A Retrospective Case Series in Regenerative Endodontics: Trend Analysis Based on Clinical Evaluation and 2- and 3-dimensional Radiology

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Abstract

Introduction: A regenerative endodontic procedure (REP) is a biologically based treatment to functionally replace the pulp of infected immature permanent teeth. The purpose of this retrospective case series was to assess the outcome of REPs of infected immature permanent teeth in terms of periapical bone healing (PBH), root development (RD), and pulp vitality. **Methods:** Five patients (1 tooth/patient) who had undergone a REP based on the cell homing concept were recalled 3, 6, 12, 24, and 36 months postoperatively. At each recall session, clinical and periapical radiographic (PR) investigations were performed. Cone-beam computed tomographic (CBCT) imaging was taken before and 36 months after REPs. Qualitative and quantitative PR assessments were performed on the teeth that underwent REPs. Quantitative CBCT analyses were performed on the teeth that underwent REP and contralateral teeth. **Results:** At each recall session, all teeth were asymptomatic but reacted negatively on carbon dioxide snow and electrical pulp testing. All teeth that underwent a REP showed complete PBH and further RD on PR and CBCT assessments when comparing the baseline with the final recall radiographs. CBCT analyses indicated increases in root hard tissue volume and RL for all teeth that underwent a REP, but they were 5 and 3 times less, respectively, than the contralateral teeth. The postoperative CBCT images presented bone ingrowth inside the root canal, calcification, or nonuniform RD. **Conclusions:** Thirty-six months after the REPs (based on the cell homing concept), this RCS resulted radiographically and clinically in functional and asymptomatic teeth with complete PBH and continued reparative RD. CBCT quantitative measurements and qualitative root development observations are more reliable and accurate than PR analysis. *(J Endod 2018;44:1517–1525)*

Key Words

Cone-beam computed tomography, dental infection, dental pulp, outcome assessment, stem cells

Significance

PR and CBCT analyses of this REP RCS resulted quantitatively in complete PBH and an overall gain in root hard tissue. Qualitatively, the REP outcome was nonuniform and unpredictable. Until 5 years after the REPs, the teeth remained functional and symptomless.

Immature permanent teeth mainly develop by means of (stem) cell differentiation and proliferation (1). During root development, the pulp of these fragile teeth might become necrotic because of dental trauma, anatomic anomalies, or decay (2). To treat teeth with open apices, an apical barrier at the root end can be induced or placed after disinfection, also denoted as apexification (3). Alternatively, a biologically based treatment known as a regenerative endodontic procedure (REP) has been proposed (4). This treatment option is based on root canal revascularization described in the 1960s (5) but currently relies on the 4 pillars of tissue engineering: stem cells, scaffolds, growth factors, and a sterile environment. Although root canal walls of "apexified" teeth remain thin and thus prone to cervical root fracture (6), REPs were introduced to replace the necrotic pulp by chemotaxis (cell homing principle) or transplantation (cell-based concept) of mesenchymal stem cells (2) in order to allow continued root development. However, because of several hurdles (7) implicated in the cell-based concept, the cell homing approach is the most clinically applied, and treatment protocols have been described worldwide to promote standardization (8, 9). High survival and success rates for REPs have been reported by numerous case reports, case series, and comparative clinical trials; nevertheless, systematic reviews claim a lack of high-level clinical trials (10, 11). One of the major drawbacks is the level of accuracy in the assessment of REP-treated teeth because generally patients are younger than 12 years of age. Obtaining accurate answers on clinical tests applied on partly erupted traumatized teeth and routinely taking aligned intraoral periapical radiographs in a growing

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dentition are often challenging. Although efforts have been made to correct distortions in 2-dimensional (2D) radiographic image assessment (12), the gold standard method (histology) questions if further root development is of a regenerative nature (13). This leads us to 3-dimensional (3D) radiography, which is much closer to histology. The application of cone-beam computed tomographic (CBCT) imaging has proven to be a valuable tool in REP assessment (14). Attempts to keep the radiation dose low in a controlled manner and without resolution loss have been fruitful (15). Skepticism and uncertainty toward this novel treatment option are present among the endodontic community (16). Therefore, more accurate assessment might suggest realism instead.

Case series are the least methodologically robust study designs and cannot be used to draw conclusions regarding treatment effect. Yet, a careful approach to report data on patients meeting the necessary inclusion criteria to receive a specific treatment protocol can provide valuable information, including case definition, trend analysis regarding outcomes, and clues to causation (17). Because there are limited data in the literature on this topic, the aim of the present study was to assess the outcome of REPs of infected immature permanent teeth (IIPT) in terms of periapical bone healing (PBH), root development (RD), and pulp vitality.

Materials and Methods

Study Design

This study was designed as a retrospective case series (RCS) and was conducted according to the principles of the 1996 Declaration of Helsinki on good clinical practice standards and with the approval of the Medical Ethics Committee of the UZ/KU Leuven, Leuven, Belgium (registration number: S58069). This article was written according to The CAse REport (CARE) Checklist of 2013 (English, 2016 revisions) (18).

Study Setting and Eligibility Criteria

A series of consecutive patients who had a REP on an IIPT by the same operator (N.M.) between August 1, 2009, and July 31, 2012, at the University Hospitals of Leuven, Leuven, Belgium, were included. Any of the following was regarded as a criterion for exclusion from the study: current malignancy or metabolic bone disease and a history of chemotherapy or radiation in the head and neck within 5 years before the study.

Intervention

The first session involved diagnosis and treatment planning. Clinical tests were performed, namely cold testing with carbon dioxide snow (CDS), electric pulp testing (EPT) with the Pulppen DP2000 Digital (Dental Electronic, Ballerup, Denmark), percussion, discoloration, and periodontal condition (pocket depth and mobility) assessment. A periapical radiograph (Digora and Minray; Soredex, Tuusula, Finland) and CBCT imaging (Accuitomo; J Morita, Osaka, Japan) were taken preoperatively followed by treatment planning. Subsequently, the first REP session was based on a modified version of Banchs and Trope (4). Local anesthetic with adrenaline was administered, and the tooth was isolated with a rubber dam. An endodontic access cavity was made, and the root canal was disinfected with sodium hypochlorite (30 mL, 2.5%). After drying the root canal with sterile paper points, a double antibiotic paste (ciprofloxacin 200 mg, metronidazole 500 mg, macrogel ointment, and propylene glycol) was injected into the root canal, and the tooth was temporarily sealed with glass ionomer cement (GIC). Two to 4 weeks later, the second REP session took place. Local anesthetic without vasoconstrictor was administered, and the tooth was isolated with a rubber dam. GIC was removed, and the root canal was again disinfected with sodium hypochlorite (20 mL, 2.5%) and subsequently with EDTA (5 mL, 17%). Blood was triggered periapically into the root canal until the cementoenamel junction (CEJ). A sterile biodegradable bovine collagen plug (CollaPlug; Zimmer Biomet, Warsaw, IN) was placed on the blood clot to serve as a scaffold for mineral trioxide aggregate (MTA) (white MTA [ProRoot; Dentsply Sirona, Ballaigues, Switzerland]), after which the tooth was sealed with a GIC liner and composite.

Participant Time Line and Outcomes

The patients were recalled at 3, 6, 12, 24, and 36 months after REP. At each recall session, clinical tests (as described previously) were performed by N.M. to assess pulp sensitivity. A periapical radiograph was taken at each recall session to assess the amount of PBH (primary outcome variable) and RD (secondary outcome variable). CBCT imaging (Accuitomo) was taken 3 years posttreatment to perform volumetric assessment of PBH and continued RD (other outcome variables).

Radiologic Analysis

2D Analysis. Two blinded assessors (M.E. and A.E.T.G.) performed the radiographic assessment. The periapical radiographs were encoded by N.M. so that the assessors were also blinded regarding the time point at which the radiographs were taken. The radiographs were aligned with a dedicated tool created in MeVisLab (MeVis Research, Bremen, Germany) for image registration, and the periapical lesions were outlined and quantified with ImageJ software (National Institutes of Health, Bethesda, MD). Additionally, the full-scale periapical index (19) was used to assess PBH qualitatively. Furthermore, the type of healing responses in IIPT with necrotic pulp tissue and apical periodontitis/abscess to REPs was assessed

TABLE 1. Case-specific Items of the 5 Included Teeth Treated with a Regenerative Endodontic Procedure (REP)

Case number	Sex and age	Tooth	Signs/symptoms	Pulpal status	Etiology	Periapical lesion	Follow-up (mo)
1	F, 8 y	Maxillary left lateral incisor	Vestibular fistula	Necrosis	Oehlers' type 2 invagination	Yes	42
2	F, 11 y	Maxillary left central incisor	Vestibular abscess and pain	Necrosis	Dental trauma	Yes	36
3	M, 8 y	Maxillary left central incisor	Lingering cold sensibility	Inflammation	Dental trauma	Yes	45
4	F, 6 y	Maxillary left central incisor	Vestibular abscess and pain	Necrosis	Dental trauma	Yes	45
5	M, 8 y	Maxillary right central incisor	Vestibular abscess and pain	Necrosis	Dental trauma	Yes	23

F, female; M, male.