# Role of the Active Form of Vitamin D (1,25 Dihydroxycholecalciferol) in Orthodontic Treatment

## An *in vivo* study

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*The aim of this study was to evaluate the role of local administration of vitamin D in influencing the rate of orthodontic tooth movement. Six dental arches were included in this study. Every arch was divided intro two hemiarches: experimental hemiarch and control hemiarch. The canines were included in this study. Control canines received orthodontic therapy compared with experimental canines which received orthodontic therapy associated with local administration of calcitriol (1,25 dihydroxycholecalciferol). The rate of tooth movement was measured in both hemiarches. We noticed a difference between the rates of orthodontic treatment in experimental and control hemiarches respectively. This might be attributed to local administration of calcitriol (1,25 dihydroxycholecalciferol).*

*Keywords: bone remodeling, orthodontic tooth movement, vitamin D, bone desorption, bone apposition*

Orthodontically induced tooth movement is the result of a bone remodeling process around the tooth on which a mechanical force was applied [1]. Remodeling of alveolar bone represents the biological response to orthodontic forces. This process is done by the activity of cells involved in bone resorption and respectively bone apposition. Bone resorption is done by osteoclastic cells, while bone apposition is made by the osteoblastics cells. These cells are triggered or stimulated by a cascade of events in which chemical messengers play an important role [1].

In the pressure-tension theory of orthodontic tooth movement, mechanical forces cause the tooth to shift position within the periodontal ligament space which provokes two different areas in the periodontal ligament: a pressure area and a tension area [2].

In the pressure area, the periodontal ligament is compressed and blood flow is decreased. On the other hand, in the tension area the periodontal ligament is under tension while the blood flow is maintained or increased. Alterations in blood flow are produced by sustained pressure on tooth crown and are responsible for changes in the chemical environment [2].

Oxygen levels fall in the pressure area and increase in the tension area. These chemical changes lead to the release of chemical messengers which are important in the cascade of events that induce bone remodeling process, acting by activation of osteoclastic cells [3]. The activated osteoclastic cells remove bone from the pression area, while osteoblastic cells form new bone on the tension side and remodel resorbed areas on the pressure side [2].

There are several pharmacological agents that are known to affect different chemical messengers involved in cells activation [4-9]. Prostaglandin E2 is known to be a stimulator of both osteoclastic and osteoblastic activity [10-15].

Vitamin D3 (cholecalciferol) is a liposoluble vitamin which plays an important role in maintaining calcium homeostasis [16]. The synthesis of cholecalciferol take place in skin under UV-B radiation and is activated by two hydroxylation reactions: one in the liver resulting calcidiol and one in the kidney resulting calcitriol or 1,25 dihydroxycholecalciferol.

The active form of vitamin D3, 1,25 dihydroxycholecalciferol (also known as calcitriol) stimulates osteoclastic activity [17] and also induces the formation of new osteoclasts from their precursors. In experimental animal models studies, local administration of 1,25 dihydroxycholecalciferol increased the rate of orthodontic tooth movement [7, 17, 18].

The aim of this study was to evaluate the effect of local administration of the active form of vitamin D3 (1,25 dihydroxycholecalciferol or calcitriol ) in influencing the rate of orthodontic tooth movement.

### Experimental part

In this study we included patients who needed orthodontic treatment. Patients were selected according to the eligibility criteria: healthy subjects, no history of chronic drug intake, no previous orthodontic treatment, healthy teeth, requirement of bilateral retraction of canines. Signed consent was obtained only from 4 patients. In two patients only the upper dental arch was included in this study, while in the other two patients, both the upper and lower dental arches were included. A total of six dental arches were included in this study. The study protocol was approved by the Research Ethics Committee of „Grigore T.

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| | Age | Gender | Studied dental arch | The rate of control canine movement | The rate of experimental canine movement |
|---|---|---|---|---|---|
| 1. | 18 years old | M | Upper | 0.85 mm | 1.55 mm |
| 2. | 34 years old | F | Upper | 0 mm | 0.44 mm |
| 3. | 15 years old | M | Upper | 1.16 mm | 1.34 mm |
| 4. | 15 years old | M | Lower | 0.89 mm | 1.18 mm |
| 5. | 13 years old | F | Upper | 0.34 mm | 1.03 mm |
| 6. | 13 years old | F | Lower | 1.17 mm | 1.98 mm |
| Average rate of tooth movement | | | | 0.735 mm | 1.235 mm |

**Table 1**
ILLUSTRATION OF BOTH EXPERIMENTAL AND CONTROL CANINE MOVEMENT RATE FOUR MONTH AFTER FIRST LOCAL ADMINISTRATION OF CALCITRIOL ON EXPERIMENTAL TEETH.

Popa" University of Medicine and Pharmacy of Iaşi and was carried out in accordance with ethics guidelines regarding research on human subjects.

Each studied dental arch was divided in two hemiarches: experimental side and control side. After application of mechanical forces for corporeal bilateral movement of the canines, local administration of 1,25 dihydroxycholecalciferol (calcitriol) (Decostriol, Mibe, Germany) was performed only on experimental canines. We administrated 0.2 mL of calcitriol (42 pg/mL).

The values of mechanical forces applied on both experimental and control canines were measured using an orthodontic dynamometer (Dynamometer, Falcon Orthodontics, Colorado).

On the control side we applied only mechanical forces on the canine, while the experimental side received mechanical forces associated with local administration of 1,25 dihydroxycholecalciferol (calcitriol).

For local administration, calcitriol was diluted with dimethylsulfoxid (DMSO, Bisolve B.V. Netherlands) which served as a liposoluble vehicle. We performed three local administrations at one week interval. We measured the rate of orthodontic tooth movement both on the control and experimental side one month after the first local administration of calcitriol. We used dental casts for these measurements made before and after one month of orthodontic treatment. The follow-up period was of one month. We noticed the differences between the control and experimental sides.

We performed X-rays examination on the dental root of the teeth studied one month and four months respectively after the first local administration of calcitriol in order to evaluate the secondary effects of vitamin D.

## Results and discussions

For weeks after the first local administration of calcitriol (1,25 dihydroxycholecalciferol) we obtained the following results:

- average rate of the experimental canine movement was 1.253 mm (table 1);
- average rate of the control canine movement was 0.735 mm (table 1) ;
- the rate of tooth movement in experimental hemiarches was 70.47 % higher compared with control hemiarches.

Average relative movement calculated as the average difference between tooth movement rate on experimental hemiarches and tooth movement rate on control hemiarches is of 0.518 mm, which represents an increase of 70.47 % in the rate of experimental tooth movement compared with the rate of control tooth movement.

In this study we associated orthodontic treatment and drug therapy in order to notice the influence of drugs on the rate of orthodontic tooth movement.

Several pharmacological agents had been studied in the context of orthodontic treatment: prostaglandin E, vitamin D, parathyroid hormone, thyroxine [9, 19-21]. Among these, the biologically active form of vitamin D, 1,25 dihydroxycholecalciferol (calcitriol) has been mentioned as the most intense biomodulator of bone tissue, increasing the rate of orthodontic tooth movement in experimental animals [22, 23] .

Scientific information regarding the effects of calcitriol on the rate of orthodontic tooth movement on human subjects is deficient, which is why we chose to evaluate the role of vitamin D in influencing orthodontic treatment results.

According to our study, the mean value of the rate of tooth movement in experimental hemiarches was of 1.253 mm, compared with the mean value of 0.735 mm found in control hemiarches. This difference represents a higher rate (70.47%) of tooth movement in experimental hemiarches. This fact suggests a correlation between local administration of biologically active form of vitamin D and an increased rate of tooth movement.

The effect of calcitriol (1,25 dihydroxycholecalciferol) on influencing orthodontic tooth movement has been studied by different authors in experimental animals [17, 21, 23]. According to this, calcitriol was found to accelerate orthodontic tooth movement [17, 21, 23].

Vitamin D influences bone metabolism through several mechanisms [23]. It is involved in osteoclastic cell formation from their precursors, it stimulates the activity of osteoclastic cells from the periodontal ligament and stimulates the osteoblastic cells to activate the osteoclastic ones [23]. *In vitro* studies have concluded that vitamin D stimulates bone resorption by increasing de number of osteoclastic cells. As osteoclastic cell activity is essential for the bone remodeling process and orthodontic tooth movement depends on surrounding bone reorganization, we might attribute the acceleration of tooth movement to the local administration of calcitriol.

We administrated a small volume of calcitriol (0.2mL) in order to reduce pain as much as possible. X-ray examination was performed using cone-beam CT exams of dental root and we noticed the absence of any modification in dental root structures.

## Conclusions

The rate of orthodontic tooth movement of the experimental canines was higher compared with the rate of orthodontic tooth movement of the control canines. This suggests that local administration of the biologically active form of vitamin D (calcitriol or 1,25 dihydroxycholecalciferol) might influence orthodontic therapy by increasing the biological response of alveolar bone to orthodontic forces.

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