Medical and Research Publications
International Open Access

Review Article **Journal of MAR Dental Sciences (Volume 5 Issue 5)**

The Scientific Evidence for the Prevention of Replacement Resorption in Traumatized Teeth.

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Received Date: June 16, 2022

Published Date: July 01, 2022

Abstract

Avulsion represents 0.5-3% of all dental injuries. Nonetheless, it is one of the most complicated and controversial traumatic injuries to treat. Replantation of the permanent teeth (mature and immature) after avulsion is advocated, especially in children and teenagers who are unable to receive implants. However, this treatment is crucially important, there are a very high risk of extensive periodontal ligament necrosis in cases with extended dry out period (i.e. more than 30 min). It is well established that replacement resorption is a destructive consequence after replantation of tooth in mentioned cases. Another complication after replantation is bacterial contamination of the pulp combined with damaged cementum, which should be taken into account in treatment planning and managing of these cases. There have been several developments regarding prevention and treatment techniques of ankylosis and replacement resorptions. In this review article, different methods of preservation and preparation of the avulsed tooth before replacement as well as further conservative treatments after replacement is discussed. This study is based on the recent published articles in trauma including systematic reviews and RCTs. Moreover, the alternative treatment in nonresponsive teeth to mentioned treatment will be presented.

Keywords: Replacement resorption, avulsion, traumatized teeth, Prevention of resorption.

Introduction and causes

Epidemiological studies illustrate that dental trauma is one of the major problems, which is current among children and teenagers. Some traumatic injuries such as sever luxation, intrusion and avulsion represent various public health problems which may contribute to high social and psychological impacts. Tooth avulsion, in which the tooth is completely displaced from the socket, is one of the most serious injuries which is responsible for the damage to the pulp and periodontal tissues. (Trope 281-294)

Avulsion represents some 0.5-3% of all dental injuries. Nevertheless, it is one of the most complicated and controversial traumatic injuries to treat. (Andreasen, Bakland, and Andreasen 90-98)

Replantation of the permanent teeth (mature and immature) after avulsion is advocated for improving the function and esthetics, especially in children and teenagers who are unable to receive implants or other definitive treatment cause of continuation of skeletal growth. However, this treatment can not be

carried out immediately. Most of the time, avulsed teeth are replanted after an extended dry out period (i.e., more than 30 min), which may lead to extensive periodontal ligament necrosis. In case of replanting immature teeth, the aim is root development and facilitate the possible revascularization of the pulp chamber. However, the risk of emerging replacement resorption or ankylosis should be born in mind. (Trope 281-294)

The necrotic tissue after replantation stimulates an inflammatory response along the root surface, where the odontoclasts and osteoclasts play a crucial role in initiating the ankylose and replacement root resorption. (Carvalho, E. D. et al. 91-99)

When avulsed tooth kept dry in long time and not stored in appropriate storage media, the remnant of PDL cells on the root surface degenerate, and the cementum layer will expose. The nude cementum will attract the osteoclasts and resorptive process starts. (Trope 281-294)

Another phenomenon after replantation is bacterial contamination of the necrosed tissue (pulp), combined with damaged cementum, result in external inflammatory resorption of the root. This kind of resorption is more common in younger patients due to wide dentinal tubules which provide a passage for bacteria. At the time the resorptive process exposes dentin, the intra-radicular bacteria can achieve the periodontal tissues, triggering release of inflammatory factors, which leads to resorption of bone and the root of the tooth. (Najeeb et al. 77-83)

The inflammatory root resorption may be prevented by early endodontic treatment (less than 3 week), while the replacement resorption is not treatable and arises form a permanent damage in periodontal ligaments. (Mohamed et al. 168-172)

There are some definite factors which are associated with replacement resorption following replantation of avulsed permanent teeth: period of extra-oral storage (less than 15 minutes or more than 15 minutes), type of storage media, extended splinting period (more than 10 days), time of endodontic treatment, antibiotic coverage of both topical and systemic (Panzarini SR, et al., 2008)(Miron RJ, et al.2016)

Regarding the IADT guidelines, signs that suggest a compromised prognosis for a replanted avulsed immature permanent tooth with an open apex are symptomatic tooth (pain or presence of a sinus tract), no mobility (ankylosis) and a sharp, doll sound in percussion, radiographic evidence of resorption, and the absence of previous root development. According to Andreasen and Pedersen, the severity of damage to the traumatized tooth or other factors associated with the injury may impact the healings prognoses. Some factors like patients age, stage of root formation, which is the most important one, type of the tooth, displacement extent of the tooth, the number of teeth which are intruded, and the potential crown fractures. (Andreasen, Bakland, and Andreasen 90-98)

Various studies illustrated that replacement resorption is a complex and periodical process. (Luso & Luder 2012, Mavridou et al.2016a, 2017b) There are three main cycles; resorptive (initiation), resorptive

(propagation) and reparative (remodeling) like what happens in bones regularly. Fig. 1 (Mavridou et al. 2016a, 2017b). These stages of resorption and repair can happen in different parts of the same lesion.

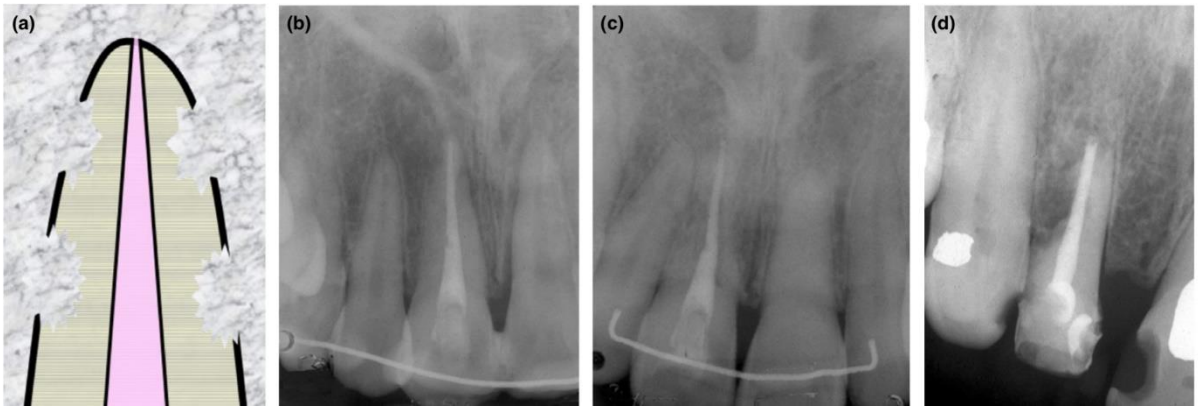

Fig. 1: a) schematic diagram of external replacement resorption b) upper right central incisor that had been avulsed c)development of slowly progressed external replacement resorption d) upper right lateral incisor has both inflammatory (on the distal surface) and replacement resorption(apically) (Abbott 82-94)

Prevention or slow down the progression

A thorough understanding of the pathology and physiology of the resorption may lead to providing strategies to prevent, control or slow down the progression of the disease.

There are different approaches prior and after the replantation of avulsed permanent teeth to prevent and improve the prognoses:

The most important measure, which enhance the chance of preventing root resorption, is not keeping the avulsed tooth dry during extra oral time. A physiological storage such as milk, saline, saliva, or special cell culture media (Hank's buffer) advised to avoid the necrosis of periodontal ligament before replantation. (Hammarstrom L et al., 1997) (Filippi A., et al. 2006) In addition, local and systemic administration of antibiotics is shown to have a favorable influence on periodontal healing following replantation.

There are a broad spectrum of antibiotics, corticosteroids and mixing materials are available in the market. However, there are a few of them which are suitable to prevent replacement or inflammatory resorption following avulsion or sever traumatic injuries. Sae_Lin et al developed a replacement resorption model in dogs and tested systematic tetracycline versus amoxicillin. (Sae-Lim, Wang et al. 1998) Results displayed that in tetracycline group, more teeth had significantly over 50% of the root surface with completely healed sites than in amoxicillin group. Hence, it is obvious that prescribing systemic tetracycline may help to prevent external replacement resorption to a limited extend. They also

tested corticosteroid drugs in their models. Corticosteroid drugs potentially inhibit the inflammation and clastic cell activities, therefor they have direct antiresorptive role.

They showed 85% complete healing in their dog replacement resorption models when dexamethasone was applied topically prior to replanting the extracted teeth. This result was significantly better than the group treated with systemic dexamethasone.

Beside the systemic medicaments, there are also a variety of intracanal medicament, which have potential to improve prevention of replacement resorption. Ledermix paste (corticosteroid/tetracycline) and calcium hydroxide paste are to most investigated ones. When Ledermix paste is placed in the root canal system, it releases its active elements (Triamcinolone and demeclocycline), which later distribute through dentine, lateral canals and apex to reach peri radicular tissues. This diffusion increases if the cementum has been removed by trauma or surface resorption. Consequently, the active component of ledermix paste act to reduce the risk of inflammatory resorption. The antibiotic component of ledermix (tetracyclin) act mainly within the root canal system, specifically in the dentine tubules by inhibiting the bacterial growth, whereas the corticosteroid component works within the peri-radicular tissues by undermining inflammation and inhibiting clastic function.

Ledermix paste provide the therapeutic effects for about 6 weeks in completely developed teeth and for about 4 weeks in unmatured permanent teeth. It is advised that ledermix paste should be removed and replaced after these time intervals. So, it would continue to be effective. (Abbott 2016)

Calcium hydroxide is popular for the PH changes in root dentine, especially when used for the management of external inflammatory resorption. Calcium hydroxide is a toxic material which results in cell necrosis. As a result, it can induce necrosis of both resorbing and reparative cells. This impact on reparative cells in the periodontal ligaments will contribute to ankylosis and replacement resorption rather than healing. Therefore, if calcium hydroxide uses in the early stages of treatment, it may predispose the tooth to ankylosis and replacement resorption, specifically when the protective cementum layer is lost due to trauma. (Abbott 2016)

Abbott and et al. suggest a cautious approach for PDL healing following most luxation and avulsion injuries. They believe that the root canal system should be medicated for at least 3 months and preferably longer time since the healing response is difficult to achieve. It is recommended using Ledermix paste for the first 3 months and based of aforementioned information, two dressings for 6 weeks each should be used in fully developed teeth, and three dressing for 4 weeks each in incompletely developed teeth. Then, a periapical radiograph should be taken to assess status of the root surface. If any evidence of inflammatory external resorption detected, Ledermix paste should be used for further 3 months to stop the progression of the resorption. Otherwise, at this stage, a mixture of calcium hydroxide and Ledermix (50:50) can be used as medicament paste. This combination undermines the toxicity of the calcium hydroxide and reduces the chance of ankylosis and replacement resorption. This

mixture also increases the antibacterial spectrum compared with pure Ledermix, while the calcium hydroxide part commences the hard tissue heling effect.

In addition, the other benefit of this mixture is slow releasing and diffusing of Ledermix active elements, under the impact of calcium hydroxide, which increases the remaining time of the medicament introduction in the root canal system for a longer period.

After using the mixture of Ledermix and calcium hydroxide for 2-3 months, another periapical x-ray should be taken to assess PDL healing and control whether any resorption is evident. If there is not seen any incidence of resorption (replacement or inflammatory), the root canal filling can be done in developed teeth using gutta-percha and cement. (Abbott 82-94)

In order to enrich nutrition and maintain cell activity in periodontal tissues following avulsion, several researchers advised that teeth should be transplanted and repositioned to the socket with regenerative tissues. These components facilitate interaction between different types of cells, growth factors, hormones, and the extracellular matrix proteins, within the environment which these events occur.

One of the suggested materials is Enamel matrix derivative (EMD), which is extracted from developing porcine tooth gems and has been quite often used as an effective material to regenerate periodontal tissues. (Ferreira et al. 589-593)

Enamel-related proteins help with formation of acellular cementum on the root of the developing tooth providing a base for all other tissues accompanying periodontal attachment. Emdogain Influences periodontal ligaments by affecting on their migration, attachment, proliferation and biosynthetic activity. Therefore, it is advocated as a therapeutic agent for management of the avulsed permanent teeth because of its effectiveness in enhancing the healing process of replanted teeth.

In the recent systematic review, the author describes Emdogain as a treatment agent which reduces resorption of replanted teeth and improves the healing of periodontal ligament. Moreover, use of Emdogain improves the regeneration of cementum, PDL fibers and bone. (Mohamed et al. 168-172)

Fridsom et al showed Emdogain as an effective substance in PDL regeneration of replanted teeth, histologically.(Fridström, Schollin, and Crossner 299-304) Emdogain promotes regeneration and reestablishment of periodontal cells on the injured root surface, thus prevents ankylosis.

Finally, based on the systematic review on Emdogain, the author deducted that Emdogain treatment before replantation might be effective in improving normal healing and minimizing inflammatory and replacement root resorption in the presence of periodontal cells. (Mohamed et al. 168-172)

Similarly, following the idea of preparing the avulsed tooth prior to replantation, the treatment of the root surface through either chemical (acidic solutions, sodium hypochlorite, antibiotics, alendronate,

vitamin C, tooth enamel protein) or mechanical (lasers, curettage with instruments) is advised in different research.

These are attempts which may contribute to improve the repair and attachment of PDL cells to the root surface and decline the severity of ankyloses and root resorption. (Lustosa-Pereira et al. 30-35) This will happen by minimizing or eliminating clastic cells attack on the necrotic cells that are remained on the surface of the replanted tooth to protect cementum and underneath dentine. (Maslamani et al. 182-187).

Removal of non-viable periodontal ligaments, which may reduce the risk of osseous replacement, is a procedure, which has always been on the spotlight. However, there are various concepts and debates about it. The latest guidelines for avulsed teeth by International Association of Dental Traumatology recommend the removal of attached non-viable soft tissue (PDL) carefully with gauze before replantation(Andersson et al. 88-96; Maslamani et al. 182-187).

However, Maslamani et al. showed, in teeth where PDL had been removed, resorption cavities were detectable in the superficial dentine within 2 weeks, after 6 weeks a large portion of the dentine, and in some teeth almost all dentine, had been resorbed and replaced by bone regardless of pretreatment of PDL. In another word, they concluded that in the long term, extensive ankylosis with extensive osseous replacement will occur whether the PDL has been removed or not. (Maslamani et al. 182-187).

Laser technology and devices has significantly evolved in dentistry in the last couple of decades. There is a believe that irradiation of high-power laser has both antimicrobial and morphology changing effects on the root surface, which play a crucial role in cell's adhesion, proliferation and subsequent attachment of periodontal tissues. (Carvalho, E. D. et al. 91-99).

Since the remaining PDL cells on the root surface of avulsed teeth with extended extra-oral dry time is responsible for initiation of the resorptive process, some studies introduce the irradiation of periodontally diseased root surfaces with high power laser such as: Er:YAGDiode, diode and Nd:YAG lasers. (Carvalho, Erica dos Santos et al. 429-436).

The study by Hamaoka et al. (Hamaoka et al. 715-720) verified that Nd:YAG laser irradiation improves the biocompatibility of dental roots. According to the author, it could be counted as an alternative treatment on the root surface prior to replantation. Other studies demonstrated that irradiation with Er:YAG and diode high-power laser enhanced morphological changes on the root surfaces which contribute in better cell adhesion. (Raldi et al. e161).

In another study, the occurrence of replacement and inflammatory resorption and ankylosis was examined in groups of diode laser and diode laser (high-power diode laser) plus FGF (Topical application of fibroblast growth gel). Results displayed improved changes in the cementum structure, following irradiation with diode laser, which make the root surface more resistance to clastic cell's action. These

effects stem from fusion and melting of the surface after irradiation with diode laser. In addition, the physical contact of optical fiber at 45 degrees with the root surface in a scanning movement, promotes the removal of necrotic PDL fibers attached to it. Such results can also be confirmed by the combination of diode laser and FGF, where diode laser eliminates microorganisms, degenerates necrotic cells, and changes the structure of cementum and FGF aids in migration and proliferation of fibroblasts, precursor cells of PDL. Consequently, reintegration of the PDL fibers to the cementum was observed. Fig 2. (Carvalho, E. D. et al. 91-99)

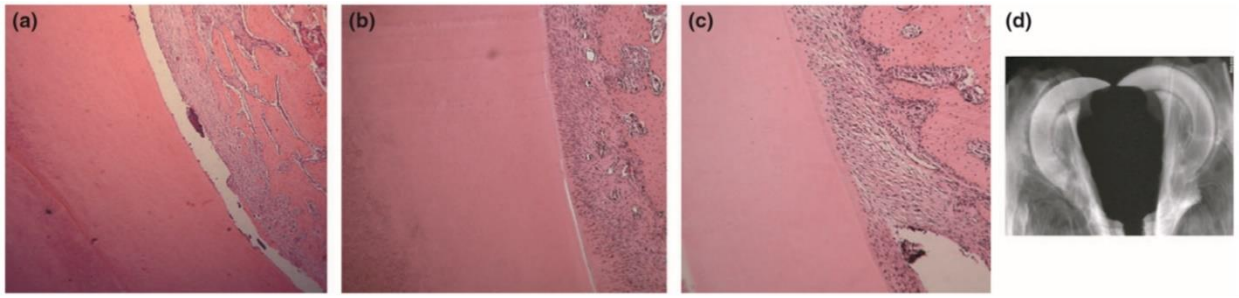

Fig. 2. Representative histological sections of group DL + FGF: (a) absence of inflammatory and replacement resorption and ankylosis. Original magnification 509 (HE staining); (b) and (c) connective tissue dense and organized PDL fibers reinserted to the cementum (509 and 1009); (d) representative radiographic image (Carvalho, E. D. et al. 91-99)

Application of bisphosphonates prior to replantation is another solution for avoiding replacement resorption. (Najeeb et al. 77-83) Bisphosphonates are a class of drugs used to treat resorptive diseases like osteoporosis and Paget's disease. There are two types of bisphosphonates available in the market, Nitrogen-containing (nitrogenous) and non-nitrogenous. Alendronate, zoledronate, and risedronate are some commonly used nitrogenous bisphosphonates. They inhibit the activity of osteoclasts by and consequently further bone resorption. These group of drugs exert their effects by inhibiting the proliferation and activity of osteoclast by inducing apoptosis. Meanwhile, bisphosphonates stimulate the production of osteoblasts resulting in bone formation. (Najeeb et al. 77-83)

Various research advised using intracanal or surface application of bisphosphonates. A current systematic review accomplished by Najeeb et al. showed that surface application of zoledronate and alendronate, prior to replantation of avulsed teeth, reduces root resorption of replanted teeth in animal models. While the efficacy of intracanal usage of bisphosphonates is still debatable and need further research. (Najeeb et al. 77-83)

Progress in tissue engineering and periodontal regeneration therapy has opened the field for new research to promote the prognosis of delayed replanted teeth and prevent the vicious consequents such as ankylosis and replacement resorption. It is shown that cytokines such as fibroblast growth factor

have an important role in periodontal regeneration, since FGF stimulates migration and proliferation of fibroblasts.

Basic fibroblast growth factor (βFGF or FGF-2) is a single chain polypeptide that induces various biological replies including mitogens for periodontal cells. Topical βFGF application has been shown to be effective in regeneration of periodontal tissues caused by progressive periodontitis. The application of βFGF has been shown to have a positive impact on stimulating periodontal healing of delayed replanted teeth. (Carvalho, E. D. et al. 91-99)

There are, indeed, some alternative treatment options such as autogenous tooth transplantation and decoronation. Autogenous tooth transplantation is a proved method to restore the arch if there is an existing suitable tooth donor tooth available.

Especially, when patient has crowding and facing with a trauma in incisors, the premolar teeth would be an option for transplanting a successful results of tooth transplantation depends on incident free extraction and replantation in the prepared socket. This treatment could be reckoned as a permanent treatment after reshaping of the transplanted tooth. (Ferreira et al. 589-593)

Decoranation is an alternative treatment that also offers good clinical outcome, when all the other mentioned treatments could not regenerate the PDL attachment and ankyloses occur. Ankyloses in adults is not a significant problem and can be managed through prosthodontics or implant treatments, whereas in immature teeth the rate of replacement root replacement is fast and may result in an un esthetic ridge deformity and tilting of adjacent teeth. Several attempts to manage ankylosed teeth in growing children have been proposed. Surgical luxation, orthodontic distraction, auto-transplantation, composite build ups. Most techniques have been linked with a questionable prognosis. It has been shown, in the current systematic review, that if the treatment is carried out in correct time, the buccopalatal alveolar as well as the vertical dimension, which is crucial for further treatments such as implant therapy, can be preserved. In addition, the vertical growth can be achieved. Studies show that in cases where ankylosis is diagnosed before 10 years old (the growth spurt), a prompt intervention would be required within 2-3 years. In contrast, after the puberty, decoronating could not be a beneficial solution, since alveolar ridge deformity or tilting of neighbor teeth, is already well-established. All in all, decoronating is an easy, safe and conservative approach comparing to extraction of the ankylosed teeth, which involves complicated surgical interventions. (Mohadeb, Somar, and He 255-263).

Conclusion

This review of articles introduces a variety of approaches that should be considered for preventing of the root resorption further to avulsion. To reduce the risk of resorption, limiting of the dry out period is extremely important. A physiological storage such as milk, saline, saliva, or special cell culture media

(Hank's buffer) advised to avoid the necrosis of periodontal ligament before replanting. Moreover, systematic use of tetracycline versus penicillin is more effective in these cases.

However, some intercanal medicaments such as Ledermix paste (corticosteroid/tetracycline) would minimize the risk of replacement resorption. Furthermore, treatment of the surface of the avulsed tooth prior to replantation with regenerative tissue materials (Emdogain), and laser irradiation would improve the root surface of the tooth which may enhance cell adhesion.

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