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RESEARCH ARTICLE

REVITALIZATION OF IMMATURE OPEN APEX THROUGH REVASCULARIZATION UTILIZING NOVEL COMBINATION OF CURCUMIN IMPREGNATED COLLAGEN AS A SCAFFOLD. A CASE REPORT

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ABSTRACT

In 21 st century endodontics regeneration of apical tissues and root elongation is possible in necrotic immature permanent teeth. The purpose of this case report is to add a novel technique in regenerative endodontic therapy by using curcumin impregnated collagen for revitalization of immature non vital tooth through blood clot. An 11year old boy with the history of trauma was diagnosed with the pulpal necrosis and symptomatic apical periodontitis in tooth #21. Intra oral periapical radiograph showed open apex with large periapical pathology. Access preparation and minimal instrumentation was done to remove necrotic debris under copious irrigation with 2.5% sodium hypochlorite. Triple antibiotic paste was packed in the canal for four weeks. During second visit, Triple antibiotic paste was removed and canal was dried and collagen impregnated with curcumin was placed with Buchanan Hand Plugger Size (#2) 2 mm beyond the confines of working length and after this procedure a sterile 23-gauge needle was placed at 2 mm beyond the working length. With sharp strokes, the needle was pushed past the confines of the canal into the periapical tissue to intentionally induce bleeding into the canal. Three millimeters of Mineral trioxide (MTA) Angelis was placed in cervical part of the root canal and permanent restoration with GIC and Composite was done. Clinical examination at 6 and 12 months revealed no sensitivity to percussion and palpation in tooth #21and it responded positively to both electric pulp and cold tests. Radiographic examination showed resolution of periapical rarefaction, further root development and apical closure of the tooth #21. On the basis of successful outcome of the present case it can be stated that curcumin impregnated collagen increases the healing kinetics and may serve as a scaffold for regeneration of necrotic immature teeth.

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INTRODUCTION

Root canal treatment of mature teeth having irreversible pulpitis has shown a high success rate of 95% (Basmadjian-Charles *et al.*, 2002; Chugal *et al.*, 2003). However, endodontic treatment of necrotic immature permanent teeth poses difficulty in management on account of thin lateral dentinal walls which are prone to fracture and have a questionable long term successful retention in the oral cavity (Cvek, 1992; Trabert, 1978).

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Characteristically these teeth in addition to thin and fragile dentinal wall also have, open apices which are very difficult to seal apically, laterally and coronally i.e. (3D seal) (Kerezoudis *et al.*, 1999). Calcium hydroxide (Frank, 1966; Steiner, 1968) or mineral trioxide aggregate (MTA) apexification is the only option conventionally (Shabahang, 2000; Witherspoon, 2001). It has been reported that 30% of such teeth fracture during or after such conventional treatment either due to hygroscopic expansion of MTA or denaturation of collagen fibrils by long term placement of calcium hydroxide for apexification (Kerekes, 1980). In last decades there is a shift in the treatment protocol of managing and treating such teeth with regenerative protocols to regenerate both hard and soft tissues of diseased tooth.

Regeneration is a biological procedure based on principle of cell homing offers a huge potential for both hard and soft tissue formation in such teeth (Rule, 1966; Iwaya *et al*., 2001) The periradicular region for regeneration is dependent upon 3 main ingredients. 1 spatial orientation of stem cells 2.Signaling molecule 3.Suitable scaffold (Hargreaves, 2008; Langer, 1993) Various studies on regenerative endodontics utilized blood clot as scaffold with the resultant increase in concentration of growth micromolecules. There is a herbal transition happening in endodontic research and now plethora of studies are undertaken to study the exact role of many herbs at molecular level. One such compound is Curcumin obtained from *Curcumalonga* (Turmeric). Its anti inflammatory / immunomodulatory to antimicrobial properties are utilized with an advantage that these herbal compounds has no known side effects and can hasten biologic healing of various tissues. *Curcumalonga* (Turmeric) an Indian spice/herb has a long history of use in Ayurvedic medicine as a treatment for inflammatory conditions. It is derived from the rhizomes of the plant (Nadkarni, 1954). The primary active constituent of turmeric and the one responsible for its vibrant yellow color is curcumin, first identified in 1910 by Lampe and Milobedzka. Turmeric is comprised of a group of three curcuminoids: curcumin (diferuloylmethane), demethoxycurcumin, and bisdemethoxycurcumin as well as volatile oils (tumerone, atlantone, and zingiberone), sugars, proteins, and resins (Leung, 1998). While curcumin has been attributed numerous pharmacological activities, including antioxidant (Chandra, 1972) and antimicrobial properties (Cooper, 1994), the anti-inflammatory effects of curcumin.

Based on the inflammatory and immunomodulatory properties of Curcumin regeneration of immature teeth was done through blood clot with collagen impregnated with curcumin as a scaffold in the present case report.

Case report: An intraoral radiograph was taken before access opening for a baseline record (Figure 1.) and under rubber dam isolation; access preparation was done in tooth #21 after obtaining the local anesthesia. Minimal instrumentation was done and the canal was continuously irrigated with 2.5% NaOCl for 15 minutes. Equal proportions of ciprofloxacin (Bayer, Leverkusen, Germany), metronidazole (Shionogi and Co, Ltd, Osaka, Japan), and minocycline (Aurobindo, Andhra Pradesh, India) were ground and mixed with ratio of 1:1:1 respectively with distilled water to form a thick paste like consistency. Canal was dried and the antibiotic mixture was packed in the canal using large endodontic pluggers. The access cavity was sealed with Cavit (ESPE, Chergy Pontoise, France). Patient was kept on follow up period of four weeks and anti-inflammatory medications were prescribed for three days. In cases in which infection persisted and drainage from the canal was present, one more dressing was applied, and revascularization was performed at a subsequent appointment. The revascularization process was completed as follows.Tooth #21 showed no sensitivity to percussion and palpation, absence of pain and swelling during follow up. Temporary restoration was removed and the triple antibiotic mixture was washed out with saline and 2.5% sodium hypochlorite. Canal was dried and collagen impregnated with curcumin (Figure 2.) was placed with Buchanan Hand Plugger Size #2 (Sybron Endo, Orange, CA) 2 mm beyond the confines of working length and after this procedure a sterile 23-gauge needle was taken, and a rubber stopper was placed at 2 mm beyond the working length. With sharp strokes, the needle was pushed past the confines of the canal into the periapical tissue to intentionally induce bleeding into the canal. When frank bleeding was evident at the cervical portion of the root canal system, a tight dry cotton pellet was inserted at a depth of 3– 4 mm into the canal and the pulp chamber and held there for 7–10 minutes to allow formation of clot in the apical two thirds of the canal. Three millimeters of MTA Angelius was placed directly over the clot and tooth was restored with GIC and composite (Esthet.X HD, Dentsply, UK) in the same sitting. The patient was kept on follow-up at 6 and 12 months (Figure 3, 4) for re-evaluation. Tooth #21was asymptomatic and was not sensitive to percussion or palpation tests. Sensitivity tests with cold and Electric Pulp Tester elicited a positive response. Radiographic examination showed resolution of the periapical lesion, further root development and continued apical closure in tooth #21 An intraoral radiograph was taken before access opening for a baseline record to be compared with follow-up radiographs to be taken at intervals of every 6 months. Both clinical and radiographic evaluation was done at each follow-up. Clinical examination on follow ups showed tooth #21 was asymptomatic. Radiographic examination was done using XCP (Dentsply) for standardization at 6 and 12 months (Fig. 3, 4) which showed resolution of the periapical lesion, further root development and continued apical closure in tooth #21.

DISCUSSION

A regenerative procedure like Apexogenesis and maturogenesis in necrotic immature permanent teeth was first introduced in the endodontics by Ostby in 1961. Regenerative Endodontics set the stage for maturogenesis in nonvital immature tooth. It has been reported that the remnants of hertwig's epithelial root sheath or cell rests of Malassez present in the apical regions are resistant to peri-apical infections (Okamoto *et al*., 2009) Thus, the signaling networks from these remnant epithelial root sheath cells may stimulate various stem cells like stem cells from apical papillae, (Huang, 2006) periodontal ligament, bone marrow and multipotent pulp stem cells to form odontoblasts-like cells in nonvital, immature and no infected teeth. These newly formed odontoblasts-like cells from dentine which helps in normal root maturation. This biological process is also mediated by stimulation of cementoblasts at peri-apex leading to deposition of calcific material at apex as well as on lateral dentinal walls. Several research groups have demonstrated the role of morphogens like statins, (Wang, 2007) dexamethasone, (Visser *et al*., 2010) LIM mineralization proteins (Ahmed, 2008) on the differentiation of odontoblasts-like phenotypes from dental stem cells. The thickened and convergent dentinal walls add to the long-term prognosis of the tooth by increasing its fracture resistance. Successful revascularization of immature teeth can be accomplished after complete disinfection, placement of a matrix in the canal for tissue in-growth and bacterial tight seal of the access opening. Minimal instrumentation and copious irrigation was done with 2.5% NaOCl, to achieve disinfection. Triple antibiotic paste (TAP) (Soffer, 2003) a mixture of ciprofloxacin, metronidazole, and minocycline was packed in the canal to achieve further reduction of microbial load. Appropriate scaffolding is necessary to give correct spatial location to stem cells and to regulate its differentiation, proliferation, and metabolism by different growth factors. Blood clot and platelet concentrates i.e., PRP (Choi, 2006) and PRF (Mazzucco *et al*., 2004) serve as natural scaffolds with numerous growth factors.

Figure 1. Preoperative IOPA X ray

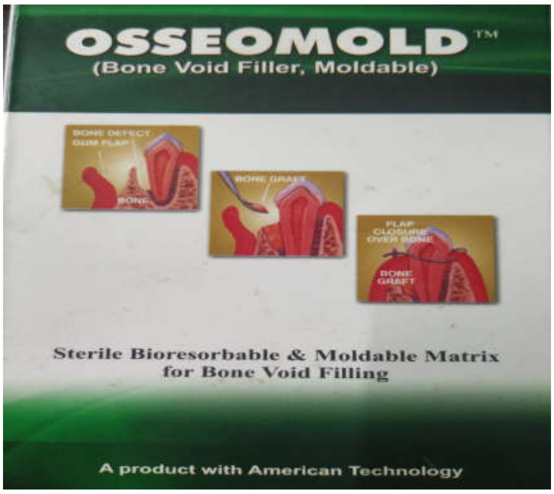

Figure 2. Collagen scaffold

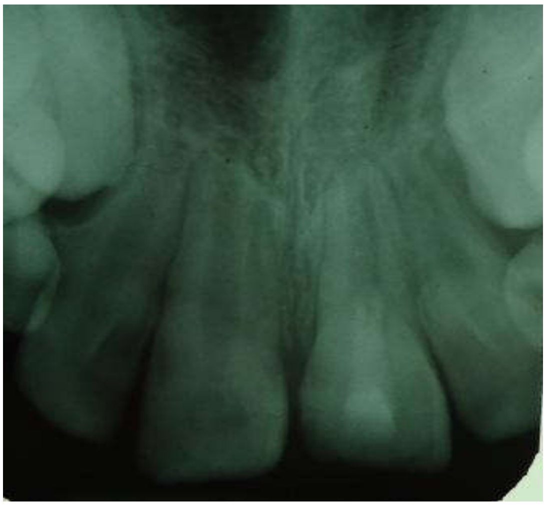

Figure 3. Follow up IOPA 6 Months

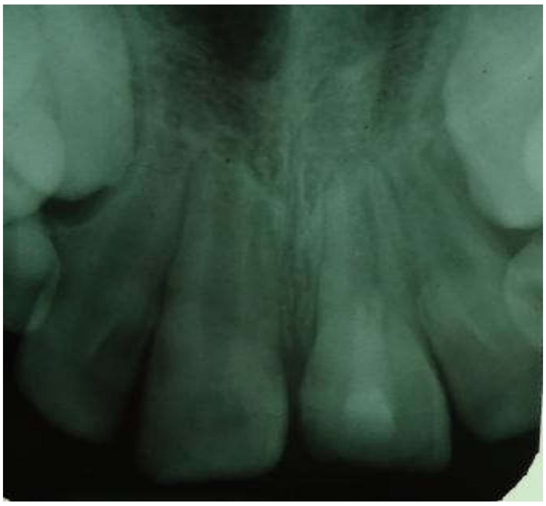

Figure 4. Follow up IOPA 12 Months

Platelet-derived growth factor (PDGF-AB), transforming growth factor β (TGF-β), and insulin-like growth factors have been evaluated for their ability to guide the stem cells to differentiate into odontoblasts-like cells (Mazzucco *et al*., 2008) Curcumin impregnated collagen a novel combination was used as a scaffold and revascularization was induced after its placement in the present case report as these natural scaffolds with curcumin can store and induce numerous growth factors like Platelet-derived growth factor (PDGF-AB), transforming growth factor β (TGF-β), and insulin-like growth factors in the vicinity of periapex after revascularization and guide the stem cells for Regeneration of Pulp Dentin complex and results acceleration of biologic healing kinetics. Mechanism of Revascularization It is possible that a few vital pulp cells remain 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, which are quite resistant to destruction, even in the presence of inflammation. The newly formed odontoblasts can lay down atubular dentin at the apical end, causing elongation of root, as well as on lateral aspects of dentinal walls of the root canal, reinforcing and strengthening the root. Another possible mechanism of continued root development could be due to multipotent dental pulp stem cells, which are present in permanent teeth and might be present in abundance in immature teeth. These cells from the apical end might be seeded onto the existing dentinal walls and might differentiate into odontoblasts and deposit tertiary or atubular dentin. The third possible mechanism could be attributed to the presence of stem cells in the periodontal ligament (He *et al*., 2009; Arpornmaeklong *et al*., 2004) which can proliferate, grow into the apical end and within the root canal, and deposit hard tissue both at the apical end and on the lateral root walls. The evidence in support of this hypothesis is presented by documentation of cementum and Sharpey's fibers in the newly formed tissues. The fourth possible mechanism of root development could be attributed to stem cells from the apical papilla or the bone marrow. Instrumentation beyond the confines of the root canal to induce bleeding can also transplant mesenchymal stem cells from the bone into the canal lumen. These cells have extensive proliferating capacity. Transplantation studies have shown that human stem cells from bone narrow can form bone or dentin in vivo (Vogel *et al*., 2006; Lucarelli *et al*., 2003). Another possible mechanism could be that the blood clot itself, being a rich source of growth factors, could play an important role in regeneration. These include platelet-derived growth factor, vascular endothelial growth factor (VEGF), platelet-derived epithelial growth factor, and tissue growth factor and could stimulate differentiation, growth, and maturation of fibroblasts, odontoblasts, cementoblasts, etc from the immature, undifferentiated mesenchymal cells in the newly formed tissue matrix. Expression of VEGF in immature and mature permanent teeth has been documented (Soffer *et al*., 2003).

There are several advantages of revascularization as observed from this study as well as from the past studies. It requires a shorter treatment time; after control of infection, it can be completed in a single visit. It is also very cost-effective, because the number of visits is reduced, and no additional material like bone graft or growth factors are required. Obturation of the canal is not required unlike in calcium hydroxide– induced apexification, with its inherent danger of splitting the root during lateral condensation. However, the biggest advantage is that of achieving continued root development (root lengthening) and strengthening of the root as a result of reinforcement of lateral dentinal walls with deposition of new dentin/hard tissue. There are only a few limitations of revascularization. Long-term clinical results are as yet not available. It is possible that the entire canal might be calcified, compromising esthetics and potentially increasing the difficulty in future endodontic procedures if required. In case post and core are the final restorative treatment plan, revascularization is not the right treatment option because the vital tissue in apical two thirds of the canal cannot be violated for post placement.

Conclusions

There are several advantages of revascularization with curcumin impregnated collagen as observed from this study. It requires a shorter treatment time; after control of infection, it can be completed in a single visit. It is also very cost-effective, because the number of visits is reduced, and no additional material like bone graft or growth factors are required. Curcumin increases healing kinetics and in tissue engineering in the apical region of immature necrotic teeth leads to the apexogenesis and maturogenesis. The thickened and convergent dentinal walls also add up to the overall resistance of the tooth to fracture and increase the longevity of the tooth. This regenerative process is accomplished after complete disinfection of the root canal and placement of a matrix in the canal for tissue in-growth. Appropriate scaffolding is necessary to give correct spatial location to stem cells and to regulate its differentiation, proliferation and metabolism by different growth factors. Platelet derived growth factor (PDGF-AB), transforming growth factor β (TGF-β), insulin like growth factors derived from platelet concentrates have been evaluated for their ability to guide the stem cells to differentiate into odontoblasts like cells so more studies need to undertaken utilizing novel combination of curcumin and collagen in revascularization through blood clot in immature non vital permanent teeth with molecular action of curcumin on stem cells differentiation and periapical tissues.

Conflict of Interest: None

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