Use of Platelet-rich Plasma in Endodontic Procedures in Adults: Regeneration or Repair? A Report of 3 Cases with 5 Years of Follow-up



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Abstract

Introduction: Regenerative endodontic procedures (REP) are a promising alternative for necrotic immature teeth in adolescents and children, but very little evidence is available on this alternative in long-lasting necrotic teeth with open apices in adults. REPs are designed to replace damaged structures of the pulpdentin complex, but no regeneration has been obtained in any of the cases described in necrotic immature permanent teeth with apical periodontitis with histologic results. The results are limited to periapical tissue repair with increasing root length, thickening of the root walls, and apical closure in young patients. In this series of cases, we report on the outcomes of the adjuvant use of autologous platelet-rich plasma (PRP) in endodontic therapy in adults by monitoring periapical tissue healing with periodic periapical radiographs and cone-beam computed tomographic scanning. Methods: Three teeth with apical periodontitis and open apices in 3 different patients from 21 to 35 years-old were evaluated. An REP was performed with the adjuvant use of PRP. Results: At controls, complete disappearance of the radiolucent lesions and the presence of calcified structures forming bridges occupying the pulp lumen were observed but not an ostensible thickening of root walls with a regeneration of pulp-dentin complex. Conclusions: The repair of periapical tissues with REPs of open apex teeth with apical periodontitis and in nonsurgical endodontic retreatment appears to be feasible in adults, but no regeneration was obtained in any of the present cases. The use of PRP may be a good choice as an autologous matrix because of its stability and induction; it contains growth factors and bioactive molecules like transforming growth factor beta, bone morphogenic proteins, insulinlike growth factors, and angiogenetic growth factors, which stimulate collagen production, angiogenesis, and cell differentiation. Anti-inflammatory and antibacterial properties have also been reported for this preparation, which are involved in all processes of repair. (*J Endod 2017;43:1294–1301*)

Key Words

Adult regenerative endodontic procedure, apical periodontitis, open apex necrotic tooth, plasma-rich growth factors

Early dental trauma to immature teeth can result in a loss of neurovascular supply, leading to pulp necrosis, interruption of rhizogenesis, and subsequent formation of

Significance

Endodontic therapy with PRP of necrotic teeth with open apices and apical periodontitis appears to be predictable at a 5-year follow-up and a good option in adults.

periapical lesions. The management of necrotic immature teeth with open apices has been performed classically using apexification with long-term application of calcium hydroxide (1). More recently, root-end barriers with mineral trioxide aggregate (MTA) have shown predictable clinical results (2). However, the difficulty in obtaining the apical stop as well as failure in the continuity of root development and the increased risk of subsequent fracture during or after treatment (77% in teeth with the least developed roots for calcium hydroxide apexification) make the retention of these teeth difficult (3).

Regenerative endodontic procedures (REPs) are designed to replace damaged structures including dentin and root structures as well as cells of the pulp-dentin complex (4). REPs follow the basic principles of tissue regeneration, being a more conservative and biological endodontic treatment. The ultimate goal of REPs is the regeneration of tooth pulp based on 3 pillars: the source of stem cells (genesis), the supply of growth factors (induction), and the presence of a scaffold (conduction) (5). No regeneration of the dentin-pulp complex has been obtained in any of the cases

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Copyright © 2017 American Association of Endodontists. http://dx.doi.org/10.1016/j.joen.2017.04.010 described with histologic results in immature permanent necrotic teeth with apical periodontitis. Despite this, REPs provide 3 advantages over traditional methods of apexification: they promote root development and increase root length, they allow thickening of the root dentinal walls, and they provide apical closure (6,7).

Disinfection of the root canal using calcium hydroxide and antibiotic pastes (8-10), obtaining a biological scaffold with bleeding into the canal, and sealing with a biocompatible material seem to be the main methods to produce the necessary environment for the success of REPs (6). To achieve vascularization of a necrotic tooth with an open apex with a diameter <1 mm may require instrumentation to approximately 1-2 mm to allow bleeding into the root canal system and thus obtain a greater likelihood of repair (4).

Despite this, sometimes it is difficult to generate the blood clot; the use of autologous growth factors and a matrix may offer an alternative that is worth investigating. Platelet-rich plasma (PRP) is an autologous scaffold that is obtained by platelet activation and fibrinogen polymerization. Several studies have shown the capacity of this preparation to stimulate collagen production, angiogenesis, and cell differentiation, and anti-inflammatory and antibacterial properties have also been reported for this preparation (11–13).

Most of the cases that reported using REPs have been limited to patients aged 8–16 years (14). This series of cases describes the technique and long-term outcome of the adjuvant use of PRP in endodontic therapy on teeth with pulp necrosis and apical periodontitis in adult patients to show that this therapy is effective in the repair and formation of mineralized tissue in open apex teeth in adults.

Case Reports

Case 1

A 35-year-old white female patient presented to the University of Barcelona Dental Hospital, Barcelona, Spain, complaining of dental pain and discomfort of 2 weeks' duration. The signs and symptoms were related to the maxillary left central incisor. Her medical history was not relevant. The patient reported a traumatic injury when she was 8 years old, but she did not remember what kind of injury; there was no history of pain or discomfort until 2 weeks before attending the clinic. Clinical examination revealed a discolored left maxillary central incisor and an intraoral sinus draining buccally. Percussion and cold vitality tests (Endo Ice; Coltène/Whaledent Inc, Cuyahoga Falls, OH) were negative. Periodontal probing performed using a periodontal probe (CP-12; Hu-Friedy, Chicago, IL) was normal. A periapical radiograph using the paralleling technique revealed incomplete root development, thin dentinal walls, and an open apex, corresponding to Nolla's ninth stage of root development. A radiolucent periapical lesion $(3 \times 3 \text{ mm})$ was also evident (Fig. 1A). The clinical and radiographic examinations were sufficiently obvious, and a diagnosis of pulp necrosis and chronic apical abscess was established.

Taking into account that the tooth exhibited an open apex, an REP with autologous PRP was considered for treatment. The patient agreed, and written informed consent was obtained.

At the first appointment, after placing a rubber dam, adequate access to the pulp cavity was obtained without administration of a local anesthetic. Drainage of hemorrhagic and purulent exudates was then performed. The root canal was irrigated with 10 mL 5.25% sodium hypochlorite (NaOCl) using Endo-Eze Irrigator Tips (Ultradent, South Jordan, UT) without instrumentation, and the canal was dried using sterile paper points. An approximation of the working length was determined with an apex locator (Root ZX; Morita, Tokyo, Japan) using a #15 K-file. The working length was confirmed using a periapical radiograph. Then, minimal mechanical instrumentation was performed 2 mm above

the apex with an ISO #70 H-file and copious irrigation with 5.25% NaOCl solution. After drying the canal, a triantibiotic paste (TAP) (metronidazole 250 mg, ciprofloxacin 250 mg, and minocycline 100 mg), obtained after mixing with sterile water until a creamy paste was generated, was introduced into the canal using a #1 Buchanan hand plugger (SybronEndo, Orange, CA) and paper points up to the apex. The access cavity was temporarily restored with 3 mm Cavit (3M ESPE, Seefeld, Germany).

At the second appointment 2 weeks later, the patient remained asymptomatic, and the intraoral sinus draining had disappeared. Local anesthesia was administered with 3% mepivacaine without a vasoconstrictor (Scandinibsa 3%; Laboratorios Inibsa SA, Lliçà de Vall, Barcelona, Spain). The root canal was accessed and irrigated with sterile saline to remove the TAP. The canal was then washed with 5.25% NaOCl solution that remained in the root canal for 10 minutes (renewing every 5 minutes). Then, a final irrigation with sterile saline was performed again. The canal was dried, and a #25 K-file was introduced until the bone to provoke bleeding from the periapical tissue into the pulp chamber.

PRP (PRGF-Endoret; BTI Biotechnology Institute SL, Vitoria, Spain) was prepared according to the instructions of the manufacturer. Briefly, 18 mL peripheral blood was extracted by venipuncture into two 9-mL extraction tubes containing 3.8% sodium citrate as anticoagulant (BTI Biotechnology Institute SL). The tubes were centrifuged at 580 g for 8 minutes at room temperature using a BTI System centrifuge (BTI Biotechnology Institute SL). Then, the plasma column was divided into 2 fractions: fraction 2 (F2) was defined as the 2 mL plasma just above the buffy coat, and fraction 1 (F1) was defined as the plasma column above the F2. This gave a total of 4 mL F2, and the volume of F1 depended on the hematocrit value of the patient. At that point, the PRP was used in the REP as follows. First, 1 mL F2 without activation was injected into the apical third of the root canal using a sterile syringe. The remaining 3 mL F2 was gently poured in a sterile glass container and activated by adding 150 μ L 10% calcium chloride solution; the latter triggered the formation of a 3-dimensional fibrin clot and the release of growth factors and proteins by autologous platelets. The obtained clot of F2 was used to fill the apical third of the root canal, extruding it through the apical foramen to the periapical tissues. In addition, the activated F1 fraction, maintained at 37°C to obtain a hemostatic and elastic fibrin membrane, was placed over the F2 clot to 3 mm below the cementoenamel junction.

Mineral trioxide aggregate (MTA) (Dentsply Tulsa Dental, Johnson City, TN) was mixed with saline solution and placed on top of the PRP to 1 mm below the cementoenamel junction to prevent the staining of the crown from worsening. The consistency of the F1 fibrin membrane allowed us to place the MTA safely and to control the level at which it was placed. A moistened cotton pellet was positioned in the pulp chamber, and then a provisional restoration with 3 mm Cavit was placed to seal the access cavity. A postoperative radiogram was taken (Fig. 1B).

After 1 week, the tooth was asymptomatic. A protocol of internal bleaching was initiated, and the final restoration was performed using an adhesive composite. Esthetic restoration was performed after the last control at 50 months because the patient did not want to do it earlier.

Follow-up visits were then scheduled after 1, 2, 6, 12, 24, 36, and 50 months of treatment. The patient remained asymptomatic and exhibited negative percussion, palpation, and thermal tests. At radiographic controls, the widening of the walls and the reduction of periapical radiolucency were not clear; for this reason, cone-beam computed tomographic (CBCT) imaging was obtained at the 36-month appointment, revealing the presence of periapical radiolucency and the loss of vestibular cortical bone in the root apical third. The apex remained

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