External Apical Root Resorption and the Release of Interleukin-1 Beta in the Gingival Crevicular Fluid Treated by a Self-Ligating System

Yuko Kanetaka-Ishikawa, Masaru Yamaguchi, Masaki Asano, Kunihiko Yamada, Mami Shimizu, Mari Funakoshi, and Kazutaka Kasai

Department of Orthodontics, Nihon University School of Dentistry at Matsudo, Matsudo, Chiba 271-8587, Japan

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Abstract
The aim of this study was to investigate the amount of external apical root resorption (EARR) and the release of interleukin (IL)-1 beta in the gingival crevicular fluid (GCF) in subjects treated with a low-force low-friction system.

Sixty patients were assigned to two groups of thirty patients each: one group received treatment with self-ligating brackets and the other received conventional ligated edgewise brackets. All patients were treated with extraction of the maxillary first premolars. The EARR of the maxillary central incisors was evaluated on the periapical radiographs and cephalograms, taken before and after orthodontic treatment. The GCF was also collected non-invasively from the mesial and distal sides of central incisors using filter paper strips before and after orthodontic treatment. Enzyme-linked immunosorbent assay (ELISA) kits were used to determine the IL-1 beta levels in the GCF samples.

A significant difference was found in the amount of EARR between the patients with self-ligating brackets and conventional brackets. The mean amount of EARR was significantly lower for self-ligating brackets than the conventional brackets (p < 0.05). The GCF levels of IL-1 beta for the patients with the self-ligating brackets application were significantly lower than for those with the conventional brackets (p < 0.05).

These results show that the mean amount of EARR and the GCF levels of IL-1 beta are significantly lower in patients treated using low-force low-friction appliances than with the conventional brackets. Therefore, self-ligating brackets may be a useful system for reducing inflammation and EARR.

Introduction
External apical root resorption (EARR) is an unavoidable pathological consequence of orthodontic tooth movement. It can be defined as an iatrogenic disorder that unpredictably occurs after orthodontic treatment, whereby the resorbed apical root portion is replaced with normal bone. EARR is a sterile inflammatory process that is extremely complex, and involves various disparate components, including mechanical forces, tooth and bone, cells, the surrounding matrix, and certain known biologic messengers (1, 2). Interleukin-1 beta (IL-1 beta) is a potent stimulus for bone resorption and osteoclastic cell recruitment during orthodontic tooth movement (3). With regard to the relationship between EARR and inflammatory cytokines, Zhang et al. indicated that interleukin IL-1 and tumor necrosis factor (TNF)-alpha are important for the induction and further processing of mechanically-induced root resorption in rats (4). Recent papers have discussed a genetic predisposition for root resorption, and have demonstrated that polymorphisms of the IL-1 beta gene are associated with EARR during orthodontic treatment (5, 6). Therefore, IL-1 beta contributes to alveolar bone resorption and EARR during orthodontic tooth movement.

Wire friction influences the forces acting in a continuous arch system. Damon suggested that the use of a nearly friction-free system, using self-ligating brackets and high-tech wires, may not cause the periodontal problems,
including alveolar bone loss, which are typically associated with orthodontic treatment (7). Other studies have reported that the static friction measured in vitro is much lower when a passive self-ligating system is used than when any other type of fixed appliance is used (8, 9). The friction force disturbs orthodontic tooth movement, thus, it is expected that the influence on the periodontal tissue would be different for the self-ligating brackets compared to the conventional appliances. We previously reported that the gingival crevicular fluid (GCF) levels of substance P (SP), one of neuropeptides which cause local inflammation, for the passive self-ligating system sites are significantly lower than those for the teeth with conventional brackets at 24 hours after initiating treatment (10). Therefore, the passive self-ligating system is useful to reduce the inflammation and pain resulting from orthodontic forces.

The purposes of this study were to measure and compare the EARR and the levels of IL-1 beta in the GCF in patients undergoing treatment with self-ligating brackets compared to those undergoing treatment using the conventional appliances.

Materials and Methods

Subject selection

Sixty subjects were selected from patients seeking treatment in the Department of Orthodontics at the Nihon University School of Dentistry at Matsudo. Sixty orthodontic patients (15 males, 45 females, mean age of 18.0 ± 5.3 years) were enrolled in the study after meeting the following criteria: [1] good general health; [2] lack of antibiotic therapy during the previous 6 months; [3] absence of anti-inflammatory drug administration in the month preceding the study; [4] healthy periodontal tissues with generalized probing depths ≤3 mm and no radiographic evidence of periodontal bone loss. Informed consent was obtained from the subjects after an explanation of the study protocol, which was reviewed by the ethics committee of Nihon University School of Dentistry at Matsudo (#10-019).

Two groups were set up, one treated with ‘conventional brackets’ (CB) and the other treated with ‘self-ligation brackets’ (SL) (Figs. 1 and 2). Thirty patients (7 males, 23 females) were treated with the self-ligating brackets (Damon 3,Ormco, Japan, Tokyo, Japan). A matched control group of 30 patients (8 males, 22 females) was selected from the same registry and treated with the conventional brackets (0.022-inch slot; Ormco). These controls were matched with the other group for age, sex, ANB, overjet, and overbite values, before orthodontic treatment (T1).

The selection criteria for the subjects were as follows: 1. a Class I malocclusion with mild crowding (≤ 6 mm; mean 5.4 ± 0.55), 2. Four premolar extractions, 3. Excellent quality records, 4. Only patients with no history or evidence of tooth injury or wear, as shown on the charts and diagnostic records, were included.

Measurement of the EARR and tooth position

To record the EARR and tooth position parameters, the following measurements and evaluations were executed. The tooth length of the maxillary central incisor at T1 and T2 (after orthodontic treatment) was measured on the periapical radiographs and cephalograms, and from the incisal edge to the apex. When a difference in the length of the 2 adjacent maxillary central incisors was evident, the shorter root length was recorded. Baseline measurements of the ANB angle, overjet (along the occlusal line), and overbite (perpendicular to the occlusal line) at T1, were made on the cephalograms.

The measurements of the root length (EARR) and tooth position were performed according to the method reported by Kocadereli et al. (11) and Brin & Bollen (12). The changes in the root length (EARR) of the maxillary central incisor were recorded as the difference between tooth lengths from T1 to T2. Maxillary incisor movements were measured as: [1] The axial inclination of the maxillary central incisor to SN (1/SN) between T1 and T2; [2] The vertical and horizontal distances that the maxillary central incisor root moved during orthodontic treatment.

GCF collection

The GCF was collected from the mesial and distal sides of the upper central incisors. GCF sampling was performed using the method described by Yamaguchi et al. (13), and was collected before (T1) and after (T2) orthodontic treatment. The tooth was gently washed with water, and then the sites under study were isolated with cotton rolls (to minimize saliva contamination) and gently dried with an air syringe. Paper strips (Periopaper, Harco, Tustin, CA, USA) were carefully inserted 1 mm into the gingival crevice and allowed to remain there for 1 minute, after which a second strip was placed at the same site. Care was taken to avoid mechanical injury. The contents were eluted out into 1x
phosphate buffer saline (PBS) containing 0.1mM phenylmethylsulphonyfluoride and stored at −80℃ until further processing.

**Enzyme immunoassay**

The levels of IL-1 beta were measured in duplicate using a commercial ELISA kit (Quantikine, R&D Systems, Inc., Minneapolis, MN, USA), with the results expressed as pg/μg of total protein in the GCF.

**Statistical methods**

The statistical analysis of the differences among the groups was performed using a one-way ANOVA and the Scheffe test to evaluate the significance of the differences between each pair of groups.

**Results**

The 2 groups were matched for sex and chronological age at T1. Good agreement was also found for the ANB angle, overjet and overbite at T1. The tooth lengths at T1 in both groups were similar: 26.5 ± 1.7 in the CB group and 26.6 ± 1.9 in the SL group (Table 1).

Table 2 shows that the duration of treatment in the SL group (25.8 ± 3.3) was not significantly different from that
in the CB group (26.4 ± 3.1) (P=0.883). In both groups, the lengths were reduced at T2 (Table 2): to 24.0mm ± 1.6 in the CB group and 25.4mm ± 1.5 in the SL group. The tooth lengths in the 2 groups were statistically different at T2 (P=0.05). The mean amount of root resorption of the maxillary central incisor as measured on the lateral cephalogram was significantly greater in the CB group than that in the SL group at T2. However, this mean difference in

Fig. 2. The dental model of self-ligating brackets and conventional ligated edgewise brackets. The wire was set into self-ligating brackets (A: the whole view, B: the close-range view). The wire was ligated into conventional edgewise brackets by ligature wire (C: the whole view, D: the close-range view).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>CB group</th>
<th>SL group</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male/female ratio</td>
<td>8/22</td>
<td>7/23</td>
<td></td>
</tr>
<tr>
<td>Mean age at T1 (y)</td>
<td>18.8 ± 5.5</td>
<td>19.0 ± 5.3</td>
<td></td>
</tr>
<tr>
<td>ANB (°)</td>
<td>3.5 ± 1.8</td>
<td>3.6 ± 1.7</td>
<td></td>
</tr>
<tr>
<td>Overjet (mm)</td>
<td>3.6 ± 1.7</td>
<td>3.7 ± 1.6</td>
<td></td>
</tr>
<tr>
<td>Overbite (mm)</td>
<td>3.4 ± 1.6</td>
<td>3.4 ± 1.6</td>
<td></td>
</tr>
<tr>
<td>Tooth length (mm)</td>
<td>26.5 ± 1.7</td>
<td>26.6 ± 1.9</td>
<td></td>
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</tbody>
</table>

Table 2. Comparison of changes (±SD) during mechanotherapy (T1-T2) in EARR and tooth position in the Conventional bracket and Self-ligation bracket groups (absolute values in parentheses)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>CB group</th>
<th>SL group</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of treatment (mo)</td>
<td>26.4 ± 3.1</td>
<td>25.8 ± 3.3</td>
<td>0.891</td>
</tr>
<tr>
<td>EARR (mm)</td>
<td>2.5 ± 1.5</td>
<td>0.88 ± 0.9</td>
<td>0.005*</td>
</tr>
<tr>
<td>Change in I/SN (°)</td>
<td>-7.2 ± 4.7</td>
<td>-7.1 ± 4.8</td>
<td>0.901</td>
</tr>
<tr>
<td>Apex (a) vertical movement (mm)</td>
<td>-0.8 ± 1.2</td>
<td>-0.8 ± 1.0</td>
<td>0.883</td>
</tr>
<tr>
<td>Apex (a) horizontal movement (mm)</td>
<td>2.6 ± 1.7</td>
<td>2.8± 1.7</td>
<td>0.750</td>
</tr>
</tbody>
</table>
EARR between the groups did reach statistical significance.

The axial movements of the central incisor—vertical and horizontal apical movements—are presented in Table 2. The 1/SN change between T1 and T2 indicated an increase in the axial inclination in both the CB and SL groups (about 6°). The change in the axial inclination of the maxillary central incisor (1/SN) was not significantly different between the CB group and the SL group (P=0.922). The amounts of vertical movement of the apex were also not significantly different between the groups (P=0.931). For the horizontal movements of the apex, similar (P=0.807) amounts of distal palatal root movement were observed in both groups.

**GCF study**

The GCF volume has previously been shown to correlate with the inflammatory state (13), however, there was no statistically significant difference in the mean volume of GCF between the CB group and SL group at either T1 (CB: 0.43 ± 0.08 μl, SL: 0.42 ± 0.09 μl) or T2 (CB: 0.42 ± 0.07 μl, SL: 0.44 ± 0.08 μl) in the present study. In all of the patients, the probing depths remained less than 2 mm and gingival health was excellent, with no gingival bleeding.

At T1, there were no significant differences in the mean IL-1 beta value between the CB and the SL groups. However, the mean IL-1 beta value in the CB group was significantly higher than that in the SL group at T2 (p<0.05) (Fig.3).

**Discussion**

In this study, the mean amount of root resorption of the maxillary central incisor measured on the lateral cephalogram was significantly greater in the CB group than the SL group at T2 (Table 2). According to Weltman et al. (14), the risk factors for EARR can be divided into treatment-related and patient-related factors. The orthodontic treatment-related risk factors include the treatment duration (15–17), magnitude of applied force (18–20), direction of tooth movement (21–23), amount of apical displacement (15, 17), method of force?application [continuous vs intermittent] (24, 25), type of appliance (26, 27), and treatment technique (28, 29).

Previous studies have found that heavy forces produce significantly more EARR than light forces or controls (18–20). Chan and Darendeliler found that the mean volume of the resorption craters is significantly (11.59 times) greater in a heavy-force group than in a control group (19). Heavy forces in both compression and tension areas produced significantly more EARR than in regions under light compression and light tension forces. Barbagallo et al. also found that heavy forces produce significantly more RR
(9 times greater than the control) than a light force (5 times greater than the control) (20). Therefore, a light force may have an advantage for preventing the occurrence of EARR or reducing the extent of EARR.

The claim of reduced friction with self-ligating brackets is often cited as a primary advantage over the use of conventional brackets (30–32). This occurs because the usual steel or elastomeric ligatures are not necessary, and it is claimed that passive designs generate even less friction than active ones (33, 34). Beger demonstrated that there is a significant decrease in the force level required for the self-ligating bracket when compared with elastomeric and steel-tie ligation in both metal and plastic bracket systems, and concluded that self-ligating brackets require less force to produce tooth movement, leading to reduced friction (8).

GCF collection, which is a non-invasive method that has been widely used for the analysis of human tooth movement, enables the easy detection of various biochemical markers, including IL-1 beta (35, 36). During the process of root resorption, organic matrix proteins and cytokines are released into the gingival crevice. In this GCF study, the mean IL-1 beta value in the CB group was significantly higher than that in the SL at T2 (p < 0.05) (Fig.3).

The expression of IL-1beta has previously been shown to increase depending on the strength and duration of the compressive force in osteoblastic Saos-2 cells (37). Nakao et al. demonstrated that the IL-1 beta expression levels from periodontal ligament (PDL) cells are increased in a compressive force-dependent manner in vitro (38). IL-1 alpha and TNF-alpha are also expressed in the bone and PDL along the roots of the orthodontically moved molars in rats (39). Moreover, IL-1 beta has been characterized as a potent bone-resorptive cytokine, and was implicated as a key component of the complex pathways leading to root resorption (40). Therefore, the IL-1 beta released in the GCF may increase depending on the strength of the orthodontic force, and the system using self-ligating brackets may inhibit the increased production of IL-1 beta in the GCF during orthodontic treatment. Taken together, these findings and our present results suggest that self-ligating brackets may reduce the inflammation and EARR associated with orthodontic treatment.

In contrast to our current results, previous studies have found no significant differences in the EARR between CB and SL groups (41). Furthermore, Wright et al. concluded that there is no evidence that treatment with self-ligated appliances, and in particular, the Damon (®) appliance is more stable (42). In the presence of identical archwire sequences, there is no evidence that Damon (®) brackets can align teeth faster or in a qualitatively differently manner when compared to conventional-ligation. There is no high quality evidence that treatment with the Damon (®) appliance takes place more rapidly or leads to a superior occlusal or aesthetic result. Indeed, the best available evidence suggests there is no difference in treatment outcome or time, at least in extraction cases. Further studies in a larger number of patients should be carried out to investigate the advantages and disadvantages of using self-ligating brackets for orthodontic treatment.

Conclusion
The present results show that the mean amount of EARR and the GCF levels of IL-1 beta are significantly lower in patients treated with the low-force low-friction appliance than with the conventional brackets. Therefore, self-ligating brackets may be useful for reducing the inflammation and EARR associated with orthodontic treatment.

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References


