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ORIGINAL ARTICLE

Comparison of platelet pellet and bioactive glass in periodontal regenerative therapy

GONCA CAYIR KELES[1], BURCU OZKAN CETINKAYA[1], DAVUT ALBAYRAK[2], HULYA KOPRULU[3] & GOKHAN ACIKGOZ[1]

[1]*Ondokuzmayis University, Faculty of Dentistry, Department of Periodontology, Samsun, Turkey,* [2]*Ondokuzmayis University, Faculty of Medicine, Department of Hematology, Samsun, Turkey,* [3]*Ondokuzmayis University, Faculty of Dentistry, Department of Restorative Dentistry and Endodontics, Samsun, Turkey*

Abstract

Objective. In recent years, platelet-rich plasma combined with graft materials has been used for periodontal regeneration. The individual role of blood products with guided tissue regeneration in periodontal regenerative therapy is unclear and needs to be elucidated. The purpose of this study was to compare the clinical and radiological effectiveness of platelet pellet/guided tissue regeneration (PP/GTR) and bioactive glass/GTR (BG/GTR) treatments in patients with periodontal disease. ***Material and methods***. Using a split mouth design, 15 chronic periodontitis patients with pocket depths ≥ 6 mm following periodontal initial therapy were randomly assigned to treatment with a combination of PP/GTR or BG/GTR in contralateral dentition areas. An absorbable membrane of polylactic acid was used for GTR. The criteria for the comparative study were preoperative and postoperative 6 months pocket depth, clinical attachment level, and radiological alveolar bone level. ***Results***. Both treatment modalities resulted in significant pocket depth reduction and gain in clinical attachment and alveolar bone level compared to the preoperative values ($p < 0.01$). Reduction in pocket depth, gain in clinical attachment and alveolar bone level were 4(3–6), 4.1 ± 0.7, 4.9 ± 1.4 mm in the PP/GTR group and 4(3–7), 4.1 ± 1.2, 5.9 ± 1.7 mm in the BG/GTR group, respectively. The differences between the two groups were not statistically significant ($p > 0.05$). ***Conclusions***. Within the limits of this study, it was concluded that PP may be effective as a bioactive glass graft material and used as a graft material for treating intrabony defects. PP thus appears to be a suitable alternative in the regenerative treatment of intrabony periodontal defects.

Key Words: *Bioactive glass, grafts, periodontal regeneration, platelet pellet, platelet-rich plasma*

Introduction

The purpose of periodontal therapy is to control the infection and regenerate the tissues that have been lost as a result of destructive periodontal disease [1,2]. Bone graft materials (autografts, allografts, xenografts, alloplasts) and guided tissue regeneration (GTR) have been used to promote periodontal regeneration [3,4].

In recent years, platelet-rich plasma (PRP) combined with graft materials has been used for the purpose of periodontal regeneration [4–10]. PRP is a volume of autologous plasma that has a higher platelet concentration than baseline. It is known that the increased number of platelets deliver an increased number of polypeptide growth factors that regulate cell proliferation, chemotaxis, and differentiation to the surgical area within PRP [4,6,11,12]. Platelets contain these growth factors in their alpha granules [4–7,13]. Concentration of platelets increases by up to 338% due to the application of PRP in surgical sites [4,6,7,14]. In the present study, platelet pellet (PP) was considered an appropriate term for the material used rather than PRP because of its higher platelet content than PRP. In addition to PP's higher platelet and lower white blood cell content, it is more adhesive than PRP owing to its gel consistency.

Recent findings in clinical studies have shown that the combination of PRP, bovine porous bone mineral (BPBM), and GTR is an effective treatment modality in periodontal regeneration [4,6,7,9]. Additionally, treatment with a combination of PRP,

Correspondence: Dr. Gonca Cayir Keles, Ondokuzmayis University, Faculty of Dentistry, Department of Periodontology, 55139 Samsun, Turkey. Tel: +90 362 4576000/3687. Fax: +90 362 4576032. E-mail: goncakeles@hotmail.com

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porous hydroxyapatite (HA) [10], and PRP, bovine-derived xenograft [8] has recently been reported as improving clinical parameters in intrabony periodontal defects. The individual role of blood products without graft materials in periodontal regenerative therapy is unclear and needs to be elucidated.

Bioactive glass (BG), alloplastic synthetic bone grafting material, forms a strong bond with bone and soft connective tissue and has a modulus of elasticity similar to that of bone [15]. It has been demonstrated that BG particles are: (i) biocompatible and easy to use, (ii) show both osteoconductive and osteostimulatory effects, and (iii) have optimal pore size for vascularization [1–3,15–21].

No data are available on evaluation of the effect of blood products alone without any graft materials in the treatment of intrabony defects with GTR. The use of PP and GTR in combination for periodontal regeneration is an interesting and clinically useful modality for the clinician treating periodontal defects because PP is autologous and cheaper than graft materials. However, it is still unknown whether a combination of these materials shows effective clinical results like graft materials, so the purpose of this study was to compare the clinical and radiological effectiveness of PP/GTR and BG/GTR treatments for intrabony defects in humans.

Material and methods

This was a randomized clinical trial of 6 months' duration using a split-mouth design; each subject was randomly assigned to treatment with PP/GTR or BG/GTR in contralateral dentition areas.

Patient selection

Fifteen chronic periodontitis patients (8 M, 7 F) with a mean age of 39.1 ± 7.4 years (range 29–51 years) exhibiting radiographic evidence of bone loss and paired, similar vertical periodontal osseous defects in each of two contralateral quadrants were recruited for the study. The criterion needed for inclusion was having two interproximal defects (two-wall or three-wall) with pocket depths of 6 mm or greater following initial periodontal therapy. The exclusion criteria were systemic diseases (i.e. diabetes mellitus, cancer, HIV, bone metabolic diseases, or disorders that compromise wound healing), chronic high-dose steroid therapy, radiation or immune-suppressive therapy, allergy or sensitivity to any drug, pregnancy, lactation, and smoking. The subjects had no history of drug therapy in the previous 6 months.

After receiving information about the study, the patients signed a consent form indicating their agreement to participation in the study. The study protocol and consent form were approved by the University Institutional Review Board.

Initial periodontal therapy

Initial periodontal therapy performed on all patients comprised oral hygiene instruction, full-mouth scaling and root planing, and occlusal adjustment when indicated. Scaling and root planing were performed using hand and ultrasonic instruments. Plaque control was assessed during each scaling and root planing session.

Four to six weeks following completion of initial periodontal therapy, a periodontal re-evaluation was performed to determine the patient's response to the therapy and to confirm the need for periodontal surgery. Furthermore, the following selection criteria had to be met: (1) probing pocket depth ≥ 6 mm; (2) radiographic and intrasurgical osseous defect depth ≥ 4 mm; and (3) two or three osseous walls.

Clinical and radiological measurements

Probing pocket depth and clinical attachment level were measured with the use of force-controlled Florida Probe (Florida Probe Corp., Gainesville, Fl., USA) on the day of surgery and postoperatively at 6 months. Probing depth was measured as the distance from the gingival margin to the base of the periodontal pocket. Clinical attachment level was recorded by combining the distance from the cemento-enamel junction to the gingival margin with probing depth. The measurements were repeated in six areas per tooth: mesiobuccal, distobuccal, midbuccal, mesiolingual, distolingual, and midlingual.

Radiological examinations were done prior to surgery (baseline) and postoperatively at 6 months. Standardized radiographs were taken using the parallel technique with a customized film-holder [21,22]. The linear alveolar bone level, which is between the radiographic cemento-enamel junction and the most apical alveolar bone, was determined using millimeter-scaled paper [23,24].

All clinical and radiological measurements were performed by the same calibrated investigator, who was blinded with respect to treatment modality.

PP preparation

On the day of periodontal surgery, the patients were sent to the hospital blood bank of the University as donors (candidates for blood bank donation). Blood was drawn by venal puncture and placed in the top and bottom with four bags. Leuko-depleted erythrocyte suspension, plasma, and leuko-depleted platelet were obtained by the standard technique. The leuko-depleted platelet bag obtained was centrifuged. PP at the bottom was placed in a syringe (mean $\pm$ standard deviation of platelets in 1 μl PP was $67768 \times 10^3 \pm 11514 \times 10^3$).

Table I. Median (minimum-maximum) of the changes in probing pocket depth (mm)*

Groups	Baseline	6 month	*p*-value	Changes	Changes (%)
PP/GTR	7 (6–9)	3 (2–4)	<0.001	4 (3–6)†	57.1 (50.0–71.4)†
BG/GTR	7 (6–10)	3 (2–4)	<0.01	4 (3–7)†	57.1 (50.0–71.4)†

Wilcoxon and Mann-Whitney U tests.
*n =15 paired interproximal defects.
†No significant difference was found between the groups.

Surgical procedure

Two experienced periodontal clinicians performed all periodontal surgical procedures on an outpatient basis in aseptic conditions with the patients under local anesthesia. The paired intrabony defects were randomly assigned to receive, by the flip of a coin, either PP/GTR treatment or BG/GTR treatment. Following buccal and lingual intra-crevicular incisions, full-thickness mucoperiosteal flaps were raised. All granulation tissue was removed from the defects, and the roots were thoroughly scaled and planed using hand and ultrasonic instruments. The surgical sites were rinsed in sterile saline.

PerioGlas (US Biomaterials Corp., Alachua, Fl., USA) was used as a bioactive glass graft material in the present study. In accordance with the manufacturer's instructions, PerioGlas was mixed with sterile saline to form a paste. At the time of application, PP was coagulated by adding 10% calcium chloride at 1:10 ratio (v/v) [25].

All defects were completely filled with either PP or BG and care was taken not to overfill the defects. Atrisorb (Atrix Laboratories, Inc., Fort Collins, CO., USA), an absorbable membrane made of polylactic acid, was used for GTR. Atrisorb was prepared in accordance with the manufacturer's instructions and placed over the BG-grafted or PP-filled defect.

To achieve primary closure, flaps were replaced and secured by a 4-0 silk suture utilizing an interrupted suture technique.

Postoperative care

Patients were prescribed a 0.2% chlorhexidine gluconate mouth rinse to be performed twice a day for 2 weeks. Silk sutures were removed one week after surgery. Recall appointments for supragingival professional tooth cleaning and oral hygiene reinforcement were scheduled every second week during the first two months after surgery and once a month for the rest of the observation period.

Statistical analysis

Statistical analysis was performed using a commercially available software program (SPSS 12.0, SPSS Inc., Chicago, Ill., USA). In the statistical analysis, only the recordings representing the deepest clinical site in each defect were used [1]. The Shapiro Wilk test was used to investigate whether the data were normally distributed or not. Statistical comparisons between preoperative and postoperative 6-month measurements in each of the treatment modalities and between the study groups were made. The Wilcoxon and Mann-Whitney U non-parametric tests were used for comparisons of the parameters not having a normal distribution. Data are shown as median (minimum-maximum). Paired t and Student t parametric tests were used for comparisons with a normal distribution. Data are shown as mean $\pm$ standard deviation. Significant levels were calculated for $p < 0.05$.

Results

Twelve two-wall and 3 three-wall defects were treated with PP/GTR, 11 two-wall and 4 three-wall with BG/GTR.

The changes in probing depth are indicated in Table I. At postoperative 6 months, probing depth decreased significantly in both treatment modalities compared to the preoperative data ($p < 0.01$). No significant difference was observed between the values of the groups at baseline and at 6 months ($p > 0.05$).

Changes in clinical attachment level are reported in Table II. The clinical attachment level improved significantly in both groups compared to the preoperative data ($p < 0.001$). No significant difference

Table II. Mean $\pm$ standard deviation of the changes in clinical attachment level (mm)*

Groups	Baseline	6 month	*p*-value	Changes	Changes (%)
PP/GTR	7.9 $\pm$ 1.3	3.9 $\pm$ 1.2	<0.001	4.1 $\pm$ 0.7†	52.0 $\pm$ 9.0†
BG/GTR	8.3 $\pm$ 1.8	4.3 $\pm$ 1.5	<0.001	4.1 $\pm$ 1.2†	49.1 $\pm$ 11.2†

Paired t and Student t tests.
*n =15 paired interproximal defects.
†No significant difference was found between the groups.

Table III. Median (minimum-maximum) of the changes in gingival recession (mm)*

Groups	Baseline	6 month	*p*-value	Changes
PP/GTR	0 (0–3)	0 (0–3)	<0.05	0 (0–1)†
BG/GTR	0 (0–4)	1 (0–5)	<0.05	0 (0–1)†

Wilcoxon and Mann-Whitney U tests.
*n =15 paired interproximal defects.
†No significant difference was found between the groups.

was found between the groups at baseline and postoperatively at 6 months ($p > 0.05$).

Postsurgical gingival recession was similar for both treatment modalities, as demonstrated in Table III.

A significant gain in alveolar bone level was observed in both treatment modalities compared to the preoperative data, as shown in Table IV and Figures 1 and 2 ($p < 0.001$). No significant difference was observed between the values of the groups at baseline and postoperatively at 6 months ($p > 0.05$).

Discussion

The results of this study demonstrate that treatment of intrabony periodontal defects with the combinations PP/GTR and BG/GTR can lead to a significant reduction in probing depth and a gain in clinical attachment level and alveolar bone level. No clinical and radiological differences in any of the investigated parameters were observed between the two treatment modalities. In most reported studies related to the field of dental surgery, PRP has been used in combination with autogenous bone graft, allograft, bovine-derived xenograft, and porous hydroxyapatite graft [4–10,14,26–28]. It is unclear whether blood products would have an effect similar to graft materials when used in conjunction with GTR membranes. This is the first report on the use of a combination of PP/GTR in intrabony periodontal defects for regeneration.

Platelets have been considered to be important in tissue regeneration, so PP with higher platelet content was used. In our study, the mean number of platelets in PP for patients was approximately 17 times higher than the mean platelet count in concentrated PRP ($3990 \times 10^3/\mu l$) that has been reported in another study [29]. In the literature, coagulation of PRP has been achieved when combined with calcium chloride and bovine thrombin, which then becomes a sticky gel consistency [4,6,7,14,26]. Compared to PRP, PP is more condense, has a gel consistency, and therefore could be placed in periodontal defects. However, in the present study PP was activated with calcium chloride before periodontal surgery.

A polylactic acid barrier was selected as the GTR membrane because the data have demonstrated that this type of barrier is successful in regenerative periodontal therapy [30–35] and shows effective clinical results like non-absorbable barriers [36,37]. Polylactic acid barrier is easily adapted to the defect and absorbs by hydrolysis with the rate controlled [34,35]. BG was selected as the alloplastic graft material which is safe and well tolerated because the histological data from animals and humans have suggested that BG demonstrates an ability to enhance a regenerative type of healing [2,3,18,20, 38,39]. The material maintains the blood clot in the osseous defect [40]. It is considered that BG will be used as a delivery system for growth factors or other materials because it increases hemostasis [3].

Shanaman et al. [26] evaluated the role of PRP in conjunction with bone allograft/GTR histologically in localized alveolar ridge defects prior to dental implant placement in a case series. It has been reported that this did not enhance the quality or quantity of new bone formation. However, in an experimental study, PRP used with allograft has been shown to improve bone formation in the defects around implants compared to using allograft alone [28]. As has been reported [27], PRP may also be effective in small (periodontal) and larger bone defects if the defects are treated with both autologous graft and PRP. The authors have also considered that PRP needs vital bone cells for stimulation [27]. However, an *in vitro* study [41] has suggested that PRP has the ability to increase periodontal ligament cell numbers and simultaneously upregulate extracellular matrix production. In a recent study it has also been suggested that PRP stimulates cell proliferation and increases alkaline phosphatase activity in periodontal ligament cells [42]. PRP may promote periodontal wound healing with these functions.

Reduction in pocket depth and gain in clinical attachment level are the most important clinical outcomes of regenerative therapy [7]. It is well documented that gain in clinical attachment after any type of regenerative and conventional periodontal treatment is dependent on the initial pocket

Table IV. Mean±standard deviation of the changes in radiological alveolar bone level (mm)*

Groups	Baseline	6 month	*p*-value	Changes	Changes (%)
PP/GTR	7.9±1.4	3.1±1.3	<0.001	4.9±1.4†	61.7±13.1†
BG/GTR	9.5±2.7	3.6±1.8	<0.001	5.9±1.7†	63.5±12.8†

Paired t and Student t tests.
*n =15 paired interproximal defects.
†No significant difference was found between the groups.

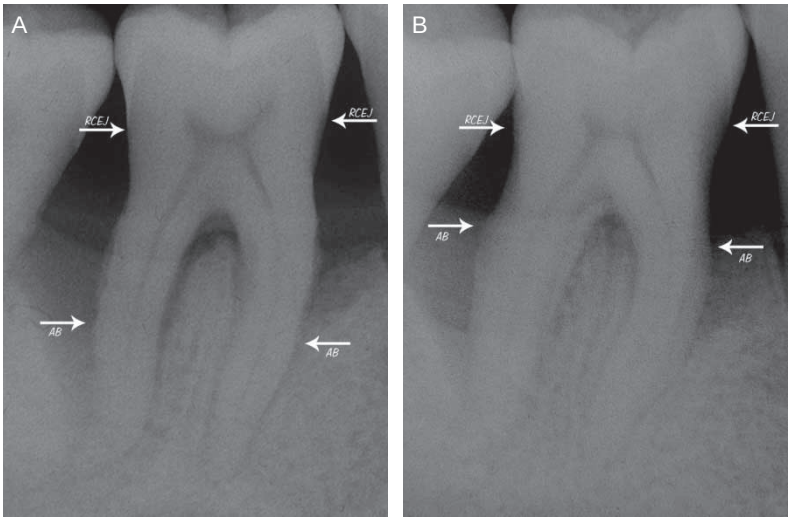

Figure 1. Radiographic appearances of the defects (RCEJ: radiographic cemento-enamel junction, AB: alveolar bone). A. Before treatment of PP/GTR. B. After treatment of PP/GTR.

depth; that is, the deeper the initial pocket depth, the greater the pocket depth reduction and clinical attachment gain [43,44]. No significant difference in probing pocket depth was observed between the two treatment modalities preoperatively in the present study. The gain in clinical attachment level might have been a result of periodontal regeneration via a new attachment or of healing by repair characterized by the formation of a long junctional epithelium between the new regenerated tissues and the root surface [45]. It is known that histological analysis of regenerative periodontal therapy is important in addition to observing clinical and radiological results. As has been reported [8,46], both radiographic interpretations and changes in measurements of clinical attachment level over time are reliable in assessing the outcome of intrabony defect treatments. In other words, the use of attachment level and radiological evaluations is in parity indicative of the outcome of periodontal therapies. When interpreting the findings of the present study, it has to be pointed out that the changes in clinical attachment level concur with the gain in radiological alveolar bone level. In addition, postsurgical healing indicated an excellent soft tissue response to both the combination of PP/GTR and BG/GTR with no adverse complications.

Radiological changes in alveolar bone level may also be used unless re-entry procedure is not performed. In the present study, re-entry surgery was not performed because of an ethical concern and the probability of alveolar bone loss following the procedure [21]. In clinical re-entry studies, it has been suggested that the combination PRP/BPBM/GTR enhances the clinical results achieved with GTR [4] or with open-flap debridement [9] in the treatment of intrabony defects in humans. Additionally, combining PRP and bovine-derived xenograft in the treatment of intrabony defects has been reported to improve clinical periodontal response compared

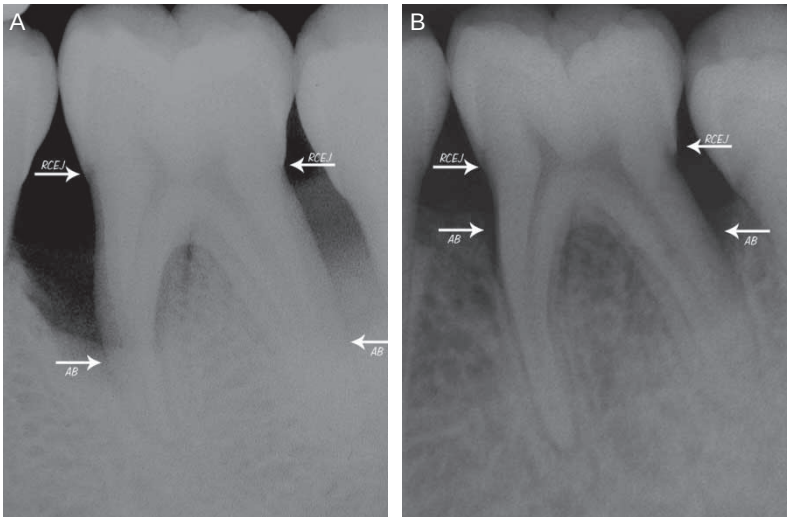

Figure 2. Radiographic appearances of the defects (RCEJ: radiographic cemento-enamel junction, AB: alveolar bone). A. Before treatment of BG/GTR. B. After treatment of BG/GTR.

to treatment with bone replacement graft alone in a 6-month clinical trial [8].

Based on the results of the present study, it is concluded that the combinations PP/GTR and BG/GTR in the treatment of intrabony defects in humans are similarly effective both clinically and radiologically. Within the limits of this study, it is suggested that PP may be as effective as bioactive glass graft materials and may be used as graft materials for treating intrabony defects. PP therefore appears to be a suitable alternative in the regenerative treatment of intrabony periodontal defects. PP is developed from autologous blood, completely safe, and it eliminates concerns about disease transmission and immunogeneic reactions associated with allogeneic or xenogeneic preparations [5,11,47]. It has been considered an economical source of growth factors by most clinical dentists. In addition, no local wound healing or systemic complications have been observed [9]. PP, which is coagulated mass, is easy to manipulate and cheaper than bone allografts and xenografts as well as alloplasts such as bioactive ceramics. However, PRP preparation has been suggested as having limited potential in promoting local bone formation histologically in rat calvaria defects [48]. Further experimental studies are necessary to elucidate the histological effectiveness of the PP and GTR combination on periodontium in periodontal regenerative therapy.

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