The Effect of Etiology on the Function of Hertwig's Epithelial Root Sheath in Regenerative Endodontic Procedures—A Review of Literature

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Abstract

The management of nonvital immature permanent teeth poses quite a challenge. The apexification procedure is in use for long-term now but the treated teeth are more prone to fracture questioning the long-term prognosis of this technique. The introduction of regenerative procedures for the treatment of these teeth is quite favorable; however, despite the increasing use of regenerative endodontic therapy procedures, inconsistent results are seen in the root development. Conservation of Hertwig's epithelial root sheath may have a prime role and selecting the cases with viable root sheath may impact on the consistent positive results treated with regenerative procedures. This article aims to look at the database to find the role of etiology and its implication on Hertwig's epithelial root sheath in the outcome of regenerative endodontics.

Keywords

- regenerative endodontic therapy
- apical revascularization
- Hertwig's epithelial root sheath

Introduction

Regenerative endodontic therapy (RET) is a procedure that works by restoring the damaged tissues biologically, like the cells of pulp–dentin complex, dentin, and root structures.[1] This treatment is indicated in nonvital tooth with an open apex and that does not require heavy restoration or post and core build up as a part of the restorative treatment.

Apexification that is the formation of calcified barrier at the open apex of nonvital tooth has been the standard treatment followed for many years now. This procedure can be done in single visit or may require multiple visits depending upon the material to be used. The most used materials are calcium hydroxide and mineral trioxide aggregate (MTA). Although both of these materials allow the healing of periodontal lesions and formation of apical stop

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necessary for obturation, none of these reinforce the treated teeth or allow the continued root development, which unfortunately makes them more prone to fracture in the cervical third of the root.[1]

In contrast, the RETs along with the periodontal healing also allow the thickening of the root dentinal walls and regeneration of the necrotic pulp. Currently, cell-free and cell-based approaches are followed for regenerative endodontics.

The cell-based approach is also known as tissue engineering method. In this technique, the stem cells and growth factors are added on a scaffold that is then introduced into the debrided root canal.[2] For clinical use in dentistry, any of the five classes of stem cells can be used. So far, the identified ones are the dental pulp stem cells, the periodontal ligament stem cells, stem cells from exfoliated deciduous teeth, dental follicle precursor cells, and the stem cells from apical papilla.[1] Other than these dental tissue stem cells, bone marrow-derived mesenchymal stem cells and stem cells taken from adipose tissues can also be utilized for the cell-based approach.[2] The stem cell transplantation method promises to be successful; however, it is technique sensitive and a costly procedure making it unfeasible for use in clinical settings.

Contrary to this, the cell-free approach, which is also known as the revascularization method, is far more realistic and popular technique. Introduced first by Nygaard otsby in the year 1960, it was adopted widely after a successful published case report on pulp revascularization in 2004.[3] This method is a two-step procedure, wherein in the first visit biomechanical preparation of the infected root canal is done followed by packing the canal with a disinfectant (antibiotic paste or calcium hydroxide) for 1 to 4 weeks. In the next visit, in the absence of any symptoms of infection, bleeding is induced with the k-file inserted 2mm beyond the apical foramen and allowing the full canal to fill with blood up to the level of cemento-enamel junction, which is then followed by placement of suitable pulp capping material (MTA, bioceramics or tricalcium silicate cements) and restoration.[4]

Like all endodontic treatments, the success is measured by the absence of any symptom and healing of the periapical area; however, for the revascularization procedures, the additional factors, which determine the favorable result, are the increase in root thickness and length and regaining of the vitality of pulp.

Although considered as a good option for the treatment of immature nonvital tooth, revascularization procedure is yet to obtain the gold standard and still has not replaced the apexification procedures for the treatment of such teeth. This could be attributed to the inconsistencies in the result of revascularization that range from 79 to 90%[2] as compared with 95% success rate of apexification[5] and also could be due to the lack of sufficient Grade A level of evidence in this area.

The inconsistent results could possibly be due to various factors like the different etiologies for which the pulp has become necrotic that in turn impacts the viability of Hertwig's epithelial root sheath (HERS) or it could be due to procedural errors and nonstandardization of measurement methods after conducting revascularization.

The main focus of the current review is on the viability of HERS and how its preservation can determine the success of RET.

Hertwig's Epithelial Root Sheath and Root Formation

After the crown is formed, a transitory two layered sheath of epithelium (without stellate reticulum and stratum intermedium) develops just below the enamel in the cervical region. Named after its discoverer Oskar Hertwig's,[6] this sheath basically acts as the main center for root formation.[7]

Root dentin is formed when the mesenchymal cells of dental papilla directly interact with the cells of inner enamel epithelium of HERS. This epithelial–mesenchymal interaction leads to the release of Laminin 5 from HERS than then leads to differentiation of cells of dental papilla into odontoblast, which in turns lays down the radicular dentin.[8]

After the formation of radicular dentin, this root sheath breaks and disintegrates; when this happens the cells of dental follicle interact with the root dentin and get differentiated into cementoblast, fibroblast, and osteoblast that then lead to the formation of cementum, periodontal ligament, and bundle bone, respectively. Recently, another process known as epithelial–mesenchymal transition has been identified in which cells of HERS can directly differentiate into cementoblast cells by the activation of transforming growth factor beta signaling.[9] At last, the cells of this sheath get embedded as epithelial cell rest of Malassez into developing periodontal ligament or mineralized matrix of cementum.

In conclusion, an uninterrupted HERS is crucial for the root structure, shape, size, number, length, and other features of root formation.[7]

Discussing the Influence of HERS on Successful Revascularization

There has been a transition from the conventional treatment to RETs in the management of necrotic tooth with open apex. The term apical revascularization was adopted by the American Dental Association in the year 2011 after providing the clinical codes (D3351, D3352, and D3354) for the practice of induced bleeding in the root canal and is slowly gaining acceptance in several asian[10] and European countries.[11] A root canal free from infection, a blood clot that acts as a medium for growth of new tissue, and a good coronal seal are must for the success of apical revascularization procedures.

In a case report on permanent teeth that had become necrotic due to trauma Lu et al[12] found RETs to be successful. Contrary to this, He et al[13] in their meta-analysis of literature including 22 studies on apical revascularization observed just the thickening of root wall without increase in the root length. Almost similar observations were made by Nosrat[14] et al in their case report, where despite being functional and formation of root apex, increase in the length of root was not seen that leads us to an important parameter that is the case selection criteria for apical revascularization procedures.

Selecting the cases on the basis of etiology could help in getting consistent result as the pathogenesis is different and the impact on HERS is variable. An immature tooth can become necrotic due to caries, trauma, or developmental dental anomalies. Of these, trauma accounts for the most common reason followed by developmental anomaly like dens evaginatus.[15]

In case of trauma if the force is transmitted directly to the sheath as seen in intrusion injuries, then this could stop the growth of the root completely or partially. However, in the avulsion injuries HERS could get damaged at the time of injury or during extraoral storage time and during reimplantation procedure; all of these could invariably affect the formation of root after apical revascularization.

Nagata et al when conducted apical revascularization procedure on luxative[16] and avulsive tooth injuries[17] under the tested protocol found both clinical and radiographic successful results. Among the outcomes, they concluded that clinically symptomless tooth can be expected at 1 year follow-up; however, the root thickening and lengthening cannot be expected in this time frame. Saoud et al[18] found that apical closure was the most consistent finding that can be observed radiographically after apical revascularization.[18]

In dens evaginatus or evaginatus odontoma which commonly involves mandibular premolars and maxillary lateral incisors bilaterally can be identified by a raised tubercle of around 3.5 mm in the occlusal surface of premolars and 6.0 mm in the palatal surface of anterior teeth.[19] This raised tubercle consists of enamel and dentin layer and sometimes may have the pulpal extension,[20] which makes these teeth more prone to early pulpal involvement following caries or occlusal trauma and this usually happens at a faster rate even before the completion of the root.

When revascularization procedure was done in immature tooth that had become necrotic due to dens evaginatus. Chen et al[16] found that the continued development of root and similar observation of successful revascularization procedure was made by Natera and Mukherjee[15] after 4 years of follow-up.

The above-mentioned studies back up the fact that the prognosis of immature teeth that become necrotic due to dens evaginatus or trauma shows a favorable outcome and good prognosis. When comparing both these etiologies in a randomized controlled study, Lin et al[17] found that teeth that had become necrotic due to dens evaginatus had better prognosis as compared with traumatized nonvital teeth. This could possibly be due to the damage inflicted upon HERS due to trauma that may create negative treatment results as compared with seen in cases with dens evaginatus.

Caries is another factor responsible for early pulpal necrosis in children and adolescent contributing to around 7% of such cases.[13] Though HERS is resistant to inflammation and continues to function in the presence of partial pulp necrosis irrespective of whether endodontic treatment was carried or not, this resistance decreases as the distance between inflammation and HERS decreases and virtually diminishes if the distance is too short, therefore arresting the root formation.

A case report by Nosrat et al[21] on revascularization in immature necrotic mandibular first molars due to extensive coronal caries observed uninterrupted root development with healing of periapical area on radiographs. Similar successful findings of revascularization on carious teeth were observed in studies of Carmen et al,[22] Algal et al,[23] and Silujjai et al.[24] When all the three etiologies were compared in a systematic review on revascularization procedure conducted between 2014 and 2019, it was observed that the highest success rate of approximately 96% was found with the teeth affected by dental caries followed by 94.8% in case of traumatized teeth and 93.1% in dens evaginatus.[10] The authors went on concluding that there is no relation in the etiology of dental caries and success of RET.

Although the success of RET is dependent on HERS, the state under which its viability is preserved is unknown.[10] However, RET has clearly proven to show better results in terms of increase in root length and thickness than apexification procedures in the treatment of immature non vital teeth,[17] but the criteria and conditions in which a persistent outcome can be obtained remain unknown.

Conclusion

The role of HERS in the formation of root has been clearly established however; no clear association between the reason `of pulp necrosis and HERS has been established. Further randomized clinical trials are required to establish the association between these two so that a successful outcome can be predicted on the basis of case selection criteria.

Conflict of Interest
None declared.

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