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Revascularization medicaments of the traumatized immature permanent incisor- A case report

***Abstract*—** Dental trauma to teeth in children often causes apical periodontitis and pulp necrosis in immature permanent teeth. Subsequently, it may lead to cessation of dentinal wall thickening and complete root development. This case report presents a revascularization therapy of the traumatized permanent upper left central incisor tooth in an 8-year-old boy. The tooth had suffered the traumatic injury about two months prior the first consultation that cause pulp necrosis and impede root development. Revascularization therapy was done onto his traumatized tooth. A sterile sodium chloride or normal saline was used solely as a canal disinfectant material and double antibiotic paste (DAP) as an intracanal medicament. Good radiographic and clinical outcomes were observed during the 12 months review since the beginning of the revascularization therapy. Considering the continuous root development and apical closed, it can be concluded that the sterile normal saline disinfectant and DAP as intracanal medicament serves a promising good outcome in an asymptomatic and immature necrotic permanent tooth.

***Keywords* — double antibiotic paste, open apex, pulp revascularization, sodium chloride**

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1 INTRODUCTION

Dental trauma involving hard tissues among children and teenagers possesses a great challenge to dental practitioners as they were often victims of falls, traffic accidents, aggression and collisions. Age and gender distribution indicated that most injuries occurred in the period between aged 13-19 years with the majority were male patients [1,2,3]. It has been reported that 35.6% of teeth with an immatured roots eventually developed pulp necrosis, compared to 64.3% in those with complete root development [4]. Secreted products of pathologic bacteria and biofilm is believed to have hindered mineralization process of apical papilla stem cells in developing a complete root [5]. During the early years of managing traumatic permanent teeth with immatured root, the aim of the endodontic treatment is to create an apical barrier through apexification procedure. The used of biocompatible Calcium Hydroxide ($Ca(OH)_2$) and Mineral Trioxide Aggregate (MTA) create an apical barrier for the immature root [6,7]. However, this conventional approach presents several treatment challenges throughout the procedure due to the thin and fragile state of the root canal wall [8,9]. Mechanical preparation from endodontic procedure will cause further weakening of the dentinal root wall that prone to root fracture in the long term [6]. Furthermore, the treatment itself will leave the root short with a fragile dentinal wall due to arrested root development and re-growth [10]. As an alternative, the recent regenerative endodontic therapy or also known as revascularization was proposed with the aim to create a revascularize episode of bleeding from the apical pulp region which form a blood clot that act as a 3-dimensional scaffold. Most of the literatures and clinical studies consistently address the important of scaffolds blood clot and their function to stimulate the residual stem cell in the pulp tissue. This stimulation will induce the formation of new dental hard tissue, thus enhance continuous root development [11,12,13,14,15].

This case report presents, a revascularization treatment of the traumatized immature permanent anterior tooth in a young boy. The tooth had suffered the trauma injury that cause pulp necrosis and impede root development. The canal disinfection was done with the use of sterile

sodium chloride as irrigation, instead of the commonly used sodium hypochlorite, followed by application of double antibiotic paste (DAP) as an intracanal medicament. Good radiographic and clinical outcomes were observed during the 12 months review since the commenced of the revascularization therapy.

2 CASE PRESENTATION

An 8-year-old boy presented to the paediatric dental clinic, Hospital Universiti Sains Malaysia with the complaint of a dislodged restoration on his upper anterior tooth. Parents claimed that the boy had a history of fractured tooth crown due to the unfortunate fall from the staircase about two months prior to this initial consultation. Further history revealed that he fell with his face facing downwards and he also sustained soft tissue injury of his upper lip. There was no history loss of consciousness or vomiting post fall. The tooth had a complete fractured leaving only one third of the cervical tooth crown and it was previously restored with the tooth coloured restoration at the other dental clinic.

However, there was no history of pain or swelling from that fractured tooth. A signed, written informed consent form was obtained from the parent for detail of examination and investigation. The upper left central incisor (UL1) showed complicated crown fracture involving about two-third of tooth crown height with pulp exposed (**Figure 1**). The tooth was firm and there was no sign of inflammatory reaction at the area including abscess or sinus. The fractured tooth was nontender on percussion and palpation. While upper right central incisor (UR1) tooth was intact. Patient's general oral hygiene was very good. The clinical diagnostic test such as electric pulp test and thermal test showed that the UL1 tooth was not responsive. Intraoral periapical radiograph showed an immature root with open apices on both UR1 and UL1 (**Figure 2**).

There was a widening of periodontal ligament and periapical radiolucency presented on UL1. The diagnosis made was immature root of non-vital UL1 tooth. Since patient was potentially cooperative, the revascularization therapy was suggested which aimed to regenerate the pulp tissue and regrowth of the root dentinal wall. Hence, to promote the apical root closure. An explanation regarding the revascularization therapy was discussed with parents and a written consent was obtained prior the procedure.

Figure 1: Anterior view shows complicated crown fracture with pulp expose of UL1.

Figure 2: Intraoral periapical radiograph shows open apices of UL1 and UR1, and periapical radiolucency (as shown by arrow).

3 REVASCULARIZATION PROCEDURES

The revascularization therapy was started after the consultation with the endodontist at the first visit. The UL1 was anaesthetized under 2% mepivacaine (Scandonest®2% L, Septodont, USA) with epinephrine (1:100,000) and isolated with a rubber dam. Access cavity preparation by using a diamond bur and a high-speed handpiece with copious sterile water. Root canal systems were slowly and carefully irrigated with 0.9% sodium chloride (B.Braun Med, Malaysia) up to the working length of 17mm which was based on radiographic estimated working length (**Figure 3**). Two type of antibiotic paste or so-called DAP which consist of a triturated ciprofloxacin 250 mg (Bayer,Malaysia) and Metronidazole 400mg(Biochemie, Malaysia) in the proportion of 1:1 mixed with distilled water to formulate 1000:1

mg/ml concentration in combination with 0.1ml of Propylene glycol (Admix International, Malaysia). A portion of 0.5 mg from the prepared paste was weigh in using analytical balances weight scale (Mettler Toledo, USA), and then applied into the clean and dried canal up to 3 mm short of the working length using a #4 Lentulo spiral RA 25mm, as shown in **Figure 4** (Dentsply Mailefer, Ballaigues, Switzerland).

Figure 3: Estimation of working length of using K-file size 30 up to 19 mm. Note the tip of K-file went about 2mm beyond the apical orifice as shown by arrow.

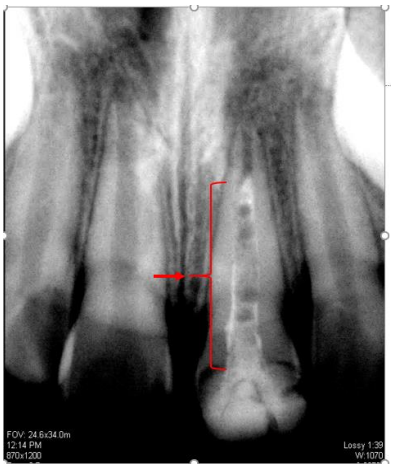

Figure 4: Intracanal DAP medicament. Note the inconsistency of canal filling.

The access cavity sealed with Cavitron (3M ESPE, Germany) before coronal of the crown was restored with Glass ionomer GIC Fuji IX (GC International, Japan). The paste was placed as an intracanal medicament for 14 days. During the review, revascularization therapy was continued by administrating the local anaesthesia using 2% mepivacaine (Scandonest®2% L, Septodont, USA) with epinephrine (1:100,000), then the UL1 was isolated under rubber dam. After canal re-accessment, it was re-irrigated thoroughly with 0.9% sodium chloride and 3 mL of 17% Ethylene Diamine Tetraacetic Acid (EDTA) (Meta Biomed, South Korea) in order to clean and remove remaining intracanal medicament and debris. The final canal irrigation was done using sodium chloride, then dried with paper points size #40. Different sizes of K-file were used to induce bleeding into the root canal, starting with the smallest size of #15 to the final size #55 (Denstply, Maillefer, Switzerland). The bleeding reach 3 mm below the cementoenamel junction and were left remained in situ for 30 minutes to allow blood clot formation. A 2mm depth of canal from the orifice opening was sealed with Mineral Trioxide Aggregate (ProRoot®MTA, Denstply Sirona, Canada). Endodontic hand plugger (SybronEndo,UK) size 2mm diameter was used for the application procedure. The whole procedure was performed under magnification 4.0x Dental Operating Microscope (Zeiss OPMI® pico, Germany). However, there were some of the MTA which excessively placed towards middle part of the canal. The remaining orifice canal space and access cavity was restored with Glass Ionomer Cement (GIC, Fuji IX) (GC International, Japan) and the final coronal structure with Zmack universal microhybrid composite moulded in a crown former (Zhermack SpA, Italy).

Patient was recalled for review on every first, third, sixth, ninth and twelve months for clinical and radiographic evaluation. During the assessment, the patient's clinical findings including the presence of pulp sensibility, spontaneous pain, tenderness, pain upon palpation, sinus tract, swelling, and crown discoloration were recorded. The radiographic examination performed by two clinicians including one endodontist to analyse the periapical lesion, root resorption, apical closure, root length, and root thickness. On the 12 months interval since the initial visit of revascularization therapy, the periapical lesion had subsided, and apical closure was noted on the periapical radiograph. Excessive MTA were also seen lining the root canal wall with part of canal sealed with GIC (**Figure 5**).

Figure 5: Apical closure of UL1 with some evident of radiopacity inside the canal (MTA plug and irregular dentin deposition) at 12 months review. Noted that no radiolucency at surrounding closed apical region. 2mm thickness of MTA in approximately 2mm depth from orifices canal, and an excessive flow of MTA (radiopacity) can be seen lining the wall.

4 DISCUSSION

The most common aetiologies of traumatic dental injury in children were fall, sport injury, assault and road traffic accident [2,3], with the most affected teeth were the upper central and lateral incisors followed by the lower central and lateral incisors [3]. Since the traumatic permanent teeth with incomplete root formation is commonly affected, it warrants a complicated endodontic treatment strategy. Revascularization therapy is a recent biologically based procedures designed by stimulation of existing stem and progenitor cells presents in a damaged and non-functioning pulp of the root canal system [16]. It was commenced by abiding some of inclusion and exclusion criteria's such as no tooth root or surrounding alveolar bone fracture [13] and based on the guideline protocol by International Association of Dental Traumatology [17].

The revascularization is aims to suppress the pathogenic microorganisms in the root canal systems and allow the vital pulp tissue healing. This promotes the continuous growth of an immature root by a formation of blood clot as a scaffold that establish a new vasculature system into the root canal [18,19]. A thorough and adequate disinfection plays a major contribution factors in the whole revascularization process. Continuous root development and thickness of dentinal wall are affected by the existing of remaining bacteria in the root canal systems [20]. Commonly, the revascularization treatment is started with a straight-line access cavity through the tooth crown until reach the pulp chamber, followed by the copious irrigation of Sodium hypochlorite (NaOCl) and application of triple antibiotic paste (TAP) which consists of mixture of ciprofloxacin 250 mg, metronidazole 400 mg, and minocycline 50 mg in the proportion of 1:1:1. The apical third received no treatment to preserve stem cells that might be present [13,14,15]. Once the infection is under control approximately after one to three weeks, the natural bleeding will be induced to obtain a fresh blood clot [21,22]. Bleeding will be initiated by mechanically irritated the apical area using sharp edge of endodontic k-Files [13,19].

Profuse bleeding will eventually fill the root canal systems to the level of cemento enamel junction (CEJ). Intracanal pressure at the CEJ by using a sterile cotton pellet soaked with sodium chloride will control the excessive blood profusion and thus form a clot throughout the root canal system. At least 3mm thickness of MTA cement is placed to cover the blood clot [14,18,22]. Autologous platelet concentrates such as platelet-rich-plasma(PRP), platelet-rich-fibrin (PRF) and platelet pellet have been used for the treatment, with the clinical and radiographic outcomes showed similar result compared to mechanically induced-blood clot scaffold [23,24,25,26]. Furthermore, collagen membrane has also been proven in promoting the vasculature progress during revascularization therapy [27].

In this present case report, our patient was presented with a very good hygiene and without any major complaint except for his aesthetic reason. The tooth had no sign of tenderness or abscess formation except for the non-vital condition and incomplete root formation. Revascularization therapy via blood clot scaffold was the best procedural option for our patient. Furthermore, patient was well cooperative and had high motivation for the treatment. Sterile 0.9% sodium chloride was purposedly chose to remove the debris and to keep apical stem cell as non-injured. A study had shown that there was lower incident of post treatment gingiva swelling and post-operative pain in root canal treated teeth using 0.9% sodium chloride as intracanal irrigant group, compared to sequential of 3% hydrogen peroxide, 5.2% NaOCl and 0.9% sodium chloride group [28]. Although the limitation of the latter study includes small sample size and short duration of post-treatment follow-up. Another recent recommendation is to use other common

desirable root canal irrigants such as 1-6% NaOCl, 2% chlorhexidine gluconate and 10% citric acid, whether as alone or in combination, in order to induce the release of many growth factors and promotes the dental pulp regeneration [29]. Majority of revascularization reported cases had choose NaOCl as the main canal irrigant [25,26,35,36,37,38], with variable of treatment outcomes.

Whereas disinfection protocol was achieved by DAP in the form of Ciprofloxacin + metronidazole 1:1 mixed with Propylene glycol which act as a vehicle for delivering antibiotic into the root canal systems. Mixture of antibiotic showed exothermic reaction was very granular and dry, therefore distilled water was added to overcome the problem. The addition of propylene glycol was to create a paste like concentration. Furthermore, it also has antimicrobial activity which provides sustained release for up to 7 – 14 days [30,31]. The clinical success of our case was based on criteria which defined successful outcome as a tooth that survive after a year with no sign of endodontic pathology including tenderness to percussion or palpation, a swelling or sinus tract or spontaneous pain [8]. It has comparable result with other clinical reports which use double antibiotic paste protocol during revascularization procedure [32,33,34].

Most of the literatures and clinical studies had found that, even though with different approach and materials, the outcome for revascularization therapy is still promising [22,25,26,32,35,36,37,38]. Different types of cases, material and their treatment outcome are summarized in **Table 1**.

Revascularization therapy promote bleeding into the root canal, which delivers undifferentiated mesenchymal stem cells in the root canal space. These cells are found in many sites of the dental element: in the pulp, in the apical papilla, and in the periodontal ligament [39,40]. The outcomes of root development and re-growth will depend on how effective the disinfection and the ability of the residual pulp and the apical and periodontal stem cells to differentiate [14]. The stem cells could generate a highly vascularized and a conjunctive rich living tissue and able to colonize the available pulp space. They will further differentiate into newly formed of odontoblasts and induce an apposition of hard tissue of the apical root development of immature teeth [41].

For this patient, yearly review has been recommended to exclude any sign of infection and non-vital tooth. Permanent crown restoration such as veneer, porcelain crown and porcelain fused metal crown has been suggested once the patient reached adulthood with possibility of growth completion.

Table 1: Revascularization therapy on immature permanent incisor with an open apex

Author	Age (in year)	Gender	Tooth	Clinical /Radiographic findings at initial consultation visit	Time interval from initial trauma	Materials	Duration of review	Outcome during last visit of review
Nagaveni et al. 2020 [25]	11	M	12	Fractured, discoloured, radiographically incompletely developed root with wide and open apex, thin dentinal walls, and wide root canal space with periapical radiolucency	24 weeks	5.25% NaOCl, ciprofloxacin + metronidazole + minocycline. Platelet Rich Fibrin. MTA	6-12 months	Root growth with complete apices closure
Nagaveni et al. 2020 [24]	11	M	22	Fractured, discoloured, radiographically incompletely developed root with wide and open apex, thin dentinal walls, and wide root canal space with periapical radiolucency	24 weeks	5.25% NaOCl, ciprofloxacin + metronidazole + minocycline. blood clot MTA	6-12 months	Root growth with complete apices closure
Arango-Gómez et al. 2019 [26]	9	M	11	Sinus tract and tender on percussion; radiographically multiple fracture lines at the cervical and middle levels of the root, an increase in the periodontal ligament space, a periradicular lesion, and inflammatory external root resorption	2 years	1.25% NaOCl, Amoxicillin (500 mg),metronidazole (500 mg), ciprofloxacin (500 mg) , Platelet rich plasma. MTA	48 months	Calcification in the apical and coronal fragments, no periapical pathology, displacement of the apical fragment of 21
Arango-Gómez et al. 2019 [26]	9	M	21	Sinus tract and tender on percussion; radiographically multiple fracture lines at the cervical and middle levels of the root, an increase in the periodontal ligament space, a periradicular lesion, and inflammatory external root resorption	2 years	1.25% NaOCl Amoxicillin (500 mg), metronidazole (500 mg), and ciprofloxacin (500 mg) Blood clot. MTA	48 months	Calcification in the apical and coronal fragments, no periapical pathology, displacement of the apical fragment of 21
John et al. 2019 [38]	10	M	21	fracture from the incisal third to the cervical of crown; Radiographically open apex	1 week	5.25% NaOCl + sodium chloride. ciprofloxacin, metronidazole, and minocycline (100 mg of each drug in 0.5 mL total volume, MTA	12 months	Asymptomatic and functional. Apical closure and dentinal wall thickening along with the attainment of root length
Nagata et al. 2015 [35]	8	M	21	Replanted avulsed, negative pulp test, external inflammatory resorption at the distal root surface	3 weeks	6% NaOCl + sterile sodium chloride + 2% chlorhexidine irrigation, 17% EDTA solution, MTA	16 months	Periapical bone healing, apical closure and calcification in the apical 4 mm of the root canal

Khoshkhouneja d et al. 2015 [36]	16	M	21	Crown fractured and luxation injury; immature root with a radiolucent periapical lesion	417 (8 years)	5.25% NaOCl + 0.2% Chlorhexidine ciprofloxacin + metronidazole+ doxycycline. MTA	6 years	Recurrence of pus discharge. No evidence of thickening of the canal walls or continuation of root development. Apexification using MTA apical plug commenced
Silva et al. 2015 [39]	6	M	11	Luxation injury; Swelling was present at the apical area of the tooth, which was symptomatic to percussion and palpation; incomplete root formation, an open apex, thin root canal walls and radiolucent area in the apical third	16 weeks	3% NaOCl, Calcium hydroxide paste MTA	36 months	Closed apex, root lengthened to the same size as that of tooth 21. Thickening of the root was not notable and radiopaque tissue partially filled the root canal space
Miltiadous & Florato, 2015 [37]	14	M	11	Intermittent pain upon biting , swelling at the buccal mucosa, discoloured crown, history of trauma 5 years back, crown fracture and pulp exposure, conventional root canal treatment was constructed. Radiographically revealed root canal filling, open apex, radiolucency	5 years	2.5% NaOCl, 500mg ciprofloxacin, 500mg metronidazole, 500mg amoxicillin. 17% EDTA, collagen membrane, MTA	36 months	Asymptomatic, functional, apical closure, negative response to cold test, no increase in the root length

Abbreviation: M, male; F, female; NaOCl, sodium hypochlorite; MTA, mineral trioxide; EDTA, Ethylenediaminetetraacetic acid

5 CONCLUSION

The protocol established for this treatment, including the use of initial canal irrigant such as sterile 0.9% sodium chloride, followed by DAP consisting of ciprofloxacin and metronidazole, seems potentially effective for eliminating bacteria in the root canal system and promote periapical healing. The placement of MTA to ensure an adequate coronal seal have been favourable for clinical success of this case. Therefore, it is concluded that this proposed revascularization treatment protocol may provide a satisfactory clinical and radiographic result in a non-symptomatic and non-vital immature permanent tooth. However, more clinical trials pertaining to variety of material and protocol are proposed to enhance significant treatment outcomes with satisfactory results.

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7 COMPETING INTEREST

The authors declare that they have no competing interests.

8 CONSENT FOR PUBLICATION

Written informed consent was granted by patient's parents, including for publication and figures taken.

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