



REVIEW

Can revascularization serve as a treatment alternative to apexification for management of immature non-vital permanent tooth? - A Review

Morankar Rahul¹

ABSTRACT : Pulpal necrosis is a relatively common sequel following dental trauma which arrests the further root development in an immature permanent tooth resulting in wide open apices. The immature root with a necrotic pulp and apical periodontitis presents multiple challenges to successful treatment. Various treatment modalities for management such teeth include calcium hydroxide apexification, MTA apexification, and endodontic surgeries. Apexification using calcium hydroxide although shown some success but it is less popular nowadays due to limitations like multiple visits, formation of porous barrier. Mineral trioxide aggregate (MTA) apexification is a commonly used treatment option for management of immature non-vital teeth. However, it does not strengthen the remaining root structure and the tooth remains fracture prone and non-vital. Regenerative endodontic procedures are designed to replace damaged structures, including dentin and root structures, as well as cells of the pulp-dentin complex. Thickening of root dentin and reestablished tooth vitality are the significant outcome with revascularization which cannot be achieved with apexification procedure. Considering the advantages, if the proper case selection protocol is followed revascularization can be used as an alternative to apexification for management of immature non-vital teeth.

Key-words: *Apexification, revascularization, immature teeth*

Introduction:

Traumatic dental injuries to anterior teeth is a common clinical problem among young children and adolescents with a reported prevalence of 6% to 59% in various studies.¹ Pulpal necrosis is a relatively common sequel following dental trauma which arrests the further root development in an immature permanent tooth resulting in wide open apices. The immature root with a necrotic pulp and apical periodontitis presents multiple challenges to successful treatment. (Fig.1)

1. The infected root canal space cannot be disinfected with the standard root canal protocol with the aggressive use of endodontic files.
2. Once the microbial phase of the treatment is complete, filling the root canal is difficult because the open apex provides no barrier for stopping the root filling material before impinging on the periodontal tissues.
3. Even when the challenges described earlier are overcome, the roots of these teeth are thin with a higher susceptibility to fracture.

These problems are overcome by using a disinfection protocol that does not include root canal

instrumentation, stimulating the formation of a hard tissue barrier or providing an artificial apical barrier to allow for optimal filling of the canal, and reinforcing the weakened root against fracture during and after an apical stop is provided.²

Treatment options

Various treatment modalities have been suggested in the literature for the management of traumatized non-vital immature permanent teeth that include calcium hydroxide apexification³, MTA apexification⁴, and endodontic surgeries.⁵

Calcium hydroxide apexification

Apexification by traditional means using calcium hydroxide has although shown some success but it is less popular today as it is associated with certain inherent limitations like multiple visits extending from 6 to 24 months, formation of porous barrier and an inadequate seal.³ Some reports have even shown that long-term calcium hydroxide therapy alters the mechanical properties of dentin which become more prone to fracture.⁶

Mineral trioxide aggregate (MTA)

apexification

Mineral trioxide aggregate (MTA) apexification nowadays has been the most commonly used treatment option for management of immature non-vital teeth.⁷ It, however, doesn't strengthen the remaining root structure and the tooth remains fracture prone and non-vital, as there is no reestablishment of tooth vitality with this approach.⁴

Other alternatives

Other treatment approaches have taken into account reinforcement of root using composite resins, but, this limits the possibility of root canal retreatment in future.⁸ Endodontic surgery to seal the wide open apex by retrograde means is an invasive approach with associated disadvantages like surgical complications and compromised crown-root ratio that further weakens the already fragile root.⁴ Thus, the ideal treatment to obtain further root development and thickening of dentinal walls in an immature tooth with apical periodontitis would be revascularization, to reestablish the vitality in a non-vital tooth to allow repair and regeneration of pulp-dentin complex.

Revascularization

Regenerative endodontic procedures can be defined as biologically based procedures designed to replace damaged structures, including dentin and root structures, as well as cells of the pulp-dentin complex. The term "revascularization" has been used for the reestablishment of vascularity in the pulp space after traumatic injuries. However, there is generation of tissues, such as cementum, periodontal ligament, bone, and dentin, or regeneration of pulp occurs rather than just the generation of vasculature in the canal space that restores functional properties of the tooth, and fosters continued root development for im-mature teeth, and prevents or resolves apical periodontitis.⁹

History

The research on this was first initiated by Nygaard-Ostby (1961) and Rule and Winter (1966) documented root development and apical barrier formation in cases of pulpal necrosis in children (Table 1).^{10,11}

Rationale for revascularization

Occasional cases of regeneration of apical tissues after

traumatic avulsion and replantation led to the search for the possibility of regeneration of the whole pulp tissue in a necrotic, infected tooth. After reimplantation of an avulsed immature tooth, a unique set of circumstances exists that allows regeneration to take place.

a) The young tooth has an open apex and is short, which allows new tissue to grow into the pulp space relatively quickly.

b) The pulp is necrotic but usually not infected, so it will act as a matrix into which the tissue can grow.

c) In addition, the fact that, in most cases, the crown of the tooth is intact ensures that bacterial penetration into the pulp space through cracks and defects will be a slow process.

Thus, the race between the new tissue and infection of the pulp space, favors the new tissue.¹² Extrapolating from this information, it is hypothesized that once the canal infection is controlled, it resembles the avulsed tooth that has a necrotic but sterile pulp space. So, the rationale of revascularization is that 'If a sterile tissue matrix is provided in which new cells can grow, pulp vitality can be reestablished.'

Factors affecting the outcome of revascularization

Root canal disinfection - There is no established protocol for revascularization procedure and different authors have suggested various modifications.⁹ Triantibiotic paste (TAP) mixture has been the most commonly used intracanal medicament for disinfection of root canals prior to revascularization. Various authors have reported the efficacy of mixture of triantibiotic paste for disinfecting the root canals and its penetration into dentin. Hoshino et al. (2005) in their study evaluated the dose-dependent effect of TAP mixture on the vitality of Stem cells from apical papilla (SCAP) and found that a concentration of 0.1 mg /ml (100ug/ml) was highly effective against endodontic microorganisms including enterococcus fecalis¹³ with minimum effect on SCAP cell survival. This is important as in majority of cases reported in literature where TAP has been used as intracanal medicament, no attempt has been made to deliver a specific concentration of drug and the only criterion of preparation of mixture has been achieving a particular physical consistency.⁹ The use of tetracycline and minocycline as intracanal medicaments leads to

extensive tooth discoloration¹⁴ so instead, doxycycline can be considered as an alternative which has found to cause less discoloration.¹⁵

Patient age and time elapsed since tooth become non-vital - Younger the patient and lesser the duration of time since the tooth become non-vital more is the likelihood that regeneration would occur. It is not advisable to carry out regenerative endodontic procedures in children younger than 8 years or older than 16 years unless the tooth has an open apex with thin walls that are at risk from subsequent fracture.¹²

The concentration of sodium hypochlorite for irrigation - Sodium hypochlorite in low concentration has been found to be equally effective as high concentration. This is because the volume of irrigating solution has more role in disinfecting the root canals than its concentration.¹⁶ Moreover, in low strength (1.5%), sodium hypochlorite has been found to be less detrimental to the vitality of cells of pulp and periapical areas. In higher concentration sodium hypochlorite (6%) has been shown to significantly decrease the survival of stem cells from apical papilla (SCAP),¹⁷ and the resorption lacunae were also readily evident in the dentin treated at this concentration.¹⁸

The role of blood clot-The purpose of inducing bleeding in the root canal is to allow blood clot formation to occur which is rich in fibrin and acts as a matrix over which new tissue growth can occur. It has been found that the apical papilla is a dense reservoir of undifferentiated mesenchymal stem cells with greater proliferative and odontogenic differentiation capacity.^{19,20} Induced bleeding results in laceration of this apical papilla with substantial influx of mesenchymal stem cells into root canals during regenerative procedure resulting in an increase in expression of mesenchymal stem cells markers by more than 700 folds.²¹

The role of stem cells - The population of Dental Stem Cells (DSC), stem cells from the apical papilla (SCAP) of incompletely developed teeth, has been identified (Table 2). Evidence for this unique DSC population is based on the observation that tooth root formation was demonstrated to continue in some immature teeth, following endodontic treatment.²²

SCAP, like DPSCs and SHED, can also differentiate into odontoblast-like cells and produce dentin-pulp

complex in vivo.^{23,24} Since the apical papilla is located at the tip of root and receives blood supply from surrounding tissues, SCAP may survive after pulp necrosis or endodontic treatment and continue to produce root dentin.²⁵

Advantages

A number of authors in the literature in their case reports and case series have reported revascularization to be a successful procedure with resultant increase in root length and thickness of dentinal walls.^{26,27} Thickening of root dentin and reestablished tooth vitality are the significant outcome with revascularization which cannot be achieved with apexification procedure. Many have also reported reestablished tooth vitality or sensitivity after revascularization procedure (Table3).

Limitations

This novel procedure produces a stronger mature root that is better able to withstand fracture but has the potential for clinical and biological complications. Amongst them, crown discoloration²⁸ development of resistant bacterial strains²⁹ and allergic reaction to the intracanal medication. A modification³⁰ of the current clinical protocol³¹ was established to avoid crown discoloration. In this novel approach, the coronal dentine was sealed with flowable composite thus avoiding any contact between the tri-antibiotic paste and the dentinal walls.

Furthermore, the stage and duration of pathosis that will ultimately lead to the complete destruction of the resistant apical mesenchymal cells and surviving dental pulp stem cells has not been determined. Under the circumstances of total pulpal and apical papilla necrosis, revascularization treatment may not be possible.

Additional complications such as various systemic health conditions and immunologic problems may offer other obstacles in achieving adequate root maturation in the presence of a periradicular infection. Long term studies are not available to tell whether the canal obliterates or whether apical periodontitis will develop at a later stage. Even if these undesirable outcomes do occur, the tooth is still likely to last for a long time, which would not have been the case if it had been treated endodontically at the time of presentation as tooth can fracture because of weakened roots.

Table 1 : History of regenerative endodontics

Author	Year	Contribution
Nygaard-Østby	1961	The role of the blood clot in endodontic therapy
Rule and Winter	1966	Root growth and apical repair subsequent to pulpal necrosis in children
Nygaard-Østby	1971	Tissue formation in the root canal following pulp removal
Iwaya et al	2001	Revascularization of an immature permanent tooth with apical periodontitis and sinus tract

Table 2: Sources of dental stem cells

Dental pulp derived	Non dental pulp derived
Dental pulp stem cells (DPSC)	Periodontal ligament stem cells
Stem cells from Human Exfoliated deciduous teeth (SHED)	Dental follicle progenitor cells
Stem cells from Apical Papilla (SCAP)	

Though, there are few limitations of revascularization. It is possible that the entire canal might be calcified, compromising esthetics and potentially increasing the difficulty in future endodontic procedures if required. Long-term clinical results are as yet not available.

Future perspective

One of the difficulties is how to confirm the clinical vitality of pulp. The histological examination can verify the vitality of dental pulp but is not practical for clinicians, who are limited to clinical and radiographic evaluations, which do not provide an accurate evaluation of pulp vitality. For this reason, more sensitive methods and/or instruments need to be developed. It is possible that pulp regeneration using autologous dental stem cells (DSC) might become a routine therapy after endodontic treatment. However, autologous DSC sources are limited. Several DSC banks have been established, and patients have started to cryopreserve their DSCs. Perhaps the most promising solution might be induced pluripotent stem cells (iPSCs), cells that have been artificially derived through stem cell gene transfer into an adult somatic cell and can be used for autologous tissue regeneration.^{32,33}

Conclusion

The clinical and radiographic success of revascularization procedure resulting in an increase in root length and thickness of root dentin along with

reestablished tooth vitality justifies the use of this treatment approach as an alternative to traditional apexification for management of traumatized immature non-vital permanent teeth.

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Table 3 . Tooth vitality after revascularization

Author / Year	Sample size	Cause	Diagnosis	Clinical results	Post-operative vitality
Cehrelli et al. 2012	1	Trauma	Not reported	Periapical healing and evidence of continued root development (3-month follow-up).	Tooth responded positively to cold tests (12-month follow-up) and electrical pulp test EPT (18monthsfollowup)
Cehrelli et al. 2011	6	Caries	Pulp necrosis with symptomatic apical periodontitis	On an average 7.7% increase in root length and 26.5% root width increase	33.3% (n = 2) responded positively to sensitivity testing (12-month follow-up)
Iwaya et al. 2011	1	Scaling and Root planning	Necrotic pulp and acute apical abscess	A dentinal bridge was formed; Tooth remained asymptomatic and demonstrated root development and apical closure (30-month and 13-year recall).	EPT elicited a response when applied to the dentinal bridge (3-month follow-up).
Thomson & Kahler 2010	1	Dens evaginatus	Pulp necrosis with chronic apical abscess	Resolution of signs and symptoms of pathosis including closure of sinus tract; evidence of root development	Positive response to EPT testing (18-monthfollow-up.)
Petrino et al. 2010	6	Trauma (complicated Crown fracture n = 2, avulsion n = 2); Caries (n = 2)	Pulp necrosis (n = 6) with asymptomatic apical periodontitis (n = 4) and chronic apical abscess (n = 2)	Periradicular healing with resolution of signs and symptoms of pathosis (100% of cases; n = 6). In addition, continued root development was seen in 3 cases (50% of cases)	Response to pulpal sensitivity testing was seen in 2 cases (33.3% of cases).



Fig.1 (a) Infected non-vital tooth with complicated crown fracture and abscess formation. (b) Intraoral periapical radiograph with thin radicular dentin and wide apical foramen.

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Address of Correspondence

Dr Rahul Morankar (Morankar R)
Room.no 202, Senior Resident
Unit of pedodontics and preventive dentistry
Oral Health Sciences Centre, PGIMER,
Chandigarh -160 012.
Phone no. 9855501651
Email adress: captainrahul88@gmail.com

Authors:

¹Senior Resident, Unit of pedodontics and preventive dentistry
Oral Health Sciences Centre, PGIMER, Chandigarh.

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