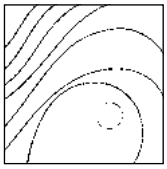
Use of Platelet-Rich Fibrin Membrane Following Treatment of Gingival Recession: A Randomized Clinical Trial



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This 6-month randomized controlled clinical study primarily aimed to compare the results achieved by the use of a platelet-rich fibrin (PRF) membrane or connective tissue graft (CTG) in the treatment of gingival recession and to evaluate the clinical impact of PRF on early wound healing and subjective patient discomfort. Use of a PRF membrane in gingival recession treatment provided acceptable clinical results, followed by enhanced wound healing and decreased subjective patient discomfort compared to CTG-treated gingival recessions. No difference could be found between PRF and CTG procedures in gingival recession therapy, except for a greater gain in keratinized tissue width obtained in the CTG group and enhanced wound healing associated with the PRF group. (Int J Periodontics Restorative Dent 2012;32:e41–e50.)

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Gingival recession is defined as the displacement and destruction of the soft tissue margin apical to the cementoenamel junction (CEJ). Obtaining predictable root coverage supported by a significant level of tissue regeneration has become an essential element of periodontal plastic surgery. Clinical and histologic data reveal that the platelet concentrate therapeutic concept would be an encouraging medium for improvement of soft tissue healing and regeneration in periodontology and implant dentistry.[1–3] Platelet-rich fibrin (PRF) belongs to a new generation of platelet concentrates with simplified processing. PRF was first developed in France by Choukroun et al[1] for specific use in oral and maxillofacial surgery. PRF preparation techniques require neither anticoagulant nor bovine thrombin. This study was designed to evaluate the implementation of PRF in gingival recession treatment. An important issue of the study was the assessment of the impact of PRF on soft tissue healing.

There are three crucial factors for healing and soft tissue maturation: angiogenesis, growth factors, and mesenchymal stem cell activity. A number of studies have confirmed that the specific dense three-dimensional (3D) structure of the fibrin gel in PRF and the action of cytokines trapped in the mesh fibrin matrix promote neoangiogenesis.[4–6] Angiogenesis requires an extracellular matrix to permit migration, division, and phenotype change of endothelial cells. Rapid neovascularization has a vital role in the tissue reparation and regeneration processes.

The published data validate that PRF membrane can be considered as an effective healing biomaterial. It features all the essential parameters permitting optimal healing. PRF membrane consists of a fibrin 3D mesh polymerized in a specific structure; the incorporation of platelets, leukocytes, and growth factors; and the presence of circulating stem cells.[7,8]

It is conceivable that concentrated growth factors within platelet concentrate entrapped in the fibrin mesh up-regulate cellular activity and subsequently promote periodontal regeneration in vivo.[9] Fibrin, fibronectin, platelet-derived growth factor (PDGF), and transforming growth factors (TGF-β) from platelet concentrate are essential for tissue reparation and regeneration. During PRF processing by centrifugation, platelets are activated, and their massive degranulation implies a very significant cytokine release.[1,7,8] Concentrated platelet-rich plasma (PRP) cytokines have already been quantified in many technologic configurations. Okuda et al[10] demonstrated that platelet concentrate contains PDGF and TGF-β at high levels and that PRP stimulates fibroblastic and osteoblastic proliferation but suppresses epithelial cell proliferation.[11] Moreover, the fibrin clot derived from PRP is able to stimulate high levels of type I collagen synthesis.[12] Biochemical analysis of the PRF composition indicates that this biomaterial consists of an intimate assembly of cytokines, glycanic chains, and structural glycoproteins enmeshed within a slowly polymerized explicit fibrin network.[1,3,13] Moreover, a specific fibrin polymerization mode in PRF provides an increased life span for these cytokines, which is especially encouraging for the healing process.[13]

Gingival recession presents loss of both soft and hard tissues. A wide variety of periodontal plastic surgical procedures have been described to correct mucogingival problems and to cover denuded root surfaces. Esthetic concerns are usually the reason to perform these procedures. Clinical studies have evaluated many such techniques. During the 1970s, the coronally positioned flap[14] and lateral sliding flap[15] were the most accepted techniques. Root coverage procedures became accepted as predictable procedures when Miller[16] demonstrated high success rates with a thick autogenous masticatory graft (free gingival graft). His studies changed the approach of the periodontist to accept that predictable root coverage was possible with a single surgical procedure. However, the procedure was not without problems, as the esthetics were usually not ideal. In an attempt to solve these problems, Raetzke[17] and Langer and Langer[18] proposed techniques using free connective tissue grafts. These techniques addressed the esthetic problems with the free gingival graft, and the results were still predictable. Others have added different variations using a connective tissue graft (CTG) and an overlaying pedicle graft.[19–21] Histologic studies on CTGs show unpredictable results related to regeneration of periodontal tissues. There is evidence of only minimal bone formation found in the most apical portion of the treated region.[22]

Several studies reported the use of platelet concentrate (PRP) in mucogingival periodontal surgery. Petrungaro[23] presented a case series in which PRP, CTG, and collagen membranes were used to cover gingival recessions. In one of these cases, a PRP-impregnated CTG was placed on the surface and the site was covered with a coronally advanced flap (CAF). The 2-month results including 3 mm of root coverage were satisfactory. Griffin and Cheung[24] compared a platelet concentrate graft and CTG for treating bilateral gingival recessions. They concluded that use of a platelet concentrate graft might result in a better esthetic outcome. Jankovic at al[25] and Keceli et al[26] compared the clinical effectiveness of CTG + PRP with CTG alone in the treat-

ment of gingival recessions. No difference in clinical parameters was recorded between groups, except for gain in keratinized tissue width.[25] Huang at al[27] evaluated the effects of PRP in combination with a CAF, and the results showed no clinically measurable enhancements on the final outcome.

To the authors' knowledge, no case report has been published regarding the use of PRF in the treatment of gingival recession. The aim of this pilot study was to evaluate and validate the clinical impact of PRF, a platelet concentrate collecting on a fibrin membrane, in the treatment of gingival recession. The main purpose of this study was to estimate the potential of PRF to accelerate wound healing. Also, the authors wanted to assess soft tissue healing and postoperative discomfort in the group of recessions treated with the PRF membrane.

Method and materials

Fifteen patients from the Clinic for Periodontology, School of Dentistry, University of Belgrade, Belgrade, Serbia, were consecutively enrolled for this clinical study. They consisted of 5 men and 10 women between 19 and 47 years of age. Prior to their selection, all patients completed a routine questionnaire, from which the following data were obtained: general medical history, age, sex, and smoking habits. All patients were systemically healthy and without any significant history of systemic diseases. Similarly, all patients underwent a full-mouth dental and periodontal examination performed by the same examiner. Patients diagnosed with periodontitis were excluded. All patients received professional tooth cleaning consisting of prophylaxis, scaling and root planing, if needed, and oral hygiene instructions. Patients were informed of the characteristics of the study and gave their written consent to the procedures. The study was approved by the Institutional Committee for Human Investigations. The inclusion criteria were: presence of either bilateral isolated or multiple defects with recession depths greater than or equal to 2 mm when measured from the CEJ on anterior teeth or premolars, all defects judged as Miller Class I or II, and the selected teeth had to be vital, free of restorations or with restorations removed, and with no bleeding on probing.

One calibrated examiner blinded to the surgical treatment collected the data at baseline and 6 months postoperative at the Clinic for Periodontology. All measurements were performed by the same operator. Randomization for test and control treatments was performed using a coin toss.

All 15 patients received bilateral surgical treatment of gingival recessions. On one side, the gingival recession was treated with a CAF and PRF membrane (PRF group). The other side was treated with a CTG in combination with a CAF (control).

PRF protocol

A blood sample was taken without anticoagulant in a 10-mL tube, which was immediately centrifuged at 3,000 rpm (approximately 400 g) for 10 minutes. Blood processing with a centrifuge for PRF allows the composition of a structured fibrin clot in the middle of the tube between the red corpuscles at the bottom and acellular plasma at the top (Fig 1). After collection of the PRF itself, resistant autologous fibrin membranes were easily obtained by driving out the serum from the clot (Figs 2 and 3).[10]

Surgical protocol

After obtaining adequate anesthesia, the exposed root surfaces in both groups were scaled and planed using hand and ultrasonic instruments (Fig 4a). The initial intrasulcular incisions in the region of the recipient site were beveled into the adjacent interdental papilla at or slightly coronal to the CEJ of the tooth with an exposed root surface. A full-thickness flap was reflected beyond the mucogingival junction and at least 5 mm apical to the most apical margin of the bony dehiscence (Fig 4b). The flap was further released by sharp dissection. The mesiodistal length of the incision was extended to the nearest distal line angle of the most mesial and distal teeth involved. Mesial and distal vertical releasing incisions were made in each procedure. PRF membrane was positioned and

Fig 1 *Blood centrifugation immediately after collection allows the composition of a structured and resistant fibrin clot.*

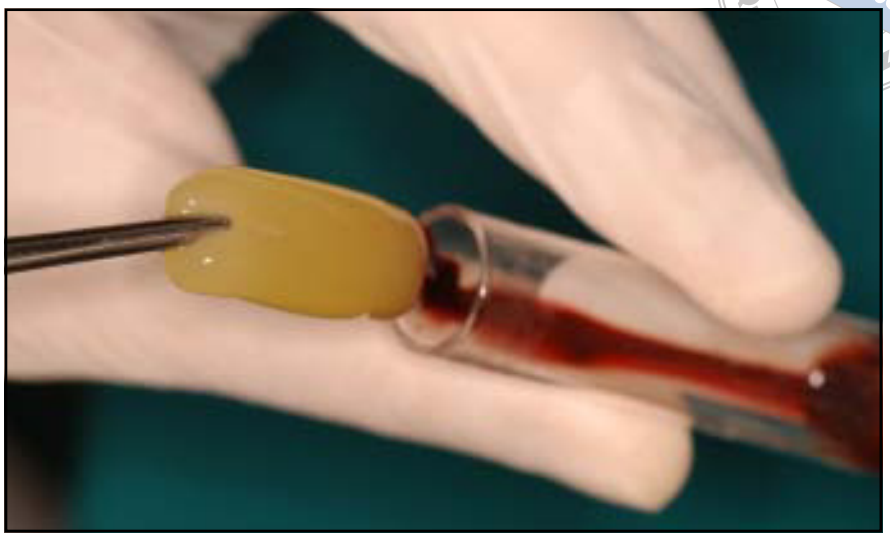

Fig 2 *PRF clot removal.*

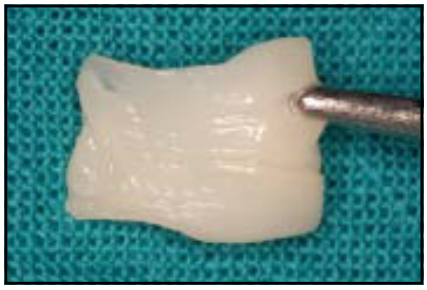

Fig 3 (left) *Autologous PRF membrane obtained by driving out the serum from the clot.*

stabilized with a horizontal mattress suture in the intended position (Fig 4c). The flap was then positioned coronally to completely cover the PRF membrane using a vertical mattress suture (Fig 4d), and periodontal dressing was positioned over the treated regions. Sutures were removed 2 weeks after the surgical procedure (Figs 4e and 4f). All patients were placed on 0.12% chlorhexidine gluconate mouthrinse for 3 weeks and advised to follow routine periodontal mucogingival surgical postoperative instructions.

The control group (CTG) was treated with the identical surgical procedure, with the exception of applying the PRF membrane. A CTG was used as the augmentation material in the control group (Fig 5).

Periodontal clinical variables were evaluated in both groups. Prior to surgery, the following measurements were performed using a standard periodontal probe and were rounded to the nearest 0.5 mm: vertical gingival recession depth (VRD), distance from the CEJ to the free gingival margin (the middle point of the exposed root was considered); clinical attachment level (CAL), distance from the CEJ to the base of the gingival crevice; clinical probing depth (PD), distance between the free gingival margin and the base of the gingival crevice; and keratinized tissue width (KTW), distance from the free gingival margin to the mucogingival junction. Clinical parameters were recorded at baseline and the 6-month follow-up by the same examiner (Figs 4f and 5d). Clinical evaluations of healing events were estimated with recordings of the Healing Index, which were performed at the first, second, and third week postsurgery. The Healing Index[28] rates healing on the basis of redness, presence of granulation tissue, bleeding and suppuration, and epithelialization. A score of 1 to 5 is given, with 1 associated with very poor healing and 5 being excellent.

Statistical analysis

Data were expressed as means ± standard deviations of the parameters evaluated. Comparisons were made within each group between the baseline and 6-month evaluations. The Student paired *t* test was used to compare intragroup and intergroup measurements at baseline and 6 months. A level of

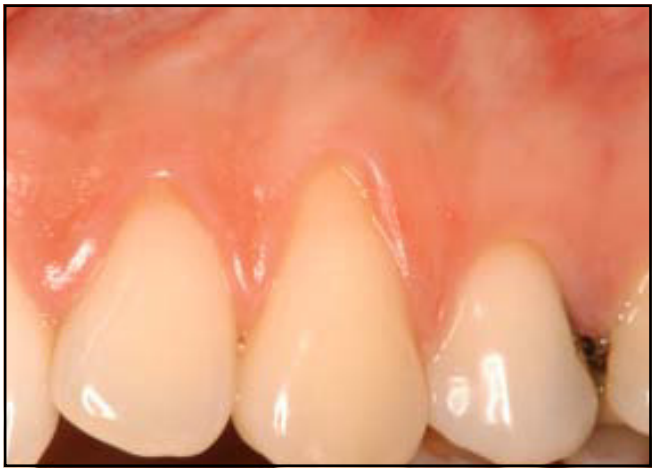

Fig 4a *A 21-year-old woman presented with a 3-mm gingival recession at the maxillary left canine.*

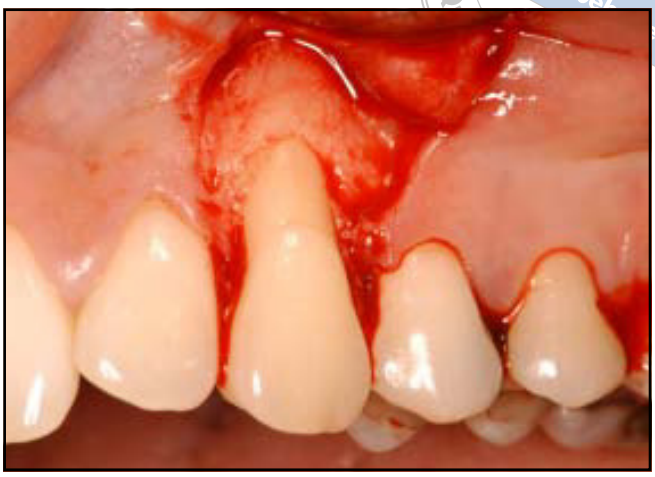

Fig 4b *A full-thickness flap with mesial and distal releasing incisions was elevated.*

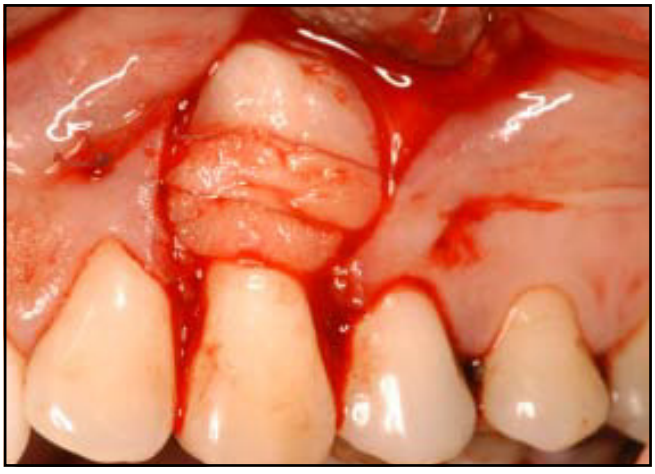

Fig 4c *PRF membrane placed and stabilized on the recipient site.*

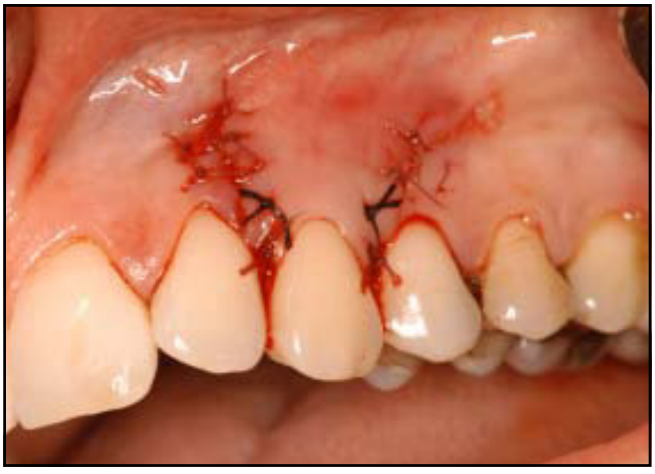

Fig 4d *CAF sutured over the PRF.*

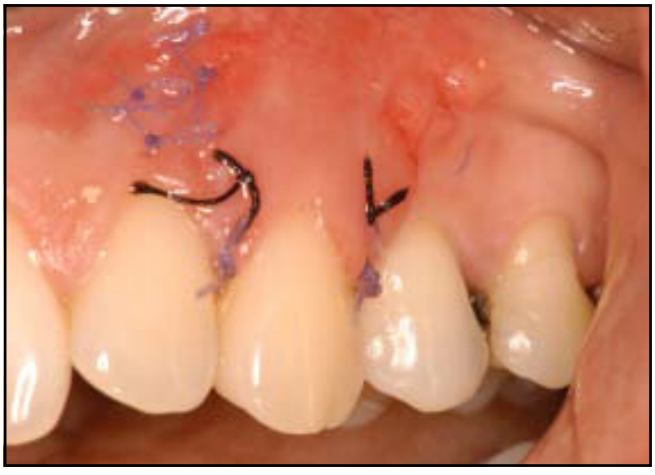

Fig 4e *Seven-day postoperative view.*

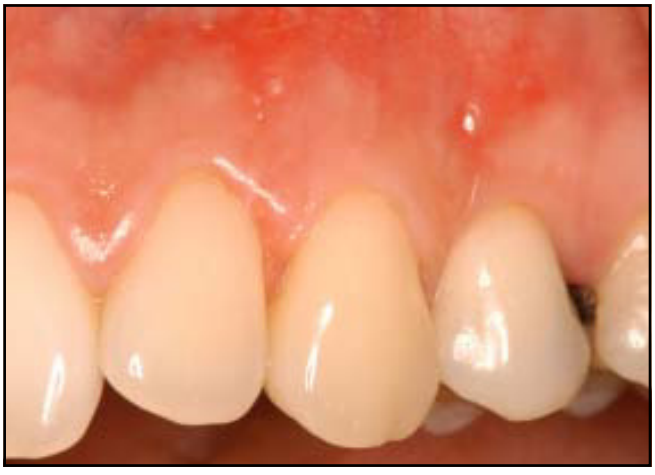

Fig 4f *Six months postoperatively, complete root coverage was obtained.*

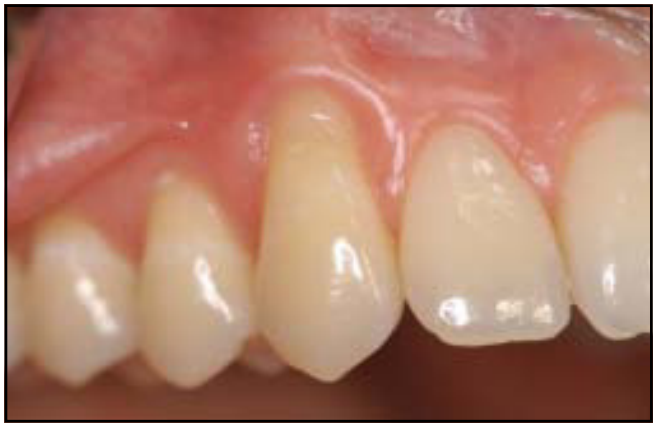

Fig 5a *A 28-year-old woman presented with a 5-mm gingival recession at the maxillary right canine.*

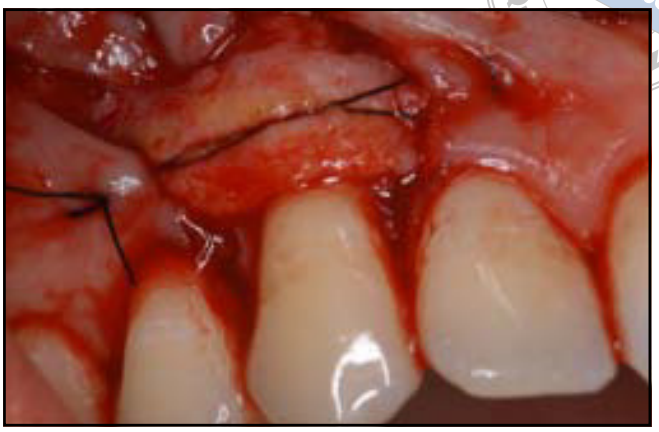

Fig 5b *CTG placed and stabilized at the recipient site.*

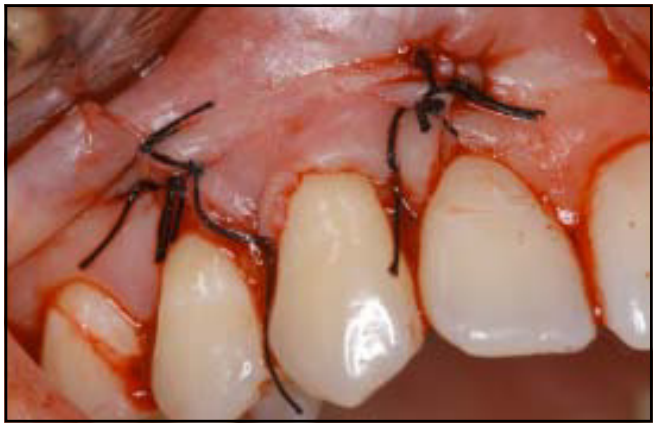

Fig 5c *CAF sutured over the CTG.*

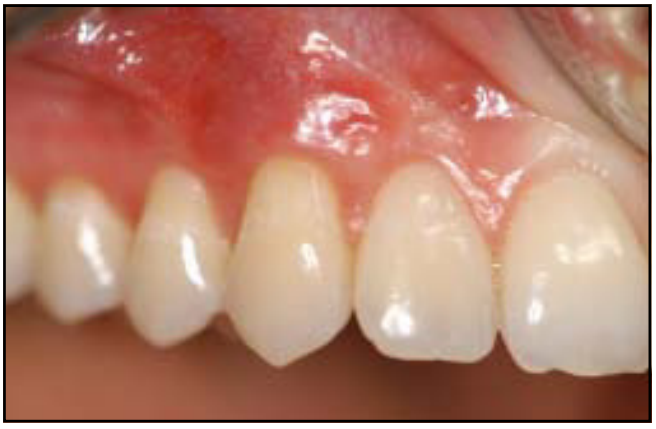

Fig 5d *Six months postoperatively, complete root coverage was obtained.*

significance of .05 was used for all statistical comparisons.

The subjects' overall postoperative pain was assessed for the first 7 days using a horizontal scale, with the left endpoint marking no pain (0), middle point marking pain (1), and right endpoint marking severe pain (2). A significance level of .05 was employed in all statistical comparisons. Pain level assessment was correlated only with control and test site symptoms. Symptoms connected with the donor site were not included in the study assessment.

Results

During the evaluation period, no side effects were reported. Tables 1 to 3 illustrate the results of the evaluations at baseline and 6 months. VRD in the PRF group decreased from 3.51 ± 0.70 mm to 0.68 ± 0.45 mm, corresponding to a mean root coverage of 88.68% ± 10.65%. In the control (CTG) group, VRD decreased from 3.45 ± 0.84 mm to 0.38 ± 0.48 mm, corresponding to a mean root coverage of 91.96% ± 15.46%. Complete root coverage was achieved in 75.85% of cases in the PRF group and 79.56% of cases in the control group. The differences between the groups were not statistically significant at baseline or 6 months (Table 3).

KTW in the PRF group increased from 1.32 ± 0.66 mm to 2.20 ± 0.54 mm. In the control group, KTW increased from 1.41 ± 0.58 mm to 2.85 ± 0.45 mm. The gain in KTW was statistically significant for both groups, although it was significantly greater for the CTG group in comparison with the PRF ($P < .05$) (Table 3).

Table 1 Clinical results of the PRF group (mm)

	Baseline	6 mo	*P*
VRD	3.51 ± 0.70	0.68 ± 0.45	.000*
KTW	1.32 ± 0.66	2.20 ± 0.54	.000*
CAL	4.35 ± 0.67	1.48 ± 0.40	.000*
PD	0.74 ± 0.53	0.95 ± 0.41	.167

VRD = gingival recession; KTW = apicocoronal width of the keratinized tissue; CAL = clinical attachment level; PD = pocket depth.
*Statistically significant ($P < .05$).

Table 2 Clinical results of the CTG group (mm)

	Baseline	6 mo	*P*
VRD	3.45 ± 0.84	0.38 ± 0.48	.000*
KTW	1.41 ± 0.58	2.85 ± 0.45	.000*
CAL	4.31 ± 0.61	1.35 ± 0.38	.000*
PD	0.86 ± 0.47	0.92 ± 0.48	.167

VRD = gingival recession; KTW = apicocoronal width of the keratinized tissue; CAL = clinical attachment level; PD = pocket depth.
*Statistically significant ($P < .05$).

Table 3 Mean changes in clinical recordings 6 mo after surgery (mm)

	PRF	CTG	*P*
VDR	2.83 ± 0.37	3.07 ± 0.30	.270
KTW	0.88 ± 0.71	1.44 ± 0.63	.013*
CAL	2.87 ± 0.39	2.96 ± 0.42	.413
PD	0.21 ± 0.10	0.16 ± 0.09	.335

VRD = gingival recession; KTW = apicocoronal width of the keratinized tissue; CAL = clinical attachment level; PD = pocket depth.
*Statistically significant ($P < .05$).

No significant changes were recorded in the two groups between baseline and 6 months for PD.

In the PRF group, CAL decreased from 4.35 ± 0.67 mm to 1.48 ± 0.40 mm, with an attachment gain of 2.87 mm. In the control group, CAL decreased from 4.31 ± 0.61 mm to 1.35 ± 0.38 mm, with an attachment gain of 2.96 mm. The differences between the two groups were not statistically significant for CAL.

Recordings of the Healing Index showed enhanced values obtained in the PRF group for the first 2 weeks after surgery in comparison with the control group. Results recorded in the PRF group after 1 and 2 weeks of surgery were 3.11 ± 0.32 and 4.20 ± 0.27, respectively. Healing Index values obtained in the control group for the first and second week postsurgery were 2.25 ± 0.54 and 3.05 ± 0.38, respectively. Results obtained in the PRF group were statistically superior in reference with data recorded in the CTG group ($P < .05$). Recordings obtained in the PRF and CTG groups 3 weeks after surgery showed a high level of equivalence (4.51 ± 0.21 and 4.29 ± 0.36, respectively; $P > .05$).

Regarding the postoperative period, 1 patient in the PRF group experienced severe pain compared to 7 patients in the CTG group. All 15 patients indicated a greater discomfort in the CTG group. The pain intensity was statistically different between groups for the first 7 days, favoring the PRF group (Table 4).

Table 4 Pain intensity in the first 7 days after surgery

Day	PRF	CTG	*P*
1	0.46 ± 0.64	1.46 ± 0.51	< .01*
2	0.40 ± 0.50	1.33 ± 0.48	< .01*
3	0.33 ± 0.48	1.20 ± 0.41	< .01*
4	0.33 ± 0.48	1.06 ± 0.45	< .05*
5	0.26 ± 0.46	0.80 ± 0.41	< .05*
6	0.25 ± 0.45	0.60 ± 0.51	< .05*
7	0.20 ± 0.41	0.46 ± 0.51	< .05*

*Statistically significant ($P < .05$).

Discussion

The ultimate goal of mucogingival plastic surgery is predictable and esthetic root coverage. The outcomes of this study revealed that both techniques, either a CTG or PRF membrane covered by a coronally positioned flap, are effective in the treatment of gingival recession defects with significant root coverage (91% and 88%, respectively) and clinical attachment gain 6 months postoperatively. Complete root coverage was obtained in 75.85% of cases in the PRF group and 79.56% of cases in the control (CTG) group. The literature reports wide variations for the clinical parameter of root coverage. Mean root coverage for the CTG in combination with CAF ranges from 70%[29] to 98%.[30–33]

Pilot study data obtained by the application of PRP in periodontal plastic surgery confirmed encouraging results regarding root coverage and esthetics. Controlled clinical trials could not document and verify any additional benefits of PRP use in root coverage except the improved wound healing in the PRP group.[25,34]

This study demonstrated that there were no statistically significant differences in PD or CAL recorded between the two groups. CAL showed significant attachment gain for both groups. For the PRF group, the mean gain was 2.87 mm, and for the control group, it was 2.96 mm. KTW was statistically enlarged for both groups, averaging 0.88 mm and 1.44 mm in the PRF and control groups, respectively. These outcomes are in agreement with literature reports for the treatment of gingival recession with a CTG and CAF.[32,34,35] The important result found in this study was a statistically significant gain in KTW obtained in the CTG group in comparison with the PRF group (Figs 5a, 5d, 6a, and 6b). Increased KTW in the CTG group is related to the ability of the connective tissue of the palatal graft to induce keratinization of the epithelium.[36] Notably, gain in KTW obtained in the group treated with the PRF membrane may be explained as a result of a tissue manifestation of the proliferation of gingival or periodontal fibroblasts as a result of the influence of the growth factors from platelets entrapped in the fibrin mesh. However, this statement must be proven clearly and scientifically in further research. While there was a statistical difference regarding gains in keratinized tissue, the final width in both groups was acceptable.

Results of the Healing Index indicated improvements in early wound healing (first and second week postsurgery) in the group treated with the PRF membrane compared to the group treated without this fraction of plasma. This outcome may be related to the extremely elevated density of fibrin fibers (100× normal) detected in the PRF membrane. High density of fibrin fibers provides additional stability of the wound and promotes rapid neoangiogenesis.[4–6] The improvements in Healing Index values achieved in the PRF group also could be explained as an action of concentrated PDGF, VEGF, and TGF—the main growth factors in PRF. These growth factors might enhance soft tissue healing by increasing the angiogenesis and matrix biosynthesis during wound healing.[27] Regardless of the fact that growth factors trapped in PRF mesh are slowly released and able to accelerate the regenerative potential,

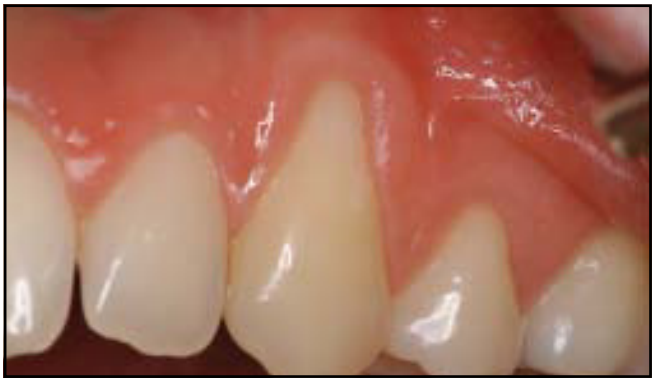

Fig 6a *Preoperative view of a gingival recession at the maxillary left canine treated in the PRF group.*

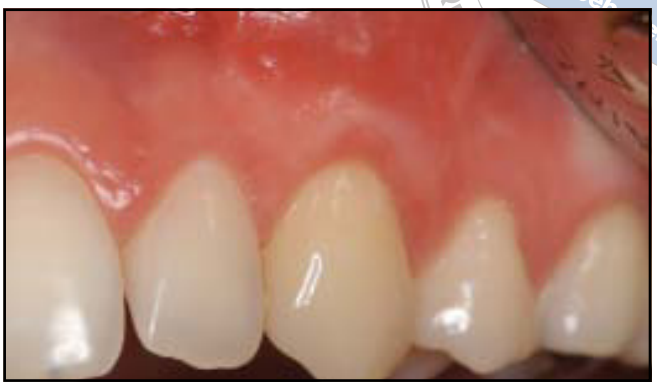

Fig 6b *Postoperative outcome (6 months) of gingival recession treatment with PRF membrane. Note the appreciably minor gain in keratinized tissue in comparison with the gingival recession treated with CTG (compare to Fig 5d).*

the structure of the fibrin network is the key element of the improved PRF healing process.[7] This effect on Healing Index values achieved in the experimental group is directly correlated with decreased patient discomfort for the first 7 days. Patient discomfort data recorded in the PRF group could be explained as a result of enhanced tissue healing and avoidance of a donor site surgical procedure. The data obtained during evaluation of the Healing Index were in high correlation with results presented by Cheung and Griffin.[37]

Recent studies have emphasized that gingival tissue thickness is essential to mean or complete root coverage and stability of the clinical outcome, and an increase in tissue thickness has been described following CTG.[38,39] To the authors' knowledge, there is only one publication[40] that separates root coverage by type or healing pattern with respect to tissue thickness. In this study, gingival tissue thickness assessment was not performed in the PRF and CTG groups. Future studies will evaluate this parameter as a promising potential predictor of root coverage. These studies will provide additional information related to the efficacy of PRF use in gingival recession treatment.

Conclusion

Results of this study indicate that use of a CTG is a highly effective method for root coverage. Clinical implications and advantages of PRF membrane as a graft material are related to avoidance of a donor site surgical procedure, advanced tissue healing for the first 2 weeks postsurgery, and a major decrease in patient discomfort during the early wound-healing period. A high level of observed clinical parameter equivalence between CTG and PRF groups powerfully supports the clinical value of PRF use. The positive tendency for PRF use should be evaluated in studies involving a larger number of subjects. No histologic evaluation was performed in the present study; therefore, the effect of PRF on the overall regenerative capacity remains to be determined.

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