Does Concentrated Growth Factor Used With Allografts in Maxillary Sinus Lifting Have Adjunctive Benefits?

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Purpose: Recent studies have shown that the use of platelet concentration products alone, or in combination with variable graft materials, accelerates the new bone formation associated with sinus augmentation. The aim of this study was to measure the adjunctive effects of concentrated growth factor (CGF) used with allograft on new bone formation and augmentation stability in sinus lifting.

Materials and Methods: This randomized controlled study included patients who presented for dental implant placement in atrophic posterior maxilla at the Department of Oral and Maxillofacial Surgery, Faculty of Dentistry, Ege University, and who needed maxillary sinus augmentation. All patients were treated with a 2-stage surgical technique using sinus lifting bilaterally and implant placement 6 months later. During sinus lifting surgery, one side was grafted with allograft (group 1) and the other side with allograft mixed CGF (group 2). Cone-beam computed tomography was carried out immediately postoperatively and also 6 months after the augmentation to evaluate vertical bone height and percentage of resorption. Bone specimens were obtained at the time of implant placement and evaluated histomorphometrically to analyze the percentage of new bone formation and residual graft particle. Statistical comparisons were conducted between groups for all these measurements.

Results: A total of 10 patients (2 females and 8 males) with a mean age of 57 years (range, 39 to 72) were enrolled in the study. Cone-beam computed tomography analysis revealed a significantly higher percentage of bone height resorption at the sixth month in group 1 (median, 9.32%) compared with group 2 (median, 6.37%) ($P < .05$). According to the histomorphometric examination, the percentage of new bone formation in group 2 (median, 36.41%) was higher than group 1 (median, 35.49%), but this difference did not reach statistical significance.

Conclusions: Using CGF with allografts supports the stabilization of gained vertical bone height after sinus augmentation, but further research is needed to determine the accelerating effects of CGF on new bone formation.

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The application of dental implants in the maxillary posterior region is a complicated operation because of the anatomic characteristics of the area. Alveolar bone resorption and maxillary sinus pneumatization after tooth loss in this area may lead to insufficient bone volume for dental implant application.

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Therefore, the most commonly used augmentation technique to obtain sufficient bone volume is sinus floor augmentation, as described by Boyne and James[1] and Tatum.[2] The critical question today is deciding the best filling material for bone augmentation in the sinus cavity.[3,4]

The autogenous bone graft is accepted as the gold standard in materials used in bone augmentation techniques because of its osteogenic potential, optimal adaptation, and the fact that it does not cause an immunologic reaction.[5] However, there are some other disadvantages of autogenous grafts, which must be considered, such as the large volume of material required in sinus augmentation, possibility of rapid resorption, need for a second surgical procedure, more traumatic formation, donor site morbidity, loss of function, prolongation of the healing period, prolonged postoperative pain, and visible movement limitation. Consequently, allogenic grafts, xenografts, and alloplastic grafts are preferred as alternatives to autogenous bone graft. Allografts are better adapted to human tissue than xenografts or synthetic materials and contain bone morphogenic proteins and growth factors, which stimulate osteoinduction. They can be supplied from tissue banks in which they are stored in sterile conditions, in ample quantities and at an affordable price.[6] However, demineralized allografts are readily resorbed, which makes it difficult to maintain a space. Therefore, they are often mixed with other allograft bones, synthetic graft materials, or platelet concentrate products.[7] In this study, demineralized allogenic bone graft material was used to provide sufficient graft material for bilateral sinus lifting augmentation.

In recent years, because of the disadvantages and limited regenerative outcomes of graft materials, attention has been focused on biological mediators to increase the clinical success of bone grafts, improve bone healing, and obtain more reliable alternative bone products.[8]

Platelets include many growth factors, which are scientifically proven to be effective in tissue regeneration in preclinical and clinical trials, and many critical differentiation factors are required for the regulation of bone healing. Therefore, the use of platelet concentrate products for bone regeneration becomes a current issue.[8-10] Several reports have been published evaluating the use of platelet concentrate products, such as platelet-rich plasma (PRP), platelet-rich fibrin (PRF), and concentrated growth factor (CGF), which accelerate new bone formation in directed bone regeneration and sinus augmentation.[11]

CGF is a second-generation platelet aggregation rich with growth factors and was first developed by Sacco in 2006.[11-13] Although CGF procedure is similar to PRF, it is different from PRP procedure. This is because biochemical additives such as calcium chloride and heterogeneous thrombin, essential for the preparation of PRP for platelet activation and fibrin polymerization, are not used in the preparation of CGF.[12,13] Thus, the disadvantages that may be encountered in the use of PRP, such as the formation of an immune reaction or the transfer of infectious diseases, do not arise in the use of CGF.[12,13] CGF is obtained by centrifugation of blood samples as in the case of PRF, but the centrifugation speed and time are different. This difference allows the CGF to have a wider, dense, and rich fibrin matrix in terms of growth factors. CGF is a concentrated autologous source of several growth factors, such as platelet-derived growth factor, insulin-like growth factor-1, vascular endothelial growth factor, and transforming growth factor-β1.[14,15] Moreover, it is reported that not only growth factors but also CD34+ cells (blood stem cells), which are involved in vascular maintenance, neovascularization, and angiogenesis, are present in the structure of CGF.[16] Therefore, it is considered that the regenerative capacity of CGF is higher in bone and sinus augmentation.[16,17] Although numerous studies have evaluated the use of PRP and PRF in augmentation procedures, only a few studies have focused on the use of CGF in these procedures.

The aim of this study was to answer the following question: Does the use of CGF mixed with allografts have superiority over the use of allograft alone in sinus augmentation procedures? The investigators hypothesized that the application of CGF with allograft accelerates new bone formation and augmentation stability in direct sinus lifting. The specific aims of the study were to estimate and compare bone height gain and bone formation radiologically and histomorphometrically between the CGF and non-CGF groups, after maxillary sinus augmentation with allograft.

Material and Methods

STUDY DESIGN

The investigators designed and implemented a split-mouth randomized clinical trial to address the research question. The study was carried out in accordance with the Declaration of Helsinki, and the study protocol was approved by the institutional ethics committee before patient selection (15-5.2/3). All patients were informed about the study/surgical protocol and provided their informed consent for participation in the study.

The study sample comprised patients presenting to the Department of Oral and Maxillofacial Surgery, Faculty of Dentistry, Ege University in 2014 and 2015 for dental implant rehabilitation bilaterally and symmetrically in the atrophic posterior maxillary region. Only the patients who needed bilateral direct sinus

augmentation before dental implant rehabilitation were considered suitable for inclusion in the study. The inclusion criteria were to have a residual bone height about 1 to 3 mm in the maxillary posterior region, sufficient alveolar crest width, and adequate interocclusal distance. Patients excluded from the study were those with systemic diseases, or pathologic or immunologic problems, which may affect wound healing and cause contraindication for a dental implant or a sinus augmentation surgery. Other factors taken into consideration in the selection process were whether the patients had previously undergone any sinus-related operations and/or whether they had had any pathologic conditions in the related region. Panoramic radiographs of the patients were taken before the operation, and residual bone heights and maxillary sinus dimensions were measured to check the limits of sinus augmentation in areas where the planned implants were to be placed. The average residual bone heights indicated on the panoramic radiographs before the operation were remeasured with a dental gauge caliper during the sinus augmentation to verify that these measurements were between 1 and 3 mm.

Before the sinus lifting surgery, randomization was achieved by flipping a coin. For each patient, the augmented sites were randomly divided into 2 study groups:

Group 1 (control): space between the sinus floor and the sinus membrane was filled only with allogenic bone material.

Group 2 (test): space between the sinus floor and the sinus membrane was filled with a mixture of CGF and allograft.

STUDY VARIABLES

The predictor variable of this prospective clinical study was the CGF application. To prepare CGF, before surgery, 2 × 9 mL venous blood samples taken from each patient's forearm were collected into 4 disposable, nonanticoagulant, and silica-coated tubes (Vacuette; Kremsmünster, Austria) and immediately placed in a single-stage specific device for centrifugation (MEDIFUGE MF200; Silfradentsrl, S. Sofia, Italy). The blood in the test tubes was centrifuged using the following CGF characteristic program: 30 seconds' acceleration, 2,700 rpm for 2 minutes, 2,400 rpm for 4 minutes, 2,700 rpm for 4 minutes, 3,000 rpm for 3 minutes, 36 seconds' deceleration, and stop. At the end of the centrifugation, there were 4 distinct layers in the test tubes: the top serum layer; the second buffy coat layer; the third liquid phase layer with white line cells and stem cells of CGFs; and the bottom red blood cell layer. The CGF (the buffy coat layer and the liquid phase layer) was separated from the red blood cell layer and divided into small pieces, using sterile scissors, for mixing with the allogenic bone grafts.

The primary outcome variable was the vertical bone height obtained by maxillary sinus lifting after 6 months. This was assessed using the cone-beam computed tomography (CBCT) that was taken immediately after the sinus augmentation and postoperatively at 6 months. The secondary outcome variables were new bone formation and residual graft particle percentages estimated by histomorphometric techniques 6 months after the sinus augmentation. The other variables included in the study were gender and age.

SURGICAL PROCEDURE

All surgical procedures were performed by the same surgeon who had 6 years of experience in conditions of asepsis and antisepsis in the Department of Oral and Maxillofacial Surgery at the Faculty of Dentistry, Ege University. All patients were treated with maxillary sinus floor elevation bilaterally via the lateral approach under local anesthesia using 2% lidocaine with epinephrine (Jetokain; Adeka Pharmaceutical Company, Samsun, Turkey). To expose the lateral wall of the maxillary sinus, a full-thickness mucoperiosteal flap was reflected. A lateral window osteotomy with a diameter of 10 × 15 mm was performed under continuous irrigation with sterile saline solution and the aid of a round-headed diamond drill.

To minimize the perforation risk of the Schniderian membrane in lateral window osteotomy, 1-mm diameter diamond rond drills were used. After the osteotomy, the sinus membrane was removed from the mesial, distal, and inferior walls by taking bone support with the special curves designed for the elevation of the sinus membrane. To control for possible perforation, the patient was frequently asked for nasal breathing, and the membrane mobility was checked.

The space between the sinus floor and the sinus membrane was filled on 1 side only with allogenic bone material (demineralized bone matrix allograft, granules: 0.25 to 1 mm) (Tissuelab Allograft, Leiden, Holland). The side selected was randomly determined by flipping a coin. The other was filled with a mixture of CGF and allograft (Fig 1).

To obtain PRF, 2 × 9 mL venous blood samples were taken from each patient's forearm, immediately placed in a single-stage centrifuge device (EBA 20; Hettich, Zentrifugen, Tuttlingen, Germany) and centrifuged at 2,700 rpm for 12 minutes. At the end of the process, 3 layers were seen in the test tubes: the top layer of serum; the second fibrin layer; and the bottom red blood cell layer. The PRF (fibrin layer) was isolated and pressed to form a membrane. The osteotomy

FIGURE 1. Preparation of concentrated growth factor and allograft mixture for group 2.

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window was then covered with the PRF device on both sides, and the surgical flap was sutured with interrupted silk sutures (4 to 0 atraumatic; Silk/Silk; Dogsan, Istanbul, Turkey).

Postoperatively, amoxicillin (1,000 mg twice per day for 5 days), naproxen sodium (550 mg twice per day for 7 days), and 0.2% chlorhexidine mouthwash (twice per day for 7 days) and, if necessary, paracetamol (500 mg up to 4 times per day) were prescribed. In addition, all the patients were instructed to take postoperative cold application, to cough or sneeze with an open mouth, and to avoid blowing their noses. Immediately after the surgery, patients underwent a CBCT scan using a patient-specific template.

All patients were scheduled for frequent routine follow-ups at the postoperative first week, first, third, and sixth months. In the postoperative sixth month, control CBCTs with templates were obtained, and planning was carried out for the dental implants. For the implant surgery, a full-thickness mucoperiosteal flap was removed under local anesthesia. Then, small dots were created with marker bursts on the crestal surfaces of the sinus regions where the implants would be placed. Taking these points as a center, and taking account of the implant size to be placed, block bone samples were taken with the aid of a trephine drill (diameter: 3.0/4.0; length: 10 mm) (Meisinger USA, LLC, Centennial, CO). Then implants were inserted

to the relevant regions in accordance with the manufacturer's instructions (Anthogyr SAS, Sallanches, France) (Fig 2). Four months postoperatively, all patients' implant-supported prostheses were fabricated.

DATA COLLECTION METHODS

Radiographic Evaluation

Radiographic examinations were performed immediately after sinus surgery and in the postoperative sixth month with patient-specific templates, which were prepared in the preoperative period to provide standardization, using CBCT with the Kodak Dental Imaging Software (Kodak 9000 3D; Dental Systems, Carestream Health, Rochester).

The patients' vertical bone heights, obtained by maxillary sinus lifting in the posterior maxillary region, were measured on images in DICOM format, and the sixth month difference rates were recorded for comparison. The patients' CBCT results, taken immediately after surgery and 6 months later, were evaluated by the same operator. During this evaluation, vertical height measurements on the coronal sections were repeated 3 times from the points determined with stents in the relevant region. For the vertical measurements, the length between the tangent line passing through the top of the alveolar crest and the tangent line passing through the top of the maxillary sinus augmentation were calculated with the aid of a drawing made perpendicular to these lines (Fig 3). Also, the percentage of resorption for the 2 groups was calculated by proportioning the reduction in vertical bone height during the 6 months to the immediately measured vertical bone heights.

Histomorphometric Evaluation

Bone samples taken from patients were immediately fixed in 10% buffered formalin (pH 7.4) (Merck, Darmstadt, Germany). All samples were decalcified in 10% ethylenediamine tetraacetic acid solution (Merck, Darmstadt, Germany) for 2 weeks. The decalcified samples were dehydrated in ascending grade alcohols with the aid of the Leica ASP 300 automatic tissue tracking device (Leica Instruments GmbH, Wetzlar, Germany) and then embedded in paraffin using the Shandon Histocentre 2 device (Thermo Shandon, Runcorn, United Kingdom). Five-micron thick sections from the paraffin blocks, parallel to the longitudinal axis of the biopsy specimen, were prepared using a Leica RM 2145 (Leica Instruments GmbH, Wetzlar, Germany) microtome device and hemotoxylin-eosin staining of the samples was performed for the histomorphometric evaluations.

Histomorphometric analyses of all sections were carried out under a light microscope (Carl Zeiss

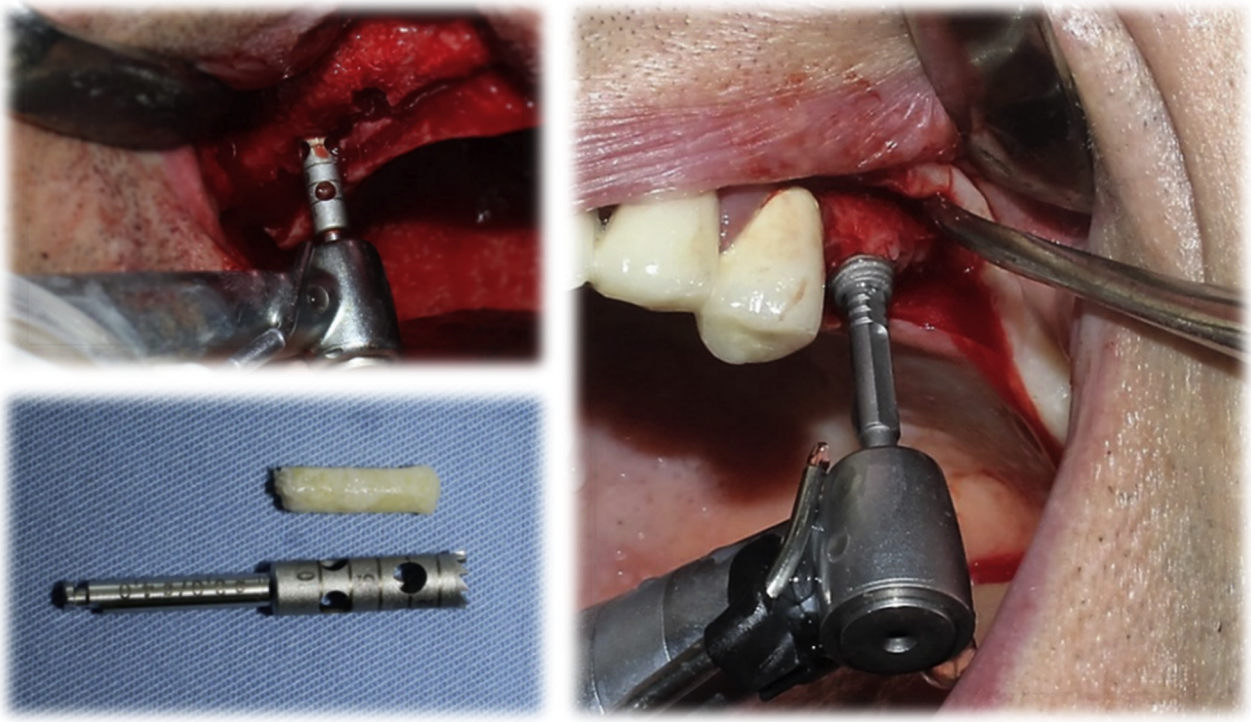

FIGURE 2. Block bone samples were taken with the aid of a trephine drill (diameter: 3.0/4.0; length: 10 mm) (Meisinger USA, LLC, Centennial, CO), and implants were inserted to the relevant regions.

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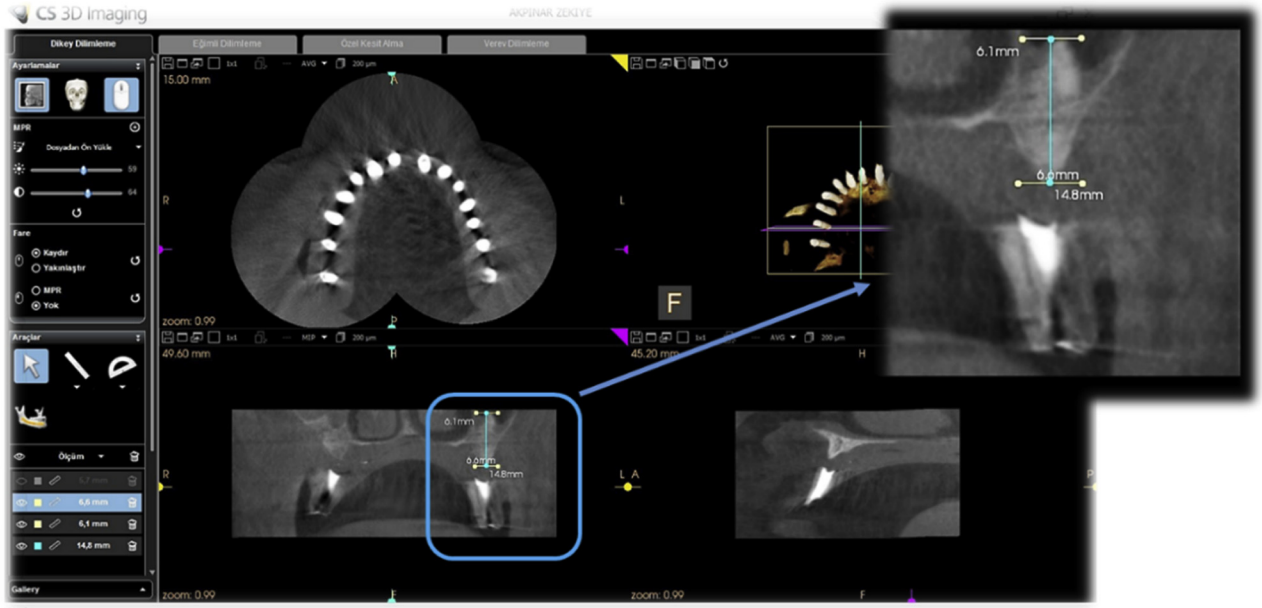

FIGURE 3. Vertical measurements on cone-beam computed tomography images.

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Microscopy GmbH, Jena, Germany). Digital images of the sections were taken with a digital camera (AxioCam HRc3; Carl Zeiss Microimaging GmbH, Jena, Germany) attached to the light microscope under a magnification of ×100 (Fig 4A). The amount of newly formed bone and residual graft particle in the sections was measured in square micrometers with the aid of the automeasure module of the AxioVision release 4.8.2. (Carl Zeiss Software GmbH, Jena, Almanya) (Figs 4B, C). The histomorphometric evaluation of the bone samples was based on the new bone formation percentage ([the mineralized and nonmineralized bone tissue/the entire sectional area] × 100) and the residual graft particles percentage ([the residual graft particles/the entire sectional area] × 100).

DATA ANALYSIS

Sample Size Calculation

The sample size of the study was determined after reference to the study by Corinaldesi et al.[18] The data were analyzed using a power analysis program (G*Power: Statistical Power Analyses for Windows; Dusseldorf, Germany). The sample size calculation determined that 6 participants per treatment group would provide 95% power to detect a true difference between test and control, using newly formed bone rate values as the primary outcome variable. Accordingly, a sample of 10 patients per group was recruited (20 observations in total) to compensate for possible dropout during the study period.

The statistical analysis was performed using the 23.0 version of the Statistical Package for the Social Sciences (SPSS Inc, IBM Corp, Armonk, NY).

The Wilcoxon signed rank test was used for the statistical evaluation of the data obtained by CBCT measurements and histomorphometric evaluation. An alpha value of 0.05 is used as the cutoff for significance; therefore, *P*-values below .05 were considered as statistically significant.

Results

This prospective randomized clinical study was composed of 10 patients (2 females and 8 males) who were referred to our clinic between 2014 and 2015 with an indication of bilateral maxillary sinus augmentation for dental implant treatment at atrophic posterior maxilla. The age range of the patients in the study was between 39 and 72 years, with a mean of 57 years.

In this study, 20 direct maxillary sinus augmentations were performed. During the maxillary sinus augmentations, Schneiderian membrane perforation (up to 2 mm) occurred in 2 of the 20 operation sites. In the sites where allograft with CGF was used as a filler, the perforation zones were repaired using the CGF as a membrane.

In the control sessions after sinus augmentation, none of the patients had any pathologic symptoms or signs of infection in the surgical site. No signs of sinusitis were observed in the patients during the 6-month healing period. At the sixth month, the 20

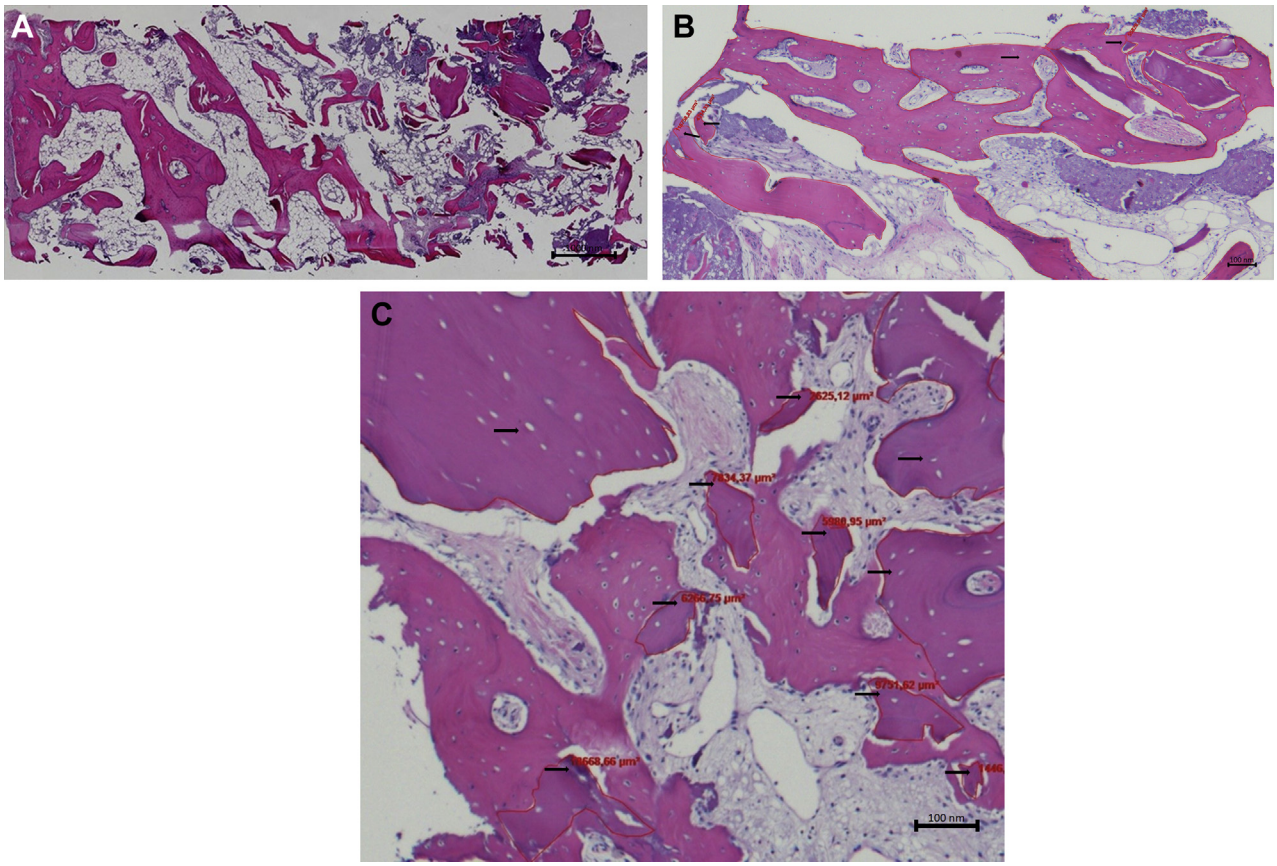

FIGURE 4. *A*, Digital images of the bone section from group 2 under magnification of ×100 (hematoxylin and eosin staining). *B*, Measurement of the newly formed bone tissue area, in square micrometers, in a bone sample from group 2 (hematoxylin and eosin staining). Arrows indicate newly formed bone bridges between residual graft particles. *C*, Measurement of the area of residual graft particles, in square micrometers, in a bone sample from group 1 (hematoxylin and eosin staining). Arrows indicate residual graft particles area.

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implants (group 1: 10; group 2: 10), with a diameter of 4.6 mm and length of 12 mm, were inserted at the sites from which bone samples were taken (first molar site). The other 32 planned implants (group 1: 16 and group 2: 16) had a diameter of 4.00 or 4.6 mm and a length of at least 10 mm. All implants had primary stabilization because all of them displayed greater than 30 N-cm insertion torque. Healing after implant surgery was uneventful in all patients. Four months postoperatively, all patients' implant-supported prostheses were placed, and occlusal loading was performed. The survival rate of implantation was 100% after 1-year follow-up.

RADIOGRAPHIC RESULTS

Comparison of the vertical bone heights obtained by CBCT immediately after the sinus surgery did not show any significant differences between the CGF and non-CGF sides, as outlined in Table 1: group 1 (median, 18.74; interquartile range, 3.41) and group 2 (median, 18.70; interquartile range, 2.76); $P = .51$.

On the other hand, the vertical bone heights obtained 6 months after sinus surgery were significantly lower in group 1 (median, 15.63; interquartile range, 4.29) compared with group 2 (median, 17.51; interquartile range, 4.62); $P = .02$ (Table 1).

The resorption percentages obtained for the 2 methods were compared using the Wilcoxon signed rank test, and a significant difference was found in the percentage of resorption between the 2 methods ($P = .047$) (Table 1). Consistent with the significant difference observed in vertical bone height between the 2 methods at 6 months, percentages of resorption were found to be higher in group 1 (median, 9.32%; interquartile range, 9.12) than in group 2 (median, 6.37%; interquartile range, 8.46) (Table 1).

Histomorphometric Results

According to the histomorphometric data analysis, although we observed a larger percentage of newly formed bone in group 2 (median, 36.41%; interquartile range, 53.08) compared with group 1 (median, 35.49%; interquartile range, 34.18) as well as a smaller

Table 1. COMPARISON OF THE VERTICAL BONE HEIGHTS MEASURED IMMEDIATELY AFTER THE SINUS SURGERY AND 6 MONTHS AFTER SURGERY

		Descriptive Statistics			Wilcoxon Signed Rank Test	
Variables		Median	Standard Deviation	Interquartile Range	Total *N*	Asymptotic Significance (2-Sided Test)
Bone height immediately after surgery	Group 1	18.7350	1.6076	3.41	10	0.508
	Group 2	18.7000	1.7693	2.76		
Bone height 6 mo after surgery	Group 1	15.6250	2.0745	4.29	10	0.022
	Group 2	17.5100	2.3243	4.62		
Resorption (%)	Group 1	9.3188	8.3044	9.12	10	0.047
	Group 2	6.3700	5.9381	8.46		

Note: Also, comparison of the resorption percentages for the 2 groups at 6 months.

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percentage of residual graft particles in group 2 (median, 5.10%; interquartile range, 21.11) compared with group 1 (median, 5.80%; interquartile range, 14.88), none of these differences were statistically significant (newly formed bone percent: $P = .29$ & residual graft particles percent: $P = .72$) (Table 2).

Discussion

The aim of this study was to answer the question of whether, for sinus augmentation procedures, the use of CGF mixed with allografts is better than the use of allograft alone. Our hypothesis was that the application of CGF with allograft would have adjunctive effects on new bone formation and augmentation stability in direct sinus lifting. The specific aims of the study were to compare bone height gain and bone formation both radiologically and histomorphometrically for the CGF and non-CGF groups after maxillary sinus augmentation with allograft. The radiologic results revealed that CGF supports the maintenance of the obtained augmentation when used with the allograft. However, histomorphometric findings showed no differences between the 2 groups with regard to new bone formation. Therefore, our hypothesis was partially accepted.

In this study, the median value of vertical bone height reduction at the end of the 6-month recovery period was 6.37% in the CGF plus allograft group and 9.32% in the allograft-only group. This difference was statistically significant and showed that the decrease in vertical height was less in the group using CGF. This indicates that CGF was effective in maintaining the volumetric stability of the graft and new bone formation. Histologic examination of the biopsies revealed no statistically significant differences between the 2 groups with regard to new bone formation and residual graft particles. More specifically, the amount of new bone formation was higher in the samples taken from the region where CGF was used (median, 36.41%) than in those from allograft-only group (median, 35.49%). Also, the median graft particle area percentage for allograft application was 5.80 compared with 5.10 for the allograft plus CGF application, but this difference was not significant. The small sample size is a limitation of the present study. Also, the large dispersion in the data may have hindered the detection of a meaningful difference in histologic examinations.

Table 2. COMPARISON OF NEW BONE FORMATION (%) AND RESIDUAL GRAFT PARTICLES (%) BETWEEN THE 2 GROUPS

		Descriptive Statistics			Wilcoxon Signed Rank Test	
Variables		Median	Standard Deviation	Interquartile Range	Total *N*	Asymptotic Significance (2-Sided Test)
New bone formation (%)	Group 1	35.4882	23.0415	34.18	10	0.285
	Group 2	36.4111	26.4774	53.08		
Residual graft particles (%)	Group 1	5.8018	13.8413	14.88	10	0.721
	Group 2	5.1006	14.6143	21.11		

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It is possible that this might be achieved with a larger sample size in future studies.

Recently, several different methods for maxillary sinus augmentation have been described, and various materials have been used for augmentation. Although the most appropriate method of augmentation varies according to individual case characteristics, the ideal graft material is still a subject for discussion. The use of recently developed platelet concentration products in bone augmentations has become popular because of their low costs and practical application. In maxillary sinus augmentation procedures, platelet concentrate products have been used alone, or in conjunction with many bone graft materials, to obtain sufficient high-quality bone for dental implant application.[8,11,14] CGF, a second-generation platelet concentrate product, has been used in various bone augmentation methods, and its effectiveness on bone regeneration has been evaluated and accepted.[11,14,19-22]

In this study, demineralized allogenic bone graft material was used to provide sufficient graft material for bilateral sinus lifting augmentation and also to benefit from its osteoinductive properties and osteoconductive effect. The radiographic results of the study showed that using CGF with allografts had an adjuvant function in maintaining bone height. However, after the healing process, sufficient bone gain was obtained for implant application in both groups.

Park et al[21] compared the effects of CGF and PRF on new bone formation in an animal study, which focused on bone defects in the femurs of dogs. According to histologic analysis, after 4 weeks of the healing period, the rate of new bone formation (52.33%) was higher in the CGF group than in the PRF group (21.00%). Furthermore, in the same study, it was reported that CGF showed a thicker and denser fibrinogen fiber network in a unit area than PRF in the scanning electron microscope examination.

Honda et al[12] evaluated the effects of using CGF with bone marrow–derived stromal cells on critical-size bone defects in the skulls of rats. They used both an in vivo and in vitro approach and reported that CGF increased cell proliferation, osteogenic maturation, and the mineralization of human mesenchymal cells in a dose-dependent manner. In an animal study performed on rabbit tibias, Durmuşlar et al[23] observed histologically the positive effects of the use of CGF with autogenous bone graft on bone regeneration in peri-implantitis defect. They stated that the skeletal structure supported by autogenous bone graft helps CGF secrete prolonged growth factor.

In addition to animal studies, the view that CGF improves bone regeneration is supported by several clinical studies. In this context, CGF alone, or in combination with autogenous bone graft, was applied to bone defects after the enucleation of intrabone cysts and periapical lesions. The results showed that CGF decreases the healing time of bone defects and increases bone regeneration.[19,24,25] Shyu et al[22] grafted a cystic lesion located in the mandibular jaw with CGF and performed dental implant application after 14 weeks. They observed a bone volume of 32.7% in microcomputed tomography results of the bone biopsy taken during dental implantation. Moreover, the radiopacity was observed to increase gradually in the radiologic follow-up of the lesion at 6 months, and periapical radiographs taken 8 months after occlusal loading showed that the crestal bone level around the implant remained stable. In a study conducted to investigate the effects of CGF on bone regeneration in immediate implant applications, Yang et al[26] evaluated buccal bone regeneration with CBCT and reported that CGF had no positive effect. They argued that the rapid absorption of CGF and the lack of sufficient density could cause this condition.

The positive effects of CGF in sinus augmentations were also determined radiologically, histologically, and clinically in various previous studies, and it was indicated that the product can be used effectively as an alternative to bone graft materials.[17,21] Sohn et al[11] reported the use of CGF only as the graft material in 61 sinus augmentations, performed with a lateral approach, and with the simultaneous application of dental implants. Five months later, histologic examination of 5 biopsy specimens from a lateral bone osteotomy revealed the presence of active new bone formation with no inflammation. Moreover, new bone formation around the implant was observed in tomographic examinations of all cases.

Kim et al[14] used CGF as a graft material in 11 sinus augmentations using a flapless transcrestal approach and a hydrodynamic piezoelectric system. They reported an average bone gain of 8.23 mm at the sinus floor, according to CBCT examinations, after an average of 23.8 weeks of healing. Also, 34 weeks after the occlusal loading of implants, the success rate of the implant was 100%.

For dental implantation in the atrophic posterior maxillary region, in patients with a residual bone height of 2 to 4 mm, Chen et al used CGF as a graft material for their osteotome sinus floor elevation technique and applied short implant applications simultaneously. In this way, they showed that the osteotome technique and short implants, usually performed in residual crests of 4 to 6 mm, can be used with CGF support at lower bone levels. The results show a mean postoperative vertical bone gain of 9.21 mm, a 2.9 mm decrease in bone height after 6 months, and a 0.14 mm decrease in the next 6 months. The implant survival rate was reported as 100% at a mean follow-up of 20 months.[19]

However, in all the aforementioned studies using CGF, an implant was placed simultaneously with CGF to hold the membrane up in the sinus augmentation process. This can be explained by the insufficiency of the CGF structure and the limited resorption times.

In maxillary sinus augmentations performed with the lateral approach, the use of absorbable or nonabsorbable membranes to cover the lateral bone window is thought to help support graft stability, prevent the invasion of soft tissue into the sinus, and increase bone regeneration. Many studies have reported that the use of membranes to improve bone quality in the lateral bone wall is effective.[27,28] Recently, absorbable membranes have become the preferred option because of some disadvantages of nonabsorbable membranes, such as the need for a second operation to remove them or sharp edges of this membranes being exposed through the soft tissue.[29] Gassling et al applied 2 different absorbable membranes, one of PRF and the other of collagen membrane, on the lateral osteotomy area in maxillary sinus augmentations and examined their relative effects on new bone formation histomorphometrically.[30] The mean new bone formation value was reported to be 17% in the area where PRF was used and 17.2% in the area where the collagen membrane was used. Taking this close similarity into consideration, they stated that PRF is preferable to commonly used membrane systems because of its low cost and the fact that it is an autogenous biomaterial.[29,30] In view of this information, in our study, PRF was used in all cases as a membrane to close the lateral bone window after augmentation. With the benefit of the particular characteristics of PRF, soft tissue invasion was prevented, and the cost of the procedure was reduced.

In our study, membrane perforation, which is the most common complication during sinus membrane elevation, was encountered twice. CGF was used as a membrane for the closure of these perforations up to 2 mm, taking account of the dense and wide fibrin structure. Chen et al[19] repaired the perforations encountered in internal sinus lifting cases with CGF and did not encounter any signs of sinusitis in the postoperative period. Similarly, in our study, there were no signs of sinusitis in the postoperative period in both cases, and the same medical treatment was applied to these patients as to all.

In the literature, there is no study on the use of CGF in grafting of the cavity formed by the elevation of the sinus membrane in 2-stage sinus augmentation and implant applications. Our study set out to rectify this position. We performed 20 2-stage sinus lifting and implant applications, applied bilaterally to 10 patients. We used CGF with allogenic bone graft as a graft material in the patients' randomly selected maxillary sinuses and examined the bone formation histologically and radiologically. The strength of our study with regard to CGF is that the control and test groups were composed of the same patients, thus eliminating the effect of individual differences between the treatment and control groups. The study was completed with 10 patients in each group. Thus, it was determined that the power of the study was more than 95%. One limitation of the study was the unequal number of males and females in the sample. Consequently, it was not possible to evaluate whether sexual dimorphism affected the outcomes or not. Moreover, we could not use CGF alone as a graft material because of ethical considerations. Therefore, we are unable to conclude that CGF alone may be as effective as other graft materials in sinus augmentations with a residual bone height below 4 mm.

CGF is an easy-to-use, autogenous, and safe material. The findings of our study show that CGF supports the maintenance of the obtained vertical bone height after sinus augmentation when used with allograft. Also, using CGF with allografts may help to regenerate new bone and replace the graft with the new bone, but further research with larger sample sizes will be required to confirm this hypothesis. Further studies are also needed to evaluate the effects of CGF as a graft material on bone regeneration in sinus augmentation and how other variables such as gender and age affect this procedure.

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