Revascularization the biological solution: A review

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Abstract
Introduction: Revascularization of necrotic immature permanent teeth is an alternative biological treatment modality to conventional apexification using calcium hydroxide or MTA. Revascularization, as defined by Andreasen, is the restoration of the vascularity to a tissue or organ. Revascularization in necrotic immature permanent teeth results in maturogenesis which allows continued thickening of root dentin and apical closure. This article gives an insight to the detailed procedure of a revascularization and its clinical update.

Keywords: Apexification, Immature permanent teeth, Maturogenesis, Revascularization.

Introduction

Trauma or carious exposure in immature permanent teeth can lead to pulp necrosis, infection and arrested root development. The consequences of arrested development include roots with thin dentinal walls, open apices and an increased risk of root fracture. The instrumentation and obturation of immature root canals are difficult or impossible with conventional techniques. Furthermore, weak teeth with thin root walls are susceptible to fracture. Traditionally, immature teeth were treated by apexification consisting of using long-term calcium hydroxide dressings in an attempt to induce a calcific barrier at the apex before filling the root canal. This is a successful treatment technique for immature teeth, but it has several disadvantages like the need for multiple visits over a relatively long period of time (an average of 12 months) and the root canal may not be reinforced. Additionally, the proteolytic action of calcium hydroxide tends to reduce the organic support of dentine due to disruption of links between collagen fibres and hydroxyapatite crystals. This reduction in microhardness of dentine renders the teeth more susceptible to root fracture. An alternative to conventional apexification with calcium hydroxide is to make an artificial apical barrier to prevent the extrusion of root canal filling materials. The material of choice is mineral trioxide aggregate (MTA) which has good sealing ability and biocompatibility. However, these techniques do not help strengthen the root, and in the absence of continued development, the roots remain thin and fragile rendering the tooth prone to fracture.

A novel concept of revascularization for immature nonvital, infected teeth was recently introduced. Several case reports have reported the use of revascularization procedures to treat immature permanent teeth with necrotic pulps with or without periapical pathosis. Nygaardost by introducing the concept of revascularizationin 1961 and in 1966. In 2001, Iwaya and in 2004 Banchs and Trope demonstrated the advantages of this treatment modality, which resulted in a radiographically apparent normal maturation of the entire root versus an outcome of only a calcific barrier formation at the apex after conventional calcium hydroxide induced apexification. Another term used to describe the development in an immature permanent teeth is maturogenesis.

Regeneration of pulp tissue in a necrotic infected tooth with apical periodontitis has been thought impossible. However, if it were possible to create a similar environment as described here for the avulsed tooth, regeneration should occur. Thus, if the canal were effectively disinfected, a matrix into which new tissue could grow were created, and the coronal access would be effectively sealed, regeneration should occur as in an avulsed immature tooth.

The development of normal, sterile granulation tissue within the root canal is thought to aid in revascularization and stimulation of cementoblasts or the undifferentiated mesenchymal cells at the periapex, leading to deposition of a calcific material at the apex as well as on the lateral dentinal walls.

Indications
- Immature Avulsed teeth.
- Immature permanent teeth with apical periodontitis.
- Immature teeth with periradicular periodontitis or abscess.
- Immature permanent tooth with apical periodontitis and sinus tract.

Case Selection
- Young patients- high healing potential, high vascularity.
- Tooth with immature apex and necrotic pulp secondary to trauma, pulp exposure, caries.
- Apex open > 1.5 mm allow in growth of tissues.
- Pulp space not needed for post and core restoration.
- Compliant patient.

Procedure\(^{7-8,13}\): Revascularization protocol advocates that the immature permanent tooth, diagnosed with apical periodontitis, should be accessed and irrigated with either 5% sodium hypochlorite + 3% Hydrogen peroxide or 5.25 % NaOCl and Peridex. An antimicrobial agent (either an antibiotic such as metronidazole + ciprofloxacin or ciprofloxacin + metronidazole + minocycline or calcium hydroxide should be then applied into root canal system, and the access cavity is sealed. After an average of 3 weeks, in the absence of symptoms, the tooth is re-entered and irrigation is done with 20ml of 17% EDTA and the periapical tissue is irrigated until bleeding is started and a blood clot produced, and then MTA is placed over the blood clot, and the access is sealed. Within the next 2 years a gradual increase in root development can be observed.

Irrigants\(^{7,15-17}\)
- The canal was slowly flushed with 20 ml of 5.25% NaOCl, and 10 ml of Peridex (0.12% chlorhexidine gluconate).
- 20 ml of saline in between sodium hypochlorite and chlorhexidine irrigation to prevent the interaction,
- A final rinse of 17% EDTA is recommended as it is found to promote the bioavailability of growth factors.
- Place the needle into the apical third and irrigate using needles with closed end and side port vents (eg. Max-I-probe needles), together with slow rate of infusion, to help to reduce any irrigants passing through the open apex.

Antimicrobial medicaments
- Triple antibiotic paste\(^{7,17}\)
- Calcium hydroxide\(^{18}\)
- Formocresol\(^{9}\)

The triple antibiotic paste produced significantly greater differences in root wall thickness than either the Ca(OH)\(_2\) or formocresol groups.\(^{19}\)

**Antibiotics (3 mix) Fig 1**
- Ciprofloxacin200mg
- Metronidazole500mg
- Minocycline100mg

**Carrier (MP)**
- Macrogol ointment
- Propylene glycol

**Fig. 1: Triple antibiotic mix**

Triple antibiotic paste was prepared as described by Hoshino et al.\(^7\)
Discolouration potential because of minocycline can be avoided by using cefaclor instead of minocycline\(^7\) and by modified novel technique which involves the application of bonding agent along the walls of pulp chamber.\(^{20}\)

Although endodontic microorganisms are unable to survive in the highly alkaline environment provided by calcium hydroxide, the compound may also have a detrimental effect on vital tissue. Direct contact between the Ca(OH)\(_2\) paste and any vital pulp tissue remaining in the canal can induce the formation of a layer of calcified tissue that will prevent the regeneration of pulp tissue into the occupied space within the canal.\(^5\)

**Blood clot formation**\(^7,8\): A sterile 23 gauge needle or file is placed with a rubber stop at 2 mm beyond the working length. With sharp strokes, needle is pushed past the confines of the canal into the periradicular tissues to intentionally induce bleeding onto the canal. When frank bleeding is evident at the cervical portion of the root canal portion, tight dry cotton pellet is inserted at a depth of 3-4mm into the canal and held there for 7-10 min to allow the formation of clot in the apical 2/3 of the canal. A small piece of colla-plug may be inserted to serve as a resorbable matrix to restrict the positioning of the MTA. About 3mm of MTA is then placed, followed by restoration. A 12 to 18 month recall should be considered.

**Mechanism of revascularization**\(^9,14,21-23\)
- Presence of few vital pulp cells at the apical end of the root canal. These cells might proliferate into the newly formed matrix and differentiate into odontoblasts under the organizing influence of cells of hertwig’s epithelial root sheath.
- The newly formed odontoblasts can lay down atubular dentin at the apical end, causing apexogenesis, as well as on lateral aspects of dentinal walls.
- Abundance of multipotent dental pulp stem cells in immature teeth.
- Presence of stem cells in the periodontal ligament. The evidence in support of this hypothesis is presence of cementum and Sharpy’s fibers in the newly formed tissues.
- Stem cells from the apical papilla or the bone marrow.
- Another possible mechanism could be that the blood clot itself, being a rich source of growth factors could play an important role in revascularization. These include platelet derived growth factor (PDGF), vascular endothelial growth factor (VEGF), tissue growth factor (TGF), platelet derived epithelial growth factor (PDEGF). A blood clot provides a scaffold/matrix for the ingrowth of new tissue. They stimulate differentiation, growth, and maturation of fibroblasts, odontoblasts, cementoblasts etc from the immature, undifferentiated mesenchymal cells in the newly formed tissue matrix.

Adjuncts to blood clot: Platelet-rich fibrin (PRF), a second-generation platelet concentrate, was first developed by Choukroun et al. (2001). It is a non-thrombonized autologous fibrin mesh that serves as a reservoir of growth factors and allows continuous release of growth factors over a period of 7–14 days. Platelet rich plasma (PRP), a first generation platelet concentrate acts as a reservoir of growth factors. In contrast, PRP exhibits sudden release of growth factors in approximately 7–14 h. After that, the release of growth factors from PRP dramatically diminishes. Studies have shown that Supplementation with PRP can potentially improve the desired biological outcome of this regenerative technique.

Limitations
- The source of the revascularized tissue has not been identified. Generally, tissue engineering does not rely on blood clot formation, because the concentration and composition of cells trapped in the fibrin clot is unpredictable.
- Difficult to achieve it in fully formed permanent teeth.
- Potential clinical and biological complications like crown discoloration, development of resistant bacterial strains (due to long term use of antimicrobial agents), allergic reaction to intracanal medicament.
- Potential risk of necrosis, if tissue is reinfected.

Discussion: The rationale of revascularization is that if a sterile tissue matrix is provided in which new cells can grow, pulp vitality can be re-established.

Revascularization protocols are derived from the observations of re-implanted and autotransplanted teeth in experimental animals in which necrotic pulp, if free of infection, provided amatrix into which the cells from the periapical issues could grow and re-establish pulp vascularity, slowly replacing the necrotic tissue.

In immature, infected, non-vital teeth, infection control is achieved with minimal instrumentation, depending more on aggressive, copious irrigation with sodium hypochlorite, chlorhexidine, orpovidone-iodine. The advantages of pulp revascularization lie in the possibility of further root development and reinforcement of dentinal walls by deposition of hard tissue, thus strengthening the root against fracture.

Recommendations: 1) Clinicians should consider the use of an anesthetic without a vasoconstrictor when trying to induce bleeding. 2) A collagen matrix is useful for the controlled placement of MTA to a desired and optimal level. 3) Patients/parents should be informed about the potential for staining, especially in anterior teeth when the paste contains minocycline.

Conclusion This procedure is preferred over apexification. The revascularization treatment is minimally invasive but technically challenging. A blood clot seems to be of importance. Future research ongoing into predictable scaffold materials, growth factors, stem cells. Regeneration of diseased tissues is the future”.

References