Longitudinal Cohort Study of Regenerative Endodontic Treatment for Immature Necrotic Permanent Teeth

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Abstract

Introduction: The treatment of immature necrotic permanent teeth presents several clinical challenges in endodontics. Regenerative endodontic procedures (REPs) permit root development, increased canal wall thickness, and apical closure. This longitudinal cohort study aimed to evaluate the long-term clinical and radiographic outcomes of REPs of immature necrotic permanent teeth over a 30-month period. **Methods:** This study was performed at the Division of Dentistry of the Montreal Children's Hospital, Montreal, Quebec, Canada. Twenty-eight immature necrotic permanent teeth from 22 patients were included in this study. All teeth were treated with a standardized REP protocol. Patients had follow-up appointments at 1, 2, 3, 6, 12, 18, 24, and 30 months. At each appointment, signs and symptoms were evaluated. Radiographic evaluation was also performed by a calibrated endodontist in order to analyze different parameters. **Results:** Our results show a high survival rate (96.4%), clinical success (92.8%), and resolution of apical pathology (100%). Significant increases in the average root length (8.1%, $P < .0001$) and root thickness area (11.6%, $P = .03$) were observed after 30 months. In the study period, a significant decrease in the apical diameter was also noted, with 30.8% of the cases showing complete apical closure. Teeth with more immature stages of root development had a higher percentage of change in root thickness, length, and apical diameter; however, these results were not statistically significant. **Conclusions:** Teeth treated with REPs presented resolution of symptoms. Although clinical meaningful change was not achieved in all cases, increased root thickness, root length, and apical closure were observed at 30 months. *(J Endod 2016;■:1–6)*

Key Words

Immature teeth, prospective cohort study, regenerative endodontics, revascularization

Significance

This is the largest longitudinal cohort study with a standardized protocol that evaluated the outcomes of REPs over a 30-month period. REPs showed high clinical and radiographic success rates. Changes in apical diameter, root thickness, and length were observed.

Regenerative endodontic therapy or revascularization is a treatment modality to manage immature necrotic teeth. These teeth present several treatment challenges for the clinician; the wide canals and open apices render mechanical debridement and obturation for a conventional root canal treatment difficult (1). Alternative treatments include long-term apexification with calcium hydroxide or immediate apexification with the placement of an apical barrier like mineral trioxide aggregate (MTA); however, these techniques do not promote root development. Therefore, they maintain a poor crown-to-root ratio and thin walls, which may result in an increased risk of fractures and a compromised prognosis (1, 2).

Studies have shown that regenerative endodontic procedures (REPs) stimulate hard tissue formation, continued root development, and root structure strengthening (3–6). This technique relies on surviving stem cells from the Hertwig epithelial root sheath and stem cells from the apical papilla (SCAPs) along with growth factor release from the dentinal walls for continued root development (7). The goals of REP are to eliminate patient symptoms, encourage healing of the surrounding tissues, increase root length and thickness, and achieve a positive response to vitality testing (8). However, the literature available consists mostly of case reports and does not report long-term results (9). Thus, this longitudinal cohort study aimed to evaluate the long-term clinical and radiographic outcomes of REPs of immature necrotic permanent teeth over a 30-month period.

Methods

This project received approval from the Research Ethics Board of the McGill University Health Center, Montreal, Quebec, Canada. Children who presented to the Division of Dentistry at Montreal Children's Hospital with immature necrotic permanent teeth were recruited to participate in this study. Inclusion criteria consisted of the following:

1. Healthy subjects
2. The presence of 1 or more necrotic permanent teeth (negative vitality test [cold test] and the presence of necrotic tissue confirmed upon access)

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3. An open apex
4. A restorable tooth
5. A cooperative and compliant patient. Exclusion criteria included medically compromised patients or patients with allergies to the antibiotics required for the procedure

At the initial examination, the cause of necrosis, including traumatic injuries, dental caries, or morphologic anomalies, was noted. Additionally, the presence of pain, swelling, tenderness, sensibility to palpation or percussion, and response to cold test was recorded. A periapical radiograph assessed the presence or absence of periapical radiolucency, the length of the root, the width of the root walls, and the width of the opening of the apex. The stage of formation of the root was defined as 1 (<1/3 root length formation), 2 (<1/2 root length formation), 3 (<2/3 root formation), or 4 (root almost complete with an open apical foramen) (10). Stage 5 of root development (complete root formation and closed apical foramen) was not considered in this study.

REPs

Three operators performed REP using the standardized protocol described later. After the initial examination, informed consent was obtained. The tooth was anesthetized with 2% lidocaine with epinephrine 1:100,000 and isolated with a rubber dam. Access was established and the canal irrigated with 5.25% sodium hypochlorite without instrumentation. The working length was determined with a periapical radiograph taken with a file inserted into the canal for length confirmation. The canal was dried with paper points, and a triple antibiotic paste was inserted to or 1 mm short of the working length of the root canal with a Lentulo spiral. The paste consisted of 100 mg cefaclor powder, 500 mg ciprofloxacin, and 500 mg metronidazole mixed with a base of propylene glycol and macrogol. Cefaclor was used instead of minocycline following the recommendation of several authors (6, 11). Afterward, the tooth was temporarily obturated with Cavit (3M ESPE, Seefeld, Germany) and glass ionomer cement (GC Fuji IX; GP Corp, Tokyo, Japan).

Patients returned 2 to 6 weeks later. The resolution of infection and swelling and absence of pain were confirmed. Mepivacaine 3% without a vasoconstrictor was used; a rubber dam was placed, and the canal was reopened and irrigated with 5.25% sodium hypochlorite. The canal was then dried with paper points. Bleeding was induced into the canal space by overinstrumenting with a file 1–2 mm into the periapical tissues to allow the formation of a blood clot. To assist in MTA placement, an average of 2 mm of matrix (CollaPlug; Zimmer Inc, Carlsbad, CA) was placed into the blood clot formed 3 mm apical to the cementoenamel junction (CEJ); however, variations in quantity may have occurred accordingly with root canal size and shape. Then, 3 mm ProRoot MTA (Dentsply Tulsa Dental, Tulsa, OK) was placed and covered with a wet cotton pellet and Cavit. One week later, the temporary restoration was removed and replaced with a final composite restoration over a glass ionomer base.

Patients had follow-up appointments at 1, 2, 3, 6, 12, 18, 24, and 30 months. At each appointment, clinical examination was performed to evaluate soft tissue swelling, probing depth, mobility, tenderness to percussion and palpation, and response to vitality test (cold test [Endo-Ice with a cotton pellet {Coltene/Whaledent Inc, Cuyahoga Falls, OH}]). A periapical radiograph was also taken.

Radiographic Analysis

Preoperative and postoperative radiographs were compared using ImageJ software (version 1.48; National Institutes of Health, Bethesda, MD) with the TurboReg (Biomedical Imaging Group, Swiss Federal Institute of Technology, Lausanne, VD, Switzerland) plug-in to correct for different angulations and minor distortions (12). One endodontist (M.C.) was designated to evaluate preoperative and postoperative study radiographs. The calibration of the examiner (M.C.) was performed on 25 selected radiographs of REP typical cases. An intraexaminer and interexaminer agreement of 95% was necessary before the beginning of evaluation. All radiographs were analyzed for the following parameters:

1. Root thickness, measured as the radiographic root area (RRA) as described by Flake et al (13)
2. Root length (perpendicular straight line from the CEJ to the radiographic apex of the tooth)
3. Apical closure (stage of maturation of the tooth) (10)
4. Resolution of periapical pathology
5. MTA placement from CEJ
6. MTA thickness and density

Clinical success was defined as the absence of any signs or symptoms (pain, swelling, sinus tract, tenderness to palpation or percussion, normal tooth mobility, or probing depth <3 mm) after REP. Also, the absence of radiographic pathosis (radiolucency or resorption) and/or bony healing had to be observed. Discoloration was noted but not considered in the criteria for success or failure. Survival was defined as retention of the tooth after REP, whereas a tooth that was extracted was considered as a failure.

Statistical Analysis

Descriptive analyses including mean and standard deviations were performed for all variables. Patients' demographic and clinical characteristics were expressed as frequencies and percentages. The repeated measures analysis of variance (ANOVA) test was used to test for significant changes in root length, thickness of canal walls, and apical closure at the baseline versus the 30-month follow-up. Associations between stage of root development and radiographic outcomes were assessed using the Mann-Whitney *U* test. Statistical significance was based on probability values $\leq .05$. All statistical analyses were conducted using Statistical Package for Social Sciences software (version 21.0; SPSS, Chicago, IL).

Results

Baseline Study Population Characteristics

Twenty-eight immature necrotic permanent teeth were included in this study. The demographic and clinical characteristics of the study population are outlined in Table 1. In this population, about half of the subjects were male (54.5%), and the average age was 9 years old. The majority of teeth treated were central incisors (75%), and the principal cause of tooth necrosis was traumatic injury (78%). The majority of the cases initially presented with a radiographic periapical radiolucency (75%) and symptoms of an abscess or cellulitis (57.1%). The average follow-up time was 30 months.

Clinical Outcomes

The survival rate of 96.4% (27/28) for a mean follow-up period of 30 months was observed; 1 tooth needing further treatment was extracted because of financial reasons. This study showed a clinical success rate of 92.8% (26/28); another tooth required further treatment (MTA apexification) because of the recurrence of symptoms. The only adverse event noted was discoloration, which was observed in more than half of the cases (57.1%, 16/28). All cases of discoloration occurred in teeth with a history of traumatic injury. During the follow-up period, vitality tests (cold and electric pulp tests) were performed at several occasions, and none of the teeth recuperated pulpal sensitivity.