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Original article

# APPLICATION OF PLATELET RICH FIBRIN IN SURGICAL PERIODONTAL THERAPY: A CONTROLLED CLINICAL TRIAL

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**ABSTRACT**

**Purpose:** The current study investigates the effectiveness of two surgical protocols for the treatment of periodontitis (Stage III or Stage IV) in the presence of angular bone defects.

**Materials and methods:** Twenty patients diagnosed with periodontitis were randomly divided into two groups, each of 10 patients with radiographically proven infraosseous defects. The first group delivered surgical treatment with bone graft and platelet rich fibrin, the second group – only with bone graft. Clinical and radiographic parameters were assessed before and 6 months after the surgical procedure.

**Results:** Statistically significant differences were found between both groups in the following parameters: probing pocket depth, clinical attachment gain, bone filling, and radiographic depth of the bone defect before and after periodontal surgery, described as bone filling in millimeters.

**Conclusion:** The results show platelet rich fibrin as an autogenous material with promising potential. Its additional application to bone replacement materials can improve the clinical parameters and the expected filling of the vertical bone defects.

**Keywords:** growth factors, periodontal regeneration, periodontitis, platelet-rich fibrin, platelet-rich plasma,

## INTRODUCTION

The destructive periodontal diseases are featured with periodontal pocket formation, loss of attachment and alveolar bone loss. The regeneration of lost periodontal structures is a goal of periodontal treatment and is characterized by the regeneration of alveolar bone, periodontal ligament, cementum and connective tissue attachment [1, 2]. The non-surgical periodontal therapy of moderate and severe periodontitis in the presence of deep periodontal sites and vertical bone loss aims to establish control of inflammation. The surgical therapy is aimed at achieving true periodontal regeneration, and the current modalities for periodontal surgery involve the use of bone grafts, guided tissue regeneration with barrier membranes, procedures with different types of flaps and additional components, such as: soft tissue grafts, root bio modifiers and growth factors [1-3].

Various growth factors have been studied since they are biologically reactive molecules which have the ability to stimulate cells responsible for regenerative processes. There is evidence showing that growth factors can promote cell proliferation, migration and metabolic activity, as well as affect chemotaxis and extracellular matrix protein production [3].

A resource of growth factors can be platelet-rich plasma (PRP) or platelet rich fibrin (PRF) - the recently preferred product, developed by Choukroun J et al. PRF is a newer generation autogenous platelet concentrate, free from biological and chemical additives. PRF is a fibrin matrix in which platelets and leukocytes are concentrated together with their growth factors and is developed as a second PRP generation. In recent years there has been increasing literature data for the combined use of bone substitutes and barrier membranes with different "growth factors", as well as on the higher regenerative potential associated with the use of growth factors expressed in stimulating the formation of mineralized and non-mineralized tissues [3, 4].

In PRF is observed a finer and more flexible fibrin network able to facilitate the incorporated intrinsic cytokines and cell migration. Such configuration of the fibrin scaffold is proven to provide better survival of platelet-derived growth factors and platelet and leukocyte cytokines. The growth factors and cytokines in PRF are: platelet-derived growth factor-AB (PDGF-AB) - promoting the migration and proliferation of mesenchymal cell lineages; transforming growth factor-β1(TGF-β1) - induces the synthesis of matrix molecules like collagen and fibronectin; insulin-like growth factor-1(IGF-1) - cellular protective agent, a regulator of proliferation and differentiation of most cell types; vascular-endothelial growth factor (VEGF) - important for the angiogenesis and the growth of the fibrin network; interleukin-1β - a key mediator of inflammatory control, able to stimulate T-helper lymphocytes; interleukin-4 - important for the proliferation and differentiation of the B-cells, plays a role in healing, inhibits the stimulation of MMP-1 and MMP-3 by IL-1;

interleukin-6 - acts synergistically with IL-3 and stimulates the proliferation of hematopoietic stem cells in vitro, supports reaction chains which lead to inflammation, destruction and remodeling. The final fibrin clot and its 3D structure is similar to naturally polymerized fibrinogen, which also carries numerous "growth factors" and gives higher strength and elasticity to the fibrin matrix. This is confirmed by the clinical properties of PRF membrane - elasticity, strength and structure, which allows being sutured. Literature data indicates that the combination of bone grafts with PRP and PRF in regenerative surgical techniques for the treatment of infraosseous defects results in better clinical outcomes [5].

The **aim** of the current study is to investigate the effectiveness of two surgical protocols for the treatment of periodontitis in the presence of angular bone defects - bone filling with bone graft alone or with bone graft and PRF together.

## MATERIALS AND METHODS

Ethical approval for this study was obtained from the Research Ethics Committee at the Medical University of Sofia (KENIMUS). All participants were informed about the design and the aim of the study and signed informed consent.

Twenty patients diagnosed with periodontitis were included in the study. They were randomly divided into two groups, each of 10 patients with radiographically proven infraosseous defects. The first group delivered surgical treatment with bone graft and PRF, the second group – only with bone graft.

**Including criteria**: systemically healthy individuals with generalized periodontitis, presence of periodontal pockets with PD ≥5 mm at least 8 teeth, clinical attachment loss ≥5 mm, radiographically proven bone loss, presence of vertical bone defects deeper than 3 mm.

**Excluding criteria**: patients with systemic disease or condition associated with loss of periodontal structures or modulating the development and progression of periodontitis (diabetes, immunodeficiency viral diseases), patients on immunosuppressive therapy, patients taking bisphosphonates, on anticoagulant or antiplatelet therapy, patients with thrombocytopenia, hypofibrinogenemia, hemophilia, with unstable haemodynamic parameters (coagulopathies). Pregnant women are not included also.

**The clinical assessment** includes: hygiene index (FMPS - full mouth plaque scores), bleeding on probing (BOP); probing pocket depth (PPD); clinical attachment loss (CAL); radiographic examination: 1) orthopantomography; 2) intraoral retroalveolar x-rays. The bone loss was assessed using a measuring scale in mm (depth and width of the bone defect). The radiographic examination was performed at the initial assessment of the patients (initial database) and six months postsurgically (evaluating the results after the surgical treatment).

**Surgical method**: The surgical procedure was performed under local anesthesia. Sulcular and interdental incisions were done, and vestibular and oral flaps were reflected to allow complete visualization of the lesion. The defects were debrided of all soft tissue, and the root surfaces were scaled and root planed. The bone defects were filled with bone graft and PRF together (Group I) or only with bone graft (Group II).

The defects were filled to the level of the remaining alveolar bone. The flaps were closed and sutured with interrupted interdental sutures using nonabsorbable silk suture 5-0.

For each patient, systemic antibiotics (Amoxicillin 500 mg, every 8 hours for 7 days), analgesic drugs (Aulin 100 mg, every 12 hours for 3 days) and 0.2% chlorhexidine gluconate solution (for 2 weeks) were prescribed.

Suture removal was done after the 7th up to the 10th day.

For the platelet rich fibrin (PRF), blood was collected by venipuncture using a closed system type "Butterfly" - 9 ml of blood in 10 ml vacuum tubes (2 tubes in total) without anticoagulants. The tubes were centrifuged at 1300 rpm for 8 min in a PRF DUO centrifuge. The absence of anticoagulants allowed activation of most of the platelets in the sample and induction of the coagulation cascade. The fibrin clot was located in the middle of the tube, between a fraction of acellular plasma on the surface and a red fraction of erythrocytes at the bottom.

The extraction of the PRF clot was performed by removing the red blood cells and placing the clot in a sterile metal cup, where it was mixed with the bone graft (Cerabone®) in a 1:1 ratio for the patients in Group I (Cerabone+PRF).

The bone graft (Cerabone®) was chosen because of its osteoconductive properties. For the current research, Cerabone® with small size particles (0.5 - 1.0 mm) was preferred.

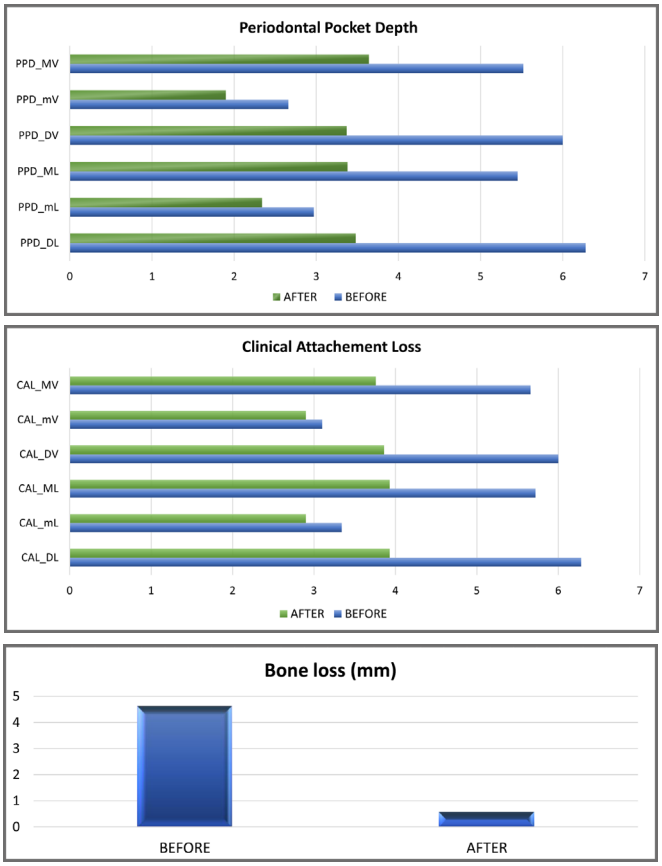
Six months after the surgery, all clinical and radiographic parameters were reassessed.

**Statistical analysis**: Data was implemented in IBM SPSS Statitics 21. For a level of significance at which the null hypothesis is rejected, was set P value of less than 0.05. The applied methods were descriptive statistics, correlation analysis, t-Test and paired t-Test.

## RESULTS:

In the study participated 20 patients diagnosed with moderate or severe periodontitis -10 women and 10 men, aged between 27 and 57 years. Figure 1. A) shows a significant reduction in the parameter probing pocket depth. The achieved results correspond to the clinical parameters of periodontal health when periodontal stability or control is established. Figure 1. B) points out a significant gain of supracrestal attachment at the sites with attachment loss as compared to baseline and after the periodontal surgery. The sites with higher clinical attachment loss show greater gain postsurgical. Figure 1. C) collates the radiographic depth of bone defects (mm) before and after surgical treatment. It shows significant bone filling in all patients with a statistically significant difference ($p<0.001$, paired t-Test).

**Fig. 1.** Changes in the parameter: A) Periodontal pocket depth before and after the surgical treatment in all patients; B) Clinical attachment loss before and after the surgical treatment in all patients; C) Bone loss before and after the periodontal surgery.




After the surgical treatment, the group treated with PRF registered significantly lower values of PPD, CAL and RA (radiographic analysis). The parameters with statistically significant difference ($p < 0.05$) are described in Table 1.

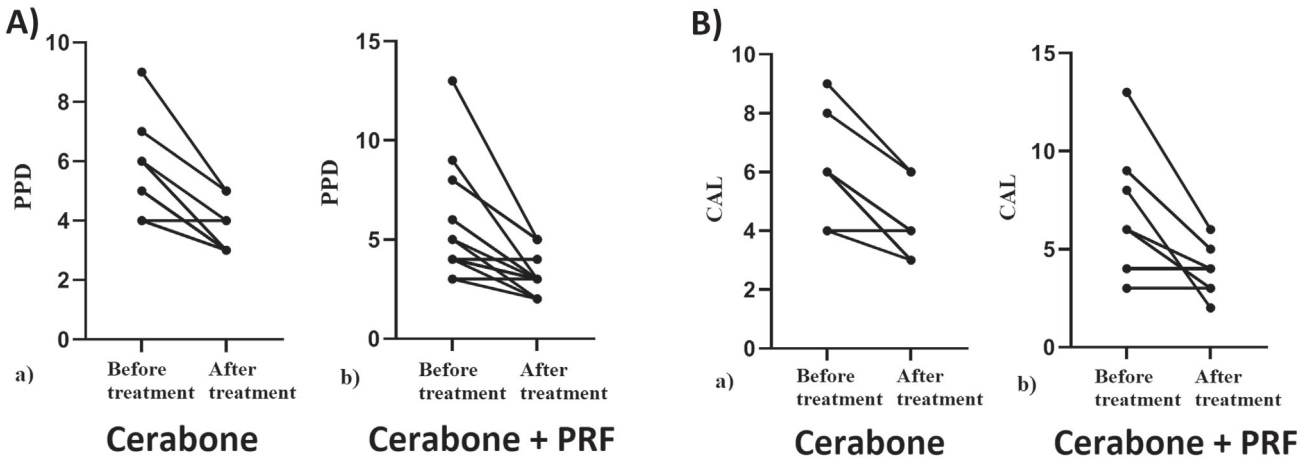
**Table 1.** Statistically significant difference between the studied groups.

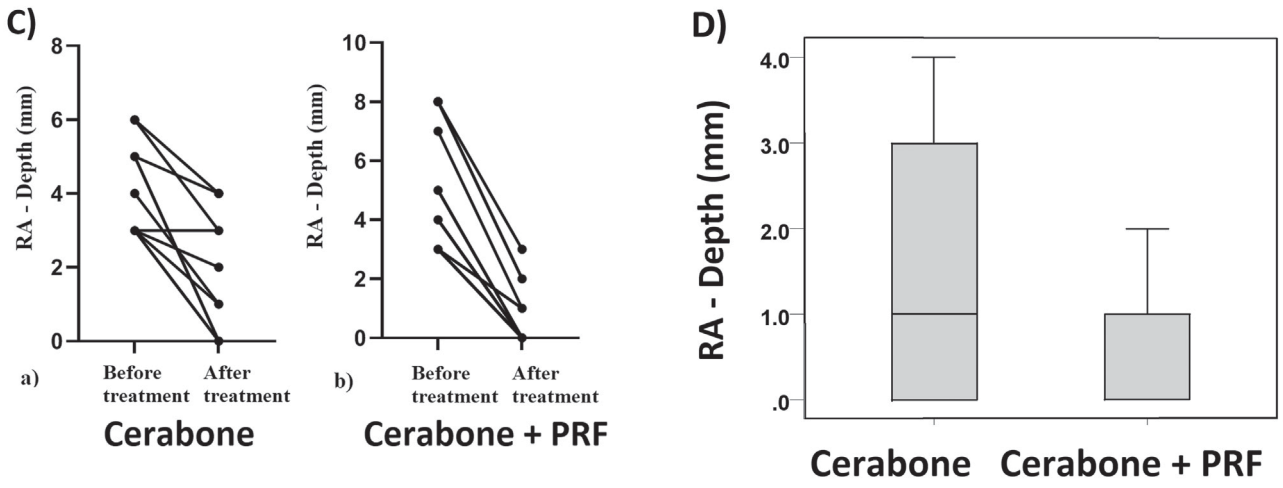
| Indicator | Cerabone | Cerabone +PRF | P coefficient /t-test / |
|---|---|---|---|
| | Mean value | Mean value | |
| Patients, N | 10 | 10 | |
| Teeth, N | 11 | 18 | |
| $PPD_2$ | 2,27 | 1,67 | 0,026 |
| $CAL_2$ | 4,55 | 3,56 | 0,032 |
| RA-after/mm | 1,64 | 0,56 | 0,03 |

Legend: PPD2 – periodontal pocket depth - after; CAL2 – clinical attachment loss - after; RA – radiographic analysis.

Between the two studied groups, statistically significant differences ($p<0.05$) were registered. In the group with PRF was achieved: a statistically significant higher reduction of probing pocket depth (Fig. 2A), clinical attachment gain (Fig. 2B) and bone filling (Fig. 2C). The differences between the results of radiographic analysis RA (in mm) in both groups before and after treatment can be seen in Fig. 2D.

**Fig. 2.** Changes in: A) PPD before and after the surgical treatment: (a) Cerabone, (b) Cerabone +PRF; B) CAL before and after the surgical treatment: (a) Cerabone, (b) Cerabone +PRF. C) Bone defect depth (mm) before and after treatment: (a) Cerabone, (b) Cerabone+PRF; D) The parameter RA (radiographic analysis) in both groups after the surgical treatment - box-plot.






A Paired Samples t-Test was performed to make an assessment in both groups, and statistically significant differences in both types of treatment before and after treatment were observed (p<0.001). Statistically significant differences were obtained for the studied parameter - depth of the infraosseous defect - before and after periodontal surgery (p<0.001) (Table 2A) and B)).

**Table 2.** Statistically significant difference in the defect depth: A) Group II; B) Group

| Paired Samples t-Test | | | Paired Differences | | | | | t | df | Sig. (2-tailed) |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | Std. Mean | Std. Error Deviation | Mean | 95% Confidence Interval of the Difference Lower | Upper | | | |
| A. Statistically significant differences in the depth of the bone defects in patients in group II (Cerabone) | | | | | | | | | | |
| Treatment = 1.00 (Ceraborne) | Pair 1 | RA(before)mm minus RA(sfter)mm | 2.545 | 1.572 | .474 | 1.489 | 3.602 | 5.369 | 10 | .000 |
| B. Statistically significant differences in the depth of the bone defects in patients in group I (Cerabone+PRF) | | | | | | | | | | |
| Treatment = 2.00 (Ceraborne + PRF) | Pair 1 | RA(before)mm minus RA(sfter)mm | 4.056 | 1.305 | .308 | 3.407 | 4.704 | 13.186 | 17 | .000 |

## DISCUSSION

The current study investigates the more innovative protocol of PRP - PRF [6-9]. PRF is developed as a second generation of PRP that uses a simplified protocol - autologous peripheral blood is centrifuged without adding any anticoagulants. PRF can be considered as a physiological scaffold - a fibrin matrix in a 3D-dimensional structure containing cytokines, platelets, leukocytes, circulating mesenchymal cells. The osteogenic ability of PRF in the treatment of intrabony defects, in the management of extraction site and in sinus lift procedures has been lately discussed in the literature [10]. It has been found that the use of PRF improves bone formation [7, 9].

**Combination of PRF and bone grafts**

A lot of research has been done on the combination of PRF with bone replacement materials for the surgical treatment of vertical bone defects. The results favor this combination, and it is accepted that PRF assists the effective organization of the space, maintaining bone graft and the implementation of its osteoconductive effect. Some authors believe that PRF can improve the quality of the used materials by providing cytokines, platelets, growth factors, etc. [11, 12]. Fibrin seems to aid the process of consolidation by keeping the bone graft particles integrated. Therefore, its use is considered to reduce the need for barrier membrane placement during surgery [9]. Studies show that PRF also promotes early bone healing. It improves the proliferation, differentiation, migration and mineralization in the process of bone formation postsurgical. A pronounced haemostatic effect of PRF is also discussed [9, 13].

**Considering the clinical attachment gain**

The clinical attachment gain results correspond to the data in the scientific literature and the results obtained from other authors [8, 14]. They confirm the possibilities of regenerative periodontal surgery using bone substitutes

alone or in combination with PRF in the treatment of vertical bone defects. The established in the study results are comparable with the criteria gain of clinical attachment as a result of reattachment – the restoration of the lost attachment.

**Considering the bone filling**

The results of the study indicate that PRF, due to the various and large amounts of growth factors, successfully promotes bone filling. This conclusion confirms the current literature data for significant radiographic bone filling [6, 8, 15]. The bone filling was monitored radiographically in the 6th month after the surgery [9]. The results demonstrate a significant bone filling in all patients - 3.48 mm (average value). However, comparing both studied groups, statistically, significant differences in the filling of the existing bone defects were found. Radiographic data presented residual bone pockets of 0.56 mm in the first group (Cerabone +PRF) compared to the second group (Cerabone alone) - 1.64 mm. In the first group, the bone fill is 4.05 mm. In the second group – 2.54 mm.

The radiographically determined angle of the bone defects were measured at a 29.34° average value. In the group treated only with Cerabone, the average angle is 26.82°. In the other group, Cerabone+PRF – 30.89°. The results confirm that the radiographic angle up to 30° - 33° is favourable for optimal bone regeneration. Considering these criteria, we have complied with the literature data, which determines a limit for predictable results of regenerative periodontal therapy at an angle of 37 °- 40 ° [16]. In the group treated with Cerabone +PRF, larger angles of the bone defect were measured, but a higher bone gain was obtained, which gives an advantage to the additional application of PRF.

## CONCLUSION

The results of the current study show PRF as an autogenous material with promising potential. Its additional application to bone replacement materials can improve the clinical parameters and the expected filling of the vertical bone defects. Statistically significant differences ($p < 0.05$) were found between both studied groups in the following parameters: probing pocket depth; clinical attachment gain; bone filling. Statistically significant differences ($p < 0.001$) were found between both studied groups in terms of radiographic depth of the bone defect before and after periodontal surgery, described as bone filling in millimeters.

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