Regenerative Endodontic Treatment versus Apical Plug in Immature Teeth: Three-Year Follow-Up

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This report compares and evaluates the treatment outcomes of regenerative endodontic treatment and apical plug as two accepted treatment protocols in a pair of necrotic immature maxillary central incisors of a 12-year old female. The patient was referred complaining of a dull pain and swelling in her upper lip area. She had a history of trauma to the anterior maxilla two years earlier. Both teeth were clinically diagnosed with pulp necrosis and periapical radiographs revealed that separate periapical radiolucent lesions surrounded the immature apices of both teeth. The left and right incisors were treated with apical plug and regenerative endodontic treatment, respectively, using calcium-enriched mixture (CEM) cement. The patient was followed-up for three years. During this period, both teeth were clinically asymptomatic and showed complete radiographic healing of the periapical lesions. The right central incisor showed root development. No tooth discoloration was evident. Apexification by apical plug placement and pulp regeneration are both reliable treatments for immature non-vital teeth. In order to choose the right treatment the advantages of either technique should be weighed against its drawbacks. CEM cement can be successfully applied for both purposes. This biomaterial causes less discoloration of the tooth.

***Key words**: Calcium-Enriched Mixture, Pulp, Revascularization, Regeneration*

INTRODUCTION

Management of immature teeth with necrotic pulp and apical periodontitis is considered as a clinical challenge because of several reasons; the root canal space is infected and the thin dentinal walls cannot be adequately instrumented [1]. In addition, the patent apical foramen lowers the chances of proper sealing and due to under-developed root structure, the tooth is still vulnerable to cervical fractures [2]. These challenges necessitate specific approaches such as a chemical disinfection protocol with minimal instrumentation [3], apical sealing through apexification by means of hard tissue barrier induction with calcium hydroxide (CH) [1] or apical plug [4] and finally reinforcement of the thin dentinal walls [2].

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Although apexification with CH was claimed to be a successful procedure [5], it is time consuming and requires patient's cooperation. It has been estimated that 30% of the teeth that have undergone CH apexification fracture during/after long-term endodontic treatment [6]. Because of the special configuration of the immature apex (the apical diameter being larger than the coronal diameter), a softened filling technique is indicated in these teeth [2]. Placement of an apical plug and then backfilling of the canal during one or two visits, based on the symptoms and presence/absence of exudation/suppuration through the root canal space, has gained popularity among clinicians [7]. An ideal plug material should seal the pathway between the root canal space and the surrounding tissues. In addition, it needs to be nontoxic, biocompatible, insoluble in tissue fluids, and dimensionally stable [8]. Calcium-enriched mixture (CEM) cement is a tooth-colored water-based cement with a different chemical composition compared to mineral trioxide aggregate (MTA) and similar clinical applications [9]. It offers favorable sealing, antimicrobial properties similar to those of CH [10], hard tissue induction properties [11] and compared to MTA, it has shorter setting time, greater flowability and lower film thickness [12].

As a biologically-based treatment alternative for immature infected teeth with apical periodontitis, tissue regeneration within the root canal space is possible when the following criteria are met: proper canal disinfection, presence of a matrix into which the tissue can grow and adequate coronal seal [13,2]. There are several reports of successful regenerative endodontic procedures owing their outcome to proper infection control [14,15]. Different technique/methods of disinfection (mainly using CH or different antibiotic pastes) have been introduced. Under ideal circumstances, the successful outcome

is defined as healing of the periapical lesion, continuation of root development, and positive response to vitality tests [7,3,5]. Despite highly successful results, there are reports of lack of root development following treatment [16-18]. In addition, since the blood clot is being covered below the CEJ level in most of the cases, there would be no increase in root thickness in this critical area.

Recent retrospective studies on comparison of apical plug technique versus regenerative endodontic treatments have shown similar survival and success rates for both treatments [19,20]. Yet there is no well-designed prospective trial on comparison of these two treatment approaches. The purpose of this paper is to present and compare the outcome of apical plug technique vs. regenerative endodontic treatment in two non vital bilateral immature maxillary central incisors using CEM cement.

Case Report

A 12 year-old female referred with complain of a dull pain and slight swelling in the upper lip area. The medical history of the patient was non-contributory. During extraoral evaluation, the upper lip was tender to palpation. There was a localized swelling in the periapical area of the left central incisor. Both central incisors were sensitive to percussion and showed a grayish discoloration. The patient reported a history of impact trauma to her upper teeth 2 years earlier. The response to electric pulp test (Analytic Technology, Redmond, WA, USA) was negative. Cold test was done by using a cotton pellet and cold spray (Coltene/Whaledent, Inc., Mahwah, NJ, USA) in contact with the labial surfaces of the teeth. The response to the cold test on the left and right central incisors was also negative.

Periapical radiographs showed presence of separate radiolucent lesions on both maxillary central incisors (Figs 1a and 1b). Both teeth had immature roots with open apices. The final diagnosis was pulp necrosis with symptomatic apical periodontitis for the right central incisor, and pulp necrosis with acute apical abscess for the left central incisor. After explaining the condition of the teeth and possible treatment modalities, an informed consent was obtained from the patient's parent. Because of the urgent condition of the tooth, the treatment of left incisor was started first.

Treatment of the maxillary left central incisor

After local anesthesia with 2% lidocaine containing 1:80000 epinephrine (Darupakhsh, Tehran, Iran) and rubber dam isolation, an ideal access cavity was prepared. Upon entrance, a continuous drainage was noticed through the root canal space. The working length (WL) was determined radiographically. The canal was filled with 5.25% sodium hypochlorite (NaOCl) and was gently instrumented with hand files (Maillefer, Ballaigues, Switzerland). The exudate was flushed with intermittent use of NaOCl. CH powder (Golchay, Tehran, Iran) was mixed with 0.2% chlorhexidine gluconate (Behsa Co, Tehran, Iran) to a creamy consistency, which was carried into the canal using a lentulo spiral. Then the access cavity was temporarily sealed. There was a noticeable reduction in the size of swelling after removal of the rubber dam, therefore incision and drainage or systemic medication was not indicated. However the patient was informed that in case intensive pain or swelling she should refer to the office.

One week later, at the second appointment, the patient was asymptomatic. After local anesthesia and rubber dam isolation, the contents of the canal were irrigated with 5.25% NaOCl. After drying the canal with paper points (Ariadent, Tehran, Iran), the CEM cement powder and liquid (BioniqueDent, Tehran, Iran) were mixed according to the manufacturer's instructions. The mixture was carried into the canal and was gently condensed by means of hand pluggers (Dentsply Maillefer, Ballaigues, Switzerland). The quality of root canal filling with CEM was confirmed radiographically (Fig 1d) and the tooth was temporarily restored. The patient was referred to her general dentist for permanent restoration.

Treatment of the maxillary right central incisor

The process of local anesthesia, rubber-dam isolation, access cavity preparation, instrumentation and irrigation was done as previously explained. The triple antibiotic paste [similar doses of ciprofloxacin, metronidazole and minocycline (Exir Co. Tehran, Iran) mixed with saline as creamy paste] was carried into the canal. Care was taken to not touch the dentinal walls of the access cavity to prevent the discoloration. The access cavity was then sealed temporarily.

The second appointment was set three weeks later while the patient was asymptomatic. During this appointment, the canal contents were removed with concomitant NaOCl irrigation and gentle hand filling. After a flush with 5.25% NaOCl and then saline, a #20 sterile hand K-file was overextended and turned around to irritate the periapical tissues and induce bleeding. The bleeding was stopped below the CEJ. After 10 minutes, when the blood clot formed, CEM cement paste was prepared and gently carried into the canal below the CEJ level.

The CEM cement was covered with flowable composite resin and then the access cavity was restored with composite resin (Filtek Z-250, 3M Dental Products Division, St Paul, Minn., USA). A final periapical radiograph was taken (Fig 1c).

During first 24 months, both teeth were functional and symptom-free (Fig 1e, 1f, and 1g). At 3-year follow-up, normal PDL around the apices of both teeth was evident and the lesions completely healed (Fig 1h). In addition, the right central incisor showed an increase in root length/wall thickness and formation of the apex (Fig 1g). Clinically, no tooth discoloration was noted; however, the restorations had marginal discoloration (Fig 2a) and were successfully replaced (Fig 2b).

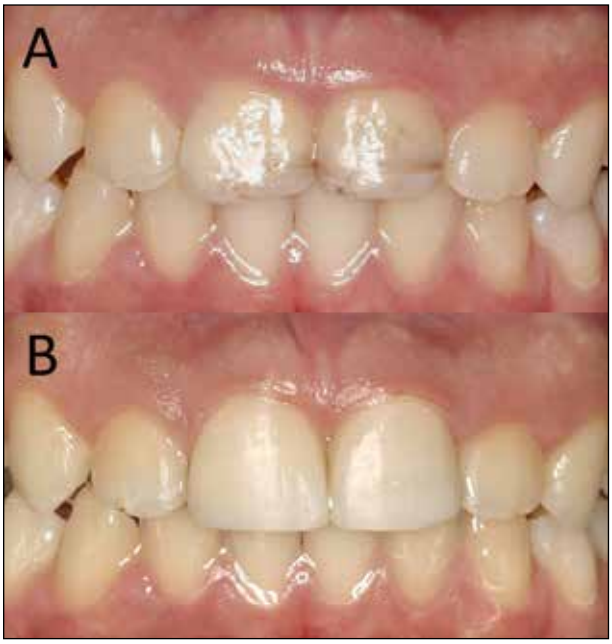
DISCUSSION

This report represented the outcome of treatment in two adjacent immature maxillary central incisors with apical periodontitis that were separately treated with pulp regeneration protocol and apical plug using CEM biomaterial. Three-year follow-up showed asymptomatic and functional teeth without discoloration and an increase in the root length of the right central incisor. For this case systemic antibiotic was not prescribed because antibiotic treatment is not recommended for healthy patients with localized infections [21]; systemic antibiotics should be considered in case of a spreading infection indicating the failure of local host response due compromised defense mechanisms [22,21].

The concept of pulp revascularization was first introduced as filling of the empty pulp space by tissues originating from the periapical area [23]. It was primarily accepted for immature avulsed teeth [24], were a combination of circumstances naming patent apical foramen and short root length, are present that allow re-growth

Figure 1 Pre-operative radiograph of the (A) right and (B) left central incisors. Note the immature roots and large periapical radiolucencies around the apices. (C) Tooth # 8 after sealing the blood clot with CEM cement. (D) Tooth # 9 after filling the canal with CEM cement. (E) One-year follow-up of regenerative endodontic treatment. (F) One-year follow-up of apical plug with CEM cement (G) Two-year follow-up; note the complete healing of periapical lesions and root development (increase in length and wall thickness and maturation of the apex) in tooth # 8. (H) Three-year follow-up; formation of normal PDL spaces is suggestive of normal intra-canal conditions

Figure 2 (A) three-year post-operative clinical photography of both central incisors; the tooth structure shows no discoloration but restorations are defective and represent marginal extrinsic stains (B) replacement of composite restorations



of the tissues into the necrotic -but not infected- pulp acting as a matrix; all these phenomena is supported by the intact crown which ensures the delay in bacterial penetration [13,2]. This treatment was deemed impossible for immature necrotic teeth until Iwaya [25] introduced the first case of revitalization in an immature premolar with necrotic pulp. Since then this concept gained acceptance and several successful treatments with variations in the protocol were reported in different studies. In clinical reports, procedure of canal disinfection in the first visit included irrigation with NaOCl or chlorhexidine in different concentrations [26-29]. Attempts for more disinfection included CH paste, triple antibiotic paste or addition of photodynamic therapy following canal irrigation [30,24,26,31]; some reports did not use the inter-appointment disinfection protocol and reported single-visit regeneration [27]. All reports have induced intracanal bleeding by irritating the periradicular tissues and almost all reports have used MTA for coronal sealing [30,28,26,24,32,27]. Only one report mentioned using CEM cement as the canal sealing biomaterial [29].

Radiographic root development and positive response to vitality tests are indicators of success in regenerative endodontic treatments [3]. Positive response to vitality tests is indicative of re-innervation of the tissues inside the canal. On the other hand, lack of response to vitality tests in the absence of other clinical/radiographic signs of failure should not be interpreted as failure of the treatment. Position of the sealing material (at the CEJ or below) might interfere with the results of the vitality tests. In the presented case, the upper right central incisor, which was treated with regenerative endodontic treatment, showed complete healing of the lesion with radiographic root development. The main advantage of regenerative endodontic treatment over apical plug technique is continued root development. Numerous clinical studies have been published showing the possibility of root development following pulpal necrosis in immature

teeth [16,29]. On the other hand, there are reports showing that root development might not be a predictable outcome for this treatment [18,17,16]. The rational is that a more developed root would be more resistant to future trauma, which indeed increases the longevity of the tooth. However, still there is no direct evidence showing that root development is correlated with longer survival. In almost all the cases, the blood clot (with/without a collagen scaffold) is controlled under the level of CEJ that leaves the CEJ area of the root narrow and still vulnerable to the future fracture. Follow-up of cases treated with regenerative endodontic treatment shows that the teeth are still susceptible to cervical fractures due to impact trauma or occlusal forces [33,34,19]. A retrospective study on the outcomes of immature necrotic teeth treated with CH apexification, MTA apical plug, or regenerative endodontic treatment, showed that while the lowest survival rate belonged to teeth treated with apexification, there was no difference between MTA apical plug and regenerative endodontic treatment [20]. Another retrospective study confirmed the absence of significant differences between the outcomes of regenerative endodontic treatments and MTA apical plug [19]. However, they reported significantly higher incidence of adverse events such as fracture, discoloration, and reinfection in the teeth treated with regenerative procedures. Although these retrospective studies show a significant increase in the root dimensions following regenerative treatments, the effect of this finding on the success and survival rate of the treated teeth is not clear. The presented case shows that patients with more than one immature necrotic tooth (a frequent finding in young patients with history of trauma) can be an appropriate model for potential prospective studies comparing regenerative endodontic treatments with apical plug technique.

The protocol of regenerative endodontic treatment using triple antibiotic paste for disinfection was first introduced by Banchs and Trope [13]. Since then, several studies have been published showing that this method of disinfection is being clinically and radiographically successful [15]. Absence of clinical signs of infection and osseous healing of the radiographic lesion is a common finding in these studies [17]. Compared to conventional root canal treatment procedures, a higher level of disinfection is required in regenerative endodontic treatments. Given the fact that microorganisms penetrate through more dentinal tubules and proceed deeper in younger individuals [35], disinfection of the root canal system in immature teeth could be another challenge. This issue becomes more challenging when *in vitro* studies show that triple antibiotic paste with the concentration of 1 gr/mL is extremely cytotoxic to the stem cells from apical papilla and can be a threat for pulp regeneration [36].

Experts are of the opinion that tissue regeneration in the root canal space may have some potential drawbacks. As a technical side effect, coronal discoloration can be associated with the use of triple antibiotic paste, with the minocycline content being the most important cause [37]. A change in the contents of antibiotic paste by replacing minocycline with doxycycline, amoxicillin and cefaclor did not prevent discoloration [38]. Single-visit regeneration without using the antibiotic paste has been advocated [32,27]. Also sealing of the dentinal walls of the access cavity by etching/bonding prior to placement of the triple antibiotic paste has been tried; although the discoloration was notably low but it was not eliminated [24]. This can be due to the discoloration potential of MTA [8] that causes cervical grayish hue [24,17]. CEM cement is a tooth-colored endodontic biomaterial and unlike MTA does not induce discoloration overtime. In one report, despite using the triple antibiotic paste in one tooth and CEM cement in both treated teeth, no discoloration was evident [29]. Conducting spectrophotometric analysis of discoloration potential of CEM biomaterial can provide more information about this fact.

The last but not least is the nature of in-growing tissue that fills the canal space. Probably the remaining vital pulp and/or apical papilla may exist in the canal spaces that regenerate the pulp after canal disinfection. If these tissues are both destroyed, periodontal tissues will fill the canal space [39]. In the lack of human studies, some histological animal evaluations have shown that the thickening of the canal walls and increase in the root length was due to deposition of cementum-like tissues that were accompanied by PDL like tissues and Sharpey's fibers. Moreover, intracanal bone-like tissues and survived pulp tissue accompanied by odontoblast cells lining the dentinal walls were found in the root canal space [39,40]. These findings raise doubts about "true pulp regeneration" following regenerative endodontic procedures.

CONCLUSIONS

Apexification by apical plug placement and pulp regeneration are both reliable treatments for immature non-vital teeth.

CEM cement can be successfully applied as an apical plug (in apexification treatments) or coronal barrier (in regenerative processes).

CEM cement causes much less discoloration when used as an apical plug or coronal barrier.

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