The purpose of this study was to compare the efficacy between the use of bovine bone graft material and platelet-rich fibrin (PRF) mixture (test group) and bovine bone graft material and collagen membrane combination (control group) in 2-stage maxillary sinus augmentation. According to specific inclusion/exclusion criteria, patients treated between 2008 and 2012 were selected. Panoramic radiographs were used for radiologic assessments. To evaluate the relationship between sinus-graft height and each implant, the bone level (BL) was divided by implant length (IL). To evaluate the change in the height of grafted sinus, the grafted sinus floor above the lowest part of the original sinus height (GSH) was divided by the original sinus height (OSH). Samples taken during implant surgery were used for histologic and histomorphometric analyses. Twenty-five patients, 32 augmentation surgeries, and 66 one-stage implants were included in the study. No implant loss or complication was observed in either group. There were no statistical differences according to new bone formation ($P = .61$) and biomaterial remnant ($P = .87$). During the evaluation period, the test group showed statistically less change in the BL/IL ratio ($P = .022$). The difference of GSH/OSH ratio was found to be insignificant between groups ($P = .093$). It was observed that the grafted sinus covering the implant apex and sinus floor was above the original sinus height in both groups. It may be concluded from this study that both combinations can be successfully used for sinus augmentation. Further studies evaluating different graft materials and PRF combinations in the early phases of healing would be beneficial.

**Key Words:** sinus augmentation, platelet-rich fibrin, bovine bone graft, collagen membrane

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**INTRODUCTION**

Several treatment options such as short implants, tilted implants, onlay bone grafts, and sinus augmentation surgeries have been proposed to allow implant placement in the atrophic posterior maxilla. The lateral window approach described by Boyne and James and developed by Tatum is very predictable, safe, and one of the most frequently performed treatment modalities. It is a well-documented technique; however, there is no consensus on the ideal grafting material for sinus augmentation surgery. Anorganic bovine bone is a biocompatible, osteoconductive, and widely used biomaterial with approved high clinical success in sinus augmentation surgery. The space-maintaining effect of the graft material permits the apposition of de novo bone formation. Schneiderian membrane and lateral access window can be covered with a resorbable collagen membrane to avoid membrane perforation, to promote bone formation and to prevent soft tissue migration. The main disadvantage of the anorganic bovine bone is the lack of osteoinductive properties. To overcome this problem, the addition of platelet concentrates—generally named platelet-rich plasma (PRP)—to grafting material may be used.

PRP is an autologous biomaterial that contains many growth factors such as platelet-derived growth factor, transforming growth factor, vascular endothelial growth factor, and insulin-like growth factor. It has been shown that PRP stimulates and enhances cell proliferation, angiogenesis, and bone regeneration. PRP techniques depend on the extraction of the patient’s own blood, followed by sequestration of platelets from blood by centrifugation. These techniques differ from each other by using different activators and release carriers. In 2001, Choukroun et al described platelet-rich fibrin (PRF). PRF is classified as a leukocyte and fibrin concentrate. The main difference between PRF and the other PRP preparations is that the PRF technique does not require any anticoagulant, carrier, or activator. In this technique, blood is collected into empty tubes and immediately centrifuged. Following blood processing, PRF is collected in the middle of the tube, between the red corpuscles at the bottom and...
acellar plasma at the top. PRF can either be cut into small pieces and mixed with graft material or packed into 2 sterile compresses to prepare fibrin membrane. It was reported that PRF can be used successfully solely or in combination with graft materials in the treatment of intrabony periodontal defect,17–19 sinus lifting surgery,20–24 socket preservation,25 and peri-implant defects.26 According to the best of the author’s knowledge, there has been no long-term follow-up study on the effect of PRF in sinus lifting surgery.

The objective of this retrospective study was to compare the efficacy between the use of bovine bone graft material and PRF mixture and bovine bone graft material and collagen membrane combination in sinus augmentation surgery. Results were obtained by means of clinical, radiographic, and histologic examination.

Materials and Methods

Patient selection

This was a single center, retrospective study. All surgical procedures, prosthetic rehabilitation, and follow-up controls were performed between July 2008 and December 2012. The study protocol was approved by Istanbul University, Istanbul Medical Faculty Ethical Committee, and performed in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from all participants during the last clinical visit. This study followed the STROBE statement.

Inclusion criteria of patients were as follows:

- generally healthy (not having diabetes, cardiovascular disease, and blood-related diseases);
- nonsmoker;
- partially edentulous;
- presence of residual crest height less than 5 mm;
- treated with 2-stage unilateral or bilateral maxillary sinus augmentation with 1 of the study combinations before dental implant treatment;
- attendance of routine controls following prosthetic treatment for at least 2 years;
- having distinct panoramic radiographs showing all borders of original sinus floor, grafted area, and implant grooves at each follow-up control; and
- having histologic biopsies 6 months after sinus augmentation surgery.

There were 2 study groups according to different grafting materials. One group was augmented with bovine bone graft (Bio-Oss, Geistlich Pharma AG, Wolhusen, Switzerland) and PRF mixture, and the other (control group) was grafted with the resorbable collagen membrane (Bio-Gide, Geistlich Pharma AG) and bovine bone graft (Bio-Oss, Geistlich Pharma AG).

PRF technique

PRF was prepared as described by Choukroun et al.14 Venous blood was drawn from antecubital vein with a blood collection set (Safety Blood Collection Set, Greiner Bio-One, Monroe, NC) prior to sinus lifting surgery; 60 mL of blood was taken in 10-mL tubes, without anticoagulant (Vacuette, Greiner Bio-One). The tubes were immediately centrifuged at 400g for 12 minutes (Process, Nice, France). Acellular plasma (platelet-poor plasma [PPP]) was concentrated at the top of the tube, and the red corpuscles were concentrated at the bottom. PPP was collected by syringe. A fibrin clot was obtained in the middle of the tube. The fibrin clot was removed from the tube and was gently separated from red corpuscles with a scalpel. This clot was either cut into small pieces or mixed with graft material or pressed between 2 sterile compresses to obtain a membrane.

Sinus augmentation surgery

Sinus lifting surgeries were done by surgeons who had at least 8 years of experience (N.B., S.E.) with the method described by Boyne and James4 and Tatum.5 All surgeries were performed under infiltrative local anaesthesia. Full-thickness muco-periosteal flap was raised to gain access to the lateral wall of the sinus. Cortical bone was removed using steel and diamond round burs. The sinus membrane was elevated by special instruments to allow the placement of the graft. The Valsalva maneuver was used to examine the membrane perforations. In the test group, PRF membrane was placed over the sinus membrane. The sinus cavity was filled with PRF and bovine bone graft mixture (0.25- to 1-mm particle size) in 1:2 ratios. PPP was used to provide a sufficient amount of wetting of the graft material. The vestibular wall was covered by PRF membrane (Figure 1a through d). In the control group, sinus membrane was covered by a resorbable collagen membrane, and then sinus was augmented with 0.25- to 1-mm particle-size bovine bone mixed with saline. Resorbable collagen membrane was also covered on the vestibular wall in order to prevent the migration of graft material and epithelial cells (Figure 2a through d). The horizontal width of the alveolar crest was sufficient in all cases; therefore, no horizontal augmentations were performed.

Flap closure was completed using 3.0 silk interrupted sutures (Drogsan Medical Supplies Industry, Trabzon, Turkey). The sutures were removed 10 days after the surgery. If bilateral surgery was planned, then a 15-day interval was left between the 2 sinus lifting surgeries. All patients received standard prescription for antimicrobial drugs, anti-inflammatory drugs, and oral antiseptics. Amoxicillin/clavulanic acid, 1 g twice a day (Augmentin BID, GlaxoSmithKline, Istanbul, Turkey), was prescribed starting from 1 day before the operation and administered for 10 days. Meloxicam, 15 mg once a day (Melox Fort, Nobel, Istanbul, Turkey), was used for 4 days, starting from the day of the operation. Patients were recommended to use mouth rinse (twice a day) containing 0.2% chlorhexidine gluconate and benzylamine hydrochloride (Kloroben, Drogsan, Istanbul, Turkey), starting from the day after surgery and for the next 10 days.

Implant surgery

The surgeon who performed the sinus lifting surgery also performed the implant surgery. Implants were placed 6 months after sinus lifting surgery under local infiltrative anaesthesia. Midcrestal and buccal vertical incisions were made to ensure adequate field of vision. In each sinus, biopsies were obtained from the most distal part of the grafted area where the implant
placement was not intended by standardized 4-mm trephine bur. Panoramic radiographs were used to select the implant length. Implant osteotomy was done according to the manufacturer's protocol. In all cases, wound closure was completed using silk interrupted sutures (Drogsan Medical Supplies Industry). The sutures were removed 1 week after surgery. Patients were given 1 g of amoxicillin (Largopen, Bilim Pharmaceuticals, Istanbul, Turkey) tablets and 100 mg of flurbiprofen (Majezik, Sanovel, Istanbul, Turkey) tablets 2 times a day for 5 days postoperatively. Also, all patients were instructed to rinse their mouths using 0.2% chlorhexidine gluconate and benzydamine hydrochloride (Kloroben, Drogsan) twice a day for 7 days.

**Prosthetic treatment**

After sinus augmentation surgeries, patients were instructed not to wear temporary removable prosthesis for a 6-month period. During 6 months of an osseointegration period, new temporary removable prosthesis were prepared and relined periodically with a soft-tissue liner (Visco-gel, Dentsply, York, Pa). Six months after the implant surgery, abutments were fastened, and implants were connected with metal-fused-to-ceramic restorations.

**Radiographic assessment**

Baseline (before sinus lifting surgery) panoramic radiographs were used to evaluate the initial bone volume. Panoramic radiographs were obtained and evaluated in 6 stages thereafter:

- 10 days after sinus lifting surgery (T₀);
- 10 days after dental implant surgery (T₁);
- 6 months after dental implant surgery (T₂);
- 6 months after the prosthetic loading (T₃).

**FIGURES 1 AND 2.**

**FIGURE 1.** Treatment stages of a patient treated with platelet-rich fibrin (PRF) and bovine bone graft material. (a) Schneiderian membrane was covered by PRF membrane. (b) Sinus cavity was filled with bovine bone graft and PRF in 1:2 ratios. (c) The osteotomy window was covered with PRF membrane. (d) Panoramic image 6 months after the prosthetic loading (T₃).

**FIGURE 2.** Treatment stages of a patient treated with bovine bone graft material and resorbable collagen membrane. (a) Schneiderian membrane was covered by resorbable collagen membrane. (b) Sinus cavity was filled with bovine bone graft. (c) The osteotomy window was covered with resorbable collagen membrane. (d) Panoramic image 6 months after the prosthetic loading (T₃).
12 months after the prosthetic loading (T4); and
24 months after the prosthetic loading (T5).

All radiologic measurements were done by a single investigator (C.B.) who was not involved in any stage of treatment and blinded to patients. Tracing paper was located on the panoramic radiographs; and alveolar crest, original sinus floor, grafted sinus floor, and implant body were traced. Measurements were performed manually with a millimeter scale according to the method of Hatano et al. 27

To evaluate the relationship between sinus-graft height and the implant, the distance from the top of the bone-to-implant contact region to the head of the fixture (BL) and the distance from the apex to the head of the fixture (IL) were calculated. BL/IL ratio showed the change in height of grafted sinus floor for each implant (Figure 3). A value of 1.0 or higher indicates that the grafted sinus covers the implant apex. If the BL/IL ratio is lower than 1.0, the implant apex does not cover the grafted sinus floor.

To evaluate the change in the height of grafted sinus, the distance from the intraoral marginal bone to the grafted sinus floor above the lowest part of the original sinus height (GSH) was divided by the original sinus height (OSH) (Figure 3). OSH was defined as the distance from the intraoral marginal bone to the lowest point of the original sinus floor. GSH/OSH values were measured at sites that did not support the implants. A value of 1.0 or higher shows that the grafted sinus floor is above the original sinus height.

Histologic and histomorphometric assessment

Tissue samples were fixed in 10% buffered neutral formalin and stored at refrigerator temperature (about 4°–8°C). Histologic samples were brought to room temperature at the beginning of the histologic evaluation. The samples were decalcified in 10% formic acid solution, which was replaced every day. After decalcification, samples were rinsed with distilled water and were subsequently dehydrated in ethanol, cleared in xylene, and embedded in paraffin. Ten transverse sections (6 μm) from the middle portion (in vertical direction) of the each sample were cut and mounted on glass slides. The sections were deparaffinized with xylene, rehydrated in decreasing concentrations of ethanol, and stained with hematoxylin-eosin.

The area of the newly formed trabecular bone, connective tissue, and remnants of biomaterial as a percentage of the total area were analyzed at ×4 objective magnification. Vascularity in connective tissue, empty lacuna, osteoblasts, osteocytes, osteoclasts, lymphocytes, and polymorphonuclear leukocytes were determined at ×40 and ×100 magnification. Osteoid matrix and trabecular structure examinations were made at ×16 magnification. All assessments were performed using a light microscope (Olympus CH20; Olympus Optical, Tokyo, Japan), and the photography was performed with a light microscopy (Leitz Laborlux K; Leitz, Wetzlar, Germany). The results of the connective tissue vascularity and inflammation were evaluated. Vascularity in connective tissues was assessed according to the number and diameter of vessel sections in defect area. Inflammation severity was evaluated according to the density of inflammatory cells (especially lymphocytes and polymorphonuclear leukocytes).

Statistical analysis

Statistical analyses were performed using SPSS for Windows (Version 10, SPSS Inc, Chicago, Ill). All statistical tests were 2-sided and performed at the 5% significance level. Data were expressed as numbers or mean ± SD. Changes in BL/IL and GSH/OSH ratios within the time points were assessed through Pillai trace test for repeated measures of the general linear model. Mann-Whitney U test was used to compare the age, new bone formation ratio, and remnants of biomaterial. Pearson chi-square test was used to compare the differences in gender, implant number, and implant location.

RESULTS

Twenty-five patients requiring 2-stage either unilateral (18 patients) or bilateral (7 patients) maxillary sinus augmentation (17 sinus sites in the test group, 15 sinus sites in the control.
group) for dental implant treatment participated to this study. Fifteen patients were female and 10 were male. The mean age was $50.06 \pm 12.15$ and $47.73 \pm 8.2$ years in the test and control groups, respectively. Sixty-six 1-staged implants with a sand-blasted, large-grit, acid-etched (SLA) surface (Straumann, Basel, Switzerland) were evaluated. The sizes of implants were as follows: $3.3 \times 10$ mm ($n = 14$), $3.3 \times 12$ mm ($n = 26$), $4.1 \times 10$ ($n = 14$), and $4.1 \times 12$ mm ($n = 12$). The number of placed implants in each group is shown in Table 1. The number of implants per site according to ADA Dental Terminology is shown in Figure 4. A total of 32 metal-fused-to-ceramic restorations were fabricated. There were no statistically significant differences with respect to age ($P = .44$), gender ($P = .76$), implant number ($P = .65$), and implant location ($P = .37$) between the 2 groups. During the sinus augmentation surgery, no adverse events or complications such as membrane perforation, wound dehiscence, and inflammation were noted in either group. No implant loss or complication was observed during the follow-up period, and overall implant survival rate was 100% in both test and control groups according to Albrektsson et al. criteria.28

**Radiographic assessment**

The mean values of BL/IL ratios are shown in Table 2. The mean values of BL/IL measured 10 days after (T1) dental implant surgery were $1.43 \pm 0.05$ in the test group and $1.46 \pm 0.05$ in the control group. These values decreased with time. In the test group, the difference between T3 and T4 was statistically significant ($P = .001$). In the control group, BL/IL decreased significantly between T2 and T3 ($P = .043$), T3 and T4 ($P = .0001$), and T4 and T5 ($P = .002$). Twenty-four months after the prosthetic loading (T5), BL/IL values were >1 in both groups. These results indicate that the grafted sinus was above the implant apex. During the study period, the test group showed statistically less change in BL/IL values than the control group ($P = .022$).

The mean values of GSH/OSH ratios are shown in Table 3. Ten days after sinus lifting surgery (T0), the mean GSH/OSH values were $4.26 \pm 0.33$ and $4.20 \pm 0.15$ in the test and control groups, respectively. These values increased during the next 6 months. Statistical analysis showed that these increases were significant in the test group ($P = .003$) and not significantly different in the control group ($P = .30$). At T5, GSH/OSH values began to decline in both groups. There was no significant change in the test group. In contrast, a significant decrease was observed between T2 and T3 ($P = .004$) in the control group. Values measured 24 months after the prosthetic loading (T5) showed that the grafted sinus floor was above the original sinus height in both groups. Although different rates of bone height gain and resorption were calculated radiologically in the test and control groups, the differences were not statistically significant ($P = .093$).

**Histologic and histomorphometric findings**

Table 4 shows the percentages of newly formed bone, connective tissue, and biomaterial remnants calculated through histologic examinations of tissue section area of both groups. No statistically significant difference was found between groups in terms of these 3 criteria percentages. Remnants of biomaterial were observed to be surrounded by bone trabeculae and connective tissue in both groups (Figure 5a and b). Statistically similar results and wound areas covered by

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**Table 1**

<table>
<thead>
<tr>
<th>Number of Implants</th>
<th>Test</th>
<th>Control</th>
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<tr>
<td>1</td>
<td>3</td>
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<tr>
<td>2</td>
<td>11</td>
<td>11</td>
</tr>
<tr>
<td>3</td>
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<td>Total</td>
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**Table 2**

<table>
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<th>Measurement</th>
<th>Test Mean ± Standard Deviation</th>
<th>Control Mean ± Standard Deviation</th>
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<tr>
<td>T1</td>
<td>1.43 ± 0.05</td>
<td>1.46 ± 0.05</td>
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<tr>
<td>T2</td>
<td>1.38 ± 0.04</td>
<td>1.43 ± 0.04*</td>
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<tr>
<td>T3</td>
<td>1.37 ± 0.04*</td>
<td>1.37 ± 0.03*</td>
</tr>
<tr>
<td>T4</td>
<td>1.32 ± 0.04*</td>
<td>1.29 ± 0.04*</td>
</tr>
<tr>
<td>T5</td>
<td>1.30 ± 0.04</td>
<td>1.23 ± 0.04*</td>
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<tr>
<td>The averages of T1–T5</td>
<td>1.36 ± 0.04</td>
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*Statistical difference.

**Table 3**

<table>
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<th>Measurement</th>
<th>Test Mean ± Standard Deviation</th>
<th>Control Mean ± Standard Deviation</th>
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<tbody>
<tr>
<td>T0</td>
<td>4.26 ± 0.33</td>
<td>4.20 ± 0.15</td>
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<tr>
<td>T1</td>
<td>4.78 ± 0.34</td>
<td>4.55 ± 0.23</td>
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<tr>
<td>T2</td>
<td>4.78 ± 0.34</td>
<td>4.52 ± 0.24*</td>
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<tr>
<td>T3</td>
<td>4.39 ± 0.28</td>
<td>4.09 ± 0.22*</td>
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<td>T4</td>
<td>4.39 ± 0.27</td>
<td>3.81 ± 0.22</td>
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<td>T5</td>
<td>4.36 ± 0.26</td>
<td>3.67 ± 0.21</td>
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<tr>
<td>Total</td>
<td>4.49 ± 0.29</td>
<td>4.14 ± 0.20</td>
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</table>

*Statistical difference.

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1. In the test group, $P = .001$ between T3 and T4. In the control group, $P = .004$ between T2 and T3. T1 indicates 10 days after sinus lifting surgery; T2, 10 days after dental implant surgery; T3, 6 months after dental implant surgery; T4, 6 months after the prosthetic loading; T5, 12 months after the prosthetic loading; and T6, 24 months after the prosthetic loading.

2. Significantly between T2 and T3 ($P = .043$ between T2 and T3. T0 indicates 10 days after sinus lifting surgery; T1, 10 days after dental implant surgery; T2, 6 months after dental implant surgery; T3, 6 months after the prosthetic loading; T4, 12 months after the prosthetic loading; and T5, 24 months after the prosthetic loading.

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**Table 4**

<table>
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<th>Test Control</th>
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<tr>
<td>New bone formation</td>
<td>35.0 ± 8.60</td>
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<tr>
<td>Connective tissue</td>
<td>30.63 ± 7.53</td>
</tr>
<tr>
<td>Biomaterial remnants</td>
<td>33.05 ± 6.29</td>
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</table>
connective tissue consisting of fibroblasts, collagen fibers, and blood vessels indicate similarity of bone-forming speed and amount, and biomaterial resorption speed and amount between groups. Mineralized trabecular structures of newly formed bones in both groups indicate the forming of cells appropriate with the area.

Osteoblasts, which are bone-forming cells in the surface of newly formed bone, were observed in cuboidal structure in both groups. The histologic details showed cuboidal osteoblasts which are active bone-forming cells (black arrows) and osteocytes within bone lacunae (white arrow) (hematoxylin and eosin, original magnification ×400). In the control group, similar histologic details were observed.

**FIGURES 5–7.**

**FIGURE 5.** (a) In the test group, newly formed bone trabeculae (BT), connective tissue (CT), and remnants of biomaterial (RB) are observable. Remnants of biomaterial were surrounded by bone trabeculae and connective tissue (hematoxylin and eosin, original magnification ×63). (b) In the control group, newly formed BT, CT, and RB are observable. Remnants of biomaterial were surrounded by bone trabeculae and connective tissue (hematoxylin and eosin, original magnification ×63).

**FIGURE 6.** (a) In the test group, histologic detail showing cuboidal osteoblasts which are active bone-forming cells (black arrows) and osteocytes within bone lacunae (white arrow) (hematoxylin and eosin, original magnification ×400). (b) In the control group, histologic detail showing cuboidal osteoblasts that are active bone-forming cells (black arrows) and osteocytes within bone lacunae (white arrow) (hematoxylin and eosin, original magnification ×400).

**FIGURE 7.** (a) In the test group, a multinucleated osteoclast (arrow) is observable at the newly formed bone trabeculae surface (hematoxylin and eosin, original magnification ×400). (b) In the control group, a multinucleated osteoclast (arrow) is observable at the newly formed bone trabeculae surface (hematoxylin and eosin, original magnification ×400).
In microscopic examination, test and control groups showed similar vascularity and inflammation.

**Discussion**

The lateral wall sinus augmentation technique is a frequently performed technique with low rates of complications and higher levels of implant survival. Different grafting materials have been researched to achieve better results. In recent years, PRF has been used alone or with different grafting materials.

In the present study, we evaluated the use of PRF and anorganic bovine bone graft material mixture in sinus augmentation surgery. Also, the results were compared with routinely used resorbable collagen membrane and anorganic bovine bone graft combination. The percentage of newly formed bone (35.0 ± 8.60 in the test group; 32.97 ± 9.71 in the control group) and residual bone substitute (33.05 ± 6.29 in the test group; 33.79 ± 8.57 in the control group) were found to be similar in both groups. The change in height of grafted sinus floor for each implant was found to be statistically lower in patients treated with PRF + graft mixture. Also, the changes in the height of grafted sinus were found to be insignificantly lower in the test group. To the best of our knowledge, there is no long-term radiologic study and very few clinical studies about PRF use in sinus augmentation. Therefore, an accurate comparison of our results with those obtained from other studies may not be possible in that aspect.

Recently Zhang et al. compared the effect of PRF and bovine bone graft combination with an only bovine bone graft-treated group in sinus augmentation. Evaluation was done clinically, radiographically, and histologically 6 months after the operation. No complications were observed during the evaluation period. Orthopantomograms or dental computerized tomography scans, which were taken immediately after sinus operation and 3 and 6 months postoperatively, revealed the presence of mineralized tissue with no signs of resorption. However, radiographic bone volume changes were not measured in this study. The percentage of newly formed bone in the PRF group was found to be higher than in the control group (18.35 ± 5.62% vs 12.95 ± 5.33%). Also, the percentage of residual bone substitute in the PRF group was about 1.5-fold lower than in the control group (28.54 ± 12.01% vs 19.16 ± 6.89%). Histologically, no statistical difference was found between the test and control groups in that study, consistent with the results of the present study. However, the present study found newly formed cells and resorption of graft material at high levels, which may be due to the fact that in the present study, the surface of the sinus membrane and lateral wall were covered with collagen membrane or PRF membrane.

Inchingolo et al. evaluated success of PRF and bovine bone graft mixture in the treatment of severe maxillary bone atrophy clinically and radiographically. The study group was composed of 23 patients and 31 1- or 2-stage sinus-lifting surgeries. Radiographic analysis showed an average increase in the peri-implant bone density of 31%. Choukroun et al. evaluated the effectiveness of freeze-dried bone allograft (FDBA), and FDBA and PRF mixture in sinus augmentation surgery in 9 cases. In histologic evaluation, they found similarity between the results of the FDBA and PRF mixture groups at 4 months and the results obtained at 8 months of the FDBA group. The researchers reported that FDBA and PRF mixture would decrease the waiting time after sinus augmentation.

Kim et al. compared tricalcium phosphate (TCP), PRF-mixed TCP and recombinant human bone morphogenetic protein 2 (rhBMP-2)-coated TCP in their effect on bone regeneration in sinus elevation in an experimental study on rabbits. Histologic samples were obtained at 3 days, 1 week, 2 weeks, 4 weeks, 6 weeks, and 8 weeks. There was no bone formation found in any of the groups at 3 days. At all time points, the TCP group showed the least bone formation. Bone formation area was found to be statistically higher in the PRF-mixed TCP group than in the rhBMP-2-coated TCP group.

The observation of higher rates of newly formed cells in PRF-applied groups in the studies of Choukroun et al. and Kim et al. compared with the rates in the present study and in that by Zhang et al. may indicate that the effectiveness of PRF may depend on the characteristics of the coadministered graft material. Also, slow resorption rate of bovine bone graft may cause a delay in the new bone formation. Further clinical studies are required to evaluate and compare the PRF and different bone-grafting-material combinations in bone regeneration.

In this study, the sinus cavity was filled with PRF and graft mixture in 1:2 ratios. PPP was also used to provide enough wetting of grafting material. Su et al. reported the release of growth factor from PRF in vitro and found that the protein profiles of the releasates and serum supernatant were similar. They suggested that platelet-poor plasma obtained by centrifugation could be used as an additional source of growth factors for grafting. Further, according to our clinical observation, this gel-like mixture accelerated the adhesive capacity, leading to easy handling and making the filling of the sinus cavity easier than graft material alone.

Bioresorbable membranes are used in guided bone regeneration to allow growing periosteal cells for bone tissue engineering. Resorbable membranes composed of collagen fibers are a generally accepted, biocompatible, and successfully used biomaterial. These collagen fibers appear to have an osteoinductive effect and therefore it is believed that collagen fibers serve as a trap for several growth factors. It is reported that vital fibrin can be used in bone-tissue engineering because it is an autologous scaffold for periosteal or stem cell transplantation. PRF is an autologous fibrin matrix in which the platelet cytokines and cells are trapped. Therefore, it could be used as a membrane to cover bone augmentation sites. Simonpieri et al. used PRF membranes as the sole protection for covering sinus membrane. The X-ray
analyses 6 months after surgery showed no invagination or fibrosis, and a cortical limit was observed after 3 years. Gassling et al.\(^{27}\) compared the PRF membrane with collagen membrane as scaffolds for periosteal tissue engineering. PRF membranes showed a higher level of proliferation and metabolic activity, but a slightly inferior biocompatibility compared to collagen membrane. Generally, the Schneiderian membrane is not covered by a membrane. In this study, PRF or collagen membranes were also used to cover the sinus membrane to avoid sinus perforation with the use of particulate graft. In the present study, no complications such as migration of graft material or opening of wound edges were observed in the test or control groups. According to the results of the present study, the use of PRF membrane could be suggested as an alternative to collagen membranes in bone regeneration. Collagen membranes are biomaterials that increase total treatment cost. On the other hand, PRF membranes, which are produced from the blood of the patient, involve many growth factors and also have no disease risk thanks to being autogenous and, therefore, would be preferred. Also, the easy application of PRF membrane to cover the sinus membrane can give additional advantage over using collagen membrane.

The similar histologic results may result from the fact that PRF is effective especially in the early phase of recovery ranging between 7 and 28 days.\(^{40–42}\) Future experimental studies may evaluate the recovery at early phases in order to evaluate the effectiveness of both combinations.

The maintenance of augmented bone volume in the sinus cavity can influence the short-term and long-term success of implants. The most dominant factor affecting long-term vertical stability of the augmented sinus is the type of grafting material.\(^{43}\) The grafting material with slow or no resorption characteristics may maintain the graft height and implant survival. Therefore, anorganic bovine has advantages in sinus augmentation.\(^{43,44}\) An acceptable bone height found in the present study with approximately 36 months of follow-up in both groups could be explained by replacement by bone with grafting materials. The studies radiologically evaluating bone height after sinus augmentation reported resorption especially during the first year, and then a decrease in resorption in the following periods, irrespective of graft type.\(^{27,43,45,46}\) The results of the present study are consistent with the results of the previous studies. A BL/IL ratio showing grafted sinus height calculated for each implant was observed to decrease between time intervals; however, apexes of all implants were observed to be covered with grafted sinus floor. Resorption rates observed radiographically are not meant to be clinically important. Compared with the control group, statistically significant lower resorption was observed in the test group. A GSH/OSH ratio evaluating bone height in areas with no implants in grafted sinus indicates higher rates of grafted sinus than the original sinus in both the test and control groups. In addition, according to measurements conducted 10 days after sinus augmentation in both groups, measurement values conducted after implant surgery were found to be higher, which may result from the increase in the bone amount radiologically observed in the first 6-month period depending on the increase in bone density. In our study, all measurements were evaluated through panoramic radiographs. Severe alveolar loss, the nearby presence of the hard palate, various magnification ratios of the radiographs, and the projections of implants at the maxillary sinus area at the panoramic radiographs affect the evaluation of bone resorption rates precisely. In that direction, BL/IL and GSH/OSH ratios were used instead of real measurements in this study. Using the same reference points described by Hatano et al.\(^{27}\) allowed us to conduct accurate comparisons within and between the groups. It is possible to measure the distances more accurately with computerized tomography than panoramic radiographs. On the other hand, from an ethical point of view, computerized tomography is not a suitable visualization technique for follow-up. Furthermore, it was reported that there were no significant differences in vertical bone height measurements between plain radiographs and tomographies.\(^{47}\) Implant survival rate following the sinus augmentation surgery was found to be >95% in many studies,\(^{31,48–50}\) and survival rate was not influenced by the type of grafting material.\(^{32,51–53}\) This study found an implant survival rate of 100% in the test and control groups, and this rate was found to be similar with the studies using anorganic bovine bone for sinus augmentation.\(^{32,51,53}\)

**CONCLUSION**

PRF and bovine bone graft material combination may be an alternative treatment option to the routinely used bovine bone graft material and collagen membrane combination. Being an autogenous and inexpensive biomaterial are advantages of the PRF combinations over the used bovine bone graft material and collagen membrane combination. PRF is effective, in particular in the first phases of wound healing, and its effectiveness may change depending on the characteristics of jointly applied graft material. Therefore, experimental studies applying PRF with different graft materials are beneficial. The current study was planned in retrospective design to control the study variables. Further long-term randomized, controlled clinical studies should be performed to evaluate various times for sinus graft healing.

**ABBREVIATIONS**

- BL: distance from the top of the bone-to-implant contact region to the head of the fixture
- FDBA: freeze-dried bone allograft
- GSH: grafted sinus floor above the lowest part of the original sinus height
- IL: distance from the apex to the head of the fixture; implant length
- OSH: original sinus height
- PPP: platelet poor plasma
- PRF: platelet-rich fibrin
- PRP: platelet-rich plasma
- rhBMP-2: recombinant human bone morphogenetic protein 2
- TCP: tricalcium phosphate

**REFERENCES**


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