External apical root resorption caused by orthodontic treatment: a review of the literature

Abstract

External apical root resorption is a common consequence of orthodontic treatment. A number of treatment-related factors have been implicated in the pathogenesis of root resorption in orthodontic patients; however recent evidence suggests that genetic factors also play a major role in the development of this condition. Herein, we review prevalence, diagnosis and aetiology of root resorption with a particular emphasis on the effect of genetic variation and orthodontic forces, as well as discuss effective prevention strategies.

Keywords Root resorption; Orthodontic treatment; Genetic predisposition; Review.

Introduction

External apical root resorption (ARR) is an undesirable complication of orthodontic treatment, which results in permanent loss of tooth structure from the root apex [Mohendesan et al., 2007]. Previous studies have demonstrated a number of treatment-related factors that are significantly associated with the development of ARR in orthodontic patients, and led to the use of the term iatrogenic consequence [Brezniak and Wasserstein, 2002]. However, a growing body of evidence suggests that single nucleotide variations in human genome are also associated with development of ARR, suggesting that orthodontic treatment is not the only culprit [Al-Qawasmi et al., 2003]. Even though there is no clinical practice guidelines on diagnosis, monitoring and management of root resorption, understanding patient- and treatment-related risk factors of this unwanted complication is of utmost importance to general dentists and orthodontists in the care of these patients.

Herein, we review prevalence, diagnosis and aetiology of ARR with an emphasis on the effect of genetics and orthodontic forces, as well as discuss prevention strategies.

Classification and prevalence of ARR

Levander and Malmgren presented a classification system for root resorption which is widely accepted in the orthodontic literature [1988]. According to this index, severity of root resorption increases from grade 1, defined as presence of irregular root contour, to grade 4, where root resorption is greater than 1/3 of the original root length (Table 1).

<table>
<thead>
<tr>
<th>Grade</th>
<th>Definition</th>
</tr>
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<tbody>
<tr>
<td>0</td>
<td>No evidence for resorption</td>
</tr>
<tr>
<td>1</td>
<td>Irregular root contour</td>
</tr>
<tr>
<td>2</td>
<td>Apical root resorption less than 2 mm</td>
</tr>
<tr>
<td>3</td>
<td>Apical root resorption &gt; 2 mm and &lt; 1/3 of original root length</td>
</tr>
<tr>
<td>4</td>
<td>Root resorption exceeding 1/3 of original root length</td>
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</table>

Previous studies reported a prevalence of root resorption greater than 2 mm (grades 3 and 4) of 10-18% [Linge and Linge, 1983; Levander and Malmgren, 1988]. However, it is important to note that plain radiography is a crude method of assessing root resorption, which may underestimate the true prevalence of this condition. Indeed, experimental and human histological studies have shown that root resorption occurs in over 90% of patients undergoing orthodontic treatment [Kural and Owman-Moll, 1998].

Diagnosis of ARR

The most widely used diagnostic technique for root resorption remains conventional radiography including panoramic and periapical views. Newer imaging modalities, including 3-D Cone Beam Computed Tomography (CBCT), were recently introduced into clinical use and serve as attractive alternatives to conventional radiotherapy in diagnosis of ARR. Dudic and colleagues [2009] assessed the effectiveness of CBCT compared to panoramic radiographs in 22 patients near the end of their orthodontic treatment and demonstrated that detection of root resorption was significantly higher in CBCT compared to panoramic radiographs (69.0% vs. 43.5%, respectively). Similarly, Alqerban et al. [2011] demonstrated, in 60 patients with impacted or ectopically erupting maxillary canines seeking orthodontic treatment, that there was a significant difference in root resorption rates obtained by CBCT versus panoramic radiograph in favor of CBCT. Taken together, these studies suggest that CBCT may be a more sensitive imaging modality for diagnostic and prognostic assessment of ARR. However, further studies are needed to assess safety and cost-effectiveness of CBCT in the management of orthodontic patients with ARR.
Aetiology of ARR

Identification of risk factors responsible for ARR has been the focus of numerous research studies in an effort to understand underlying mechanisms and develop prevention strategies and treatment methods. Collectively, these studies suggest that the aetiology of ARR is complex and multifactorial including patient-related and treatment-related risk factors [Weltman et al., 2010]. Patient-related risk factors implicated in the pathogenesis of ARR include age, gender, genetic predisposition, severity of malocclusion, tooth and root morphology, as well as systemic conditions such as allergy, asthma, and alcoholism. Treatment-related risk factors implicated in the pathogenesis of ARR include magnitude of orthodontic force, direction of tooth movement, amount of apical displacement, and duration of treatment.

Genetic predisposition to ARR

Growing lines of evidence suggest that genetic factors play a major role in the development of root resorption. Genetic epidemiology defines heritability as the ratio of genetic variance to total variance for a given trait, which represents the proportion of the phenotypic variance attributable to genetic factors. In a sibling pair study design, Harris et al. [1997] estimated heritability for root resorption to be 80% for the maxillary incisors. In a separate retrospective twin study, phenotypic concordance for quantitative detection of root resorption was 49.2% in monozygotic twins compared to 28.3% in dizygotic twins with an estimated heritability of 34% [Ngan et al., 2004]. Taken together, these findings suggest that there is a strong genetic component of root resorption trait. Interestingly, in the latter study, concordance for monozygotic twins was less than 100% suggesting that environmental factors also play a role in the development of ARR.

Al-Qawasmi and colleagues [2003a] performed a family study to assess the potential effect of single nucleotide polymorphisms (SNPs) in two closely-located pro-inflammatory candidate genes (IL-1A and IL-1B) on root resorption. These genes have been selected for their potential involvement/activation in periodontitis as well as tooth movement process. Interestingly, the transmission disequilibrium test identified evidence for significant linkage disequilibrium of IL-1B SNP (+3954) with clinical ARR. Patients who were homozygous for IL-1B allele 1 have a 5.6 fold (95% CI 1.9-21.2) increased risk of ARR compared with those who were not homozygous for the IL-1B (+3954) allele 1. Allele 1, which was shown to decrease the production of IL-1 cytokine in vivo, significantly increases risk of ARR in this patient group. An independent verification study for this SNP trait association was published by a group of investigators from Brazil [Bastos Lages, 2009]. In this case-control study of 61 patients, the authors demonstrated that carrying patients who were homozygous for IL-1B allele 1 have a 4.0 fold (95% CI 1.23-12.9) increased risk of ARR compared with those who were not homozygous for the IL-1B (+3954) allele 1. However, Gulden et al. [2009] from Germany failed to demonstrate such relationship in a study of 96 ARR cases and 162 controls. Indeed, IL-1B (+3954) allele 1 was observed more commonly in the control group. Conversely, this study demonstrated a significant association between IL-1A (-899) genotype and root resorption. Reasons for this discrepancy remains unknown, however it might be related to differences in genetic background of the populations, analytical methods, as well as Type I and/or Type II statistical errors.

Another candidate locus implicated for the development of ARR is located on chromosome 18 [Al-Qawasmi et al., 2003b]. Using a sibling correlation design by calculating shared IBD (identical by descent) for candidate markers, Al-Qawasmi and colleagues identified evidence for linkage (LOD score of 2.5) between a microsatellite marker D18S64 which lies close to the candidate gene TNFRSF11A and root resorption trait. The TNFRSF11A gene encodes the receptor activator of nuclear factor-kappa B (RANK), an essential signaling molecule in osteoclast formation and activation as a potential mechanism in pathogenesis of root resorption.

Although the aforementioned preliminary studies are promising, their results need to be carefully evaluated. First of all, it is important to remember that SNP-trait association may not necessarily represent a causal relationship, and the marker SNP may in fact be in LD with the causal SNP. Secondly, sample sizes of these studies are extremely small and subject to Type II error. Lastly, candidate gene approach is subject to selection bias and limits analysis to a few markers compared to millions of different variations present in the human genome. Genomewide association studies or next-generation sequencing techniques in a large group of patients with case-control design may provide an unbiased approach to detect candidate genes and/or markers in this complex genetic disease. Nevertheless, these studies provide the basis for evidence that genetic markers of root resorption

<table>
<thead>
<tr>
<th>Study</th>
<th>SNP</th>
<th>n (cases)</th>
<th>n (controls)</th>
<th>Odds Ratio</th>
<th>95% CI</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Al-Qawasmi et al.</td>
<td>IL-1A (-899)</td>
<td>33</td>
<td>40</td>
<td>NR</td>
<td>NR</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>IL-1B (+3954)</td>
<td>33</td>
<td>40</td>
<td>5.6</td>
<td>1.9 - 21.2</td>
<td>0.004</td>
</tr>
<tr>
<td>Bastos-Lages et al.</td>
<td>IL-1B (+3954)</td>
<td>23</td>
<td>38</td>
<td>4.0</td>
<td>1.2 - 12.9</td>
<td>0.014</td>
</tr>
<tr>
<td>Gulden et al.</td>
<td>IL-1A (-899)</td>
<td>45</td>
<td>44</td>
<td>9.3</td>
<td>1.1 - 77.8</td>
<td>0.040</td>
</tr>
<tr>
<td></td>
<td>IL-1B (+3954)</td>
<td>45</td>
<td>49</td>
<td>0.5</td>
<td>0.2 - 1.0</td>
<td>0.062</td>
</tr>
</tbody>
</table>

*Odds Ratio calculation based on 2/2 genotype vs. 1/1 and 1/2 genotypes for IL-1A SNP and 1/1 genotype vs. 1/2 and 2/2 genotypes for IL-1B SNP.

NR= not reported, NS= non-significant.

TABLE 2 - Candidate gene studies of root resorption.
do exist, and in the future may serve to identify patients at risk prior to initiation of treatment.

**Role of orthodontic forces**

Previous studies have shown that teeth subjected to orthodontic forces had significantly more ARR than the control teeth from the same subjects, suggesting that orthodontic forces have a significant role on the development of ARR, irrespective of patient-related factors [Harris et al., 2006; Barbagallo et al., 2008]. It has also been demonstrated that heavy forces induce significantly more ARR compared to light forces factors [Harris et al., 2006; Barbagallo et al., 2008; Chan et al., 2005]. This may be attributed, at least in part, to rapid lacuna development as well as compromised repair process observed with heavy force application.

The direction of force has also been implicated in the aetiology of ARR. Chan et al. [2005] indicated that compressive forces on the periodontal ligament cause more root resorption than tensile forces. Han et al. [2005] suggested that the intrusion of teeth causes about four times more ARR than extrusion, however it should be noted that extrusion of teeth may also cause ARR in susceptible individuals. Several reports indicated that jiggling and movement caused by application of intermaxillary elastics are likely to increase the risk of ARR [Baumrind, 1996; Mirabella, 1995; Weltman, 2010]. Taken together, intrusive forces with and lingual root torque appear to be strongly associated with ARR following orthodontic treatment.

One of the other established treatment-related risk factors for ARR is duration of treatment. In a meta-analysis of 8 independent studies, Segal et al. [2004] demonstrated that mean apical root resorption was strongly correlated with total apical displacement (r = 0.822) and treatment duration (r = 0.852). Apical root resorption and duration of treatment reported from these 8 trials were a scatterplot (Fig. 1). Given that duration of treatment is proportional to severity of root resorption, investigators have explored whether treatment pause would have a favourable effect on root resorption. Levander et al. [1994] studied 40 patients with evidence of root resorption after 6 months of orthodontic treatment, and randomised these patients to either continuation of treatment or a treatment pause of 2 to 3 months after which the treatment was resumed. They observed that the amount of root resorption was significantly less in patients who underwent treatment interruption. Acar et al. [1999] indicated that the application of discontinuous force results in less ARR than does the application of continuous force.

Rudolf et al. [2001] investigated the effect of different types of orthodontic tooth movement on stress distribution using a three-dimensional finite element model of maxillary incisor. In this single-tooth model, authors have demonstrated that the greatest amount of relative stress at tooth apex occurred with tipping, intrusion, and extrusion forces. Field et. al. [2009] extended these observations into a multi-tooth finite element model with tipping forces and suggested that the disto-cervical region of tooth experiences the greatest stress. An important message of these preliminary studies is that, in parallel with the advances in imaging techniques, it might be possible to mathematically model stress distributions based on different treatment approaches in orthodontic patients prior to initiation of treatment, therefore tailoring treatments in susceptible individuals.

**Long-term outcomes of ARR**

Remington et al. [1989] have first reported long-term outcomes of 100 orthodontic patients who had undergone active orthodontic treatment and subsequently exhibited root resorption. In their analysis, maxillary incisors seemed to be affected more frequently and to a more severe extent than the rest of the dentition. They also reported that ARR associated with orthodontic forces did not progress radiologically following the termination of active orthodontic treatment, and reparative processes took place including smoothing and remodeling of sharp edges. There was no evidence of tooth loss, however hypermobility was observed in 2 cases. This finding is inconsistent with the reports indicating that the apical part of the root has relatively minor importance for total periodontal support [Weltman et al., 2010]. In a recent long-term study by Jonsson et al. [2007], patients who had experienced moderate, severe, and extreme ARR were recalled 5 to 15 years following orthodontic treatment for quantitative assessment of tooth mobility by periotest method. They noticed increased mobility only in teeth with extremely resorbed roots (root length less than 1 mm). The increase in mobility was minimal and non-significant in teeth with longer root lengths. The length of the follow-up period did not influence severity of root resorption, again suggesting that root resorption process does not progress following termination of the treatment.

**Prevention and management strategies**

Several points merit consideration prior to initiation of orthodontic treatment. First of all, patient and parents should be informed about root resorption as a potential

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**FIG. 1 - Association of Root Resorption and Duration of Therapy.** Trial level data obtained from Segal et al. [2004].
consequence of orthodontic treatment and long-term outcomes. Collecting a good medical history particularly focusing on the presence of potentially predisposing clinical conditions, such as allergy or asthma, is of utmost importance. Patients with positive family history of root resorption should be carefully investigated, and records of siblings and/or parents with root resorption should be reviewed. Currently, there is not enough evidence to support screening individuals for genetic susceptibility on a routine basis.

As discussed above, heavy forces are particularly harmful, and until more evidence is obtained, it is recommended to apply light forces particularly for intrusive movements. Following initial 6 months of treatment, periapical radiographs should be obtained to assess the early development of root resorption. Whenever tooth resorption is identified, patient and parents should be informed of the finding. Interruption of treatment with a passive archwire may be considered to reduce root resorption. In cases of severe root resorption, the treatment plan should be reassessed with the patient.

Upon completion or termination of the treatment, final radiographs should be obtained. Fixed appliances for retention should be carefully designed to prevent further root resorption. Patients should be informed about the importance of maintaining a proper oral hygiene to prevent periodontitis. Serial radiographs should be obtained in patients with severe root resorption until evidence for progression is no longer present. In cases of extreme resorption, endodontic treatment and calcium hydroxide may be considered.

Conclusion

The fundamental principle of medicine primum non nocere (first do no harm) by Hippocrates also applies to the field of orthodontics. Orthodontists should be well aware of the risks and benefits of orthodontic treatment, specific to each case. Despite recent advances in molecular biology, imaging modalities and clinical care of patients, our understanding of root resorption remains limited. Large clinical and genetic association studies are needed to further understand biology, detection, and treatment of this undesired complication.

References