1,18,19] Various biological methods include the use of Prostaglandin (PG), Osteoprotegerin (OPG), Interleukin (IL), RANK & RANKL, Vitamin D, Parathormone (PTH) and Relaxin. One such biological method includes the local intraoral delivery of Vitamin D and it has been associated with variable results with studies reporting the increase in orthodontic tooth movement when injected locally in different dosages.[20–23] The oral administration of Vitamin D in animal studies has shown some promising results regarding the acceleration of tooth movement but oral intake in humans had limited literature either in favour or against its use.[14,20,23] A recent systematic review and meta-analysis by Tini A et al.[24] had also elucidated the weak relation in enhancement of orthodontic tooth movement with Vitamin D supplementation either in the form of local or systemic manner and concluded that future human studies devoted toward investigating the influence of vitamin D in the realms of OTM should be undertaken. Therefore, this study was undertaken to study the effect of oral administration of Vitamin D and comprised of thirty-two patients with 16 patients in the experimental group administered calcitriol in its recommended initial dosage of 0.25 mcg/day and monitored at every follow-up with determination of Serum vitamin D levels at monthly

intervals. The increase in the orthodontic tooth movement was observed at all time intervals after oral intake of Vitamin D and the result was statistically significant. These results can be attributed to the osteoclastic action of vitamin D on reaching its higher concentration. This concept of osteoclastic resorption by 1α,25$(OH)_2D_3$ is again discussed in the systematic review by Arqub et al.[1] in which the effects of Vitamin D on bone turnover have been explained and depend on the stage of osteoblast differentiation.[25,26] It has been reported that normal levels of Vitamin D act via the vitamin D receptor (VDR) in mature osteoblasts, decreasing the Receptor Activator of Nuclear Factor Kappa-B Ligand (RANKL)/Osteoprotegerin (OPG) ratio and leading to reduction of osteoclastic bone resorption. Similarly, calcitriol acts in mature osteoblasts increasing bone formation rate.[12] However, increased levels of Vitamin D act in less-mature osteoblasts elevating the RANKL/OPG ratio, thus stimulating osteoclastic bone resorption.[27] Studies of conditional deletion of the VDR from the osteoblast lineage suggest that early osteoblastic cells may mediate an increase in bone resorption induced by Vitamin D. Thus, the effect of Vitamin D is related to increasing the expression of RANKL by local cells and therefore activation of osteoclasts and hence increases rate of orthodontic tooth movement.

The rate of canine retraction was measured on digital models with the help of Mesh Lab software which is a well-established method and used in various studies for measurement.[28] The mean increase in the rate of canine retraction between the experimental and control sides was found to be 0.26, 0.31, 0.30, and 0.39 mm during the 4th week, 8th week, 12th week, and 16th week respectively and hence, the experimental group showed 23.62 % times faster tooth movement than the control group. The results of the study correlate with the findings of Ciur et al. who showed a statistically significant difference in total tooth movement between the vitamin D supplemented group and conventional orthodontics group.[20] The present study findings are also in consensus with the findings by Al-Hasani et al. who injected either 15 pg, 25 pg, or 40 pg/0.2 ml calcitriol diluted with 10 % dimethylsulfoxide (DMSO) in three groups and found that the dose of 25 pg calcitriol produced about 51 % faster rate of experimental canine movement compared to control, while each of the 15 pg and 40 pg doses resulted in about 10 % accelerated OTM.[23] However, the findings are contradictory with a previous study by Varughese et al. [21]which indicated that the effect of locally administered calcitriol (50 pg/ml) on OTM is highest (during 8th and 12th week) when administered in doses relatively equivalent to the normal physiologic level, after which the rate of movement decreased in the 16th week. The results of our study are also in contradiction to the study conducted by Shetty et al.[29] which involved the locally administered Vitamin D3 in a vehicle of local anaesthetic (LA) solution into the buccal vestibule immediately distal to canine to be retracted on experimental side and only LA solution on contralateral side on the 7th, 21st, and 47th days of canine retraction. The amount of canine retraction 60 days was 1.14 mm on the experimental side and 1.86 mm on the control side which is opposite to the findings of our study. This may be attributed to the fact that 25(OH) vitamin D is concerned with the effects of bone formation and higher levels of 1α,25$(OH)_2D_3$ is concerned with osteoclastic bone resorption.

The direct comparison of oral administration of Vitamin D with other biological methods has not been elucidated in the literature. In comparison with other biological agents affecting tooth movements the present study corroborates with findings of study using the leucocyte platelet rich fibrin inside the extraction socket and observed an increase in tooth movement, but its effects are for short term only.[4] While studies by Tehranchi et al.[30] and Eltimamy et al.[31] showed no increase in the OTM after the use of platelet rich plasma (PRP). The studies determining the effect of PGE1 had also shown the positive influence of its use in increasing the tooth movement but those studies are either non-randomized or had some serious biases.[32,33] Therefore, oral administration of Vitamin D can be a better alternative as biological agent in increasing orthodontic tooth movement.

The inter-group comparison of root resorption of retracted canines (13, 23) showed no statistically significant difference in volumetric root resorption between the experimental and control groups. This finding is in association with the other studies evaluating the effect of root resorption of Vitamin D and other biological agents.[3,4,30] This proves the efficacy and safe nature of the calcitriol supplemented in our study.

The study has some limitations regarding the non-evaluation of effects based on gender differences and a longer follow-up is needed for better assessment of the long-term effect of systemic administration of calcitriol.

5. Conclusion

The systemic administration of Vitamin D showed statistically significantly increase in the rate of tooth movement. There is no difference in volumetric root resorption with this intervention as compared to the conventional method. The systemic administration of calcitriol may become a readily available and effective treatment modality to accelerate orthodontic treatment with excellent patient acceptance.

Ethical clearance and registration

Ethical approval from the institutional ethical committee (PGIDS/IEC/2019/20) was obtained prior to the start of study. The trial was registered prospectively in Clinical Trials Registry (NCT05202496).

Consent

Patients were informed that they will be enrolled in a study after explaining the objectives of the study and only those patients who had given consent were included.

Disclosure of interest

The authors declare that they have no competing interest.

Contributions of authors

1. Dr. Davender Kumar - Concept, design, data analysis, manuscript preparation, manuscript editing and manuscript review.
2. Dr. Revathi MN - Literature search, clinical studies, data analysis, manuscript editing and manuscript review.
3. Dr. Rekha Sharma–; Concept, Design, definition of intellectual content, statistical analysis, manuscript preparation, manuscript editing and manuscript review.
4. Dr. Ashuma Sachdeva- Design, definition of intellectual content, manuscript editing and manuscript review.
5. Dr. Nameksh Raj Bhupali - Definition of intellectual content, literature search, clinical studies, data analysis, manuscript preparation, manuscript editing and manuscript review.
6. Dr. Ravinder Solanki - Clinical studies, data analysis, manuscript preparation, manuscript editing and manuscript review.

The manuscript has been read and approved by all the authors, that the requirements for authorship have been met, and that each author believes that the manuscript represents honest work.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Abbreviations

CBCT: Cone Beam Computed Tomography
OTM: Orthodontic Tooth Movement
STL: Standard Tessellation Language
DICOM: Digital Imaging and Communications in Medicine
ROI: Region of Interest
RR: Root Resorption
VDR: Vitamin D Receptor
RANKL: Receptor Activator of Nuclear Factor Kappa Ligand
OPG: Osteoprotegerin
PRP: Platelet Rich Plasma
13: Right Maxillary Canine
23: Left Maxillary canine