Effect of PRF and Allograft Use on Immediate Implants at Extraction Sockets with Periapical Infection
—Clinical and Cone Beam CT Findings—

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Abstract

Immediate implant placement can be successful, even at infected sites. The adjunctive effects of concomitant use of platelet-rich fibrin (PRF) and decalcified freeze-dried bone allografts (DFDBA) at periapically infected sites remains to be determined, however. The purpose of this prospective study was to investigate the effect of combined use of PRF and DFDBA on immediate implant survival at tooth extraction sites exhibiting periapical lesions. Implants were immediately placed in 8 patients under a standard chemotherapeutic protocol. Adin titanium implants were used in all cases. The combination of PRF and DFDBA was used to fill the gap between the implant body and the surrounding socket wall. The final restoration was placed after 3 months. The full-mouth plaque, gingival bleeding index, and gingival esthetics scores were assessed at 3, 6, and 12 months. Cone beam computed tomography images obtained at baseline and at 12 months after implant loading were analyzed. The plaque index scores showed statistically significant differences at 3, 6, and 12 months (p<0.05). The gingival bleeding index score showed no significant difference. No difference was noted in buccal gingival level on the implant surface or adjacent teeth at 91.7% of sites. Complete closure of the interproximal space was seen in 91.7% of the implant sites. Crestal bone levels on all implant surfaces were non-significant. Implant survival was 91.67% at 12 months. The adjunctive use of PRF with DFDBA at periapically infected sites yielded a significant reduction in bone resorption and accelerated bone healing during the initial post-extraction stage. A significant improvement was achieved in the gingival esthetic score at the interproximal and midfacial surfaces. The combined use of growth factors with pre- and postoperative broad-spectrum antibiotics over a short time resulted in a higher implant survival rate at the end of the 1 year post-restoration period.

Key words: Immediate implants — Periapical/endodontic infection — Platelet-rich fibrin — Cone beam CT — Gingival esthetics
Introduction

The placement of a dental implant involves extracting the compromised tooth and allowing several months for the extraction socket to heal. This entails a prolonged treatment period, however, which means that patient compliance is often poor\(^1\). Therefore, the majority of patients are interested in shortening the treatment time between tooth extraction and implant insertion\(^50\).

With this in mind, immediate implant placement offers many advantages, including a reduction in the total treatment period, preservation of both hard and soft tissues, and a good emergence profile. Furthermore, it obviates the need for the patient to undergo additional surgical procedures, as bone grafting and implant placement can be done in one single appointment. This also allows restoration of function to occur faster, providing a psychological benefit to the patient.

Immediate implantation is usually avoided, however, at sites showing signs of infection, whether periodontal or endodontic\(^57\). Some studies have suggested that immediate implant placement should be contraindicated in the presence of infectious disease due to fear of failure of osseointegration. This is possibly due to bacterial contamination of the implant surface during the initial stages of healing\(^8,46\). A high rate of implant failure has been reported in sockets with periapical lesions, especially with placement of machined-surface implants\(^5\). Moreover, many studies have reported an increase in loss of endosseous implants at sites associated with periodontal disease\(^12,24,35\), whereas few have reported satisfactory results\(^15,20\). Similar success rates have been reported, however, with immediate implant placement whether the site was infected or not, provided infection was controlled thorough debridement of alveolar tissue by curettage and administration of broad-spectrum antibiotics\(^17,20,31,32,50,55\).

It is sometimes difficult to match the dimensions of the implant with those of the extracted tooth. A gap between the implant body and the extraction socket wall requires a biocompatible material to enhance 3-dimensional osseointegration. A number of materials have been tried as regenerative materials, including expanded polytetrafluoroethylene membranes, bioabsorbable membranes, demineralized freeze-dried bone allografts (DFDBA), freeze dried bone allografts, bone autografts, hard tissue replacement polymer, hydroxyapatite, xenografts, growth and differentiation factors, and particulate and block grafting materials. None of these materials has shown any superior clinical outcome in bone regeneration when compared \textit{in vivo}, however\(^9,42\).

Moreover, although DFDBA and modified hydroxyapatite granules have been used extensively in regenerative procedures, to the best of our knowledge, no studies to date have supported their use in immediate implant placement.

Histological studies have demonstrated numerous newly proliferative vascular endothelial cells and regenerative molecules in areas of inflammation. Platelet-rich growth factor (PRGF) has been proposed as an aid in enhancing hard and soft tissue regeneration in the field of oral surgery\(^14\) as it is a simple, natural, and inexpensive tool for production of leucocyte and platelet concentrates\(^21–23\). It is a consistent fibrin biomaterial and not improved fibrin glue from the platelet rich plasma family\(^21\). \textit{In vitro} studies have shown that growth factors, such as TGF-\(\beta\), PDGF-\(\alpha\beta\), and VEGF, together with matrix glycoproteins, such as thrombospondin-1, are released in high amounts during the initial 7 to 11 days of wound healing\(^22\).

\textit{In vitro} studies, animal experiments, and clinical studies have shown that PRGF can effectively enhance regeneration of osseous and soft tissue, as well as reduce inflammation, pain, and allergic side effects\(^20\). To the best of our knowledge, however, no studies to date have investigated the adjunctive role of second-generation growth factors, such as platelet-rich fibrin (PRF) or DFDBA allografts, for example, in immediate implant placement in periapically infected extraction sockets. Whether elimination of apical infection through mechanical debridement, with or
without systemic medication, and incorporation of growth factors in the healing socket is beneficial in immediate implant placement remains to be determined. Therefore, the purpose of the present study was to investigate the effect of concomitant use of PRF and DFDBA on the survival rate of immediately placed implants at tooth extraction sites exhibiting chronic periapical lesions.

**Materials and Methods**

This prospective case series was conducted at the Department of Periodontology of this institute. Prior approval was obtained from the institutional ethical committee for immediate placement of implants and use of DFDBA and PRF in infected extraction sockets. All the patients were given a detailed explanation of the study protocol and the risks and benefits associated with the proposed treatment. All signed a consent-to-treat agreement prior to commencement of the procedure.

All the patients enrolled in this study were systemically healthy and aged ≥18 yr. All had a full-mouth plaque score of <10% and at least one tooth with periapical infection showing as a periapical radiolucency on an intraoral periapical radiograph. No tooth that was indicated for extraction due to cervical fracture or endodontic failure, or that was nonrestorable was permitted. The exclusion criteria were as follows: a systemic disease/condition that might interfere with implant placement; active signs of periodontal infection; a history of parafunctional habits; smoker; alcohol consumption; undergoing corticosteroid therapy; chemotherapy and/or radiotherapy; lack of stable posterior occlusion; and lactating and/or pregnant females.

A detailed medical and dental history was obtained and assessment of periodontal and endodontic status performed in all patients; intraoral periapical radiographs using parallel technique and/or cone beam computed tomography (CT) scans were obtained as required to assess the implant site and adjacent vital structures. Routine blood investigations were performed before implant surgery.

1. **Pre-surgical protocol**

The standard protocol was followed at all periapically infected sites. This comprised application of a full mouth oral prophylaxis, chlorhexidine digluconate (0.2%) mouthwash (Dr. Reddy’s Laboratories Ltd., Hyderabad, India), and a broad spectrum antibiotic (amoxicillin 500 mg TID) 24 hr before commencement of surgical procedures; sometimes accompanied by abscess drainage in acute cases to control periapical infection. When required, root canal access opening involving the periapical lesion was performed 1 day prior to implant surgery. In these cases, the area concerned was irrigated thoroughly with normal saline.

2. **Surgical protocol**

All procedures were performed under aseptic conditions. The patients were advised to rinse with 10 ml of 0.2% w/v chlorhexidine digluconate immediately before surgery. The surgical area was anesthetized with lignocaine hydrochloride 2% and adrenalin (1:200,000) (EL-Ligno ADR, Elder pharmaceuticals, Mumbai, India). Implant size was determined using pre-treatment records. Venous blood was aspirated (10 to 15 ml) from an antecuboidal area for the preparation of PRF. The blood was deposited in 5-ml laboratory sterile glass-coated plastic test tubes without anticoagulants. The tubes were centrifuged at 2,700 rpm at room temperature for 12 min in a centrifuge unit (REMI R-8C Laboratory Centrifugal Machine, Andhra Surgical Emporium, Hyderabad, India).

The tooth was extracted atraumatically using periotomes. The extraction socket was thoroughly debrided using a Lucas curette and irrigation with normal saline. The integrity of the socket walls was assessed. A mucoperiosteal flap was elevated if a bone defect was observed. The final osteotomy site was prepared for implant placement to a depth of 2 to 3 mm beyond the root apex. An Adin
Titanium implant (Touareg™-S, Adin Dental Implant system, Afula, Israel) was stabilized into the osteotomy site with a minimum insertion torque of 25 Ncm. All implants were placed 2 to 3 mm apical to the gingival margin at a level corresponding to the facial cemento-enamel junction of the adjacent teeth. The gap was filled with freshly prepared PRF and DFDBA (300 to 500 μm) bone graft. The graft was compacted to within 1 mm of the planned gingival margin of the restoration. The PRF membrane was placed over the grafted site and implant and secured with a Vicryl 5-0 resorbable suture (Ethicon, Johnson & Johnson Ltd., Aurangabad, India) in a horizontal mattress fashion to secure the gingiva lightly to the PRF material to prevent immediate displacement. Provisionalization with an acrylic crown was performed within 2 to 3 days and the final restoration placed after a healing period of 3 to 4 months.

3. Postoperative protocol

A standard post-surgical medication protocol was followed. As an antibiotic, amoxicillin 500 mg TID was continued for a further 5 days. Analgesic (aceclofenac sodium, 100 mg BD) and serratiopeptidase (10 mg BD) were prescribed from 1 day preoperatively to 5 days postoperatively. All patients were advised to gargle twice daily with chlorhexidine digluconate (0.2%) mouthwash for 2 to 3 weeks. Any complications such as swelling and abscess were recorded and treated as necessary. All the patients were followed on a weekly basis for the initial 4 weeks. All were recalled for further examination at 3, 6, and 12 months following the final restoration.

4. Data collection

The full mouth plaque, bleeding, and gingival esthetic scores on the mid-facial and interproximal surfaces were recorded immediately postoperatively after implant placement (baseline) and again at 3, 6, and 12 months post-restoration. The cone beam CT images were analyzed to assess crestal bone levels (implant collar to marginal bone) on 4 surfaces (facial, lingual/palatal, mesial, and distal) at baseline and at 12 months post-restoration. Implant survival/success was assessed in accordance with the Implant Health Scale at the end of study period.

5. Statistical analysis

The data were analyzed using SPSS software (v21.0). An ANOVA and Post Hoc (Tukey HSD) test were used to compare the full-mouth plaque scores. The full-mouth bleeding index and gingival mid-facial and interproximal esthetics scores were analyzed with the Chi-square test. The circumferential bone levels around the implants immediately after placement and at 12 months postoperatively were analyzed using a student’s paired t test. A p value of <0.05 was considered to be significant.

Results

Age ranged from 23 to 44 yr among the total number of patients (men = 6, women = 2). A total of 12 implants were placed in 8 patients in either the maxilla or mandible. Seven implants were placed in the anterior region and 5 in the posterior region. At the time of prosthesis placement, all the implants were non-mobile. At the end of study, all the implants were functional according to the Implant Health Scale score.

Table 1 shows a comparison of the full-mouth plaque scores between each time point. The intergroup comparison revealed a statistically significant result in plaque scores (ANOVA value, F = 11.57, p = 0.00). A statistically significant difference was observed in plaque score between the pre- and postoperative data at 3, 6, and 12 months in all patients. No statistically significant difference was observed between postoperative 3, 6, and 12 months, however (Table 2). The full-mouth gingival bleeding index score showed statistically non-significant results throughout the study period (Table 3).

Table 4 shows the frequency distribution of gingival esthetic scores at the mid-facial surface. At the end of 12 months, no difference
was noted in buccal gingival level on the implant surface or adjacent teeth at 91.7% of sites. Statistically significant differences were observed in gingival esthetic score at 3, 6, and 12 months compared to at baseline (Table 5). Only 66.7% of proximal gingival embrasures showed gingival esthetic scores of 2, and the remaining sites showed less than half of the gingival embrasures (Table 6). At the end of the study, complete closure was achieved in 91.7% of gingival embrasures, and this was statistically significant (Chi-square value, 0.000; p < 0.05) (Table 7, Fig. 1).

Table 8 shows descriptive statistics and a comparison of bone levels around the implant at baseline and at 12 months after implant restoration. No statistically significant difference was observed in crestal bone levels around the implant between at baseline and at 12 months (Figs. 2, 3).

Eleven implants were still viable at 12 months following implant restoration (91.67%). One implant showed compromised survival. Radiographic bone loss was more than half of implant length in the facial aspect only. Probing depth was 4 to 5 mm, however.

Extraoral swelling was observed in only 1 patient within 24 hours postoperatively. This was probably due to this patient failing to observe the antibiotic and/or oral hygiene

| Table 1 | Comparison of full mouth plaque index score at different time intervals by ANOVA |
|------------------|------------------|------------------|------------------|------------------|------------------|
| Plaque score     | Sum of squares   | Degree of freedom | Mean square      | F-value          | p-value (2-tailed) |
| Between Group    | 12,029.94       | 03               | 4,009.98         | 11.57            | 0.00*             |
| Within Group     | 11,093.83       | 32               | 346.68           |                  |                  |

F: ANOVA test value, *: Significant at 0.05 level

| Table 2 | Comparison of full mouth plaque index score at different time intervals by Post Hoc test |
|------------------|------------------|------------------|------------------|------------------|------------------|
| Interval         | Mean Difference  | Std. Error       | p-value (2-tailed) | 95% CI           |
| Baseline         |                  |                  |                  |                  |
| 3 months         | 34.01*           | 8.77             | 0.003*           | 10.23 57.79      |
| 6 months         | 39.16*           | 8.77             | 0.001*           | 15.38 62.94      |
| 12 months        | 48.37*           | 8.77             | 0.000*           | 24.59 72.15      |
| 3 months         | -34.01*          | 8.77             | 0.003*           | -57.79 -10.23    |
| 6 months         | 5.14             | 8.77             | 0.936            | -18.64 28.93     |
| 12 months        | 14.356           | 8.77             | 0.374            | -9.43 38.14      |
| 6 months         | -39.16*          | 8.77             | 0.001*           | -62.9364 -15.38  |
| 3 months         | -5.14            | 8.77             | 0.936            | -28.93 18.64     |
| 12 months        | 9.21             | 8.77             | 0.722            | -14.57 32.99     |
| 12 months        | -48.37*          | 8.77             | 0.000*           | -72.15 -24.59    |
| 3 months         | -14.36           | 8.77             | 0.374            | -38.14 9.43      |
| 6 months         | -9.21            | 8.77             | 0.722            | -32.99 14.57     |

*: Mean difference significant at 0.05 level
Table 3  Comparison of full mouth bleeding index score at different time interval by Chi-square test

|                      | Baseline | 3 months | 6 months | 12 months |
|----------------------|----------|----------|----------|-----------|
| Chi-square           | 0.000    | 0.750    | 1.000    | 0.750     |
| Degree of freedom    | 7        | 6        | 5        | 6         |
| Asymptomatic significance | 1.000 | 0.993    | 0.963    | 0.993     |

Table 4  Frequency distribution of gingival esthetic (GE) score at mid-facial implant location

| GE score | Baseline | 3 months | 6 months | 12 months |
|----------|----------|----------|----------|-----------|
|          | n  | % | n  | % | n  | % | n  | % |
| 0        | 7  | 58.3 | 8  | 66.7 | 10 | 83.3 | 11 | 91.7 |
| 1        | 3  | 25.0 | 3  | 25.0 | 1  | 8.3  | 0  | 0   |
| 2        | 2  | 16.7 | 1  | 8.3  | 1  | 8.3  | 1  | 8.3  |
| 3        | 0  | 0   | 0  | 0   | 0  | 0   | 0  | 0   |
| 4        | 0  | 0   | 0  | 0   | 0  | 0   | 0  | 0   |
| Total    | 12 | 100 | 12 | 100 | 12 | 100 | 12 | 100 |

n: Number of implants, %: Percentage

Table 5  Comparison of gingival esthetic (GE) score at mid-facial implant location by Chi-square test

|                      | Baseline | 3 months | 6 months | 12 months |
|----------------------|----------|----------|----------|-----------|
| Chi-Square           | 3.500    | 6.500    | 13.500   | 8.333     |
| Degree of freedom    | 2        | 2        | 2        | 1         |
| Asymptomatic significance | 0.174 | 0.039* | 0.001* | 0.004* |

*: significant at 0.05 level

Table 6  Frequency distribution of gingival esthetic (GE) score at interproximal implant location

| GE score | Baseline | 3 months | 6 months | 12 months |
|----------|----------|----------|----------|-----------|
|          | n  | % | n  | % | n  | % | n  | % |
| 0        | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  |
| 1        | 4  | 33.3 | 5  | 41.7 | 0  | 0   | 0  | 0   |
| 2        | 8  | 66.7 | 7  | 58.3 | 5  | 41.7 | 1  | 8.3  |
| 3        | 0  | 0   | 0  | 0   | 7  | 58.3 | 11 | 91.7 |
| 4        | 0  | 0   | 0  | 0   | 0  | 0   | 0  | 0   |
| Total    | 12 | 100 | 12 | 100 | 12 | 100 | 12 | 100 |

n: Number of implants, %: Percentage
protocols. The condition was treated with an antibiotic (Augmentin 625 mg for 5 to 7 days) and the swelling subsided completely within 2 to 3 days with no further complications.

**Discussion**

Restoring function and improving esthetics are the primary goals of implant therapy. Many studies have investigated immediate implant placement in infected extraction sockets due to periapical lesions\(^5,12,17,20,24,31,32,35,55\). Few have investigated the potential adjunctive effect of concomitant use of PRF and DFDBA bone grafts in such cases, however, which was, therefore, the purpose of the present study.

Periapical microbial infection at a site scheduled for implant placement is considered a potential risk factor to its success. This is because the mixed population of anaerobic pathogens arising from such an infection may contaminate the implant during the healing process. Retrograde peri-implantitis may also arise from a number of other factors, including the persistent presence of bacteria in peri-radicular healed bone, even after vigorous debridement of the socket\(^6\); incomplete obtur-ration of the root canal\(^11\); and reactivation of bacteria in healed alveolar bone\(^36\). One study found histopathological evidence of subclinical infection at an edentulous site due to biofilm formation\(^28\). Meticulous debridement, drainage of abscesses, and antibiotic administration can reduce the inflammatory response, which is a prerequisite for favorable osseoin-marative healing of the implant.

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**Table 7** Comparison of gingival esthetic score at interproximal implant location by Chi-square test

| Number of implants | 12 |
|-------------------|----|
| Chi-square value  | 30.93 |
| Degree of freedom | 3 |
| Asymptomatic significance | 0.000* |

*: p<0.05

**Table 8** Comparison of bone loss around immediate implant placement at baseline and 12 months by paired ‘t’ test

| Bone Levels (n=12) | Mean ± SD | Standard Error | Baseline v/s 12 months | t-value | p-value (2-tailed) |
|--------------------|-----------|----------------|------------------------|---------|-------------------|
| Facial surface     |           |                |                        |         |                   |
| Baseline           | 0.37 ± 1.25 | 0.36           | –0.60 ± 1.24           | –1.67   | 0.12              |
| 12 months          | 0.97 ± 1.06 | 0.30           |                        |         |                   |
| Lingual surface    |           |                |                        |         |                   |
| Baseline           | 0.41 ± 1.05 | 0.30           | –0.48 ± 1.33           | –1.25   | 0.24              |
| 12 months          | 0.90 ± 0.86 | 0.25           |                        |         |                   |
| Mesial surface     |           |                |                        |         |                   |
| Baseline           | 1.37 ± 1.55 | 0.45           | 0.7 ± 1.93             | 1.27    | 0.23              |
| 12 months          | 0.66 ± 0.68 | 0.20           |                        |         |                   |
| Distal surface     |           |                |                        |         |                   |
| Baseline           | 1.05 ± 1.34 | 0.39           | 0.49 ± 1.81            | 0.94    | 0.37              |
| 12 months          | 0.56 ± 0.78 | 0.22           |                        |         |                   |

n: total number of implants
Integration during the early stages of wound healing. On the other hand, some clinical studies have reported satisfactory results when following the above guidelines with no biological complications. Hence, the presence of periapical infection should not be considered as a potential contraindication for immediate implant placement. Furthermore, human clinical studies have reported that implant survival rate ranged from 92 to 100% after 12 to 60 months of follow-up. One study reported that the implant survival rate was 100%, and that hard and soft tissue integration was similar and favorable between the healthy and infected groups. The present findings showing that 11 implants were successful (survival rate, 91.67%) at the end of 1 year according to Misch’s criteria are in agreement with these earlier results.

The use of pre- and/or postoperative antibiotics is controversial in immediate implant placement at infected sites. Although several antibiotic regimens have been proposed, the evidence remains inconclusive. In some studies, clindamycin was administered at 600 mg at 1 hour preoperatively, whereas in another 1.5 gm amoxicillin was given over a 4-day period preoperatively and then continued for 10 days postoperatively. A case of Pseudomembranous colitis was reported as a result of prolonged administration of antibiotics. In other studies, postoperative administration of antibiotics was recommended. In the present study, 1,500 mg amoxicillin per day was administered from 1 day preoperatively to 5 days postoperatively. Chlorhexidine digluconate (0.2%) was also recommended for a further 2 to 3 weeks. No adverse effects were observed due to the antibiotics given, and pain subsided within 5 days.

All the patients presented with a 4-wall extraction socket morphology, except at 1 implant site, where there was buccal bone dehiscence of 3 to 4 mm. Guided bone regeneration (Colaguide, resorbable membrane) was accomplished in combination with DFDBA and PRF gel to aid in osseous healing in the peri-implant region. All implant fixtures showed sufficient primary stability and a minimal torque of 25 Ncm, which corresponds to a stability quotient value of at least 60. At the completion of the study, all the implants showed clinical stability with no detectable mobility, reflecting functional ankylosis.

For an implant to be successful over the long-term, stable vertical bone levels are of great significance. Following tooth extraction, facial cortical bone will resorb faster (>25%) than the other walls within 2 to 3 months. Conventional radiographic assessment of marginal bone loss is highly specific, but limited to the proximal aspect of the implant. Buccal sites are more susceptible to dehiscence-like defects than proximal bone. The success or survival criteria of implants was classified based on proximal bone loss on conventional radiographs. Nevertheless, considering only change in volume of proximal bone may lead to the success of the implant therapy being overestimated. Therefore, assessing change in volume of
facial bone is important in evaluating long-term success, particularly with immediate implant placement. In the present study, only 1 implant showed complete facial bone loss at 12 months. No proximal bone loss was observed, however. From these findings, it is difficult to say whether the success of an implant should be assessed solely based on proximal bone loss or whether facial bone levels should also be taken into consideration from a prognostic point of view.

Implant bone levels were stable at 12 months. The mean bone loss observed on cone beam CT ranged from 0.40 to 2.4 mm. This disparity was statistically non-significant on all 4 surfaces at the end of the study in comparison with at baseline, however. These results were comparable to those of other studies. Crespi et al.\(^\text{17}\) reported mean proximal bone loss of 0.86 ± 0.54 mm after 2 years. Using PRF grafting material, Marrelli et al.\(^\text{33}\) reported mean proximal loss on cone beam CT of 0.4 to 1.7 mm after 30 months of follow-up. At 5 years, vertical bone loss of 1.98 ± 0.21 mm and 1.7 ± 0.45 mm was reported for Branemark and Astra implants, respectively; and an average increase of 0.5 mm in vertical bone loss was observed after 12 months\(^\text{9}\). Mean mesial bone resorption of 0.49 ± 0.11 mm and distally of 0.53 ± 0.12 mm was observed in immediate implant placement compared to in delayed placement at the end of 1 year\(^\text{31}\). In the present study, only 1 implant showed complete facial bone loss at 12 months. This may have been due to the development of immediate postoperative infection. The implant was clinically immobile and functional, however, with no gingival recession at the end of the study.

One difficulty faced in implantation is that a gap may be created between the body of the implant and the socket wall due to the configuration of the tooth root. Numerous grafting materials have been used in an attempt to overcome this problem. Decalcified freeze-dried bone allografts have both osteoconductive and osteoinductive properties. Bone morphogenetic proteins (BMPs) aid in mesenchymal cell migration, attachment, and osteogenesis. They also act as a scaffold for osteoconduction and create and maintain space. In the present study, PRF, a platelet concentrate, was used as a source of growth factors to accelerate the initial stages of wound healing\(^\text{45}\) and minimize the rehabilitation time required of an edentulous site. Obtaining growth factors from the fibrin matrix over the initial 7 days prolongs their chemotactic properties and promotes fibroblast and osteoblast proliferation, extracellular matrix deposition, mesenchymal cell differentiation, vascular proliferation, and extracellular matrix deposition\(^\text{4,26}\). Animal and experimental studies revealed that they exert effects similar to those of autogenous bone graft materials\(^\text{4,40}\). In contrast, BMPs act primarily at the later stages of osteoinduction, such during mesenchymal cell differentiation and vascular proliferation. Platelet-rich fibrin entraps circulating stem cells, resulting in superior healing of large osseous defects where there is migration of stem cells differentiating into the osteoblast phenotype\(^\text{15}\). Combining graft materials such as DFDBA with PRF enables these two distinct wound healing processes to take place concurrently. Their combination may promote bone regeneration and enhance the biological activity of the graft material\(^\text{10}\). The use of PRF aids in retaining the bone graft material within the walls of the socket, and, as it is a fibrin clot, it also aids in the arrest of bleeding\(^\text{54}\). Platelet-rich fibrin fragments serve as a biological connector between bone particles. Moreover, the gradual release of cytokines plays a significant role in the self-regulation of inflammatory and infectious phenomena within the grafted material\(^\text{52}\). Using less nonviable DFDBA to make room for PRF may result in higher viable bone formation\(^\text{53}\).

In humans, the addition of PRF to DFDBA significantly enhanced bone regeneration compared to with bone graft alone in the treatment of intrabony periodontal defects\(^\text{2,7,44,49}\). It also has the additional benefit of preserving ridge width and height at intervals of 90 to 180 days\(^\text{44}\). Choukroun et al.\(^\text{15}\)
reported faster healing with leukocyte-PRF mixed with DFDBA after sinus lift (4 months) than with DFDBA alone (8 months). In an experimental rabbit model, the combination of PRF and DFDBA yielded the highest bone-implant contact (73.43 ± 3.86%) and percentage of new bone formation (63.09 ± 2.10%) at the defect area when compared with antibiotic or saline. One in vivo canine study reported complete bone fill as early as within 3 to 12 weeks with use of PRF alone and/or in combination with DFDBA allograft in the extraction socket. A histological examination of 6-week post-extraction healing of extraction sockets with use of PRF gel revealed an approximately 30% acceleration in trabecular bone formation, and that this bone was composed of delicate, newly-formed bone and numerous lacunae lined with osteocytes and osteoblast cells. Atraumatic extraction technique was identified as another important factor in successful immediate implant placement and enhanced maintenance of maximum bone volume. This allows preservation of the buccal bone wall (preventing perforation or alveolar bone fracture), without which an immediate implant might be contraindicated. In addition, complete degranulation of the extraction socket followed by availability of growth factors during wound healing contributes to maintaining the integrity of the socket wall and osseous support around the implant restoration.

The underlying osseous support determines or predicts the soft tissue esthetic outcome with immediate implants. In the present study, the gingival esthetics in the mid-buccal and interproximal regions were maintained after 12 months of implant restoration. There was complete fill of interdental papillae at between 6 and 12 months after restoration. The interdental gingiva achieved greater stability at between 6 and 12 months. Similarly, a statistically significant improvement was observed in the mid-buccal gingival surface throughout the study period. Another earlier study also reported no difference in interdental papilla esthetics between immediate and delayed implant placement, as observed also in the present study. Immediate implant placement may be beneficial in maintaining the integrity of the extraction socket and contribute to the maintenance of the interdental papillae around the implant restoration.

Any incongruity between the implant diameter and morphology of the alveolus that is worsened by the presence of a bone defect due to periapical infection is challenging. Some authors have stated that a minimum of residual apical bone of 3 to 5 mm in the vertical dimension is required in such cases. Another critical aspect is the diameter of the periapical lesion. It may be necessary to obtain implant stabilization more apically, if it exceeds the diameter of the planned implant. Conversely, initial stability may be sufficient, if the implant diameter is larger than the diameter of the periapical lesion, without extending 3 to 5 mm apically to the extraction socket.

This study had a number of limitations. These include the small single-cohort sample size. This was perhaps unavoidable, however due to ethical considerations. Validation of the present results, however, will require further controlled clinical trials with larger sample sizes. Furthermore, the outcome measures were often not related to the type of infection. A clearer classification also needs to be implemented by clinical evaluation based on more specific periapical pathology. Further exploration is needed with histopathological appraisal.

**Conclusion**

Immediate implant placement in extraction sockets with periapical infection can be considered as a safe and viable treatment option, if strict aseptic protocols are followed. The present results showed that adjunctive use of PRF with DFDBA significantly reduced bone resorption and accelerated bone healing during the immediate postoperative period in sockets with periapical infection. A significant improvement was achieved in gingival esthetic scores on the interproximal and mid-facial surfaces. The combination of
growth factors with allograft and short-term pre- and postoperative broad-spectrum antibiotics improved the implant survival rate at 1 year after implant restoration.

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Competing Interests

All authors (Raghavendra S. Medikeri, Vinayak Meharwade, Parikshit M. Wate, and Suresh V. Lele) certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers’ bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements) or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

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