

Evaluation of the use of plasma rich in growth factors with immediate implant placement in periodontally compromised extraction sites: a controlled prospective study

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Abstract. This study was conducted to evaluate the use of plasma rich in growth factors (PRGFs) with immediate implant placement in periodontally compromised extraction sites. Fifteen patients with chronic periodontitis were included. Each received two implants placed immediately after extraction in the anterior region of the mandible. One of the two implants was treated with PRGFs (group I), while the other was not and served as a control (group II). Implant survival, plaque index (PI), bleeding index (BI), probing pocket depth (PPD), and marginal bone loss (MBL) were evaluated for both groups. Complete soft tissue healing occurred in all patients and all implants were successfully osseointegrated over 12 months. At 12 months, results showed mean PPD values of 3.8 ± 0.3 mm at the control site (group II) and 3.4 ± 0.4 mm at the test site (group I); the mean MBL values were 1.1 ± 0.1 mm at the control site and 0.6 ± 0.1 mm at the test site. There were no statistically significant differences between the test and control groups regarding PI or BI, while there were statistical differences between the test and control groups regarding PPD and MBL throughout the follow-up period.

Key words: bleeding index; immediate implant; implant survival; marginal bone loss; periodontally compromised sites; plaque index; plasma rich in growth factors; probing pocket depth.

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Severe periodontitis leads to the loss of alveolar bone. In such cases, the extraction of a tooth and its replacement with an implant-supported prosthesis may be the

appropriate treatment option for some patients. The standard protocol requires a delay of at least 6 months before the placement of an implant in the extraction

socket.¹ However, immediate implant placement in post-extraction sites, without waiting for the site to heal, is a treatment modality that has received much attention

and has shown favourable results, such as the preservation of aesthetics, shorter total treatment time, maintenance of socket walls, and reduced surgical time.²⁻⁷ In some studies, periodontal disease has been considered a risk factor in implant therapy; a statistically significant, greater long-term peri-implant marginal bone loss (MBL) has been observed in those with periodontal disease compared to periodontally healthy subjects.^{8,9}

Plasma rich in growth factors (PRGFs) is derived from autologous blood by sequestering and concentrating the platelets by centrifugation.¹⁰ It is suggested that platelet concentrations can enhance oral wound healing by releasing abundant growth factors, including platelet-derived growth factor, transforming growth factor, insulin-like growth factor, and epidermal growth factor.¹¹ Recently, PRGFs have been applied clinically to facilitate bone and tissue healing. Some trials have shown that the use of PRGFs during the placement of dental implants promotes osseointegration and bone regeneration.¹² The use of autologous platelets appears to improve early bone apposition around the implant and thus results in an increased rate of osseointegration.¹³ Contradictory results have been reported in an animal study by Casati et al.,¹⁴ who investigated the influence of platelet-rich plasma (PRP) on bone regeneration in dehiscence-type bone defects around dental implants. They demonstrated that PRP alone does not enhance bone regeneration for peri-implant defects.

There is a lack of scientific evidence in the literature regarding the results of the use of PRGFs and immediate implant placement in terms of accelerating the rate of osseointegration or reducing crestal bone resorption around dental implants. The aim of this study was to evaluate the clinical and radiographic outcomes of the use of PRGFs with immediate implant placement in periodontally compromised extraction sites.

Materials and methods

The present study was conducted on 15 patients (eight females and seven males) who ranged in age from 30 to 55 years. The study protocol had the necessary ethics committee approval. All patients had to be in good health, with no chronic disease or smoking habits; all were physically able to tolerate the procedure. Patients were excluded if they had any disease, condition, or medication that might compromise healing or osseointegration, or if they were unable or unwilling to return for follow-up visits.

All implants in this study were Euroteknika implants (Euroteknika, Salanches, France), which are compatible with the Astra system (Dentsply International, Waltham, MA, USA). Primary stability (torque 25 N/cm) of the implants was achieved during the surgical procedure. Preliminary diagnostic procedures included a digital panoramic radiographic evaluation.

The present study was conducted on patients with chronic periodontitis in the anterior region of the mandible. Treatment was required in order to replace the residual hopeless teeth, which had lost 75% of the supporting bone or had a probing depth (PD) >8 mm. A fixed partial implant-supported restoration was used in the presence of four bony walls of the remaining alveolus with at least 5 mm depth on both sides and the presence of 5 mm of bone beyond the root apex. Patients were excluded if there was a need for grafting of the implant site. Each patient received two implants in the region of the lateral incisors of the mandible, which were placed immediately after extraction. One of the two implants was treated with PRGFs (group I), while the other was not and served as a control (group II). The test and control sides were switched according to the order of patients.

Preparation of PRGFs

Before surgery and the administration of local anaesthesia, 10 ml of peripheral blood was drawn. The blood was deposited in laboratory glass tubes pre-treated with 3.8% trisodium citrate. The tubes were centrifuged at 270 rpm at room temperature for 7 min in a centrifuge unit specifically designed for use with this technique (PRGF System; BTI Biotechnology Institute, Vitoria-Gasteiz, Álava, Spain). This allows the separation of blood into distinct layers: a cellular layer at the bottom, PRP in the middle, and platelet-poor plasma at the top. The cellular components (mostly red blood cells and a thin layer of white blood cells) remain at the bottom of the tube, above which is the plasma component consisting of PRGFs and finally a layer of plasma poor in growth factors. The middle layer was collected and stored in a sterile glass container until use. Leukocytes were not collected in this preparation. At the time of the application, approximately 50 µl of 10% CaCl₂ solution was added per 1 ml of PRGF concentrate to enable clot formation. A platelet cell count was done before and after centrifugation.

Procedure

One hour before the surgical procedure, the patient began a prophylactic regimen of 600 mg clindamycin. All procedures were performed after the administration of 3.6–5.4 ml of a combination consisting of local anaesthetic (mepivacaine HCl 2%) and a vasoconstrictor (levonordefrin) at a ratio of 1:20,000. A full-thickness mucosal flap was raised and the teeth extracted gently with extraction forceps, with minimum surgical trauma and without any damage to the adjacent hard tissues (Fig. 1A and B). The extraction sites were then carefully debrided with a sharp curette to remove any granulation or fibrous tissue that was present and were irrigated with sterile saline. The depth of the socket was measured to determine the drilling needed after the root apex. Osteotomies were performed via standard protocols in all cases, including slow-speed sequential drills and copious irrigation. At the test sites, the prepared PRGFs were injected slowly at low pressure into the drill holes immediately before implant placement (Fig. 1C). In addition, the implant was dipped in PRGFs before seating. Implants were manually screwed into the prepared osteotomies at the crestal ridge (Fig. 1D). Implant stability was monitored and noted upon placement. Closure of the wound was obtained by coronal repositioning of the flap.

Postoperative phase

Postoperative instructions were given to the patient, which included the application of extraoral ice packs for 2 h on the first day in order to minimize oedema. Oral hygiene instructions included the use of warm 0.2% chlorhexidine HCl as an anti-septic mouthwash twice daily for 7 days, the use of a soft toothbrush, and gentle cleaning with dental floss. Patients were also required to take 300 mg clindamycin orally every 6 h for 5 days and to take ibuprofen 600 mg twice daily for 7–10 days. A direct panoramic radiograph was taken immediately after implant placement to evaluate the implant position. Patients were recalled after 1 week for the removal of sutures and to assess the presence of any pain, swelling, or infection. After a healing period of 3 months, the second-stage surgical procedure was performed with the placement of a healing abutment on the implant. Prosthetic rehabilitation started 2 weeks after the second-stage surgical procedure, in which the crowns were cemented with temporary cement.

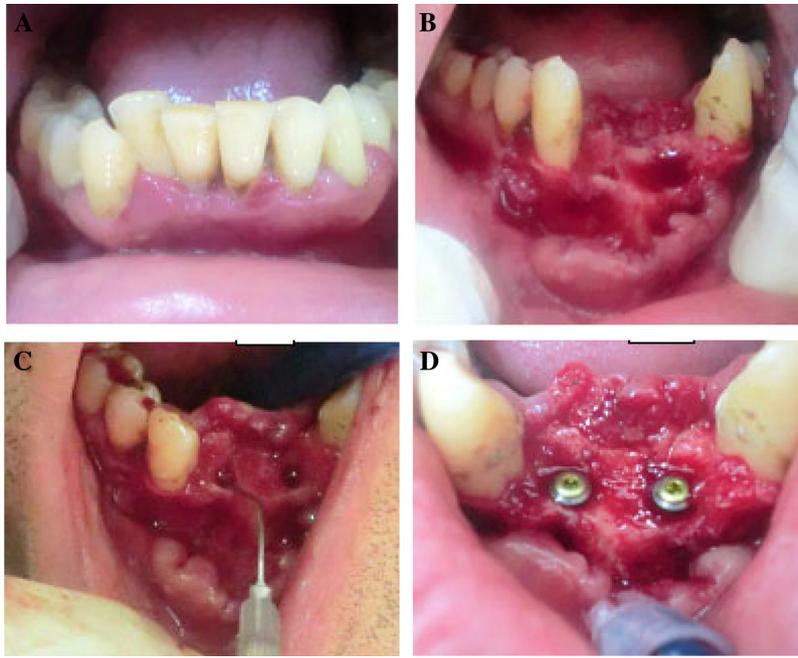


Fig. 1. (A) Before extraction. (B) After extraction. (C) Injection of PRGFs into the test site. (D) Implant placement. (Test: right side; control: left side.)

Follow-up phase

Clinical evaluation

All patients were examined immediately after surgery and during the first week to check if there was pain, discomfort, swelling, or infection. The plaque index (PI) and the bleeding index (BI) were used for clinical evaluation at 6 and 12 months after insertion of the final restoration. In accordance with Mombelli et al.,¹⁵ the probing pocket depth (PPD) around the implant was measured at the four aspects of the implant (the facial, lingual, and proximal surfaces) using a probe graduated in millimetres, and the mean was then calculated. PPD was also evaluated after 6 and 12 months.

Radiographic evaluation

Radiographic examinations with digital panoramic radiographs were performed within 7 days after surgery as the baseline and at 3, 6, and 12 months (Fig. 2). An independent radiologist analyzed the radiographs without knowledge of which implant was treated with PRGFs. The saved image was opened in ImageJ program. The reference for measurements was the implant–abutment interface and the scale was determined in reference to the known implant length. From the ‘Analyze’ command, the ‘Set Scale’ command was selected to convert pixel dimensions into millimetres. A line was

drawn from the implant apex to the implant shoulder. The length of the implant fixture was measured and compared to the real implant length to determine the magnification factor in the image. The distance from the implant apex to the first seen point of bone–implant contact was measured. The difference between this and the implant length represents a vertical marginal bone defect. The measurements were

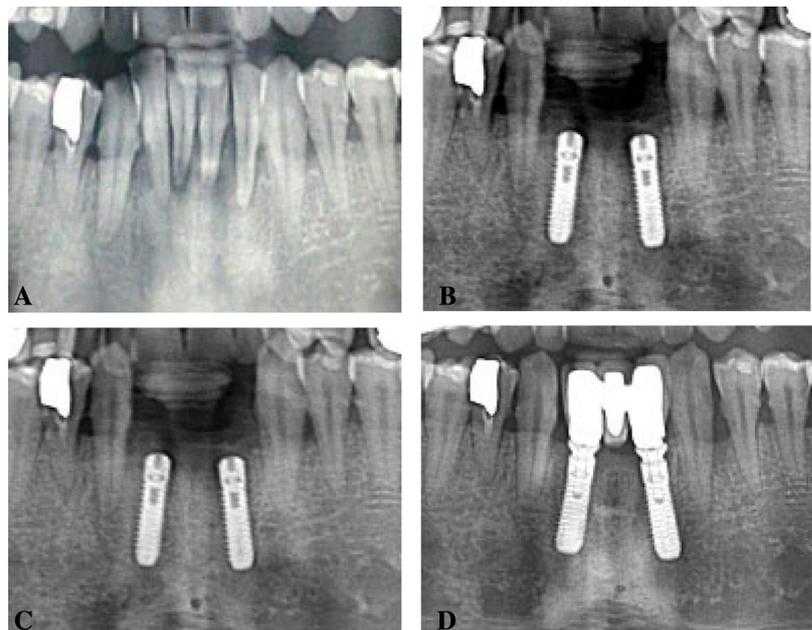


Fig. 2. Radiographic evaluation. (A) Before extraction. (B) Immediately after implant placement. (C) After 3 months. (D) After 1 year. (Test: right side; control: left side.)

noted mesially and distally and the mean was calculated in millimetres according to the magnification factor of the image. In accordance with Buser et al.,¹⁶ an implant was classified as having survived if the following parameters were met: (1) absence of recurring peri-implant infection with suppuration; (2) absence of persistent subjective complaints such as pain, foreign body sensation, and/or dysesthesia; (3) absence of a continuous radiolucency around the implant; and (4) absence of any detectable implant mobility.

Data analyses

The statistical analyses were performed using SPSS version 17 software (SPSS Inc., Chicago, IL, USA). Comparisons between quantitative variables were carried out by Student *t*-test of two independent samples. The results were considered to be significant at *P*-values of less than 0.05.

Results

Each patient received two implants with a diameter of 3.6 mm and a length between 10 and 12 mm. All patients showed good compliance and the healing period was uneventful for both treatment groups, without infections or complications. The survival rate was 100% in both groups and none of the implants lost osseointegration. The baseline analysis showed no significant differences between group I and group II for any of the variables assessed,

Table 1. Plaque index (PI) and bleeding index (BI) of the tested groups at 6 and 12 months of follow-up.^a

	PI			BI		
	Group I	Group II	P-value	Group I	Group II	P-value
6 months	0.5 ± 0.4	0.5 ± 0.3	0.890	0.6 ± 0.4	0.6 ± 0.3	0.784
12 months	1.0 ± 0.4	0.9 ± 0.1	0.357	1.0 ± 0.3	1.0 ± 0.2	0.583

^a Results are the mean ± SD (n = 15). Group I, treated with PRGFs; group II, control.

Table 2. Marginal bone loss (MBL) and probing pocket depth (PPD) in the tested groups (I and II) at the different follow-up assessments.^a

	MBL (mm)			PPD (mm)		
	Group I	Group II	P-value	Group I	Group II	P-value
Baseline	0.0 ± 0.0	0.1 ± 0.1	0.817	–	–	–
3 months	0.2 ± 0.1	0.6 ± 0.0	0.000	–	–	–
6 months	0.4 ± 0.1	0.9 ± 0.1	0.000	2.4 ± 0.4	2.9 ± 0.2	0.002
12 months	0.6 ± 0.1	1.1 ± 0.1	0.000	3.4 ± 0.4	3.8 ± 0.3	0.025

^a Results are the mean ± SD (n = 15). Group I, treated with PRGFs; group II, control.

thus allowing the post-treatment results to be compared.

Plaque index (PI)

As shown in Table 1, there were no significant differences between the control and test groups at 6 and 12 months, at the 5% level (P > 0.05). Mean PI values were 0.5 ± 0.3 at the control site and 0.5 ± 0.4 at the test site after 6 months. These values were 0.9 ± 0.1 at the control site and 1.0 ± 0.4 at the test site after 12 months.

Bleeding index (BI)

As shown in Table 1, there were no significant differences between the control and test groups at 6 and 12 months, at the 5% level (P > 0.05). Mean BI values were 0.6 ± 0.3 at the control site and 0.6 ± 0.4 at the test site after 6 months. These values were 1.0 ± 0.2 at the control site and 1.0 ± 0.3 at the test site after 12 months.

Probing pocket depth (PPD)

As shown in Tables 2–4, there were significant differences between the control and test groups at 6 and 12 months, at

the 5% level (P < 0.05). Mean PPD values were 2.9 ± 0.2 mm at the control site and 2.4 ± 0.4 mm at the test site after 6 months. These values were 3.8 ± 0.3 mm at the control site and 3.4 ± 0.4 mm at the test site after 12 months.

Marginal bone loss (MBL)

Results revealed that at 3 months of follow-up, the mean MBL values were 0.6 ± 0.0 mm at the control site and 0.2 ± 0.1 mm at the test site (Tables 2–6). At 6 months of follow-up, the mean values were 0.9 ± 0.1 mm at the control site and 0.4 ± 0.1 mm at the test site. At 12 months of follow-up, the mean values were 1.1 ± 0.1 mm at the control site and 0.6 ± 0.1 mm at the test site. There were statistically significant differences in mean MBL between the two sites for the different observation periods (P < 0.05).

Discussion

The purpose of this study was to evaluate the clinical and radiographic outcomes following the use of PRGFs with immediate implant placement in periodontally

compromised extraction sites. PRGFs have been used in the field of bone grafts for regeneration around implants, as well as for the pre-grafting of future implant sites.^{17,18} In the present study, the combination of PRGFs and immediate post-extraction implant placement led to excellent clinical outcomes. Soft tissue healing was uneventful in all patients. At 6 and 12 months of follow-up, none of the patients suffered from pain or peri-implant infection. No implants were lost in either group throughout the study period—the survival rate of dental implants in the present study was 100%.

Clinical parameters were measured at 6 months and 12 months at both sites in each patient. There was no statistically significant difference in mean BI or PI between the test and control sites. Evian et al.¹⁹ studied the effects of periodontal disease and immediate placement on implant survival and found the survival rate to be 78.18% in the immediate group. They found that implant survival was compromised by a history of periodontitis but was not affected by the immediate or delayed placement. In the study of Horwitz et al., the survival rate after immediate implant placement in the periodontally compromised extraction sites group was 65%.²⁰ In another study by Horwitz et al.,²¹ the effect of immediate restoration on radiographic bone changes was evaluated and MBL was 1.23 ± 0.20 mm in the immediately restored implants group.

The interaction of PRP with titanium implants with acid-etched surfaces has been examined by environmental scanning electron microscopy in previous experimental studies.^{22,23} Histomorphometric analysis of the bone-implant interface in goats performed after 8 weeks showed that the implant surface adsorbed the protein-rich material and that osseointegration was enhanced when the surface was covered with PRGFs.¹²

In the present study there were statistically significant differences between the test and control groups regarding PPD and MBL throughout the follow-up period.

Table 3. Mean probing pocket depth—group I (treated with PRGFs).

Case no.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
6 months	2	2.5	2.5	2	2.25	2.25	3	2.25	2.5	2.25	2	2.5	3	2.25	3.25
12 months	3.25	3.5	3.25	3.25	4	3.25	3.25	3.25	3.25	3.25	3.5	3.25	3.25	3	4.75

Table 4. Mean probing pocket depth—group II (control).

Case no.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
6 months	3.25	2.5	3	3	2.5	3	3	2.75	3	3	3	3.25	2.5	2.75	3
12 months	4	3.5	3.5	3.75	3.5	3.75	4.25	3.25	3.75	3.75	3.25	4.25	3.75	3.75	3.5

Table 5. Mean marginal bone loss—group I (treated with PRGFs).

Case no.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Baseline	0.1	0.0	0.0	0.0	0.0	0.7	0.0	0.7	0.0	0.0	0.0	0.7	0.0	0.0	0.0
3 months	0.2	0.3	0.2	0.3	0.3	0.3	0.3	0.2	0.3	0.3	0.1	0.3	0.3	0.1	0.3
6 months	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.5	0.5	0.4	0.5	0.4	0.4	0.4	0.4
12 months	0.5	0.7	0.5	0.7	0.5	0.5	0.4	0.5	0.5	0.5	0.7	0.5	0.5	0.5	0.5

Table 6. Mean marginal bone loss—group II (control).

Case no.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Baseline	0.1	0.1	0.1	0.3	0.1	0.0	0.3	0.1	0.1	0.0	0.0	0.1	0.1	0.1	0.1
3 months	0.5	0.6	0.5	0.5	0.6	0.6	0.6	0.6	0.5	0.6	0.6	0.6	0.5	0.6	0.5
6 months	0.8	0.9	0.8	0.8	0.9	0.8	0.9	0.8	0.8	0.9	0.8	0.9	0.8	0.9	0.8
12 months	1.1	1.1	1.2	1.1	1.2	1.1	1.2	1.1	1.1	1.1	1.0	1.1	1.0	1.1	1.1

After 12 months, the mean MBL values in this study were 1.1 ± 0.1 mm at the control site and 0.6 ± 0.1 mm at the test site; the difference in MBL between the two groups was 0.5 mm. According to the criteria of Alkerktsson et al.,²⁴ the implant is considered successful if MBL is <1.5 mm in the first year, hence the difference of less than 1 mm over 1 year is unlikely to be of any clinical relevance for implant success.

Del Fabbro et al.,²⁵ in a single-cohort study, evaluated the clinical outcome of implants placed immediately into fresh extraction sockets of teeth affected by chronic peri-apical pathological findings, using PRGFs as an adjunct during the surgical procedure. They concluded that the use of PRGFs combined with an immediate implant placement procedure can be considered a safe, effective, and predictable treatment option for the rehabilitation of fresh post-extraction infected sockets. Contradictory results were reported in a recent animal study by Casati et al.,¹⁴ who investigated the influence of PRP on bone regeneration in dehiscence-type bone defects around dental implants. They demonstrated that that PRP alone did not enhance bone regeneration for peri-implant defects.¹⁴ The results of the study by El-Marssafy et al. are also contradictory; they studied the effects of adding PRP with immediately loaded self-tapping dental implants placed in healed bony sites on the acceleration of osseointegration or reduction of crestal bone resorption around these implants.²⁶ They concluded that the local application of autologous PRP into the prepared drill holes immediately before implant placement did not accelerate the rate of osseointegration or decrease the crestal bone resorption in immediately loaded dental implants placed in the posterior maxillary area.²⁶

Within the limits of the present study, the use of PRGFs with the immediate placement of dental implants in periodontally compromised extraction sites reduces marginal bone loss around the implant. The results of this study need to be confirmed over a longer follow-up and with a larger number of patients.

Funding

Nothing to declare.

Competing interests

Nothing to declare.

Ethical approval

This study was approved by an ethics committee of Al-Andalus University of Medical Sciences.

Patient consent

Written patient consent was obtained.

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