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Vitamin D and Orthodontic Tooth Movement

Project Submitted to

The College of Dentistry, University of Baghdad, Department of Orthodontics in Partial Fulfillment for the Bachelor of Dental Surgery

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Certification of the Supervisor

I certify that this project entitled "**Vitamin D and Orthodontic Tooth Movement** " was prepared by the fifth- year student **Ali Hassan Abdel-Hadi** under my supervision at the College of Dentistry/University of Baghdad in partial fulfilment of the graduation requirementsfor the Bachelor Degree in Dentistry.

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B.D.S ., M.Sc.

Dedication

I would like to dedicate my humble effort to my supportive **Father** and **Mother.** Their affection, love, encouragement and prays at day and night made me able to succeed with honor.

Ali Al-Taie

Acknowledgment

First and foremost, praises and thanks to **Allah** Almighty for helping me fulfill my dream, for his blessings throughout my work to complete it successfully.

I would like to extend my deepest respect and gratitude to the Dean of College of Dentistry, University of Baghdad, **Prof. Dr. Raghad Al-Hashimi**.

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I would like to show my deep and sincere gratitude to my research supervisor, **Lect. Alaa Faleh Albo Hassan** for her advice, encouragement, and guidance in planning and conducting this project.

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List of Abbreviations

Abbreviation	Meaning
OTM	Orthodontic tooth movement
RCT	Randomized clinical trial
Pg/ml	Picogram per milliliter
ECM	Extracellular matrix
COR	Center of resistance
PDL	Periodontal ligament
RANKL	Receptor activator of nuclear factor kappa-b ligand
OPG	Osteoprotegerin
Mg/ml	Milligram per milliliter
ng/mL	Nanograms per milliliter
OH	Hydroxy
mL	Milliliter
nmol/L	Nanomoles per liter
GCf	Gingival crevicular fluid
PDL	Periodontal ligament
HMGB1	High mobility group box-1
VEGF	Vascular endothelial growth factor
DMSO	Dimethylsulfoxide
CT	Computed tomography
UV	Ultraviolet
T0	Base line time (at start of treatment)
T1	First time interval (after 4 weeks)
T2	Second time interval (after 8 weeks)
T3	Third time interval (after 12 weeks)
Ng/ml	Nanogram per milliliter
IU	International unit
%	Percentage

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Introduction

When force is applied, it alters the local blood flow, which triggers the release of numerous inflammatory mediators and causes the periodontal ligament and alveolar bone to remodel **(Jiang *et al.*, 2016)**. This results in orthodontic tooth movement (OTM). One of the biggest issues with orthodontic therapy continues to be lengthy treatment timeframes. According to **(Tsichlaki *et al.*, 2016)**, complete orthodontic treatment with fixed appliances may take an average of two years, however this time frame may be increased depending on the degree of the malocclusion, the difficulty of the operation, or factors specific to the patient and practitioner **(Fisher *et al.*, 2010).**

Several surgical and nonsurgical techniquesthat aim to speed up tooth movement and improve bone remodeling have been devised in an effort to shorten treatment times **(Mavreas and Athanasiou, 2008).** Vitamin D3 was one of the nonsurgical methods that increased osteoclast activity and hastened OTM **(Collins and Sinclair, 1988)**. By forcing osteoclasts to differentiate from their progenitors and by increasing current osteoclast activity, vitamin D3 increased bone resorption **(Kogawa *et al.*, 2013).**

Aim of Study

The aim of the study to know the possible sources and the normal level of vitamin D and it’s effect on orthodontic tooth movement.

Chapter One: Review of Literature

1.1 Orthodontic Tooth Movement

When orthodontic force is used to shift teeth, dental and parenthetic tissues, such as the gingiva, alveolar bone, periodontal ligament (PDL), dental pulp, which are remodeled. These tissues express extensive microscopic and macroscopic changes when exposed to varying degrees of frequency, magnitude, and duration ofmechanical loading. Dental eruption and physiological tooth drift are very different from orthodontic tooth movement. The former is characterized by the instantaneousformation of regions of pressure and tension in the PDL **(Jiang *et al.*, 2016).**

1.2 Physiology of Tooth Movement

Orthodontics is a special discipline dedicated to the investigation and practice of moving teeth through the bone. Moving teeth through the dentoalveolar complex is a synergistic sequence of physical phenomenon and biological tissue remodeling **(Li *et al.*, 2018).** By contrast, dependent on the physical features of the force applied and the size and biological response of the PDL, OTM may occur slowly or quickly. This force produced pressure change blood flow and the vascularityof the PDL, directing to the local creation and liberation of various key molecules, like cytokines, growth factors, colony stimulating factors, neurotransmitters, and metabolites of arachidonic acid. Such molecules can produce many cellular reactionsaround and in teeth by different cell types, generating a beneficial microenvironmentfor tissue resorption or deposition **(Cattaneo and Cornelis, 2021).**

OTM process is express by remodeling of collagenous extracellular matrix (ECM) of bone and periodontal ligament (PDL) stimulated by external mechanical force **(Rangiani *et al.*, 2016).** In PDL, pressure and tension areas are created after force starting **(Asiry, 2018).**

1.3 Types of orthodontic tooth movements

Orthodontic tooth movements can be defined as the initial displacement of the toothwithin the socket region, **(Graber *et al.*, 2016).**

Orthodontic tooth movement can be categorized into the following basic types **(Graber *et al.*, 2016)**:

1.3.1. Tipping Movement

It is the simplest tooth movement and is achieved by theapplication of single point of force to the crown of a tooth. As a result, the tooth moves under the influence of force in the direction of least resistance. So that the crown moves in the direction of applied force and the apex is in the opposite direction. (Figure 1)

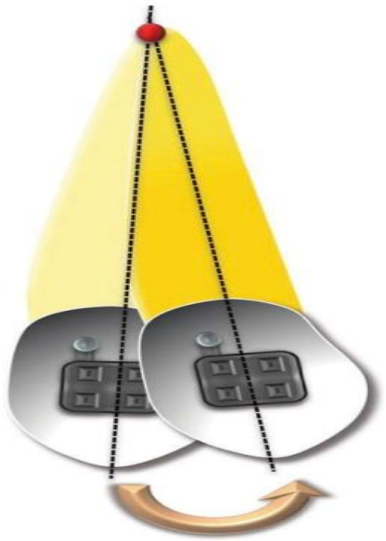

Figure 1. Tipping Movement (Nanda, 2015)

1.3.2. Bodily movement:

Bodily movement or translation of teeth occurs when the crown with the root moves an equal distance in the same direction. This happens when the applied force passes through a tooth's center of resistance (COR). The COR of a single-rooted tooth

lies between one- third and one-half of the root, while in a multi-rooted tooth, it lies between the roots (Figure 2).

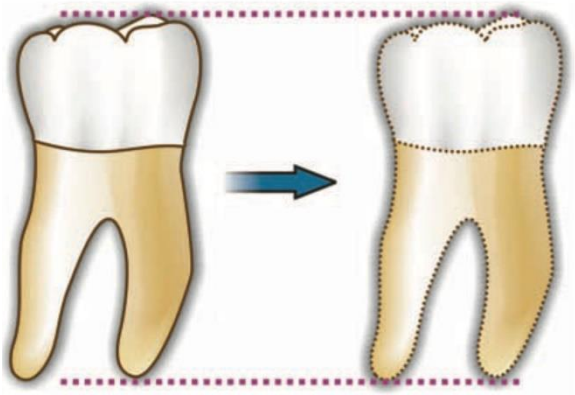

Figure 2. Bodily movement (Singh, 2007)

1.3.3. Rotation:

Rotation is said to take place when there is movement of points of a tooth along the arc of a circle, with the center of resistance being the center of the circle, pure rotation (Figure 3). The rotation takes place on the long-axis of the tooth (the angulation of the long-axis of the tooth remains unaltered) (Figure 4).

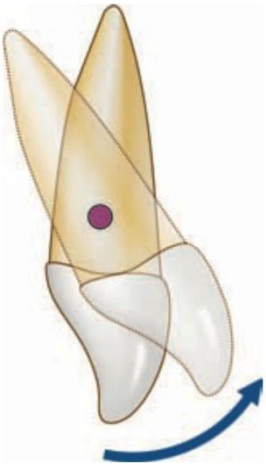

Figure 3. Pure rotation (singh, 2007)

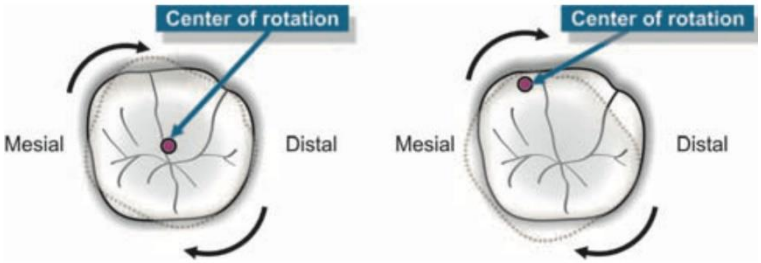

Figure 4. Rotation on the long-axis of the tooth (Singh, 2007)

1.3.4. Vertical movement

It is primarily bodily movement; it may be either intrusion or extrusion of the tooth from the socket. Intrusion occurs when a tooth bodily moves along its long axis in an apical direction (towards the gingiva). In contrast, extrusion is the bodily movement of a tooth along its long axis towards theocclusal plane (Figure 5).

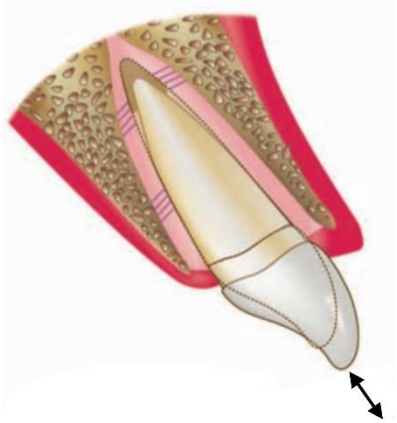

Figure 5. Intrusion and extrusion movement (singh, 2007)

1.3.5. Root Movement (Up-righting and Torqueing)

Torque movement is achievedby keeping the crown of a tooth stationary and applying a moment of force to movethe root only. Up-righting is defined as deliberate mesial or distal movement of the apices (Figure 6).

Figure 6. Root movement (Nanda, 2015)

1.4 Theories of Orthodontic Tooth Movement

The mechanisms involved in conversion of orthodontic forces into biologic activity are not completely understood **(Sabane *et al.*, 2016).**

Three possible theories of tooth movement are advocated:

1.4.1 Bone-bending theory:

Farrar was the first to propose in **(1888)** that alveolar bone bending is essential for the movement of orthodontic teeth. Any tissues close to the orthodontic force application site will be affected when it is applied to the tooth. These stresses cause the solid periodontal ligament, teeth, and bones to bend **(Reddy *et al.*, 2015).**In comparison to other tissues, bone was shown to be more elastic and to bend significantly more easily in response to force application **(Asiry, 2018).** According to this theory: **(Patel *et al.*, 2012)**

1.4.2 The bio-electric theory:

This theory was first put forth by **Bassett** and **Becker** in **(1962)** when they noticed that any mechanical distortion of the crystalline structures of collagen and hydroxyapatite resulted in the generation of electron migration and the formation ofan electric field. This phenomenon was known as "piezoelectricity," and it was theorized that this was what caused tooth movement **(Reddy *et al.*, 2015).** These signals have the following characteristics: **(Proffit, 2012)**

They have a quick decay rate which means when the force is applied it is initiated and at the same time it disappears quickly even with the force maintained. Production of an equivalent signal in the opposite direction upon force removal. The Bio-electric theory of tooth movement is explained by the alveolar bonedeflection brought on by orthodontic forces and the ensuing alteration in theperiodontal ligament (figure 7). According to observations, when abone bends, an electronegative field is created, causing the concave side to lead tobone deposition and the convex side to elicit bone

resorption **(Patel *et al.*, 2012).**Thus, external electric current and orthodontic pressures work together to speed upthe movement of the teeth during orthodontic treatment **(Sabane *et al.*, 2016).**

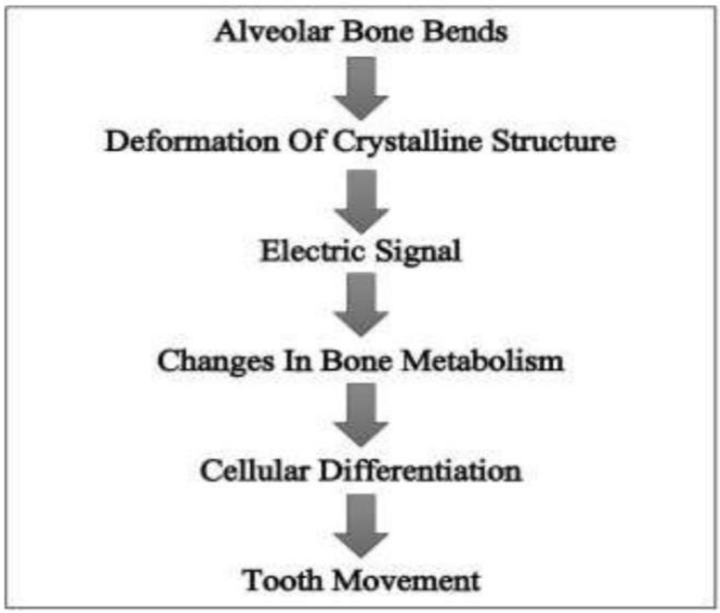

Figure 7. Bio-electric theory of tooth movement. (Asiry, 2018)

1.4.3 Pressure-tension theory:

A tooth moves in the periodontal space by producing a pressure and tensionside, according to the histology studies of **Sandstedt, Oppenheim, and Schwarz in1905, 1911, and 1932,** respectively **(Patel *et al.*, 2012).** According to this view, thePDL detects a change in mechanical forces or stresses when orthodontic force is applied. In order to cause bone resorption and apposition, respectively, PDL progenitor cells differentiate into compression-associated osteoclasts and tension- associated osteoblasts **(Jiang *et al.*, 2016).**

Due to the periodontal ligament's compression and the resulting change in blood flow, oxygen levels are decreased on the pressure side, which is followed by hypoxia,

and increased on the tension side. Other metabolite proportions also fluctuate; these variations might affect cellular activity and differentiation directly or indirectly (through the release of other physiologically active substances) **(Niklas *et al.*, 2013; Sabane *et al.*, 2016)** To control the bone and periodontal ligament remodeling during tooth movement, compression and tension sides are linked to specific signaling factors, including secreted factors like receptor activator of nuclear factor Kappa-B ligand (RANKL) and osteoprotegerin (OPG), transcription factors like hypoxia-inducible factor, cytokines, prostaglandins, tissue necrosisfactors, and proteases **(Li *et al.*, 2018).**

1.5 Phases of Orthodontic Tooth Movement

Orthodontic tooth movement consists of three phases:

1.5.1 Initial phase

The initial phase occurs immediately after the application of force onto the tooth. This results in rapid tooth movement over a short distance and then stops. Thismovement displaces the tooth within the periodontal membrane and bends the alveolar bone to a certain extent. The initial phase results in about 0.4 to 0.9 mm oftooth movement and usually occurs within a week after applying initial force **(Asiry,2018; Maltha *et al.*, 2021).**

1.5.2 Lag phase

The Lag phase shows little to no tooth movement and witnesses the formationof hyalinized tissue in the periodontal ligament. This hyalinized tissue must undergo resorption before further tooth movement can occur **(Li *et al.*, 2021).** The duration of the lag phase depends on the amount of force applied. Supposedly a clinician applies lighter force, the amount of hyalinized tissue will be less; hence resorption of the same will occur faster. In contrast, a more prolonged lag phase is seen when heavier forces are applied orthodontically. The duration of the lag phase also dependson factors such as the patient's age and the density of the alveolar bone **(Li *et al.*, 2021).**

1.5.3 Post lag phase

After the resorption of the hyalinized tissue or the lag phase, tooth movement progresses rapidly. This occurs in the post-lag phase, where bone undergoes resorption via the help of osteoclasts, resulting in direct resorption of the bone that faces the periodontal ligament **(Maltha *et al.*, 2021).**

1.6 Acceleration of Tooth Movement

When deciding on a course of treatment, patients should carefully examine the length of their orthodontic therapy. According to **Tsichlaki *et al.*, (2016),** regularactive treatment lasts an average of two years. Due to therapy challenges, a convoluted treatment plan, and/or personal factors, some patients require more time**(Fisher *et al.*, 2010).** According to **Segal *et al.*, (2004)** and **Talic (2011),** long-term orthodontic treatment can have a number of negative side effects, including pain anddiscomfort, gingival recession, dental cavities, and root resorption. Additionally, many adult patients wish to complete their orthodontic treatment sooner for social or cosmetic reasons **(Rosvall *et al.*, 2009).** Because of this, orthodontists and patients have a fundamental interest in accelerating tooth movement and shortening treatment times **(Nimeri *et al.*, 2013; Uribe *et al.*, 2014; Fathimani *et al.*, 2015).**

1.7 Methods of Acceleration Orthodontic Tooth Movement

There are many ways of acceleration OTM like Surgical approach **(Keser and Dibart, 2013; Alikhani *et al.*, 2015)**, Laser **(Salehi *et al.*, 2016)**, Vibration **(Leethanakul *et al.*, 2016; Liao et al., 2017)**, Medication **(Nimeri *et al.*, 2013; Graber *et al.*, 2016)** and Vitamin D3 **(Feldman *et al.*, 2017).**

1.8 Vitamin D

1.8.1 Definition

Vitamin D is a fat-soluble steroid hormone that is naturally present in very few

foods, added to others, and available as a dietary supplement **(DRI, 2010).** It has mainly been known for its effects on bone density. The current therapeutic practices expand to cancer research, pediatrics, nephrology, dermatology, immunology, and genetics effects **(DRI, 2010; David *et al.*, 2011).**

1.8.2 Form and metabolism

Vitamin D is an essential steroid hormone. It can be found in two forms: vitamin D2 (ergocalciferol) and vitamin D3 (cholecalciferol) **(Barral *et al.*, 2007).** The major source of vitamin D, and of vitamin D3 in particular (which is endogenous in origin), is its storage in the cutaneous tissue after exposure to Ultraviolet-B (UV-B) radiation, a process which leads to vitamin D synthesis. Over 90% of vitamin Dis endogenous in origin, and the other 10% to 20% is provided by diet. Vitamin D is indispensable and extremely important **(Holick, 2008; Castro, 2011).** Vitamin D3 is absorbed through the consumption of animal products and isprimarily found in deep-water, oily fish. Meanwhile, vitamin D2 can be ingested through the consumption of plants and is most commonly produced by fungi. It is important to note that exposure to UV-B radiation through the skin is responsible foractivating vitamin D by converting 7-dehydrocholesterol to pre-vitamin D3, which,in turn, is quickly converted to vitamin D3, also known as cholecalciferol, in the dermis **(Castro, 2011).**

Vitamin D-binding protein, a carrier 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)2 D 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 the vitamin D receptor(VDR) **(Murray, 2014).**

1.8.3 Physiological effect of vitamin D

It is known that 1.25(OH)2D is one of the main regulators of calcium metabolism.

Though it does not originate from an endocrine gland, it is the only vitamin thought to have a hormonal function, since its pathway of molecularmodification yields active metabolites and its mechanism of action is similar to thatof steroid hormones. Vitamin D is important to bone mineralization, and a vitamin D insufficiency or deficiency can increase the chances of certain diseases (in addition to bone diseases), such as cardiovascular diseases, neoplasms, diabetes, multiple sclerosis, dementia, infectious diseases, and rheumatoid arthritis **(Alves *et al.*, 2013).**

Castro in (2011) states that the crucial action of vitamin D consists of maintaining calcium and phosphorus homeostasis in order to ensure bone mineralization, which is essential to all stages of life. (Vitamin D does play other roles and is active in up to 3% of the human genome). According to **Murray *et al.*,in (2014)** this homeostasis can be produced by the regulation of intestinal calcium absorption, reduced excretion through renal calcium reabsorption, and bone mineralmobilization. Moreover, vitamin D is involved in other events such as insulin secretion, differentiation of monocytic precursor cells, synthesis and secretion of parathyroid hormone and thyroid hormones, and inhibition of interleukin and immunoglobulin synthesis.

1.8.4 Vitamin D sources

Fatty fish like salmon, tuna, and mackerel are considered good dietary sources of vitamin D **(Wagner and Greer, 2008)**. Other foods that contain smaller amounts of vitamin D include egg yolks, cheese, and beef liver **(Shils and Shike, 2006)**. Certain foods like milk, orange juice, and breakfast cereals are also fortified with vitamin D to increase intake **(Wagner and Greer, 2008)**. Vitamin D supplements in the forms of vitamin D2 (ergocalciferol) and vitamin D3 (cholecalciferol) are commonly recommended for individuals who have limited sun exposure, are older, or have conditions that affect vitamin D absorption or metabolism **(Holick, 2007)**.

When consumed concomitantly with vitamin D-rich food, some substances can

increase or decrease the bioavailability of vitamin D in the body. Milk, for instance, increases vitamin D bioavailability; when it is concomitantly consumed with natural sources of vitamin D, it maximizes vitamin D absorption by a factor of3 to 10 due to the lactalbumin in its composition. Long- chain fatty acids also supportthe absorption of this vitamin. Alcohol and fiber, on the other side, contribute to calciferol loss through the bile, which reduces vitamin D bioavailability in the body**(Bueno *et al.*, 2008).**

1.8.5 Vitamin D levels

The level of vitamin D that determines its efficacy is obtained by measuring the serum concentration of 25(OH)D. This plasma dosage also contributes to the evaluation of endogenous intoxication. Considering 1 ng/mL as 2.496 nm values of 25(OH)D ≤ 20 ng/ mL indicate vitamin D deficiency, while values ranging from 21-29 ng/mL indicate vitamin D insufficiency, and values ≥ 30 ng/ mL indicate normal levels **(Lichtenstein *et al.*, 2013).**

The biologically active compound 1.25(OH)2D is not usually measured for this purpose, since (OH) D plasma levels are approximately one hundred times higher and have a much greater half-life than 1.25(OH)2D **(Freitas et al., 2017).**

Measurements of 1.25(OH)2D serum levels are indicated in patients with chronic kidney disease, rickets influenced by vitamin D levels, and granulomatous disease caused by hypercalcemia **(Lichtenstein *et al.*, 2013).**

An optimal concentration of 25(OH)D would be able to maintain adequate levels of parathyroid hormone. Therefore, this association produces improved definitions of calciferol deficiency and insufficiency that the use of increased serum PTH. When 25(OH)D levels are reduced to a level lower than 30 ng/mL or 75 nmol/L, serum calcium decreases, stimulating parathyroid gland to release parathyroid hormone. This change increases PTH levels and results in calcium reabsorption in the kidneys and bones **(Melhus *et al.*, 2007).**

1.8.6 Vitamin D3 deficiency

Inadequate food intake, decreased absorption and utilization, increased need, or higher excretion are the usual causes of nutrient deficiencies. Vitamin D deficiency can develop from the folwing causes: When regular Intake falls below recommended levels over time, sun exposure is restricted, the kidneys cannot convert 25(OH)D to its active form, or when vitamin D absorption from the digestive tract is insufficient, a vitamin D deficiency can develop.

Milk allergy, lactose intolerance, ovo-vegetarianism, and veganism are all linked tovitamin D deficiency diets **(DRI, 2010).**

The two most common illnesses caused by a vitamin D deficiency are rickets and osteomalacia. Rickets is a condition that affects children and is brought on by vitamin D insufficiency. Rickets is defined by the improper mineralization ofbone tissue, which leads to soft bones and skeletal abnormalities **(Wharton and Bishop, 2003).**

Adults with vitamin D deficiency may develop osteomalacia, which results in brittle bones. **Jones (2008) and DRI (2010)** Inadequate vitamin D levels can be indicated by symptoms like bone pain and muscle weakness, although these signs might be mild and go unnoticed at first.

1.8.7 Risk of vitamin D inadequacy

It is challenging to get enough vitamin D from natural food sources alone. For many people, taking foods fortified with vitamin D and, maybe, getting some sun exposures are crucial for preserving a healthy vitamin D level. For some populations, dietary supplements may be necessary to obtain the recommended dailyintake of vitamin D **(Alorabi and Hanaa, 2018).**

1.8.8 Vitamin D3 daily requirements

The average patient needs 800–1000 IU of vitamin D3 daily, however thosewho are still deficient require higher dosages. For mild deficiency of 15–25 nmol/L,an oral supplement of 300–5000 IU per day can be administered for 6–12 weeks, followed by

a maintenance dose of 1000–2000 IU per day. Vitamin D3 status shouldbe checked 3 to 4 months after starting medication since vitamin D3 is stored in fatand muscle and there is a lag time before serum concentrations normalize **(Rusinska*et al.*, 2018).**

For a severe vitamin D3 insufficiency, defined as 25-hydroxyvitamin D3 below the 15 nmol/L, the intramuscular form of 1000000 IU cholecalciferol (megados treatment) will more suitably replenish the reserves quickly and efficiently. This is especially useful for those who have nutritional compliance issues, acute medical issues, and malabsorption. These formulations are currently only available under a limited access program for specialists **(Vanlint, 2005).**

1.8.9 Vitamin D and orthodontics

By causing the development of osteoclasts from their progenitors and enhancing the activity of existing osteoclasts, vitamin D enhanced bone resorption **(Castillo *et al.*, 1975; Weisbrode *et al.*, 1978)**. Bone remodeling, following the application of orthodontic forces, includes resorptive and bone formation phases at the alveolar process **(Kawakami and Yamamoto, 2004)**. There is a connection between vitamin D receptor polymorphisms and periodontitis and bone metabolism**(Martelli *et al.*, 2014).**

Based on radiographic findings, it was concluded that acceleration of canine retraction by local injection of vitamin D3 enhanced the periodontal ligament response, does not exacerbate apical root resorption nor adversely affect the alveolarbone integrity, and the procedure does not entail significant extra chair-side time **(Al-Hasani and Ibrahim, 2021).**

The duration of lower incisor alignment therapy was shorter in the group with normalized vitamin D3 level, and the percentage of alignment improvement was significantly higher in this group during the various stage of treatment. Vitamin D3 plays a role in reducing pain associated with OTM, but had no effect in reducing orthodontically induced root resorption. The reduction in pain perception observed in patients with optimal vitamin D3 levels may improve patient compliance and

satisfaction with orthodontic treatment **(Huang *et al.*, 2021; Al-Attar and Abid, 2022).**

1.8.10 Animals studies

Vitamin D3 induced bone resorption in some trials by allowing osteoclasts to differentiate from their precursors and elevate the activity of current osteoclasts **(Reynolds *et al.*, 1973; Castillo et al., 1975; Weisbrode *et al.*, 1978)**. The effects of vitamin D3 metabolite injection and calcium-rich diets on bone remodeling in rats. On the first day, treated rats had more osteoclasts than controls. The researchersfound a decline in the number of osteoclasts on days 3 and 4; this pattern occurred on days 6, 8, and 10. Meanwhile, there was a large rise in the number of osteoblastsin treated rats relative to controls over the same experimental period. Calcium and phosphorus levels have also been raised **(Boyce and Weisbrode, 1985).**

Intra-ligamentary injections ofvitamin D3 metabolites increase the number of osteoclasts and, as a result, the rate of bone resorption, which in turn accelerates canine retraction **(Collins and Sinclair,1988).**

Cui *et al.* (2016) investigates how 1,25(OH)2D3 affects the expression of HMGB1 (High mobility group box-1), a late inflammatory cytokine that is crucial for the remodeling of periodontal tissue during orthodontic tooth movement. Male Wister rats that were seven weeks' old were used in the experiments. To measure tooth movement, a nickel-titanium coil spring was employed to deliver mechanical loading to the tooth for five days. After that, every other day for up to 28 days, either 1,25(OH)2D3 or ordinary saline was administered via gavage. These results suggestthat by inhibiting HMGB1 expression in PDL, OTM increase **(Cui *et al.*, 2016).**

Contrarily, a recent study **(Nareswari *et al.*, 2019)** reported that vitamin D3 supplementation did not significantly increase the expression of vascular endothelial growth factor (VEGF) and the quantity of angiogenesis in the OTM of pregnant rats **(Nareswari *et al.*, 2019).**

1.8.11 Human studies

The effect of local application of calciterol (the active form of vitamin D3) on OTM was studied by **Al-Hasani *et al.* in 2011**. Patients were divided into three groups with five patients each. The concentration of calciterol that was injected distally to a canine in the experimental side was 15, 25, and 40 pg/0.2 ml calcitriol diluted with 10% dimethylsulfoxide (DMSO), respectively; while control sidereceived 0.2 ml DMSO. Each patient had a five-visit follow-up period spaced by oneweek, during which two injections were administered three times (at the first, second, and third visits) and checked for OTM, GCf collection, and radiographic inspection. OTM found no statistically significant differences between the three groups, the experimental side, and the control side. On a level of therapeutic effectiveness, the 25 pg calcitriol dosage caused experimental canine movement to occur 51% more quickly than it did under control, while the 15 pg and 40 pg doses each caused OTM to occur 10% more quickly. Additionally, according to periapical radiographs, calcitriol had no impact on the tissues beneath the skin **(Al-Hasani *etal.*, 2011).**

Another study done by **(losub et al., 2016)** by split into experimental side and control side, the experimental side benefited from an interaction between orthodontic therapy and intra-ligamentary vitamin D3 administration (0.2 mL of vitamin D3 (42 pg/mL) was given, once a week for three weeks). The control side only received traditional orthodontic treatment. On average, tooth movement on the experimental side has been 70% greater than on the controls. Additionally, no root resorption was found on cone-beam computed tomography three months after the first vitamin D3 administration **(Iosub *et al.*, 2016).**

The clinical and radiographic effects of locally administered 1,25-dihydroxycholecalciferol (1,25 DHC) on canine distalization were recently investigated in a split-mouth RCT.

Local periodontal injections of 1,25DHC on the experimental side was provided

at monthly intervals and placebo gel was performed on the control side ofthe maxillary canine distally. Patients were tested at the beginning (T0), four weeks(T1), eight weeks (T2), and twelve weeks (T3). In order to assess changes of bone density, CT scans were taken at T0 and T3. The amount of difference in canine distalization and bone density changes were assessed on the experimental and control sides, respectively. The findings revealed a significant rise in the rate of canine distalization and a decline in bone density on the experimental side relative to the control side **(Varughese *et al.*, 2019).**

The available human studies about the effect of vitamin D3 on OTM are summarized in table **1**: **(Al-Attar, 2022)**

Table 1. The available human studies about the effect of vitamin D3 on orthodontic tooth movement.

Authors/Year	Study design	Country	Aim	Sample size	Gender	Age	Findings
Al-Hasani et al., 2011	RCT Split mouth	Iraq	To evaluate the clinical efficacy of locally injected vitamin D3 (calcitriol) in accelerating orthodontic teeth movement (OTM)	15	Not reported	17-28 years	Statistically non-significant, but clinically significant differences were reported for OTM between the control and experimental sides, and among the three groups
Iosub et al., 2016	RCT Split mouth	France	To assess the effect of local administration of vitamin D3 on the rate of orthodontic tooth movement - To evaluate secondary effect of locally administration of vitamin D3 on dental roots.	four patients Six arches (four maxillary and two mandibular)	M:2(50%) F:2(50%)	13-34 years	70 % more tooth movement
Varughese et al., 2019	RCT Split mouth	India	Evaluate the clinical and radiographic effects of locally delivered 1,25 dihydroxycholecalciferol (1,25 DHC) on the amount of canine distalization.	15	Not reported	15-30 years	Statistically significant increase in the amount of canine distalization and decrease in cancellous bone density on the experimental side

Chapter Two: Discussion

Orthodontic tooth movement has been defined as "the result of a biologic response to interference in the physiologic equilibrium of the dentofacial complex by an externally applied force **(Davidovitch, 1991).**

The sequence of cellular, molecular, and tissue-reaction events during orthodontic tooth movement has been extensively studied **(Krishnan *et al.*, 2006)**. Several factors, alone or in combination, might influence re- modeling activities and ultimately tooth displacement **(Davidovitch, 1991)**, and the alterations in bone turnover and density may affect the rate of movement. In this sense, many biological agents play a role in the inflammatory process and alter the pathways related to bone remodeling that accompanies OTM **(Proffit et al., 2018)**. Vitamin D3 was mentioned in literature as the most important bio-modulator of bone tissue **(Yamasaki *et al.*, 1982; Long *et al.*, 2013)**.

Collins and Sinclair in (2020), reported a 60% increase of the rate of orthodontic tooth movement in ex-perimental animals after intra-ligamentary administration of vitamin D3 **(Santana *et al.*, 2020)**. This is explained by the effect of vitamin D3 on osteoclasts cells **(Yamasaki *et al.*, 1982)**.

Vitamin D may modulate the inflammatory response to orthodontic forces **(Cui et al., 2016)**. Vitamin D deficiency has been associated with a higher risk of periodontitis and delayed tooth movement during orthodontic treatment **(Abreu *et al.*, 2018)**. Moreover, Vitamin D supplementation during orthodontic treatment could improve tooth movement and reduce the risk of root resorption. **Yao et al. (2020)** Additionally, found that optimal Vitamin D3 levels were associated with reduced pain perception during orthodontic treatment, which could improve patient compliance and satisfaction. **Huang et al. (2021).**

Chapter Three: Conclusion and Suggestions

3.1 Conclusion

From our study we can conclude the following:

- Only a small number of foods naturally contain vitamin D3, and it is also sometimes added to others and made available as dietary supplements. Additionally, it is endogenously created when sunlight's UV rays strike the skin and trigger the production of vitamin D3.
- The normal range for vitamin D levels in the blood is generally considered to be between 30- 100 ng/mL (75-250 nmol/L), although optimal levels may vary depending on individual factors such as age, health status, and sun exposure.
- Vitamin D has been found to enhance bone resorption by promoting the development of osteoclasts and increasing their activity.
- The local application of vitamin D3 and its active form, calcitriol, may have a positive impact on orthodontic tooth movement and bone density. These findings could have significant implications for orthodontic treatment and patient outcomes, as shorter treatment times and reduced pain during treatment could improve patient satisfaction and compliance.

3.2 Suggestions

We suggest do further in vivo study to know the relation of vitamin D and orthodontic tooth movement with different doses of vitamin D.

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