



Progesterone Effects on Experimental Tooth Movement In Rabbits

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ABSTRACT The effect of progesterone on tooth movement was evaluated for nine weeks. Twenty-four rabbits were assigned into three groups of long-term, short-term and no progesterone injection. Orthodontic force was applied to incisors for three weeks. Statistical tests showed no significant difference at the seventh and eighth week; but at the ninth week, tooth movement was significantly lower in the long-term group. Long-term progesterone administration could reduce the rate of tooth movement.

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Extending the duration of orthodontic treatment will accentuate its side effects such as caries, white spots, and periodontal diseases. Recognizing different factors affecting the velocity of tooth movement including drugs, age, and nutrition is of particular importance, which should be considered during treatment planning. Progesterone as a feminine estradiol hormone can affect bone metabolism. It is believed this hormone stimulates bone formation and reduces renal secretion of calcium.¹ Progesterone could also specifically prevent corticosteroid-induced osteoporosis.²

Today, women comprise a major part of the whole population of orthodontic patients.³ Many of these patients use estrogen-progesterone compounds as a definite method for contraception. On the other hand, female hormone levels undergo major changes during pregnancy

or the menopausal period, which could effectively alter bone metabolism.

In a histological study on ovariectomized rats, it was concluded that ovariectomy induces osteopenia and accelerates skeletal metabolism in rats.⁴ In another study, it was demonstrated that estrogen therapy after ovariectomy in rats has a complete protective effect against osteopenia.⁵ Heersche mentioned that estrogen and progesterone deficiency together cause bone mass reduction.⁶ Additionally, it is even claimed that in postmenopausal women, progesterone deficiency and not lack of estrogen is the principal factor in the pathogenesis of menopausal osteoporosis.⁷

On the other hand, some studies questioned the role of progesterone on bone turnover and claim that this hormone does not have considerable effects on bone density by itself. However, they believe that progesterone therapy



FIGURE 1. Force application method to rabbit's incisor teeth.

increases serum levels of osteocalcin that is a marker for bone matrix synthesis.^{8,9}

When a force is applied to a tooth, alveolar bone formation and resorption occurs and the tooth moves while alveolar bone remodeling increases.¹⁰ Estrogen promotes alveolar bone formation and prevents bone resorption, and its deficiency accelerates tooth movement.¹¹⁻¹³ It also has been shown that progesterone affects tooth movement in pregnant rats and has a positive effect on periodontal ligament reconstruction during tooth movement.¹⁴

Orthodontic tooth movements vary in different stages of the estrous cycle in rats and the estradiol level of serum has a negative correlation with tooth movement, which suggests that bone formation activity depends on the progesterone level in the estrous cycle.¹⁵

It seems there is no general agreement concerning the role of progesterone on bone metabolism and there is lack of data about its influences on tooth movement. Therefore, it was considered appropriate to investigate the influences of the progesterone hormone on the rate of experimental tooth movements. The aim of the present study was to evaluate progesterone effects on the rate of tooth movements in rabbits.

Materials and Methods

In this interventional animal study, 24 prepubertal female albino rabbits with the mean age of 8 weeks and a mean weight of 1850 grams were randomly assigned into three equal groups.

TABLE 1

Mean and SD of the Rate of Tooth Movement in Three Groups at the End of Seventh, Eighth, and Ninth Weeks (mm/week)

Group	Sample size	7th week	8th week	9th week
		Mean ± SD	Mean ± SD	Mean ± SD
LTG	6	0.7±0.2	0.9 ± 0.2	1.06 ± 0.1
STG	5	0.64 ± 0.1	1.02 ± 0.2	1.34 ± 0.2
CG	8	0.73 ± 0.2	1.2 ± 0.2	1.5 ± 0.15
ANOVA		p=0.398	p=0.07	p=0.001

TABLE 2

Tukey Test Results in Comparing the Three Groups (Two by Two)

Comparing groups	Mean difference	p-value
LTG & STG	-0.27	0.044
LTG & CG	-0.43	0.001
STG & CG	-0.16	0.256

In the first, long-term group, LTG, 5 mg intramuscular progesterone was injected in the leg muscle everyday for nine weeks. In the second, short-term group, STG, the rabbits did not receive any injection in the first six weeks, but they did get intramuscular injections of progesterone at the last three weeks with the same dose and method of group one. The third, a control group, CG, served as the authors' control group and did not receive any injection during the nine weeks of experiments.

At the end of the sixth week, general anesthesia was performed in all groups via intramuscular injection of 0.5 ml of rompon and ketamine (1:2) solution. After the rabbits were unconscious, the two upper incisors were pumiced, etched (37 percent phosphoric acid for 30 seconds), rinsed, and dried. Then Microlock edgewise brackets were bonded on the buccal surface of these teeth by a no-mix self-cure composite (Dentaurum, Germany). These brackets were positioned parallel to the long axis of rabbit incisor teeth, and with 5 mm distance from their incisal edge (almost in the middle of the clinical crown).

In order to apply orthodontic force, the authors used a spring as in the Akin method with 0.014-inch stainless-steel wire in the vertical slot of these brackets¹⁶ (FIGURE 1). All the springs had similar diameter and height, and were activated only once from one arm at the end of sixth week to insert 50 gr distal force.

The distance between the mesial corners of incisors was measured blindly at the end of the seventh, eighth, and ninth weeks by a caliper calibrated 0.1 mm. SPSS software was used to analyze data. The Kolmogorov-Smirnov test revealed normal distribution of data, and the ANOVA and the Tukey test were used to compare the three groups.

Results

The rate of tooth movement at the end of the seventh, eighth, and ninth weeks is demonstrated in TABLE 1. The ANOVA test did not reveal significant difference in the rate of tooth movement between three groups at the end of the seventh and eighth week, but it demonstrated a significant difference among these groups at the end of the ninth week (p=0.044) (TABLE 1).

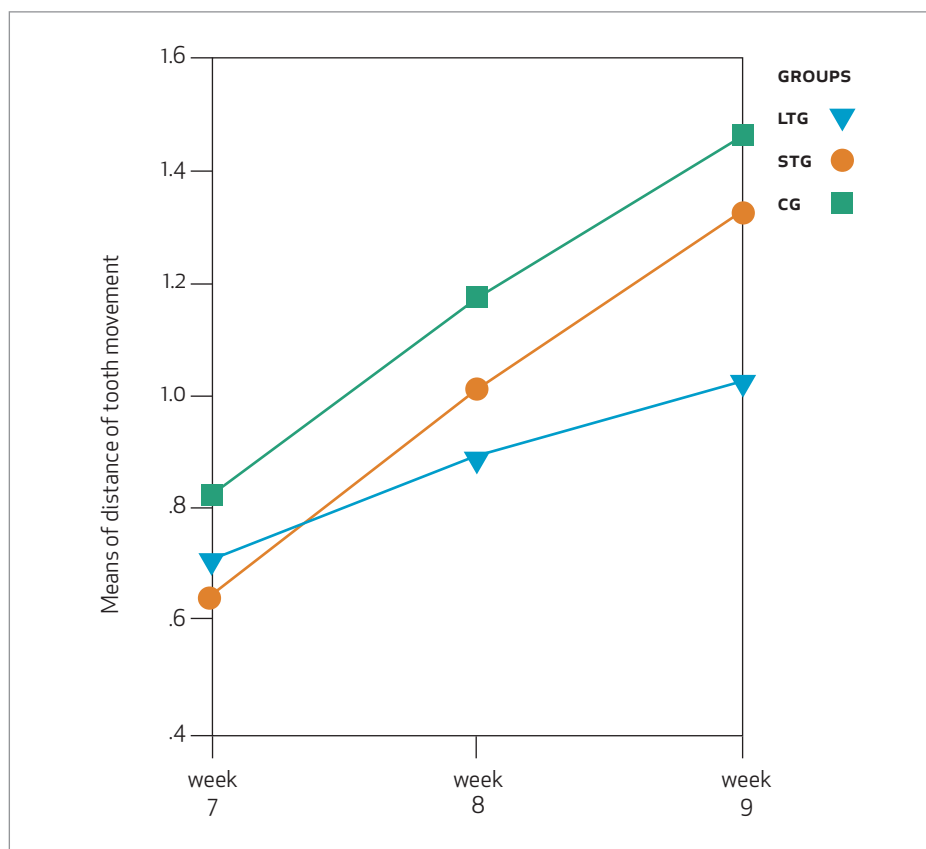


FIGURE 2. Comparison of tooth movement velocity in the three experimental groups.

The results of the Tukey test revealed significant differences between LTG and STG ($p=0.044$), and also between LTG and CG groups ($p=0.001$) (TABLE 2).

The interincisal distance in the CG group increased 105 percent between the seventh and ninth week, but this parameter had only 51 percent increase in the LTG group in the similar period of time. Comparison of tooth movement velocity between three groups is demonstrated in FIGURE 2.

Discussion

Scientists' efforts have always been to find the relationship between biochemical markers in bone remodeling and the rate of bone metabolic turnover in clinical situations. However, it is usually difficult to interpret the effects of different variables such as age, puberty, and endocrine regulations on this procedure.¹⁷

Various hormones have been recognized in association with tooth movement. For example, the growth hormone directly enhances anabolic modeling of bone via its receptors on osteoblasts. Androgens produce a masculine body through a secondary response of bone to the increased muscular forces.² Parathyroid hormone receptors exist on osteoblasts and osteocytes that indicate its direct effect on bone formation.

It has been found that estrogen accentuates osteogenic response of spongy bone to mechanical loading. This mechanism may have an important role on enhancing bone turnover in estrogen deficiency conditions.²

Although a number of studies with various results have been performed on progesterone effects on different parts of the body's skeleton, there is lack of research on progesterone influences on

jawbones in the literature. There is no evidence that changes in mandibular and maxillary bone mass are parallel to the alterations of other parts of the skeleton. The mastication force is a major factor that differentiates the maxilla and the mandible from other parts of the skeleton. However, there is a strong possibility that the rate of bone resorption after tooth extraction is coordinated with alterations in bone mass in other parts of the body.⁷

In the present study, there were attempts to evaluate the independent effect of progesterone on tooth movement in prepubertal female rabbits. These animals had appropriate tooth size for bonding orthodontic attachments and since the effects of sex hormones is gender related, female rabbits were selected.^{9,18} On the other hand, it has been shown that orthodontic forces in different periods of the estrous cycle induce various responses.¹⁵ To eliminate the latter effect, prepubertal female rabbits were chosen for this study.

The complete remodeling cycle in rabbits takes six weeks.¹⁹ Because of that, the progesterone injections were initiated weeks before force application in one of the authors' groups while in the other group, progesterone administration and force application were started simultaneously to evaluate the long-term and short-term effects of progesterone prescription.

According to the results of the present study, only a long-term progesterone application significantly decreased the rate of tooth movement, which means that the incisor teeth in rabbits moved significantly slower when progesterone was prescribed for nine weeks compared to three weeks application ($p=0.044$) and the control group ($p=0.001$). Although this finding corroborates He's study, there are controversial results in the literature about progesterone mechanism of action.¹⁴ Some investigators believe that progesterone in

combination with estrogen will reverse estrogen effects, but when prescribed alone, will increase bone formation and create positive calcium balance.^{19,20}

Kalu and Abe believe that progesterone does not affect either bone resorption or formation, but other investigators such as Yamamoto claim progesterone inhibits the bond between glucocorticoids and osteoclasts, and consequently prevents bone resorption.^{8,21,22}

Human osteoblast cells have specific receptors for progesterone but there are even controversial findings in humans about progesterone effects. Prior claims progesterone causes an increase in bone formation and estrogen only reduces bone resorption, while Verhaar demonstrated that these hormones have anabolic effects on osteoblast cells.^{23,24} It also has been shown that women with a shorter luteal phase, which indicates a shorter duration of endogen progesterone secretion, demonstrate more severe osteopenia.²³

However, whether progesterone prohibits bone resorption or induces bone formation, the result could interpret slower tooth movement in rabbits receiving progesterone in comparison to other groups. Tooth movement is a multifactorial procedure and further studies are recommended to evaluate the velocity of tooth movement associated with the differences between male and female patients.

The authors suggest histological and histochemical assessments in future studies about progesterone effects on tooth movement, and it is also better to differentiate the estrogen and progesterone effects on tooth movement in ovariectomized rabbits.

Conclusion

1. Short-term progesterone injection (three weeks) in rabbits does not significantly affect the velocity of orthodontic tooth movement.

2. Long-term progesterone prescription (nine weeks) significantly reduces the rate of tooth movement in rabbits. ■■■■

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