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Original Article

Revascularization of Non-vital Permanent Teeth with Open Apices: A New Treatment Modality

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Abstract

Objective: To determine increase in root(s) length and thickness and closure of apical foramen in patients undergoing revascularization of immature, permanent, necrotic teeth

Material and Methods: This study was conducted at outpatient department of Operative Dentistry, Pakistan institute of medical sciences (PIMS), Islamabad, from 22nd January 2011 to 22nd January 2013. All the patients were assessed with the detailed history and clinical examination. On the first visit, pulp chambers of the teeth were opened followed by minimal instrumentation. Disinfection of the root canal was done with 2.5% sodium hypochlorite (NaOCl), saline, and 2% chlorhexidine (CHX). Then triple antibiotic paste (TAP) was placed in the canal till next visit. In the next visit, in the absence of clinical signs and symptoms, under local anesthesia without vasoconstrictor, bleeding was induced in the root canal. Blood clot was allowed to form beyond the level of cementoenamel junction (CEJ) which was then covered with non-setting formulation of calcium hydroxide{$Ca(OH)_2$}and bacteria tight coronal seal with glass ionomer cement or composite was made. Patients were evaluated clinically and radiographically at 0, 3, 6, 12, 18 till 24 months.

Results: Efficacy of revascularization was measured on 24 months follow up of patients having immature, permanent and necrotic teeth. Out of 36 teeth, 34 (94.4%) showed increase in root length and whereas only 2 (5.6%) teeth showed no increase in root length. Similarly, 33 (91.7%) teeth showed increase in root thickness and 3 (8.3%) patients showed no increase in root thickness.

Conclusion: On the basis of follow-up period of at least 24 months, the present study demonstrates favorable outcome of the revascularization procedure in terms of increase in root length and thickness in immature permanent necrotic maxillary anterior teeth. The cases remained successful even with the use of non-setting formulation of $Ca(OH)_2$ in place of mineral trioxide aggregate(MTA).

Key words: Immature teeth, Calcium hydroxide, Regenerative endodontics, Revascularization.

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Introduction

Trauma to anterior teeth, commonly found among young children, accounts for one third of all traumatic injuries in males and one fourth in females. In these cases of trauma, tooth fracture constitutes about 4 to 5% of the cases.[1] As root development takes place for almost two to three years after tooth eruption into oral cavity, an incompletely formed apex is most common feature seen in traumatized teeth which in turn poses many potential complications. For example, difficulty in cleaning and shaping of the wide canal, difficulty in disinfecting necrotic debris in wide root canal and absence of apical constriction against which obturation can be done etc. Moreover, thin root canal walls render it susceptible to future fracture.[2] Endodontic management of such teeth includes surgery and retrograde sealing, conventional $Ca(OH)_2$ induced apexification and placement of an apical plug of mineral trioxide aggregate (MTA) followed by gutta percha obturation. But these procedures are not associated with more root development in terms of apical maturation and thickening of the dentinal walls and tooth will be more prone to further fracture due to being weak internally.[3,4]

Recently introduced regenerative endodontic procedures (e.g. revascularization) have the potential to allow for continuation of root development to reinforce dentinal walls and strengthen the tooth against future fracture and might therefore offer an alternative therapeutic approach in the management of immature permanent teeth with compromised integrity.[5,6] Although no randomized controlled trial related to regenerative endodontic therapy has been conducted yet. However, current best available evidence undeniably allows clinicians to provide this treatment modality safely and successfully to the patients.

Present study was conducted to evaluate the effectiveness of revascularization procedure in terms of complete resolution of signs and symptoms and increase in root length and thickness and closure of apical foramen radiographically.

Material and Methods

This study was conducted at outpatient department of Operative Dentistry, Pakistan institute of medical sciences (PIMS), Islamabad, from 22nd January 2011 to 22nd January

2013. All the patients were assessed with the detailed history and clinical examination. Patients with immature necrotic teeth with at-least 1 mm wide open apex mesiodistally, teeth not needing future post and core restoration, physically and mentally healthy children of both genders and patients with age group between 9 to 14 years were included in the study. As root lengthening and apex formation are possibly related to vitality and interaction between hertwig epithelial root sheath and stem cells of apical papillae which could be threatened in case of longer lasting periapical infection, so to avoid this, the younger patients having plenty of vital stem cells with no history of longer lasting infection were selected. Periapical radiographs were taken with the help of beam aiming device (Endoray11, Dentsply) by parallel angle radiographic technique for future comparison of radiographic findings. The study was approved by the ethical committee of PIMS. The parents of the patients were informed and explained about the whole procedure and informed consent in written was taken. On first visit, pulp chambers of the teeth were opened with round diamond bur of ISO size 018 (Mani Dia-Burs, Japan) under rubber dam isolation (Safe Touch, Medicom, USA) followed by disinfecting the root canal(s) by using 2.5% sodium hypochlorite solution (Pfizer), normal saline solution and 2% chlorhexidine (Clinica, Platinum). Canals were dried with paper points. No instrumentation was done. Then triple antibiotic paste (TAP), consisting of equal amounts of ciprofloxacin, metronidazole and minocycline mixed with propylene glycol liquid was placed as intracanal medicament for at least one week and access cavities were resealed with cavit (Provis, Germany). On next visit, in case of infection free, dry root canals, local anesthesia without vasoconstrictor (plain lidocaine, Huons Co, ltd) was administered and rubber dam was re-applied. Access cavities were re-entered followed by same irrigation protocol comprising of sodium hypochlorite, saline and chlorhexidine. Then bleeding was induced in the root canal with 25 # or 30 # sterile k-file (Mani, inc. Japan) while going 2 to 3 mm beyond the measured working length. Bleeding was controlled by sterilized cotton pellet by placing it for about 10 minutes beyond CEJ. After formation of blood clot, non-setting formulation of calcium hydroxide (Hidroxido Calcio. A, Biodinemica) was applied over the blood clot. Finally bacteria tight coronal seal with glass ionomer cement (Kross Fill, Kross Dent inc, USA) or composite was made (tgmicrohybrid, UK). (Fig.1a-h)**.** Patients were evaluated clinically and radiographically with beam aiming Deviceat 0, 3, 12, 18 till 24 months. WHO software was used for sample size calculation with Confidence level: 95%, Anticipated population proportion:70 % and absolute precision 15%. All collected data was entered on SPSS version 17.0. Number and percentage was calculated for effectiveness, gender and increase in root length and thickness at 24 months. Mean and standard deviation was calculated for age of patient.

Results

According to inclusion criteria of our study, total 36 subjects (teeth) were included in our study from the outpatient department with detailed history and clinical examination for the duration of two years. Age of our patients ranged from 8-14 years with mean age of 10.61±1.85 SD; 24 (67%) were males and 12 (33%) were females. Patients were evaluated clinically and radiographically at 0, 3, 6 and 12 months till two years (24 months). On clinical examination at 24 months, number and percentages of TTP (tender to percussion) and Sinus Tract was 2 (5.6%) and 1 (2.8%), whereas only one patient was found without intact coronal seal. Similarly, no patient was found with mobility, showing that revascularization is effective in terms of complete resolution of signs and symptoms clinically.

Efficacy of revascularization was also measured on 24 months follow up of patients having immature, permanent and necrotic teeth. About 34 (94.4%) out of 36 teeth showed increase in root length (fig 1a-f) and whereas only 2 (5.6%) teeth showed no increase in the root length. Similarly, 33 (91.7%) patients showed increase in root thickness and 3 (8.3%) patients showed no increase in root thickness, revascularization is effective in terms of complete resolution of signs and symptoms clinically and also with an increase in root length and thickness of teeth radiographically which would help in preventing further root fracture as shown in Table 1.

Table 1: Frequency of clinical examination and efficacy of revascularization radiographically on 24 months.

		n (%)
Clinical examination	TTP	02 (5.6)
	Mobility	0 (0)
	Sinus Tract	01 (2.8)
	Coronal Seal (intact)	35 (97.2)
EFFICACY		
Root length	increase	34 (94.4)
	No increase	02 (5.6)
Root thickness	increase	33 (91.7)
	not increase	03 (8.3)

Fig 1a: Pr-eop PA radiograph of Maxillary left central incisor

The 18- months follow-up.

Fig 1d: Pre-op. PA radiograph The 20-months follow up

Maxillary right central incisor

Fig 1b: Pre-op. PA radiograph Maxillary left central incisor

The 12-months follow up

Fig 1e: Pre-op. PA radiograph The 18-months follow up

Maxillary rightcentral incisor

Fig 1c: preop. PA radiograph The 24-months follow up.

Maxillary left central incisor

Fig 1f: Pre-op. PA radiograph The 12-months follow up

Maxillary leftcentral incisor

Fig 1g: Pre-op. PA radiograph Maxillary leftcentral incisor

The 10-months follow up(resolution of PA radiolucency)

Discussion

Individuals between 6-16 years have sequential permanent tooth eruption and maturation of roots. Any factor that interrupts the normal physiological process of pulp may arrest the root growth and prevents it from completion.[2] Losing immature teeth is difficult to manage as the jaws are still developing and any restorative procedure is likely to be a temporary measure.[7] Because of the important role of hertwig epithelial root sheath (HERS) in continued root development, after pulp injury, every effort should be made to maintain its viability.[8] Before applying any clinical approach to traumatized immature teeth, two clinical situations must be considered. First is dealing with immature teeth with vital pulp where apexogenesis can be attempted with high rate of success. Second is immature teeth with non-vital pulp where apexification can be attempted.[9.10] But more recently introduced is revascularization/ maturognesis which can be applied on immature non-vital permanent teeth, whereby not only the apex is closed but entire root is allowed to mature.[11] Regeneration of tissues rather than replacement with artificial substitutes is a novel and exciting field in the health sciences.[12] There has been great deal of discussion as to the correct terminology for what has been called pulp revascularization,[2] whether the correct term should be a revascularization, revitalization, regeneration or matuarogenesis? It would be difficult to impossible to assign a proper term unless complete histological analysis is performed of reformed/revascularized pulp tissue. A few histologic case reports have been published after completion of regenerative procedures. Two reports found evidence of pulp-like loose connective tissue and one study reported an in- growth of cementum, bone, and connective tissue. Animal studies examining regeneration procedures have shown that the types of tissues found within the root are not pulp but consist of bone, cementum, and connective tissue.[13]

Our study population undergoing 'revascularization' comprised 36 subjects (teeth) of 24 patients with the age range of 8 to 14 years. All teeth being maxillary anterior teeth. All patients presented with non-vital teeth with or without periapical. Necrosis of the teeth occurred secondary to coronal fracture with the exception of one patient in whom necrosis occurred due to enamel hypoplasia followed by bacterial invasion of root canal systems. Periodontally all teeth were found to be sound with healthy gingiva and periodontal depth being ≤ 3 mm.

Radiographically teeth were immature (with open apices being at least 1mm wide mesiodistally upto being blunderbuss with thin and short radicular dentinal walls). A critical aspect prior to providing regenerative endodontic procedure to immature necrotic teeth is the size of the apical foramen. Amazingly two of our subjects (teeth) of the same patient showed apical diameter of about less than 1mm or almost closed as detected radiographically but root canals being still wide. One tooth of the same patient was found to be involved in large periapical lesion that was diagnosed to be an infected cystic- like lesion, also involving adjacent lateral incisor and canine. These teeth underwent revascularization procedure. After period of 13 months, not only radiographic evidence of periapical healing was observed but amazingly teeth responded very strongly to cold and electric pulp test (EPT) tests. These findings suggest that teeth with roots showing very narrow apical openings could be revascularized along with periapical healing (perhaps even of cyst, too). This finding may give two new prospects to think of applying regenerative procedure; first, Revascularization procedure can be attempted on mature teeth with the hope that canal space will be re-occupied with healthy tissue carrying the immune cells to combat further bacterial invasion. This result is similar to the findings of case report of Khimiya paryani who demonstrated the resolution of clinical signs and symptoms with complete periapical healing in mature permanent incisors with apical periodontitis after regenerative endodontic treatment.[14] Second, Revascularization procedure can be applied on immature/ mature necrotic permanent teeth involved in cyst-like lesion similar to the results of Tarek Mohamed who successfully revascularized two mature, permanent teeth with large cyst-like lesions.[7] It can be hypothesized that disinfection of the root canals with NaOCl, saline and CHX and intracanal placement of triple antibiotic paste could eliminate the source of infection from the canal system thus providing suitable environment conductive for healing.[15] CHX has been used along with gold standard NaOCl because of its antimicrobial properties, substantivity, low toxicity. This may be safe alternative if comes in contact with periapical tissues of immature teeth.[9] Moreover stem cells of apical papillae (SCAPs) being supplied with collateral circulation survived even in necrotic condition of dental pulp thus ensuring the in-growth of the blood vessels

and regenerating tissue either from healing periapical tissue or periodontal ligament(PDL) with associated periodontal ligament stem cells (PDLSCs).[7] Both points are not more than a hypothesis that require further investigation at molecular level. At the same time, the above described findings could be able to expand the inclusion criteria in selecting the cases for revascularization.

Although $Ca(OH)_2$ mixed with 2% Chlorhexidine has been used successfully in place of triple antibiotic paste to disinfect root canal system,[15]our studies remained different from previously described studies on revascularization in that non- setting formulation of $Ca(OH)_2$ was placed over blood clot below the level of CEJ (instead of MTA used in previous studies). To the best of our knowledge, it is the first study in which $Ca(OH)_2$ has been used but surprisingly continued growth of the roots observed with positive responses to sensibility tests. Although some cases underwent clinical and radiographic failures in terms of re-infection, pain and swelling and non-healing of periapical lesion respectively, but it is uncertain to say that only the use of $Ca(OH)_2$ is responsible for failure as previously reported studies done on revascularizations using MTA also showed some failures.[16] But again this point opens the new field of research on the use of $Ca(OH)_2$ in place of MTA where financial constraints limit the application of revascularization procedure.

Among the findings observed in revascularized teeth, one of the teeth showed complete root canal calcification and three teeth showed partial calcification starting coronally and progressing apically. Partially calcified teeth responded negatively to cold test and electric pulp tester (EPT). Among two of the three partially calcified teeth, radiopaque masses or well demarcated calcified deposits on apical areas were detected on periapical radiographs along with the diffused haziness in coronal side extending apically. The hard tissue may begin as calcific particles originating or being associated with blood vessels and perineurium sheaths. Interestingly these are also the locations where pulp stem cells are believed to exist i.e. the SCAPs. Whether these stem cells are activated by low grade inflammation to undergo osteogenic differentiation is unclear at present. This finding is similar to a case report of maxillary incisor which underwent progressive calcific metamorphosis after being successfully revascularized.[17]

As hypothesized previously, longer standing of an infection, and long term use of $Ca(OH)_2$ as an intra canal medicament, may be detrimental to the process of successful revascularization[18.19] but contrary to this hypothesis, one of the patients with the age of 14 years in our study presented with non-vital maxillary central incisors with periapical radiolucencies from last six years and had been attempted unsuccessfully for $Ca(OH)_2$ induced apexification before referral to us. The revascularization procedure was performed and after the period of 12 months, successful healing of periapical lesion and continued root growth was detected radiographically, although one of the teeth redeveloped infection so it was re-entered and re-apexified. This unique set of findings requires establishing strict evidence-based guidelines that teeth with which type of pulpal and periapical status (i.e. teeth with irreversible pulpitis, partially/completely necrotic pulp, with apical periodontitis/abscess or cyst-like large lesions) are best candidates for revascularization. Moreover, it must be known that how long the placement of $Ca(OH)_2$ in the root canal and duration of infection will completely damage hertwig epithelial root sheath (HER), stem cells of apical papillae(SCAPs) and dental pulp stem cells(DPSCs) etc.

As far as blood clotting is concerned after induction of bleeding in the canal system, we observed frequent bleeding, infrequent bleeding and very difficult to induce bleeding in different cases. We observed no significant increase in root length and thickness in cases despite of the fact that profused bleeding was induced at the bleeding induction phase. So at this time it is difficult to say that how much amount of the blood is sufficient to give adequate quantity of fibrin-rich clot that will be conductive for in-growth of new tissue. Regarding response to sensibility tests (cold test and EPT), although successfully revascularized cases showing increase in root length and root thickness radiographically, responded positively to sensibility tests but point of interest arises when revascularizing teeth responded positively to cold test but no response to EPT or negative response to both tests. The lack of response might not even be related to the presence or absence of regenerated pulp nerve tissue, according to Torabinejad et al, both the coronal level of regenerated tissue and thickness of coronal filling material placed over this tissue may affect the presence and absence of response to cold test or EPT.[8]

Our study remained different in many aspects from previously described studies on revascularization in that; first, a large number of the patients were selected. second, $Ca(OH)_2$ was used instead of MTA over blood clot, thirdly discoloration was taken as one of the clinical parameters. Discoloration of the crowns of revascularized teeth increased over time in some cases. It may be due to residual TAP left in the pulp chamber. Two patients presented with pain and partially dislodged filling after being revascularized which subsided by prescribing non-steroidal anti-inflammatory drug (NSAIDs) and repairing the existing restoration. Pain may be ascribed due to some inflammatory reaction in the canal system as a result of possible micro leakage from defective coronal restoration. One explanation of subsiding the pain may be related to age of the patient. As the patients were young and healthy with fully mature immune system and defense cells so repairing the restoration and administrating of non-steroidal anti-inflammatory drug (NSAIDs) could subside inflammation and pain and immature teeth continued to develop their roots.[20] In the last if the objective of revascularization is to

achieve more clinical and radiographic success (rather than biological failure) in terms of healing of periapical tissue, no signs and symptoms, increase in root length and width and closure of apical foramen, then it can be claimed with certainty that present study succeeded to achieve that objective.

Conclusion

Our study showed that revascularization of immature necrotic permanent teeth is a clinical possibility with the benefits of revitalizing the teeth irrespective of the fact whatever the tissue inside the canal space because we were not focused primarily on histological findings in newly revascularized teeth. Overall effects (clinically as well as radiographically) were more promising in terms of revitalizing teeth again. It can be hypothesized that revascularized/ regenerated tissue carrying the full range of immune cells can better fight against future microbial challenges just like the pulp tissue of healthy, vital and mature teeth. This treatment modality may explore the vast field of research on tertiary dentine formation capability of regenerated pulp in future in the same way as do vital, healthy and mature teeth.

Conflict of Interest

This study has no conflict of interest as declared by any author.

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Authorship Contribution

Author1: Active participation research, analysis and discussion

Author2: Conception, planning and final review of article