

# Biological aspects and treatment of external replacement resorption: literature review

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## ABSTRACT

Replacement external root resorption consists in the replacement of dental structure into bone tissue. The current consensus is that there is no relevant therapy for that process. A Literature review focused on therapeutic protocol used on traumatized teeth and its effects about the replacement external root resorption is presented. For this purpose, English scientific articles were attached by using the data bases Pubmed Central, Scopus, Embase Medline, Ovid and Cochrane, with the keywords: Tooth Resorption, Root Resorption, Tooth Injuries, Root Canal Therapy, Ankylosis. Studies demonstrated that ankyloses and the replacement external root resorption were developed in

dental surfaces independently from the medicine used on the root's interior. Teeth treated with calcium hydroxide and gutta percha showed greater predominance of bone deposition. Intracanal corticosteroids showed promising results, where it was observed favorable repair and having less rates of replacement external root resorption. Articles that relate interceptive attempts against the replacement resorption process were not founded. Despite its frequency, attempts to control the installed process are relevant, considering that the treatment absence results on the worst consequence as possible, the tooth loss.

**Keywords:** Root Resorption. Tooth Resorption. Tooth Injuries. Root Canal Therapy. Ankylosis.

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## Introduction

Replacement external root resorption (RERR) is characterized by the loss of mineralized structure of the root and subsequent deposition of bone tissue in its place.<sup>1</sup> It is the result of the dental trauma, mainly in Avulsions followed by reimplantation and intrusions, where the injuries due to the cementum and periodontal ligament are more significant.<sup>2</sup> It is theorized that such structures are responsible for the protection and maintenance of the periodontal space, therefore, when damaged, allow close contact between root and alveolar bone, triggering the process.<sup>3</sup> Therefore, clastic cells reabsorb the root surface and osteoblastic cells deposit bone in its place, being the root gradually replaced by bone.<sup>4</sup> The knowledge of the clinical and radiographic aspects of the pathology is extremely important, however, early diagnosis is complex.<sup>5</sup> This fact is due to the absence of pain and the bidimensional limitation of conventional x-rays, because the defects often impair the palate/lingual surface of the teeth.<sup>6,7,8,9</sup> Clinically, it is noted infraocclusion, metallic sound high to percussion and absence of physiological or pathologic dental mobility.<sup>5,6,8</sup> Radiographically, it is observed the absence of pericementary space, irregular contour of the root and presence of bone trabeculate in its place.<sup>6,8</sup> Pulpal limits and contours remain preserved.<sup>7</sup>

The current consensus is that there is no relevant therapy for such reabsorption.<sup>1,6,7,9,10</sup> The initial inflammatory response resulting from mechanical damage is considered to be reversible, however, the root resorption and subsequent bone replacement are considered physiological, based on the fact that the bone reabsorbs and regenerates the whole life.<sup>4</sup> In situations of avulsion, utmost importance is given to the alveolar extra time, means of storage and treatment of root surface prior to re-implantation, with the aim of maintaining the viability of the periodontal ligament or retard the RERR evolution.<sup>11</sup> The protocol currently used in an attempt to prevent this process follows the guidelines of the International Association for Dental Traumatology (IADT),<sup>12</sup> suggesting endodontic treatment and treatment of root surface. Intracanal Agents, such as: Calcium hydroxide [ $\text{Ca}(\text{OH})_2$ ],<sup>13-21</sup> Ledermix®,<sup>16,21,22</sup> Corticosteroids,<sup>16,23</sup> Bisphosphonates,<sup>14,18</sup> Acetazolamide,<sup>17,20</sup> gallium nitrate<sup>9</sup> e Gutta-Percha<sup>13,16,22,23</sup> were investigated as to

the potential preventive process. Strategies that govern the progress of the pathology may extend the viability of the tooth, keeping function, aesthetics and phonetics.

The objective of this study was to review the literature with a focus on therapeutic protocols used in traumatized teeth and their effects on the RERR.

## Material and method

For the present study, scientific articles in English, with a focus on the topic Replacement external root resorption were searched in the databases Pubmed Central, Scopus, Embase, Medline, Ovid, Web of Science and Cochrane. There was no definition of publication date. The key words used were: Root Resorption OR Tooth Resorption AND Tooth Injuries AND Root Canal Therapy AND Ankylosis.

The search had 44 articles in Pubmed Central, 40 articles in Scopus, 1 article in Embase Medline, 1 article in Ovid, 1 article in Web of Science and no article in Cochrane. Counter references were used to increase the quantity and improve the search. After exclusion of repeated articles and that had no focus specifically on the objective of this work, 11 articles were included.

## Literature review

Studies of the effects of the medications and materials for intracanal filling about the occurrence of Replacement external root resorption (RERR) are summarized in table I. All of them were in vivo experimental studies in vivo and their results evaluated by hystomorphometric analysis Avulsion was the injury assayed in all of them, with dry extra-alveolar time ranging between 30 and 60 minutes. In four of the studies,<sup>17,18,19,20</sup> the extra-cellular period was 30 minutes, and in three of these<sup>18,19,20</sup> the teeth were immersed in a solution of sodium hypochlorite at 1%, and in one of these,<sup>17</sup> the root surface was scraped using scalpel blade. Therefore, the remnants of the periodontal ligament were undermined by both the extra alveolar time extended and by means of damage caused by chemicals or mechanical actions. The filling substances and materials assessed were Calcium Hydroxide<sup>13-21</sup>, Ledermix®,<sup>16,21,22</sup> Corticosteroids,<sup>16,23</sup> Bisphosphonates<sup>14,18</sup>, Acetazolamide,<sup>17,20</sup> gallium nitrate<sup>19</sup> and Gutta-Percha.<sup>13,16,22,23</sup> The de-

bridement and filling of the root canal were made on extra-orally in most studies, except in one,<sup>16</sup> in which both the steps were performed from 7 to 9 days after implantation in the group treated with  $\text{Ca}(\text{OH})_2$ . No medication or filling material has demonstrated efficacy in preventing RERR.

Evaluating the results of studies that have used calcium hydroxide intracanal,<sup>13-21</sup> it is possible to observe their Anti-resorptive ability and their positive effects, especially in reducing the occurrence of external inflammatory root resorption (EIRR). When compared to the gutta-percha,<sup>13</sup> it showed higher

**Table 1.** Studies of the effects of the medications and materials for intracanal filling about the occurrence RERR.

Authors	Type of study	Injury	Extra-alveolar time	Stage of root development	Intracanal substance	Splint	Observation time	Results
Lengheden et al. <sup>13</sup> 1991	<i>In vivo</i> (monkeys)	Avulsion	60 min. -dry	Complete	$\text{Ca}(\text{OH})_2$ Gutta-Percha	No	8 weeks	Ankylosis significantly more evident in the group $\text{Ca}(\text{OH})_2$ .
Lengheden et al. <sup>15</sup> 1991	<i>In vivo</i> (monkeys)	Avulsion	60 min. -dry	Complete	$\text{Ca}(\text{OH})_2$	No	8 weeks	Ankylosis and External reabsorption present, being more evident RERR.
Bryson et al. <sup>21</sup> 2002	<i>In vivo</i> (dogs)	Avulsion	60 min. -dry	Complete	Ledermix® $\text{Ca}(\text{OH})_2$	No	4 months	RRES significantly more evident in the group $\text{Ca}(\text{OH})_2$ .
Wong et al. <sup>22</sup> 2002	<i>In vivo</i> (monkeys)	Avulsion	60 min. -dry	Complete	Ledermix® Gutta-Percha	No	12 weeks	Favorable repair significantly higher in group Ledermix, with lower rates of RREI and RERR.
Mori et al. <sup>20</sup> 2006	<i>In vivo</i> (rats)	Avulsion	30 min. -dry	Complete	Acetazolamida $\text{Ca}(\text{OH})_2$	No	15 days 30 days 60 days	Ankylosis present in both groups
Mori et al. <sup>19</sup> 2006	<i>In vivo</i> (rats)	Avulsion	30 min. -dry	Complete	Gallium nitrate $\text{Ca}(\text{OH})_2$	No	15 days 30 days 60 days	Results similar to $\text{Ca}(\text{OH})_2$ .
Mori et al. <sup>18</sup> 2007	<i>In vivo</i> (rats)	Avulsion	30 min. -dry	Complete	Alendronate $\text{Ca}(\text{OH})_2$	No	15 days 30 days 60 days	Similar results to the $\text{Ca}(\text{OH})_2$ , minimizing but not preventing the occurrence of Ankylosis and Resorptions.
Chen et al. <sup>16</sup> 2008	<i>In vivo</i> (dogs)	Avulsion	60 min. -dry	Complete	Ledermix® Triamcinolone Demenocyclin Gutta-Percha	No	4 months	Favorable repair significantly higher in groups Ledermix and Triamcinolone, and Reabsorption significantly more evident in the group treated with tetracycline and Gutta-Percha.
Thong et al. <sup>14</sup> 2009	<i>In vivo</i> (monkeys)	Avulsion	60 min. -dry	Complete	Sodium Etidronate $\text{Ca}(\text{OH})_2$	No	8 weeks	Ankylosis and RERR present in both groups
Kirakozova et al. <sup>23</sup> 2009	<i>In vivo</i> (dogs)	Avulsion	40 min. or 60 min. -dry	Complete	Corticoids Gutta-Percha	No	4 months	Favorable repair significantly higher in groups treated with corticosteroids.
Mori et al. <sup>17</sup> 2013	<i>In vivo</i> (rats)	Avulsion	30 min. -dry	Complete	Acetazolamida $\text{Ca}(\text{OH})_2$	No	15 days 60 days	Ankylosis and RERR present

RERR = Replacement External Root Resorption, EIRR = External Inflammatory Root Resorption

rates of ankyloses not associated with reabsorption. The authors<sup>13,15</sup> attributed this fact to the mechanism of action of calcium hydroxide and its cytotoxicity, causing injuries to both resorptive cells as the healing cells of the periodontal ligament.

The studies that have experienced efficient therapeutic agents in controlling bone resorption, such as bisphosphonates<sup>14,18</sup> and gallium nitrate,<sup>19</sup> showed similar effects when compared to the  $\text{Ca}(\text{OH})_2$ , minimizing but not inhibiting the occurrence of resorptions of any kind. The exact mechanism by which these drugs inhibit the resorption is still not well understood.<sup>14,18,19</sup> It is suggested that there should be incorporation of these to the tissue, preventing its dissolution, and still, action on the clastic cells, interfering with their function.<sup>18,19</sup> These medications were suggested due to the similarities between the bone reabsorption processes and the dental reabsorption.<sup>14,18,19</sup> Two other studies that evaluated the Acetazolamide in solution<sup>20</sup> or in paste,<sup>17</sup> showed a low incidence of resorption, but presence of ankyloses in all specimens. This medicine is responsible for inhibiting carbonic anhydrase, an important enzyme released by clastic cells, responsible for catalyzing the reaction between carbon dioxide and hydrogen, enabling the maintenance of the acid pH and degradation of mineralized tissues.<sup>17,20</sup>

Studies using Ledermix® intracanal demonstrated favorable repair and small rates of resorption, both inflammatory as by replacement, when compared with the gutta-percha<sup>16,22</sup> and with calcium hydroxide.<sup>21</sup> The paste is made up of 1% of triamcinolone associated with 3% of tetracycline.<sup>16,21,22</sup> Its beneficial effects have been attributed mainly to corticosteroids, for its ability in controlling the inflammatory response against the damage caused by trauma, responsible for the destructive response of greater severity. When its components were tested together, individually and compared with each other, the positive effects of the corticosteroids and antibiotics were reaffirmed in the healing process, and also concluded that the corticosteroids, when used individually, showed similar action to the paste. The tetracycline showed lower performance when compared to both substances.<sup>16</sup>

Another study,<sup>23</sup> using various corticosteroids intracanal also demonstrated its positive performance in providing favorable healing.

## Discussion

No medication or filling material evaluated in the studies reviewed demonstrated efficacy in preventing RERR. Implanted teeth in favorable conditions that include: preservation of the periodontal ligament vitality, integrity of the cementum and minimum bacterial contamination, usually have good prognosis and survival rate.<sup>24</sup> The necrotic periodontal ligament is considered one of the main factors for the development of the ankyloses and reabsorption by replacement.<sup>6</sup> Based on this precept, studies where the teeth were kept dry, for an extended extra-cellular period, were selected. Even in such a situation, some studies,<sup>16,21,22,23</sup> have shown the presence of formed periodontal ligament associated with areas of RERR. Other findings in all studies in this review showed that the care with the pulp extirpation and debridement of the canal, have resulted in a smaller amount of gaps of inflammatory resorption, associated with absorption by replacement. Although normally being consequent to the same traumatic injuries, in which significant periodontal injuries occur, the resorptions of inflammatory nature are attributed to the presence of pulp infection, while the resorptions by replacement occur when the contamination of root canal is under control.<sup>24,25,26</sup>

The reason why the RERR occurs and continues evolving until the entire structure roots is replaced by bone, is still not well-elucidated. The theories proposed attribute its triggering essentially to periodontal injuries, in which damage to the cementum and the periodontal ligament are brought about. It is assumed that these structures are responsible for the protection of the external surface of the root against the resorption and subsequent deposition of bone in its place.<sup>27</sup> Despite its similar composition with the bone tissue, the cementum is less prone to the reabsorption process, because its more external surface is covered with a layer of cementoblast cells laid upon the non-mineralized matrix.<sup>6,8</sup> These cells do not have receptors for the mediators of bone remodeling and, furthermore, the non-mineralized matrix is a unfavorable surface to the osteoclasts adherence.<sup>6,8,9</sup> Therefore, when the cementum is damaged and the cementoblasts and pre-cementum are lost, cells responsible for degradation of mineralized matrix, similar to those observed in the process of bone resorption,

install on the root surface and reabsorb it.<sup>9,28,29</sup> The maintenance of the resorptive process is justified by two hypotheses: 1) osteoblastic cells, responsive to mediators of bone remodeling, cover the defects of the reabsorption by integrating the root to the process of bone remodeling<sup>9,10,30</sup> and; 2) the dentine, which is protected from the immune system during the development of the natural tolerance, when exposed, behaves like a sequestered antigen, triggering an immune pathologic response and the root destruction.<sup>31</sup> The deposition of bone in the reabsorbed region from the root is attributed to damage caused in the periodontal ligament and, consequently, the remnants of the epithelial sheath of Hertwing, responsible for the bone resorption of alveolar periodontal surface and maintenance of the distance between the tooth root and the bone.<sup>1,8</sup> These assumptions are not irrefutable when confronted to a surgical parendodontic procedure in root surface, often extensive, in that the cementum and the periodontal ligament are also lost, the dentin exposed and worked with tips of surgical instruments; and even so, the repair is performed and the resorption by replacement does not take place. In addition, Holland et al.<sup>32</sup> In their study, implanted tubes of dentin prepared from roots of human teeth in the subcutaneous tissue of rats, and the resorption was not observed.

The existence of infectious pulp is attributed by several authors as responsible for the absence of periapical and lateral periodontal repair.<sup>1,2,3,5,8</sup> The importance of removing the necrotic pulp for the repair of the periodontium is well demonstrated in the study by Holland et al.<sup>33</sup>, in which defects at the level of the dentin were performed in the dogs' root surface, and even though, it was observed repair of the cementum and the periodontal ligament. Due to their predisposition to contamination and increasing the risk of resorptive changes on the external part of the root, the pulp necrotic tissue should be removed as soon as possible. Products of post-traumatism pulpar alterations spread through the pulpar tissue, reach the periapex via root apex and the lateral periodontium via dentinal tubules. If there is loss of cementum in this region, these products [factors], originating from the amendment or even the decomposition of the pulp, when getting in touch with the injured periodontium, may exercise immunogenic or cytotoxic action on the

surrounding connective tissue, which can hinder or even prevent the development of a satisfactory repair process that would occur under physiological conditions, just as it happens in the exposures of dentin consequent to a periradicular surgery. Even if immediate endodontic treatment is done, perhaps, many of these products or factors may already be present in the dentin mass, which would not change the response of the surrounding connective tissue. Therefore, a true inflammatory reaction and mobilization of immunocompetent cells are attracted to the site with the aim to neutralize or destroy these factors present at the dentin mass. As a result, there is the total destruction of the dentin structure until the entire immunogenic content is eliminated from this site. This may be the reason why a uniform repair and the reconstitution of the layer of Cementum and periodontal ligament in traumatized teeth are not possible. Regarding the Replacement root resorption be attributed to the absence of pulpar contamination, it can be assumed that these factors resulting from pulpar injury and that spread through the dentin, exert a role of stimulation of osteoblasts due to the concentration in which they are. Similarly, a study carried out by Pinero et al.<sup>34</sup>, demonstrated that low concentrations of lipopolysaccharides (LPS) produced stimulation of fibroblasts with collagen production and not the typical inflammatory reaction known by the literature before the LPS. Relevant studies should be carried out with the objective of evaluating this possibility.

The International Association for Dental Traumatology (IADT) provides guidelines updated periodically with the aim of guiding the treatment of traumatized teeth. Concerning the Replacement external root resorption, full attention is given to the insertion of the avulsed tooth in order to maintain its viability and prevent the occurrence of this process. The immediate reimplantation is preferable, and when not feasible, the tooth should be maintained in proper storage medium and the patient immediately sent to the dentist. For teeth with prolonged extra-alveolar period, in that the prognosis is unfavorable, and ankyloses and RERR are expected, proposals for moderation of this pathology are geared to the external root surface. Necrotic cells of the periodontal ligament should be removed from the root surface, with the objective of reducing possible sub-



sequent inflammations. With the aim of maintaining the tooth more resistant to the action of clastic cells, it is recommended the immersion of the tooth in solution of sodium fluoride to 2% for 20 minutes, before reimplantation. For these cases, exceptionally, the retainer is indicated for 4 weeks. Regardless of the apex condition, the endodontic treatment is recommended, and may be performed prior to or seven to ten days after the reimplantation<sup>12</sup>. These recommendations are based on the principle that the reabsorptive process starts and develops from the injury to the periodontal tissues, and has as its main focus the attention on the root surface, with the aim of reducing the inflammatory process caused by the structures in degeneration and stimulate the ankyloses, with the aim of delaying the loss of dental element. The treatment of root surface for removal of the remnants from the periodontal ligament should be better studied, since that technically, the removal of these structures, without causing damage to the underlying cement, is difficult to control. In addition, it is questionable the recommendation for the obturation of the root canal beforehand or between 7 to 10 days after implantation. This approach demonstrates the inobservance of the properties of the dentin structure - especially its permeability-, which can provide changes in the external root surface from the use of intracanal substances, and lead to delay and, possibly, inhibition of the RERR process.

In spite of the occurrence of RERR have proved inevitable, interceptive attempts before the process installed are relevant, since the absence of treatment results in the worst possible consequence: the tooth loss. The main therapies should have intracanal focus, because in addition to representing a reservoir for release of medication in the long run, corresponds to the main route of spread of the same to the area of resorption, both through dentine tubules and through the apex root. In this review, all medications presented demonstrated ability to minimize the occurrence of the pathology, most of them with their mechanism of action aimed at clastic cells and derived from their activity. The calcium hydroxide still seems to be the most widely used medicine, because its ability to change the dentin environment, through the elevation of the pH, allows the neutralization of acids and inhibition of enzyme activity,

slowing down possibly, the action of the resorptive cells and inducing the formation of hard tissue by activation of alkaline phosphatase<sup>35</sup>. The corticosteroids showed promising results, and due to their anti-inflammatory ability, possibly provided a more favorable environment for repair, furthermore, its immunosuppressive potential could inhibit clastic and osteoblastic cells, responsible for the resorption and deposition of bone on the root surface, resulting in favorable results in the containment of the reabsorption process by replacement. Due to their additional effects regarding the  $\text{Ca(OH)}_2$ , the corticosteroids deserve further studies, so that their real applicability are evaluated. Other medications mentioned in this review showed similar results to the  $\text{Ca(OH)}_2$ . At the studies in this review, the medications observational time was at most 4 months, and in none of them changes for renewal of the drugs were performed. Perhaps, if a longer duration of treatment was intended to teeth affected by RERR, in which changes of medications were performed, additional effects could be observed.

Alternative therapies could also be suggested, as main or adjuvant treatment, requiring studies to prove their effectiveness. Ozone and laser have been used in various situations in dentistry, with very promising results regarding the repair processes, therefore, their effects on Resorptions by replacement, deserve to be evaluated.

### Final considerations

Little has been done in an attempt to preserve teeth affected by resorption by replacement, because therapies proposed for the control of this pathology have not demonstrated to be effective. The use of the intracanal path for the treatment of the external surface of the root may be a significant alternative in control of the reabsorption process by replacement. The studies in this review showed that, among the therapeutic possibilities aforementioned, treatment with corticosteroids as intracanal medication, was promising in providing favorable repair, however, the calcium hydroxide is still the medication that brings more ideal properties. Due to being consequence of more severe dental traumas, in which more than one variable is involved, the triggering and maintaining mechanisms of this pathology remain unclear.

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