Orthodontic Tooth Movement and Root Resorption Following Treatment with Various Doses of Celecoxib in Rats

Mahdi Hashemi 2Atefe AOtoufi *3Mohamadreza Badiee 2Zahra Abdolazimi 4Farnaz Younesian

1Orthodontist, Tehran-Iran.
2Dentist.
*3Corresponding Author: Postgraduate Student, Dept. of Orthodontics, Dental School, Shahid Beheshti University of Medical Sciences, Tehran-Iran. E-mail: mr.badiee@sbmu.ac.ir
4Postgraduate Student, Dept. of Orthodontics, Dental School, Shahid Beheshti University of Medical Sciences, Tehran-Iran.

Abstract

Objective: Consumption of nonsteroidal anti-inflammatory drugs for treatment of orthodontic pain can reduce tooth movement. At present, COX2 selective inhibitors are suitable alternatives for current anti-inflammatory medications. The present study was designed to evaluate and compare the effect of three different doses of Celecoxib on orthodontic tooth movement and root resorption in rats.

Methods: This in-vitro experimental study was conducted on 40 male rats that were randomly divided into four groups of control group D (use of orthodontic appliance and no drug consumption), control group E (no intervention at all), test group A (Celecoxib consumption with a dosage of 25 mg/kg), test group B (Celecoxib consumption with a dosage of 50 mg/kg) and test group C (Celecoxib consumption with a dosage of 100 mg/kg). A nickel-titanium spring was ligated between the maxillary right first molar and incisor. The animals were sacrificed after 2 weeks and the distance between the two teeth was measured with a caliper (in mm). Histological sections were cut and the rate of tooth resorption, number and the maximum depth of the largest resorption lacunae in the mesial root surfaces of the first molar tooth were determined. ANOVA and Tukey’s HSD and LSD tests were used for statistical analysis of the obtained data.

Results: The highest mean rate of tooth movement was observed in group A (0.8537 mm) followed by groups D, C, B, and E. Statistical analyses revealed that various doses of Celecoxib did not interfere with tooth movement. Consumption of Celecoxib especially with a dosage of 100 mg/kg resulted in a significant reduction in number of resorption lacunae in the mesial root of first molar tooth (P<0.05).

Conclusion: Dosage of 100 mg/kg was selected as the optimal dose of Celecoxib with the lowest interference with tooth movement and the highest protection against root resorption in rat model.

Key words: Orthodontic tooth movement, Root resorption, Celecoxib, Rat

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Introduction:

Tooth movement is the key in orthodontic treatments. Despite extensive investigations on humans and animal models, the exact mechanism and cause of root resorption following orthodontic treatments have yet to be fully understood (1-3). However, fundamentally, it is a biologic response to long-term controlled mechanical orthodontic forces that result in formation of pressure and tension areas in the periodontium and production of inflammatory mediators like prostaglandins and leukotrienes. Eventually, the tooth socket will move following resorption and formation of bone through the function of osteoclasts and osteoblasts, respectively (4). Osteoclasts cause bone resorption and tooth movement. They also attack root cement. Root resorption is considered as a complication of orthodontic treatment (1) which was first described by Bates in 1856. In 1914, Ottolengui linked root resorption to orthodontic
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He reported that root resorption occurs in 93% of orthodontic patients. According to him, in 1-5% of these patients this resorption is so severe that involves one third of root length (5). Patients undergoing orthodontic treatment usually experience some degrees of pain and discomfort. Researchers consider these conditions as one of the reasons why some patients become uninterested in continuation of their treatment (6). Nonsteroidal anti-inflammatory drugs (NSAIDs) are the most commonly used group of analgesics by orthodontic patients. Their mechanism of action is through the inhibition of cyclooxygenase (COX) enzyme (6-8). Production of prostaglandins from the arachidonic acid present in cell membrane is mediated by this enzyme (8). COX1 is normally found in a variety of tissues and organs and results in production of prostaglandins that play a role in protection of gastrointestinal lining. Therefore, COX1 inhibitors like aspirin cause gastrointestinal problems. Several studies have demonstrated that NSAIDs lead to inhibition of prostaglandin release, accumulation of osteoclasts and reduction of tooth movement (7). COX2 is an enzyme induced by the action of inflammatory mediators that plays a part in pathophysiologic processes like fever and edema (8). Thus, medications inhibiting this enzyme do not have GI side effects and at the same time possess anti-inflammatory effects comparable to those of COX1 inhibitors (8). That is why in the recent years use of COX2 selective inhibitors like Celecoxib has become increasingly popular. Gameiro et al, (2007, 2008) in their study on the short- and long-term effects of Celecoxib on orthodontic tooth movement and root resorption revealed that although consumption of this drug has no effect on number of osteoclasts, it can decrease their function which justifies the inhibition of tooth movement in animals treated with Celecoxib. Furthermore, results failed to find a statistically significant difference between the effects of short-term and long-term administration of this drug on root resorption (3, 6). Gonzales et al. (2008) evaluated the effect of steroidal and nonsteroidal anti-inflammatory drugs (prednisolone, Celecoxib, aspirin, acetaminophen and meloxicam)on tooth movement and root resorption of molar tooth in rats and observed a reduction in root resorption and tooth movement rate only as the result of consumption of prednisolone (0.67 and 0.13 mg/kg) and Celecoxib in high doses (16 mg/kg). Although by administration of low dose Celecoxib (3.2 mg/kg) rate of tooth movement significantly decreased, rate of root resorption was similar to the control group (2). In a study by Carlos et al, (2007) on the effect of parecoxib, celecoxib and rofecoxib on orthodontic tooth movement in rats no tooth movement was observed in the group treated with rofecoxib. Rate of tooth movement in the group treated with celecoxib was greater than the rate in the control group. However, this difference was not statistically significant (9). Gerome et al, in 2005 also demonstrated that celecoxib and parecoxib did not interfere with tooth movement; whereas, rofecoxib inhibited tooth movement (10). Inflammatory mediators activated during the process of orthodontic treatment are among the effective factors on root resorption, pain and tooth movement because they induce and activate osteoclasts and stimulate pain receptors. However, other factors like long-term treatments, type of orthodontic force, abnormal form of root, ethnicity and systemic diseases may also play a role in this regard (3, 11).

At present, considering the popularity of orthodontic treatment and its role in regaining health, function, esthetics and comfort of dental system, reducing its unwanted complications and side effects such as pain and root resorption are among the important goals of practitioners. Since celecoxib is a new generation NSAID used in orthodontic treatment, the present study was undertaken to compare the effect of various doses of celecoxib on rate of orthodontic tooth movement and root resorption in rats. By doing so, the effective dosage of this drug for pain relief of orthodontic patients with the minimal side effect on treatment outcome is determined.

Methods:

This was an in-vitro, single blind randomized experimental study. Data were collected through observation, completion of data sheets and use of specific tables. All approved standard
protocols for animal studies were thoroughly followed. Samples were selected among those who met the inclusion criteria using nonprobability convenience sampling method and were then divided into 5 groups of three tests (A, B and C) and two controls (D and E) using simple random sampling method. A total of 40 male Wistar rats (SCL, Shizuoka, Japan) with a mean age of 4 months and mean weight of 220±30 g were transferred from Mashhad Institute for Serums and Vaccines to the animal house of the Pharmacology Department of Zahedan University of Medical Sciences. In order to adapt to the new environment, the animals were kept for 7 days under similar light and nutrition conditions. Rats were randomly divided into 5 groups of 8 each and after numbering were kept in separate cages. Eight rats in the control group D received orthodontic appliance without any drug consumption. Rats in control group E received no intervention (neither an orthodontic appliance nor drug administration). During the study, group E rats only received the anesthetic drug. The remaining 24 rats were randomly divided into three celecoxib receiving groups of A (with drug dosage of 25 mg/kg), B (with drug dosage of 50 mg/kg) and C (with drug dosage of 100 mg/kg). The rats in the test groups received oral administration of celecoxib. At the beginning of study, each rat was weighed with a digital balance and then prepared for anesthesia. Ketamine (Ketamine Hydrochloride, Rotexmedica, Trittau, Germany) with a mean dosage of 120 mg/kg (range 100-140 mg/kg) was injected intramuscularly with an insulin syringe for induction of anesthesia. Post-anesthesia care included vital signs monitoring, maintaining adequate temperature in the environment, and rotating the rats from side to side once every few minutes in order to prevent pulmonary edema. A NiTi closed coil spring (American Orthodontics NiTi close coil, 855-180, 010x030 inch, 9 mm/EYELET, Sheboygan) and steel ligature wire (0/01 inch, 3M, Unitek, Monrovia, USA) were bonded to the right maxillary permanent first molar and incisor and fixed with self-cure composite resin (Radiopaque Type I self-cure composite resin, King Dental Crop, West Palm Beach, FL, USA) (Figure 1).

Figure 1- Placement of orthodontic appliance

The amount of applied force by the orthodontic appliance was 60 mg which was measured by a force meter at the time of placement. Type of tooth movement was tipping. In order to protect the orthodontic appliance from any possible damage, lower incisors were shortened and rats were provided with soft diet throughout the study. Before the rats regained consciousness, the distance between the right molar and incisor teeth was measured with a digital caliper (Pro-Cal digital caliper, Mitutoyo, Tokyo, Japan) and recorded. Celecoxib in the form of powder was obtained from Daroopakhsh Company (TalayeAfagh Manufacturing Company, Tehran, Iran). The required dosage for each rat was calculated based on the weight of animal using a digital balance with 0.0001 g readability (61189, Shimadzu, Kyoto, Japan) and 100 units were administered in the form of suspension using a disposable 1ml insulin syringe and oral gavage with animal feeding needles (Fisher Scientific, Waltham, Ma, USA) at specific times a day during the two-week study period (Figure 2).

Figure 2- Administration of celecoxib

Drinking water of rats in all groups was changed from tap water to distilled water. After the
completion of two-week study period, rats were weighed and placed in the anesthesia container containing ether. Elevation of ether concentration in the body of rats caused their death. The animals were then decapitated and before removing the orthodontic appliances, the distance between the right maxillary first molar and incisor was measured with a digital caliper. In order to assess the rate of root resorption, samples were sent to the Pathology Department of Zahedan University of Medical Sciences, School of Dentistry. Maxilla of animals was separated and removed with a chrome cobalt disc and placed in formalin 10% for 10 days to become fixed. For decalcification, the specimens were stored in formic acid 10% for 15 days and placed in formalin again for 24 hours for fixation. Right maxillary first molars in all the test and control groups were extracted and parasagittal 4-6 µm thickness sections were made mesiodistally with a microtome (RM20355, Leica, Wetzlar, Germany) and stained with Hematoxylin-eosin. Histological analysis of root resorption in the mesial and distal surfaces of mesial root of the right maxillary first molar was done. Slides showing the highest root length and maximum number of deepest resorption lacunae were selected for analysis. Study of the selected slides and measurement of root resorption rate were done directly by a pathologist blinded to the phases of study using a micrometer (CarlZeiss, Jena, Germany) and a light microscope (437530 Labophot-2, Nikon, Tokyo, Japan). All measurements were done and repeated three times by one operator and one instrument and the mean rate was reported as the final value.

Results:

The total mean rate of tooth movement in all groups was 0.6100 mm during the two-week period. The highest mean rate of tooth movement was observed in groups A with a mean rate of 0.8538 mm, D with a mean rate of 0.7813 mm, C with a mean rate of 0.7736 mm, B with a mean rate of 0.6274 mm and E with a mean rate of 0.0138 mm (Table 1).

According to paired t-test, the changes in distance between the right maxillary first molar and incisor teeth during the study period in all the test groups and the control group D with orthodontic appliance were statistically significant (P<0.05). However, this change in control group E (with no orthodontic appliance) was not statistically significant (P>0.05)(Diagram 1).

![Diagram 1- The mean distance between the right maxillary incisor and first molar teeth at the beginning and at the end of study in each group](image)

The mean tooth movement in different groups is demonstrated in Table 1 and ANOVA showed a significant difference in this respect between groups (F=7.003, P<0.05). For pairwise comparison of mean tooth movement between different groups, Tukey’s HSD test was used. By using this test, significant differences were detected in mean tooth movement between all three test groups with control group D (with orthodontic appliance) and control group E (without orthodontic appliance)(P<0.05). However, the mean tooth movement was not significantly different between three test groups with each other or with the control group D (with orthodontic appliance) (P>0.05)(Table 1).

Another variable that was evaluated in this study was the rate of root resorption in the mesial and distal surfaces and its total rate in the mesial root of the right maxillary first molar tooth (Figure 3). The highest mean of root resorption was observed in the mesial surface of mesial root in group A which was equal to 0.3500 mm. The lowest mean of root resorption was observed in
group E and was equal to 0.0375 mm. Distal surface of mesial root in group B had a resorption rate equal to 0.2500 mm which was the highest mean of distal surface root resorption among all groups. The lowest mean in this respect was noted in group E which was equal to 0.0375 mm. The mean total mesial root resorption was observed in group A which was equal to 0.2875 mm. The lowest mean in this respect belonged to group E in an amount of 0.0375 mm. ANOVA found significant differences in mean total, mesial surface and distal surface root resorption between all groups (P<0.05)(Table 1).

Table 1. Mean ±SD of tooth movement (mm), root resorption (mm) and number of resorption lacunae in the mesial and distal surfaces and their total number in the mesial root of the right maxillary first molar in different study groups

<table>
<thead>
<tr>
<th>Groups</th>
<th>Rate of tooth movement</th>
<th>Rate of root resorption</th>
<th>Number of resorption lacunae</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>A</td>
<td>B</td>
<td>C</td>
</tr>
<tr>
<td>Rate of tooth movement</td>
<td>0.8537±0.4224*</td>
<td>0.6274±0.3549*</td>
<td>0.7736±0.3763*</td>
</tr>
<tr>
<td>Mesial surface root resorption</td>
<td>0.3500±0.1690+</td>
<td>0.3125±0.1246+</td>
<td>0.2000±0.0755</td>
</tr>
<tr>
<td>Distal surface root resorption</td>
<td>0.2250±0.1753*</td>
<td>0.2500±0.1414*</td>
<td>0.1375±0.0916</td>
</tr>
<tr>
<td>Total root resorption</td>
<td>0.2875±0.1598+</td>
<td>0.2813±0.1280+</td>
<td>0.1687±0.0753</td>
</tr>
<tr>
<td>Mesial surface number of resorption lacunae</td>
<td>2.500±0.7559+</td>
<td>2.625±1.060+</td>
<td>2.625±0.7440</td>
</tr>
<tr>
<td>Distal surface number of resorption lacunae</td>
<td>1.625±0.7440</td>
<td>2.000±0.7559</td>
<td>1.125±0.6409</td>
</tr>
</tbody>
</table>

*Statistically significant difference with group E (P<0.05)
+Statistically significant difference with group C (P<0.05)

For pairwise comparison of various groups in terms of mean total, mesial surface and distal surface root resorption LSD test was used. This test found that mesial surface mean root resorption in group C was significantly different from the rates in groups A, B and E (P<0.05). Also, significant differences were detected in distal surface mean root resorption between groups A, B, D with group E (P<0.05). The mean total mesial root resorption in group C was significantly different from groups A, B and E (P<0.05)(Table 1).

The mean root resorption between the mesial and distal surfaces of first molar mesial root was also compared. The mean root resorption was similar in mesial and distal surfaces in group E. However, in other groups, the mean root resorption in the mesial surfaces was higher than in the distal surfaces. Paired t-test was used for statistical analysis of the mean root resorption at mesial and distal surfaces. This test showed statistically significant differences in mean root resorption between mesial and distal surfaces in the test groups (P<0.05)(Diagram 2).

Diagram 2- Mean root resorption at mesial and distal surfaces of the right maxillary first molar mesial root in each understudy group
Number of resorption lacunae at mesial and distal surfaces of the first molar mesial root was
another variable that was evaluated for root resorption. The highest number of resorption lacunae in both mesial and distal root surfaces was observed in group B. Comparison of mean number of resorption lacunae at mesial and distal surfaces in each group using Paired Sample Test revealed statistically significant differences in this respect in all test groups and control group D (P<0.05)(Diagram 3).

Diagram 3- Mean number of resorption lacunae at mesial and distal surfaces of the right maxillary mesial root in each group

Except for group E, in all other groups the mean number of resorption lacunae at mesial surface was more than the rate in distal surface of the mesial root. Comparison of the mean number of resorption lacunae between mesial and distal surfaces of the mesial root in all groups using ANOVA revealed statistically significant differences in this respect (P<0.05).

LSD test was employed to compare the mean number of resorption lacunae at the mesial and distal surfaces of the mesial root between all groups. Significant differences were detected between group C and groups A, B and E in the mean number of resorption lacunae at the mesial surface of the root (P<0.05). Statistically significant differences were also found between group C and groups B and E in terms of the mean number of resorption lacunae at the distal surface of the mesial root (P<0.05)(Table 1). In the present study, rats were weighed at the beginning and at the end of study and variations in weight were calculated. All rats lost weight during the two-week study period except for half the rats in group E, one rat in each of the groups B and C and two rats in group D that gained weight during the study period. Based on Paired Sample Test these changes in weight during the study period were statistically significant in all three test groups (P<0.05) but the weight variations were not statistically meaningful in the two control groups (P>0.05)(Diagram 4).

Diagram 4. Mean weight at the beginning and at the end of study in different groups

ANOVA found significant differences in weight alterations between different groups (P<0.05, F=3.279). For comparison of weight changes between different groups Tukey’s HSD analysis was used. This test indicated that the difference between groups A and C with group E was statistically significant (P<0.05).
Discussion:

The present study evaluated the effect of celecoxib which is a selective NSAID and inhibitor of cyclooxygenase II enzyme on the rate of orthodontic tooth movement and root resorption in 40 rats in three test and two control groups. The highest mean tooth movement was observed in group A. However, this rate was not significantly different than the rate observed in group D (P>0.05). Therefore, we can conclude that celecoxib does not cause significant changes or a reduction in orthodontic tooth movement. Various dosages of celecoxib were tested on different groups. The mean tooth movement was different in these groups as well however this difference was not statistically significant (P>0.05). Thus, this study revealed that the dosage of celecoxib had no effect on the reduction of tooth movement. After group A, the highest mean tooth movement was observed in group C with the highest dosage of celecoxib. Also, the mean tooth movement in group C was almost similar to that in group D and the difference between these two groups was not statistically significant either (P>0.05). As a result, higher doses of celecoxib can be used safely with no interference with the orthodontic tooth movement in rats.

As mentioned earlier, prostaglandins are important inflammatory mediators in orthodontic tooth movement and NSAIDs are capable of inhibiting different inflammatory mediators especially prostaglandins. Thus, reduction in orthodontic tooth movement can be expected when using NSAIDs. Our study results regarding tooth movements are in accord with those of Sari et al, in 2004 (12). They compared the effects of aspirin and rofecoxib on tooth movements. Rofecoxib just like celecoxib is a selective NSAID and inhibitor of cyclooxygenase II enzyme. In their study, they demonstrated that Rofecoxib had no significant effect on level of PGE2 and can be safely administered during orthodontic tooth movements. However, reduction in PGE2 synthesis and consequent decrease in orthodontic tooth movement due to aspirin were significantly greater compared to Rofecoxib. Sekhavat et al, in 2000 showed increased tooth movement following the consumption of Misoprostol which is a PGE1 analog in all test groups compared to controls in rat model (13). Chumbley and Tunkey in 1986 also indicated that indomethacin, which is a NSAID and strong inhibitor of PG synthesis, decreases tooth
movement in cat model (14). Kyrkanides in 2000 confirmed the effects of cyclooxygenase inhibitors especially indomethacin during orthodontic treatment and believed this drug to be effective on reducing enzymatic activity involved in the process of tooth movement (15). In a study by Seifi and colleagues (2003) the greatest reduction in tooth movement in rabbits was observed in the aspirin group. Aspirin is the only NSAID that irreversibly inhibits cyclooxygenase enzyme and has a greater effect on COX1 enzyme. Aspirin acts more efficiently in inhibition of PGE synthesis compared to ibuprofen and acetaminophen (1). In a study by Cohen and Zarrinnia (1996) ibuprofen which is a nonselective NSAID clearly reduced orthodontic tooth movements in Guinea pigs (16). The mentioned studies all show the effect of NSAIDs on reduction of orthodontic tooth movement. This is especially true for the nonselective NSAIDs that inhibit both cyclooxygenase I and II enzymes. However, as observed in Sari et al, study (2004)(12) as well as the present study, selective NSAIDs that only inhibit cyclooxygenase II enzyme had no interfering effect on tooth movement. The difference between the present study results and those reporting reduced orthodontic tooth movements due to the consumption of NSAIDs is the selection of nonselective NSIAD in those studies versus the administration of a selective NSAID in the current study.

It should be noted that according to studies conducted by Kanzaki (2006), Kohno (2005), Akin (2004), Kale (2004) and Soma (2000) other inflammatory mediators in addition to PGE may also play a role in orthodontic tooth movement because inhibition of cyclooxygenase enzyme and PGE synthesis in none of the studies could entirely inhibit and cease tooth movement (17-21).

In the present study, effect of different doses of celecoxib on root resorption was evaluated. Number of resorption lacunae and the highest depth of the largest resorption lacunae in the mesial and distal surfaces of the mesial root of right maxillary first molar were recorded and compared. The evaluated parameters for root resorption in the present study were almost similar to those of other studies. Akin (2004) in his study used number of resorption lacunae, osteoclasts and capillaries for evaluation of root resorption in rats (19). Sekhat and coworkers (2000) in their study assessed the depth of resorption lacunae in histological samples (13). Kale (2004) evaluated the number of Howship’s lacunae, capillaries and osteoblasts in the prepared specimens (20). Boekenoogen in 1996 determined the number of resorption lacunae at the mesial and distal surfaces and the greatest depth of resorption lacunae in the mesial root of first molar tooth in rat (22). In our study, the mean maximum depth of the largest resorption lacunae at the mesial surfaces was the greatest in group A. This rate was significantly different from the calculated mean value in group C and control groups (P<0.05). It may be assumed that higher rate of root resorption in the mesial surfaces is related to the greater tooth movement observed in this group. The mean maximum depth of the largest resorption lacunae at the mesial surfaces decreased by increasing the dosage of celecoxib from groups A to C. Reduction in depth of resorption lacunae in group C compared to groups A and B was statistically significant (P<0.05). Thus, 100 mg/kg celecoxib in rat model provides higher protection against mesial surface root resorption. Although the mean depth of resorption lacunae at the mesial surface of the root was the smallest in group E, this rate was not equal to zero. This finding can confirm the theory of Bishara (2001) stating that root resorption also occurs in teeth that have never undergone orthodontic treatment (23). The anesthetic drug may also play a part in this respect. The mean maximum depth of the largest resorption lacunae at the distal surface of the mesial root was the greatest in group B. However, its difference only with the value in group E was statistically significant (P<0.05). The mean maximum depth of the resorption lacunae at distal surfaces was smaller in group C compared to other test groups and group D; but, these differences were not statistically significant (P>0.05). Thus, we may conclude that 100 mg/kg dosage of celecoxib provides a greater protection against root resorption at the distal surfaces of root compared to lower doses or no drug consumption. Although the depth of resorption lacunae at the distal surfaces of roots in most rats in group E was equal to zero, the mean maximum depth of resorption lacunae at
distal surfaces of root in this group was not equal to zero. The mean maximum depth of the largest resorption lacunae in both mesial and distal surfaces of the mesial root (total root resorption) was the greatest in group A. This rate was significantly different from the mean rates calculated for groups C and E (P<0.05). Highest rate of root resorption observed in group A can be attributed to the greater tooth movement in this group. Increasing the dosage of celecoxib from group A to C resulted in a decrease in mean total root resorption. This reduction in group C compared to groups A and B was statistically significant (P<0.05). We may assume that low doses of celecoxib (25 and 50 mg/kg) cannot protect the root surface against resorption but higher dosage of this drug (100 mg/kg) can have a greater protective effect against root resorption or at least does not have any destructive impact in this regard.

The present study also compared the mean maximum depth of resorption lacunae between the mesial and distal surfaces of the mesial root of the first molar tooth. This comparison showed that except for group E, in all groups the mean maximum depth of the largest resorption lacuna was greater in the mesial surface compared to distal surface. This may be due to the fact that the mesial surface is subjected to more pressure during orthodontic tooth movement of first molar. These findings are in accord with those of Sekhavat et al, (2000)(13). In their study, root resorption in the distal surface of the mesial root of the maxillary first molar was smaller than that in the mesial surface in all samples (13). Mesial surface of the mesial root of maxillary first molar also showed greater root resorption compared to distal surface in Boekenoogen study in 1996 (22). In the present study, the difference in root resorption between mesial and distal surfaces of the mesial root in all three test groups was statistically significant (P<0.05). However, this difference in group D was not statistically significant (P>0.05). This finding may reveal the greater protection of the distal surface against resorption by celecoxib.

The mean number of resorption lacunae at mesial and distal surfaces of the mesial root was the highest in group B. This rate showed a statistically significant difference with the mean number of resorption lacunae at mesial and distal surfaces of the root in groups C and E (P<0.05). The mean number of resorption lacunae at mesial and distal surfaces of root was significantly different in group C compared to groups A, B and D. Also, the mean number of resorption lacunae in the mesial surface in group C was significantly different from the rate in groups A and B (P<0.05). However, in distal surface, this rate was significantly lower than the rate in group B (P<0.05). Thus, celecoxib at a dosage of 100 mg/kg reduces the number of resorption lacunae in the mesial root of the first molar tooth in rats. The mean number of resorption lacunae in all groups except for group E was greater in the mesial than in the distal surface. This finding is in concord with the results obtained from measuring the mean maximum depth of resorption lacunae in this study. Our findings regarding the protective effect of NSAIDs against root resorption during orthodontic tooth movement have also been confirmed by Seifi et al, in 2003. They noted a significant reduction in root resorption due to the consumption of aspirin and reported the causing mechanism to be the inhibition of PG production by aspirin (1). Sekhavat et al, in 2000 observed an increase in maxillary first molar mesial root resorption as the result of consuming Misoprostol. However, this increase was not statistically meaningful (13). Boekenoogen in 1996 revealed that injection of exogenous PGE2 in rat model during the two-week study period increased maxillary first molar mesial root resorption (22). These results confirm the fact that PGs not only affect orthodontic tooth movement, but also play a role in root resorption.

In the present study, the rats were weighed at the beginning and at the end of study and their exact weights were recorded. Comparison of weight changes at the end of study in all groups demonstrated weight loss in almost all animals. The exceptions were half the animals in group E and 4 rats in groups B, C and D that gained weight during the course of study. In the present study weight loss in all three test groups that received celecoxib was statistically significant (P<0.05). The highest changes in weight were observed in group A followed by group C but the difference between these two groups was not statistically significant (P>0.05). Groups A and
C had significant differences with group E in terms of changes in weight (P<0.05). The reason can be the interference of orthodontic appliance with the nutrition of animals (orthodontic treatment in humans can also change the nutritional regimen of patients). Other possible reasons can be the injection of anesthetic drug and related side effects and complications or changed living environment of animals (being transferred from Mashhad to Zahedan). Weight loss observed in our study was not in agreement with Kale’s findings in 2004 (20). They did not report weight loss in any of the groups in their study on rats (20). Roche in his study in 1997 (24) on rabbit model reported weight gain in all animals in the control group at the end of the 21-day study period. In the test group, except for weight loss in two animals, other rabbits gained weight at the end of study (22). In a study by Carlos et al, in 2007 (9) animals lost weight immediately after surgery but the change in weight at the end of study was not statistically significant. However, Akin in his study in 2005 (19) reported a significant weight loss in all groups (compared to the control group) at day 3 in comparison to the baseline value at the onset of study. The mentioned finding regarding weight change is in accord with our study result.

**Conclusion:**

Consumption of celecoxib and its dosage do not have a statistically significant effect on orthodontic tooth movement. Celecoxib dosage of 100 mg/kg had the lowest interference with tooth movement and offered greatest protection against root resorption.

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