Efficacy of Platelet-rich Plasma as a Scaffold in Regenerative Endodontic Treatment

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Abstract

Introduction: Current research is concerned with discovering better scaffolds for use in regenerative endodontic treatment. This study aimed to clinically and radiographically evaluate the efficacy of platelet-rich plasma (PRP) used as a scaffold in regenerative endodontic treatment and compare it with that of a conventional blood clot (BC) scaffold. Methods: A total of 20 necrotic, single-rooted immature teeth were randomly distributed into 2 groups. After disinfecting the root canal space with triple antibiotic paste (1:1:1 ciprofloxacin, metronidazole, and cefaclor), a tissue scaffold was created by using either PRP or BC and covered with white mineral trioxide aggregate. Clinical and radiographic follow-up examinations were performed once every 3 months during an 18-month period. Differences in root area were calculated from preoperative and postoperative radiographs. Fisher exact and Mann-Whitney U tests were used to evaluate differences between groups, with P value <.05 considered to be statistically significant. Results: All 20 teeth were clinically asymptomatic during 18-month follow-up period; however, 1 tooth in the BC group exhibited periapical pathosis and was judged radiographically unsuccessful. Complete apical closure was observed in a mean of 8.1 months in the PRP group compared with 9 months in the BC group. The PRP group exhibited 9.86% increase in root area, compared with 12.6% in the BC group. The difference in success rates between the groups was not statistically significant (P > .05). Conclusions: PRP successfully created a scaffold for regenerative endodontic treatment; however, treatment outcomes did not differ significantly between PRP and conventional BC scaffold. (J Endod 2015;41:36–44)

Key Words

Blood clot, immature teeth, platelet-rich plasma, regenerative endodontic treatment

Materials and Methods

A total of 22 teeth in 20 children (8 girls, 12 boys) aged 7–13 years (mean age, 9.95 years) were initially selected from among patients attending the pediatric dentistry clinic. Each child had at least 1 necrotic, immature, single-rooted tooth requiring root canal treatment. None of the teeth had been previously treated for necrosis. All children were healthy and cooperative. After receiving ethical approval from the Institutional Review Board, the risks and possible outcomes of RET, as well as subsequent treatment in case of failure, were explained to parents, who gave their informed consent for their children’s participation in the study.

Inclusion criteria for teeth were as follows:

1. Pulp necrosis, with or without periapical lesions
2. Possibility of restoration
3. No root fracture, ankylosis, pathologic mobility, or probing depths >3 mm (2, 7)
Pulp necrosis was tentatively diagnosed by dental history and clinical examination, which included electric pulp testing (Digitest, Parkell, NY) and cold stimulation testing (Chloraethyl, Wehr Baden, Germany). Clinical signs and symptoms such as pain, swelling, fistula, and sensitivity to percussion and palpation were also noted. Teeth with periapical lesions were grouped according to the size of the lesion as follows:

Size 1: Lesion in the apical region only
Size 2: Lesion involving one third to one half of the root
Size 3: Lesion involving more than one half of the root

**Treatment Procedures**

Teeth were randomly distributed between the 2 treatment groups by assigning each tooth a number and then assigning all odd-numbered teeth to the PRP group ($n = 11$) and all even-numbered teeth to the BC group ($n = 11$). All treatment was performed by the same pediatric dentist.

RET was performed according to the American Association of Endodontists’ protocol described below. Local anesthesia was administered (2% lidocaine with 1:100,000 adrenaline), teeth were isolated with a rubber dam, the pulp chamber was accessed, and the working length was determined by using a size 20 sterile K-file. The diagnosis of total pulp necrosis was confirmed while determining the working length, with 1 tooth assigned to the PRP group that showed sensitivity in the apical third of the root canal rediagnosed as having partial necrosis and excluded from the study. Canals were not instrumented but were irrigated copiously with 2.5% NaOCl (20 mL), sterile saline (20 mL), and 0.12% chlorhexidine (10 mL) and dried with sterile paper points. After sealing the pulp chamber with a dentin bonding agent to minimize

**TABLE 1.** Interexaminer and Intraexaminer Kappa Values for Preoperative Lesion Size, Bony Healing, and Apical Closure

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<th>Lesion Size</th>
<th>Kappa</th>
<th>P value</th>
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**Figure 1.** (A) Concentrated PRP application to the root canal. (B) Photograph showing MTA placement.

**Figure 2.** (A) Outlining of total root area in preoperative radiograph. (B) Outlining of canal space in preoperative radiograph. (C) Outlining of total root area in 18-month follow-up radiograph. (D) Outlining of canal space in 18-month follow-up radiograph.
the risk of staining, equal proportions of metronidazole (Flagyl; Eczacıbaşı Inc Co, Istanbul, Turkey), ciprofloxacin (Cipro; Biofarma Inc Co, Istanbul, Turkey), and cefaclor (Sanocef; Sanovel Inc Co, Istanbul, Turkey) were ground to a powder and mixed with distilled water into a creamy paste that was placed in the canal below the cemento-enamel junction (CEJ) by using a lentulo spiral in a slow-speed handpiece. Canals were sealed with cotton pellets and reinforced with zinc oxide–eugenol cement (IRM; Dentsply, Milford, DE). Patients were recalled after 3 weeks, and in cases of persistent signs of infection (ie, purulent drainage, failure to resolve pain, swelling, fistula, and sensitivity to percussion and palpation), triple antibiotic dressing was applied again.

In the following visit, teeth were re-accessed under a rubber dam, the antibiotic paste was removed by rinsing with a solution of 5% EDTA (20 mL) and sterile saline (20 mL), canals were dried with sterile paper points, and scaffolds were created according to the assigned group. Because PRP application involves no dental pain, no anesthetic was applied in the PRP group. PRP was prepared according to Dohan et al (23). Coagulation was achieved by combining PRP with equal volumes of sterile saline solution containing 10% calcium chloride and sterile bovine thrombin (100 U/mL). The PRP mixture was injected into the canal space up to the level of the CEJ and allowed to clot for 10 minutes (Fig. 1A). Final restoration was completed with white MTA (Angelus, Londrina, Brazil) prepared according to the manufacturer’s instructions (Fig. 1B), reinforced glass ionomer cement (Ketac Molar Easymix; 3M ESPE, Seefeld, Germany), and composite resin (Filtek Supreme XT; 3M ESPE, St Paul, MN) during the same visit.

In the BC group, an adrenaline-free local anesthetic solution (Citanest; AstraZeneca, London, UK) was applied, and a size #20 K-file was used to evoke bleeding in the root canal. Once bleeding reached the level of the CEJ, the tooth was allowed 10 minutes to form a blood clot, and the final restoration was completed as described above for the PRP group. Bleeding could not be achieved in the root canal of 1 tooth, which was subsequently excluded from the study.

### Clinical and Radiographic Examinations

Clinical and radiographic follow-up examinations were performed once every 3 months during an 18-month follow-up period by 2 experienced pediatric dentists blinded to the scaffold used in treatment.

Treated teeth were examined for vitality by using both electric pulp and cold testing, and teeth were recorded as responding positively to vitality testing only if they responded positively to both tests. At the end of 18 months, periapical radiographs were independently evaluated by 2 pediatric dentists for periapical healing and apical closure. Radiographs were reexamined 1 month after the initial examinations by the same pediatric dentists, and intraexaminer and interexaminer validity was assessed by using kappa statistics. Kappa values ranged from 0.8 to 1, demonstrating good reliability (Table 1).

In addition, preoperative and 18-month recall radiographs of teeth judged successful were digitally scanned, and radiographic root area (RRA) measurements were performed by using the Image J software (version 1.44) by a radiologist with experience using the program and who was blinded to the study groups. The ImageJ TurboReg plug-in was used to align and normalize preoperative and postoperative films. RRA was calculated from all radiographs according to Flake et al (24) (Fig. 2). Measurements were repeated after 3 weeks, and increases between preoperative and postoperative RRAs were calculated by using the averages of the 2 measurements. Wilcoxon signed rank test showed good intraexaminer reliability (Table 2).

After these examination periods, the 2 pediatric dentists jointly evaluated all clinical and radiographic findings with addition of RRA measurements and scored the final success rates for all patients, as follows:

![](image1.png)

**Figure 3.** (A) Radiograph of teeth #8 and #9 showing size 1 lesion. (B) Radiograph of tooth #8 showing size 2 lesion. (C) Radiograph of tooth #20 showing size 3 lesion.
TABLE 3. Treatment Outcomes after 18-month Follow-up

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<th>Tooth type</th>
<th>Etiology</th>
<th>Preoperative acute symptoms</th>
<th>Preoperative lesion size</th>
<th>Months to complete healing of periapical lesion</th>
<th>Complete apical closure</th>
<th>Increase in RRA (%)</th>
<th>Positive response to vitality testing</th>
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BC, blood clot; F, female; M, male; PRP, platelet-rich plasma.

Score 0 (unsuccessful): Teeth with clinical signs/symptoms (pain, tenderness to percussion, swelling, fistulization, or pathologic mobility) and/or radiographic pathology (evidence of periradicular pathosis, increase in periapical radiolucency, or internal/external root resorption)

Score 1 (satisfactory): Elimination of symptoms and evidence of bony healing but no increase in RRA or apical closure

Score 2 (good): Elimination of clinical symptoms and evidence of bony healing, with apical closure achieved with/without increase in root area

Score 3 (excellent): Score 2 + positive response to vitality testing

Statistical Analysis

Statistical analysis was performed by using the software program SPSS 20.0 (SPSS 20.0 for Windows; SPSS Inc, Chicago, IL). Clinical and radiographic data were assessed by using Fisher exact test, and differences in RRA between the 2 groups were assessed by using the Mann-Whitney U test, with P value < .05 considered to be statistically significant.

Results

Preoperative Clinical and Radiographic Findings

Of 20 necrotic teeth (PRP, 10; BC, 10) in 18 children (8 girls, 10 boys), 14 were maxillary incisor teeth exhibiting pulp necrosis in conjunction with a history of traumatic injury (either crown fracture or luxation), and 6 were premolar teeth (1 maxillary second premolar, 5 mandibular premolars) exhibiting pulp necrosis that was due to deep dentin caries or secondary caries.

Preoperative acute symptoms including night pain, spontaneous pain, and extreme sensitivity to percussion were observed in 16 teeth (PRP, 8; BC, 8), and preoperative apical abscesses were recorded in 7 teeth (PRP, 4; BC, 5). Moreover, 2 teeth assigned to the PRP group and 3 teeth assigned to the BC group required 2 sessions with triple antibiotic paste until teeth were symptom-free.

With regard to periapical lesions: 4 teeth (PRP, 3; BC, 1) had no lesions, 7 teeth (PRP, 3; BC, 4) had size 1 periapical lesion, 5 teeth (PRP, 1; BC, 4) had score 2 periapical lesion, and 4 teeth (PRP, 3; BC, 1) had score 3 periapical lesion (Fig. 3).

Postoperative Clinical and Radiographic Findings

The clinical and radiographic findings of both groups are given in Table 3. All 20 teeth were available for 18-month follow-up examination. All teeth were clinically asymptomatic; however, 1 tooth in the BC group exhibited enlargement of a preexisting periapical pathology and was judged radiographically unsuccessful (Fig. 4), whereas the remaining 14 periapical lesions showed appreciable healing. Differences in healing time according to lesion size were statistically insignificant (P > .05), although size 1 lesions required a mean time of 4.2 months for complete healing, compared with 8.3 months for both size 2 and size 3 lesions. Differences in healing time between the PRP and BC groups were also statistically insignificant, although complete healing occurred sooner in the PRP group (mean, 6.4 months) than in the BC group (mean, 6.8 months). Differences in time required for complete apical closure were also similar between the groups, although the PRP group required a mean of 8.1 months for complete apical closure, compared with 9 months in the BC group. However, the time required for complete apical closure was significantly longer in patients with acute preoperative symptoms such as night pain, spontaneous pain, and extreme sensitivity to percussion (10.2 months) when compared with patients without signs and symptoms (6 months) (P < .05).

In terms of RRA, teeth in the BC group exhibited a mean increase of 12.6% in RRA, compared with 9.86% in the PRP group; however, the difference between groups was statistically insignificant (P > .05) (Table 3).
No discoloration in relation to the triple antibiotic paste containing cefaclor was observed; however, crown discoloration caused by MTA placement was common, with unaesthetic results in 12 of 20 cases (60%).

Partial pulp canal obliteration was observed in 8 cases (PRP, 4; BC, 4) (Fig. 5); however, no relationship was found between obliteration and any of the variables (lesion presence/size, necrosis etiology, preoperative symptoms, treatment group) ($P > .05$).

A total of 7 teeth responded positively to vitality testing (PRP, 5; BC, 2), with no statistically significant difference between the groups ($P > .05$).

**Treatment Outcomes**

Treatment outcome was evaluated after an 18-month follow-up period on the basis of subjective and objective clinical findings and radiographic evidence. Scores for both groups ranged from “satisfactory” to “excellent” (Table 3) (Figs. 6–8), and although the PRP group had a higher rate of “excellent” scores, indicating better outcomes, the difference between groups was statistically insignificant ($P > .05$).

**Discussion**

This study found a PRP scaffold to be effective when used in RET of necrotic immature teeth; however, treatment outcomes did not vary significantly between PRP and conventional BC scaffold. Therefore, the null hypothesis was rejected.

Geisler (2) has stated that regenerative therapy outcomes may vary between teeth exhibiting partial necrosis (ie, teeth with some vital tissue in the apical portion of the canal) and those exhibiting full necrosis (ie, teeth in which the pulp has been completely lost). Huang (3) has suggested that the type of pulpal regeneration varies
according to these different clinical situations. In the case of partial pulp necrosis, the remaining pulp tissue may hypothetically recover after disinfection and help to regenerate the lost portion of pulp; therefore, the prognosis of these teeth is good. By contrast, in the case of complete loss of pulp tissue requiring de novo synthesis of pulp, prognosis is poor, and a separate protocol and scaffold may be required (2, 3). This study evaluated the efficacy of PRP used alone as a scaffold in cases of de novo regeneration; at the end of 18 months, all teeth in the PRP group showed resolution of signs and symptoms, and 90% of teeth in the PRP group showed various degrees of root maturogenesis.

The RRA measurements used in this study are considered to provide a valid assessment of the amount of root maturogenesis obtained as an outcome of RET (24). Flake et al (24) consider a mean RRA increase of 31% to represent obvious root development. In this study, an overall mean increase of 11% was detected. The amount of increase in RRA may be related to the preoperative root maturation stage of treated teeth, with small increases in RRA occurring in successfully treated teeth that were relatively more developed before treatment. Because RRA provides no information about periapical status, in addition to RRA, the present study relied on visual assessment of bony healing and apical closure in evaluating treatment outcomes.

**Figure 5.** (A) Preoperative radiograph of tooth #13 showing deep carious lesion and incompletely developed apex. (B) Twelve-month follow-up radiograph. (C) Partial pulp canal obliteration observed at 18-month follow-up.

**Figure 6.** (A) Preoperative radiograph of tooth #9. (B) Immediate post-treatment periapical radiograph. (C–G) Three- to 15-month follow-up radiographs. (H) At 18-month follow-up, bony healing was evident without root maturogenesis.
After an 18-month follow-up period, no statistically significant differences in outcomes were observed between the PRP and BC groups in the present study, although more "excellent" scores were obtained in the PRP group. Previous studies by Jadhav et al. (17, 19) found PRP to be more effective than BC; however, because these studies used PRP as an addendum to a BC matrix and with collagen as a carrier, the results cannot be attributed to PRP alone but may be due to synergy among the materials. The present study's finding that PRP alone did not significantly affect treatment outcomes is in line with recent histologic reports (20, 25, 26). Zhu et al. (26) used PRP and dental pulp cells for pulp regeneration in a dog study model. They found that the rate of root canal wall thickening was lower and mineralized tissue formation was less when PRP was used alone. This result was attributed to faster degradation of growth factors in PRP, which caused them to have shorter activity. In addition, growth factors were shown to have varying effects that may enhance or inhibit osseous and soft tissue repair, depending on the dynamics of the wound environment (21, 27). Martin et al. (20) concluded that PRP may enhance wound healing only if parenchymal tissue has not been completely destroyed but may not otherwise induce tissue regeneration. This would explain the similar outcomes between PRP and BC in the present study, because only totally necrotic teeth were included.

In the present study, 6 teeth (PRP, 3; BC, 3) showing bony healing but no further root development were rated "satisfactory," the lowest possible rating for a successful outcome. Nosrat et al. (28) also reported a case in which no further root maturation occurred in 6 years, despite the resolution of periapical pathology, and Kahler (29) reported root maturogenesis in 2 patients after 36 months and recommended longer periods of review. Geisler (2) suggested that even if no further root maturation has occurred, teeth showing resolution of periapical pathology do not necessarily require further endodontic treatment if they are asymptomatic. In the present study, teeth exhibiting bony healing but no root maturation were considered successful because they were asymptomatic. In the present study, teeth exhibiting bony healing but no root maturation were considered successful because they were asymptomatic. Moreover, because an 18-month period may not allow sufficient time to observe root maturogenesis, follow-up of all patients in this study is ongoing.

On the basis of the hypothesis that treatment outcome may be affected by the extent of periapical pathology, with larger lesions requiring more time for apical closure or bony healing, teeth in the present study were assessed according to size of radiolucency. A

![Figure 7](image1)

**Figure 7.** (A) Preoperative radiograph of tooth #29 showing radiolucency lesion and open apex. (B) Immediate post-treatment radiograph. (C–G) Three- to 15-month follow-up radiographs. (H) At 18 months, apical closure and complete healing of periapical lesion can be appreciated. Clinically, tooth gave negative response to vitality tests.

![Figure 8](image2)

**Figure 8.** (A) Preoperative radiograph of tooth #20. (B) Immediate post-treatment radiograph. (C–G) Three- to 15-month follow-up radiographs. (H) At 18-month follow-up, apical closure by narrowing of apical foramen and convergence of apical walls was observed with positive response to vitality tests.
number of previous studies (12, 14, 29) reported a possible relationship between the duration of pulp necrosis and treatment outcome and suggested that longstanding infection might destroy cells capable of pulp regeneration. Although large periapical lesions could be indicative of an extended period of pulp necrosis, the present study found no significant difference in treatment outcomes by lesion size.

A conventional apexification study has reported a correlation between acute symptoms such as spontaneous pain and night pain and a delay in root closure (30). Although another study reported no correlation between pretreatment symptoms and barrier formation time (31), that study made no differentiation between acute and chronic symptoms. In the present study, apical closure time was significantly longer in patients with preoperative acute symptoms; however, this finding cannot be compared with other RET studies because this issue has not been previously mentioned.

With respect to innervation, in the present study, 5 teeth in the PRP group and 2 teeth in the BC group were rated “excellent” because of positive responses to vitality testing. Previous studies have also reported positive responses to cold and/or electric pulp testing after RET (4, 8–10, 15, 16). Hargreaves et al (4) stated that positive responses to pulp sensitivity tests after RET are an indication that previously vacant space may become occupied by innervated tissue. In this study, less than 50% of all teeth showed a positive response to pulp testing. This may be due to the criteria used to define vitality (ie, a positive response to both cold and EPT tests). It is also possible that as suggested by Johns and Vidyanath (32), negative responses to vitality testing may be attributed to the thick layers of MTA (3–4 mm) and glass ionomer cement (2 mm), followed by permanent restoration. Moreover, dentin sensitivity in the natural pulp-dentin complex is related to the hydrodynamic activity of dentin tubules in association with α-β sensory fibers, whereas newly regenerated, mineralized root canal tissue does not appear to have well-organized dentin tubules and thus may not exhibit the same sensitivity as natural tissue (5).

In the present study, 8 teeth (PRP, 4; BC, 4) showed pulp canal obliteration. Varying degrees of obliteration have been previously reported in RET (8, 14, 15). This may be related to the osteoinductive activity of MTA (33). Shah et al (34) stated that obliteration after RET could be a sign of calcification of the entire canal, which could make future endodontic treatment more difficult. However, the major limitation of this study was the absence of a differentiation between acute symptoms such as spontaneous pain and night pain and a delay in root closure (30). Although another study reported no correlation between pretreatment symptoms and barrier formation time (31), that study made no differentiation between acute and chronic symptoms. In the present study, apical closure time was significantly longer in patients with preoperative acute symptoms; however, this finding cannot be compared with other RET studies because this issue has not been previously mentioned.

Recent reports (18, 36) have reported successful RET with cefadroxil used in place of minocycline in the triple antibiotic paste to avoid discoloration. Therefore, the present study not only used cefadroxil instead of minocycline, it also used a dentin bonding agent to seal the dentinal walls of the access cavity as a precaution against discoloration, which was not observed in any patient. However, discoloration of the crown after MTA placement was a common consequence. MTA is widely used as a coronal plug in RET; however, crown discoloration represents a potentially serious complication, especially in anterior teeth (2), and other studies have successfully used biocompatible MTA-like cements or glass ionomer cement instead (2, 8, 34, 37). These materials may be preferable for more aesthetic results, especially when anterior teeth are involved.

Conclusion

PRP was found to be useful in constructing a scaffold for RET; however, treatment outcomes did not differ significantly between PRP and conventional BC scaffolds.

Acknowledgments

The authors thank Ms Deborah Semel Demirtas for proofreading the manuscript.

The authors deny any conflicts of interest related to this study.

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