Review

Revascularization: A promising alternative treatment for traumatic permanent immature necrotic teeth

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ABSTRACT

Endodontic treatment of traumatic immature permanent teeth has been questioned for its long term prognosis. The treatment options for such cases include multivisit apexification with calcium hydroxide or with single visit Mineral trioxide aggregate plug. The objective of conventional root treatment is not only difficult to achieve in such cases but even if it is met, the formed root is found to be short with thin and weak dentinal walls with higher risks of fracture. Revascularization has been suggested as promising alterative treatment for necrotic immature permanent teeth. The desirable outcome of the treatment is continuous growth of the root, maturation of the lateral dentinal walls and apical closure. This review provides an overview of revascularization and its goals, mechanism of revascularization, clinical protocols along with summary of some recently published clinical reports on revascularization.

Keywords: apexification; immature permanent teeth; non vital teeth; revascularization.

INTRODUCTION

20-30% of young children suffer from dental injuries with peak incidence for boys found at 9-10 yrs whereas girls at 11-12 yrs. These injuries may vary from avulsion, intrusion, lateral displacement, fracture, subluxation or just a concussion. The root development takes place for almost 2-3 yrs after the tooth have erupted into the oral cavity(1). Pulp necrosis is one of the complications of traumatic injuries to teeth. Loss of pulp vitality may be caused by bacteria or its toxic products, acting through the dentinal tubules or directly to the pulp; or may be due to rupture of the neurovascular supply around the root apex resulting in ischemia. However, both mechanisms may act simultaneously leading to pulp necrosis(2). So any assault during the formative stage results in arrest of the further root development; resulting in tooth with short root, thin dentinal walls and wide open apex. The treatment of immature necrotic tooth presents multiple challenges to successful outcome as(3);

The infected root canals cannot be disinfected using standard root canal protocol of mechanical cleaning with instrumentation because the root canal wall is already thin which further weakens on removal of dentin.

The large apical opening does not provide the mechanical blockage necessary to confine the obturating material within root canal.

The compaction of the root filling material may risk root fracture.

Endodontic management of such cases include periapical surgery and retrograde filling; apexification and most recently revascularization (4).

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The clinical procedure with apexification depends on the use of the material. As described in multivisit procedure: calcium hydroxide, Ca(OH)2 is used as an intracanal medicament to induce an apical closure. Alfred L.frank was first to report apical closure using calcium hydroxide in 1966. Since then it has been universally used as endodontic procedure. Here, the calcium hydroxide paste is filled inside the canal till the measured working length and tightly sealed coronal restoration is placed to prevent any marginal leakage. Then the case is periodically followed up at 2-3 months interval for the radiographic assessment of signs of apical barrier formation and if evident, the canal is finally filled with permanent obturating material like gutta percha with good coronal restoration. This procedure requires multiple visits within a long period of 16-24 months (avg. 1 yrs ± 7 months)(5). Owing to the long term treatment duration and risk of further dentinal wall thinning during each step of cleaning and filling, Toranbinejad and Chivian suggested an alternative procedure termed as single visit Mineral trioxide aggregate(MTA) method. In this method, the apical 3-5 mm of the root canal was filled with MTA and the rest of the canal was subsequently filled with gutta percha(6).

Although single visit procedure limits the number of appointments, the major drawbacks of apexification are;

- Lack of growth in length of the root thus compromising the crown root ratio.
- No lateral dentin deposition on the root wall thus rendering tooth root to fracture.

Considering the short coming of the conventional apexification procedure, ideal treatment to obtain further root development and thickening of the dentinal walls in an immature tooth with or without apical periodontitis would be revascularization; i.e. reestablishment of vitality in a non vital tooth to allow repair and regeneration of pulp dentin complex. A novel concept of revascularization was put forward by Nygard ostby in the early 1960s who showed that new vascularized tissue could be induced in the apical third of the root canal of endodontically treated necrotized mature permanent tooth(7). The term revascularization has been used for the reestablishment of vascularity in the pulp spaces after traumatic injuries. However, no vascular neo-formation is seen but the regeneration of tissues such as cementum, periodontal ligament and dentine or pulp-dentin complex is noticed. So the term revascularization has been questioned(8). Huang and Lin proposed that revascularization is inappropriate term for the procedure designed to stimulate tooth maturation and suggested that induced or guided tissue generation and regeneration would be better term(9). In 2008, Hargreaves et al. used the term maturogenesis to describe the continued root development in infected immature permanent teeth rather than revitalization or revascularization(10). Hopefully, universally accepted term for the procedure will be considered and resolved by American Association of Endodontic.

Revascularization with continued root development and deposition of hard tissue in the root canal has shown to occur over time in immature teeth that are reimplanted after intentional or traumatically related avulsion. The pulp in such cases is necrotic but usually not infected, so it will act as a matrix into which the tissue can grow. In most of such cases the crown of the teeth is seen to be intact assuring that bacterial penetration in the pulp space through cracks and defects will be a slow process. Based on these studies it is stated that once the canal infection is controlled, it resembles the avulsed tooth that has a necrotic but sterile pulp space. The concept of revascularization generally evolved based on the studies that if a sterile tissue matrix is provided where new cells can grow then pulp dentin complex can be regenerated(11).

MECHANISM OF REVASCULARIZATION

Basically three factors are considered in mechanism of revascularization.

- **Sterile canal space:** Most of the revascularization procedures recommend minimal to no mechanical debridement but promote the use of root canal irrigants and intracanal medicaments in such cases. The irrigation with sodium hypochlorite (NaClo) alone has proven ineffective and hence placement of medicaments to achieve adequate reduction of intracanal bacteria is recommended. A mixture of ciprofloxacin, metronidazole and minocycline commonly known as triple antibiotic paste has been shown

to be very effective and also have demonstrated to be well tolerated in vital pulp tissue. Owing to the potential risk of dentin staining by minocycline, cefaclor is used as a substitute(12). In 2013, Adriana de Jesus Soaresone et.al in their study used 2% chlorohexidine (CHX) and calcium hydroxide as root canal irrigants and dressing for revascularization procedure. The study concluded that intracanal dressing composed of $Ca(OH)_2$ and 2% CHX gel leads to satisfactory root development in necrotic immature teeth, and also suggested that the side effects of triple antibiotics such as antibiotic resistance, allergic reaction and coronal discoloration could be prevented by using this combination for disinfection of root canals(13).

- **Scaffold for growth of new cells**: Scaffolds are used in revascularization procedure to provide a framework in which cells and a vasculature can grow. In revascularization of infected immature teeth stable blood clot has been used as a scaffold in numerous researches. The assumption behind this is that by inducing bleeding into the disinfected canal, a stable blood clot can be established, that will not only serve as a scaffold but also provide factors that stimulate the cell growth and differentiation into odontoblast like cells. Recently published studies reflect the use of collagen with or without an induced blood clot as a scaffold with promising results obtained when used along with blood clot(14).
- **Cells having capacity to regenerate and induce formation of pulp dentin complex:**

a) In teeth with open apices, it is possible that some pulp tissue and Hertwigs epithelial root sheath may have survived apically. These vital pulp tissue might proliferate into the newly formed matrix and differentiate into odontoblasts under the organizing influence of cells of Hertwigs epithelial root sheath(15).

b) Multipotent dental pulp stem cells are found in the apical end of permanent teeth and are abundantly present in immature teeth. This cells might be seeded onto the existing dentinal walls and differentiate into cells forming pulp dentin complex(16).

c) Stem cells in the periodontal ligament can also grow into the apical end and within root canal, and deposit hard tissue both at the apical end and on the dentinal root canal wall(4).

d) Stem cells from the apical papillae (SCAP) or the bone marrow can be transported along with the bleeding into canal lumen. SCAP has extreme proliferating capacity and is believed to be prime cell involved in revascularization in immature necrotic teeth(17).

CLINICAL PROCEDURE OF REVASCULARIZATION

In 2004, Dr. Trope presented a modified clinical protocol for revascularization which has been widely used in endodontic clinics(18). The clinical procedure is basically divided in three visits but may need more appointments in case of persistent clinical symptoms (19).

First visit: An access cavity is made. Removal of root canal content is accompanied by gentle irrigation with minimum of 20ml 2.5%Naclo dispersed through 20 gauge needle. When irrigating with Naclo, the needle should be introduced at a point 2 mm short of the root canal length to avoid damage to periapical tissue as the canal is wide open apically. Initial Naclo irrigation is followed by irrigation with 5 ml sterile saline to prevent possible interaction between Naclo and CHX which is used as final rinse. Then the root canal is carefully dried with large sterile paper points. The root canal is then medicated with combined triple antibiotic paste to a length of 1 mm short of measured root canal length. This medication is prepared in paste like consistency by mixing equal doses of antibiotics in sterile saline. Reynolds et.al used a mixture of 250 mg each of metronidazole, minocycline and ciprofloxacin the antibiotics in sterile water (20). Preventing coronal leakage of bacteria into the cleaned and medicated root canal is a prerequisite for successful revascularization. Thus double coronal restoration is recommended which is accompanied by placing a sterile cotton pellet over canal medicaments and then sealing with temporary filling materials like cavit and finally covering with GIC (Glass ionomer cement) or composite material. The medicament is left inside the canal for a period of 14 days to several weeks.

Second visit: In this appointment whether the clinical signs and symptoms have ablated or not should be

assessed first. If there is persistence of any clinical sign and symptom then the procedure as in the previous visit is repeated again, otherwise the canal is irrigated gently with 2.5% Naclo until no medicament is evident in the canals .In this visit 17% EDTA (Ethylene diamine tetra acetic acid) is used instead of CHX in final rinse, which acts as chelating agent exploring collagen fibers that contain adhesion motifs for the adhesion of new cells. In addition, degradation of dentine releases the growth factors that can attract new cells and promote their differentiation into cells having odontoblast like properties. Then a sterile k file (size number # 15 or 20) is placed 2mm pass the apical extent of the canal to induce bleeding from periapical tissue into the root canals. The blood clot is formed by applying intracanal blockage with a sterile cotton pellet soaked in saline to a point approximately 3mm apical to CEJ (cemento enamel junction). Once the stability is confirmed, the clot should be carefully covered with MTA cement that is back filled to the level of the CEJ. After its initial set, a wet cotton pellet should be placed over the MTA and seal access opening with temporary restoration.

Third visit: The patient is recalled after 24 hours. Cotton pellet is meticulously removed and a permanent restoration is placed.In majority of cases the resolution of any apical lesion and signs of root maturation are expected to occur within 12-24 months. Most clinicians suggest that the patient to be followed-up at every 3 months during first year then followed by a 6 monthly follow-up unless signs of apical closure and root length elongation are evident. There are many published case reports on success of revascularization/regenerative endodontic procedure. Summary of the most recently published case reports on revascularization are summarized on Table 1.

Table 1. Summary of recent clinical studies on revascularization

Author	Sample size Age, teeth number	Diagnosis	Treatment protocol	Treatment outcome
Nagy et al. 2014 Feb.(21)	N=36, 8-13 yrs. Maxillary lateral incisors.	Immature necrotic teeth due to trauma.	Grp1= MTA plug Grp2=revascularization(blood clot) Grp3=revascularization(blood clot + inject able scaffold)	At 18 months interval all teeth showed radiographic signs of healing with grp 2 and 3 with increase in root length and thickness and decrease in apical diameter and change in periapical bone density.
Jadhav GR et al,2013 Nov.(22)	N=2, mandibular premolars.	Nonvital immature teeth.	Grp1=revascularization with blood clot. Grp2=revascularization with platelet rich factor.	At 6-12 months interval both grp shows signs of root maturation but with more success in grp2.
Forghani et al. 2013(23)	N=2,9yrs, incisors.	Nonvital immature teeth due to trauma.	Grp1=apexification Grp 2=revascularization with blood clot.	After 18 months, both group were asymptomatic with grp2 showing continued development of root.

Sonmez et al. 2013 spring.(24)	N=3, molars	Nonvital immature toot.	Revascularization with blood clot.	After 24mnts, molars were asymptomatic with continuation of root development.
Yang et al. 2013 feb.(25)	N=9	Immature permanent teeth with chronic or acute apical periodontitis.	Revascularization with blood clot.	After 18-24 months, in 6 teeth complete resolution of radiolucency, closure of apex and thickening of dentinal walls was seen. In 1 tooth no root maturation seen and in rest 2 teeth recurrence of apical periodontitis with no evidence of healing was seen.
Keshwai et al 2013 Nov.(26)	N=1, 7 yrs, maxillary central incisors.	Immature non vital tooth due to trauma.	Revascularization with platelet rich fibrin.	After 12-15 months, tooth responded to sensibility test with radiographic signs of root maturation.
Gelman et al, 2012.(27)	N=2, 8 yrs.	Nonvital immature teeth due to trauma.	Revascularization with blood clot.	After 11 months follow up healing of the periapical lesion with increase in breadth of the root evident.
Jung et al, 2012 Jan.(28)	N=8, 9-10 yrs.	Immature permanent teeth with pulp necrosis and apical periodontitis.	5 teeth treated with MTA plug and rest 3 with revascularization with blood clot.	At 2-5 yrs, all treated teeth shows sign of periapical healing with root maturation.
Kim et al, 2012.(29)	N=3, mandibular left second molar with age 12 yrs. Bilateral mandibular second premolars age 10 yrs.	Immature necrotic tooth.	Revascularization with blood clot.	42-48 months after loss of periapical radiolucency with increased root canal wall thickness were observed.

Aggrawal et al, 2012 Jan.(30)	N=2, central incisors.	Immature non vital teeth.	Right teeth with conventional apexification. Left teeth with revascularization.	At 24 months, left teeth showed signs of maturogenesis.

The limitation of the revascularization procedures is that there is no human histological evaluation following the procedures. Radiographic evaluation has been reported on human based clinical studies while histological evaluation has only been reported for animal studies(31). However, the evaluations of the clinical studies suggest that revascularization could be a better alternative to the conventional apexification procedure.

CONCLUSION:

Since 1960s and 1970s when Ostby and Torneck demonstrated the potential of necrotic infected root canals with continuous functioning and regeneration of pulp dentin complex, there has been many researches and clinical studies in this field with promising results. The revascularization treatment procedure represents an improvement over conventional treatment protocols that have left the teeth root with short length and thin lateral dentinal walls of the canals. This could be a better alternative for the treatment of immature necrotic permanent teeth.

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