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Bone Regeneration in the Maxillary Sinus Using an Autologous Fibrin-Rich Block With Concentrated Growth Factors Alone

Dong-Seok Sohn, DDS, PhD,* Jeung-Uk Heo, DDS, PhD,† Dong-Ho Kwak, DDS, PhD,‡ Dong-Eung Kim, DDS, PhD,§ Ji-Min Kim, DDS,‖ Jee-Won Moon, DDS,¶ Ju-Hyoung Lee, DDS,¶ and In-Sook Park, DDS, PhD¶

Purpose: *The purpose of this study was to evaluate the predictability of new bone formation in the maxillary sinus using an autologous fibrin-rich blocks with concentrated growth factors (CGFs) alone as an alternative to graft material.*

Materials and Methods: *A total of sixty-one sinus grafts were consecutively performed using the lateral window approach. After making replaceable bony window, the sinus membrane was elevated to make a new compartment. After 113 implants (average 13 mm high) with 11 different systems were placed simultaneously, the collected fibrin-rich blocks with CGFs alone were inserted in the sinus. To seal the lateral window, the bony window was repositioned. Radiographic, clinical, and histologic evaluation was performed to verify sinus augmentation.*

Results: *No significant postoperative complications developed. New bone consolidation in all augmented maxillary sinus was observed along the implants on plain radiographs and on cone-beam computed tomograms. The success rate of implant was 98.2% after an average of 10 months loading.*

Conclusion: *Fibrin-rich blocks with CGFs act as an alternative to bone grafting and can be a predictable procedure for sinus augmentation. (Implant Dent 2011;20:1–000)*

Key Words: maxillary sinus augmentation, fibrin, growth factor, platelet aggregate, replaceable bony window

The atrophic posterior maxilla is a challenging site for oral rehabilitation with dental implants due to insufficient bone volume to accommodate dental implants. Crestal approaches or lateral window approaches for sinus augmentation are the most common surgical techniques to overcome vertical deficiencies of the atrophic posterior maxilla.[1–5] For the past several decades, bone grafts have been considered a prerequisite for the success of sinus augmentation. Thus, variable bone grafts, such as autografts, allografts, xenografts, alloplasts, or combinations of different graft materials, have been used widely to augment the maxillary sinus. As space makers, all bone grafts are considered highly predictable for new bone formation in the sinus.[6–11] However, successful bone augmentation in the maxillary sinus without bone grafting and osseointegration of implants have been reported in human and animal studies.[12–15] In addition, bone reformation in the maxillary sinus, using patients' own venous blood alone and absorbable gelatin sponges alone as alternatives to bone grafts, has been reported in clinical studies.[16,17]

Platelet aggregates, such as platelet-rich plasma and platelet-rich growth factors, have been used to accelerate new bone formation associated with guided bone regeneration and sinus grafts.[18–20] However, the effect of platelet-rich plasma on new bone formation is debatable.[21] The expression of growth factors from collected platelet aggregates is variable.[22] Recently, successful bone reformation in the sinus using fibrin-rich blocks with concentrated growth factors (CGFs) as an alternative to bone grafting has been reported with limited data.[23] To date, there have been no studies indicating implant survival rate on bone formation using fibrin-rich blocks with CGFs alone. The aim of this study was to verify the bone reformation by the application of only fibrin-rich blocks with CGFs in the new compartment between the elevated sinus membrane and the sinus floor in terms of radiologic, histologic, and clinical results.

*Chairman and Professor, Department of Dentistry and Oral and Maxillofacial Surgery, Catholic University Hospital of Daegu, Republic of Korea.
†Private Practice, President, Goodwill Dental Hospital, Pusan, Republic of Korea.
‡Private Practice, President, Kwak's Dental Hospital, Daegu, Republic of Korea.
§Private Practice, President, Dr. Kim's Dental Clinic, Daegu, Republic of Korea.
‖Resident, Department of Dentistry and Oral and Maxillofacial Surgery, Catholic University Hospital of Daegu, Republic of Korea.
¶Instructor, Department of Dentistry and Oral and Maxillofacial Surgery, Catholic University Hospital of Daegu, Republic of Korea.

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Reprint requests and correspondence to: Dong-Seok Sohn, DDS, PhD, Department of Oral and Maxillofacial Surgery, Catholic University Hospital of Daegu, 3056-6 Daemyung-4 Dong, Namgu, Daegu 705-718, Republic of Korea, Phone: +82 53-6504288, Fax: +82 53-6227067, E-mail: dssohn@cu.ac.kr

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Table 1. Summary of Characteristics and Findings of Patients

No. of Patient	Average Age (y)	No. of Sinus Graft	Average Bone Height (mm ± SD)	No. of Implant	Average Healing Time (wk ± SD)	Average Vertical Bone Gain (mm ± SD)	Average Loading Period (wk ± SD)	Success Rate (%)
53	51.3	61	3.9 ± 2.1	113	21.4 ± 5.6	9.53 ± 2.64	40 ± 15.5	98.2

MATERIALS AND METHODS

Patient Selection

The present study population comprised 61 consecutive sinus grafts in 53 patients, 30 men and 23 women, ranging from 27 to 75 years of age (mean age, 51.3 years). The surgery was performed at the Department of Oral and Maxillofacial Surgery, Catholic University Medical Center, and at 2 private practices in Daegu, Korea, from September 2008 to October 2009. All patients were informed about the treatment procedure, and oral and written consent was obtained. Before the sinus graft procedure was performed, patients' medical histories were carefully evaluated, and patients with disease known to affect bone metabolism were excluded. Smokers were not excluded from the study but were informed that smoking could compromise the quality of the sinus lift and reduce the success rate of implants. Preoperative plain panoramic radiograms and cone-beam computed tomograms (Combi; Pointnix Co., Seoul, Korea, or i-Cat; Imaging Sciences, Hatfield, PA) were taken to evaluate preoperative sinus conditions and residual bone heights and later to assess postoperative bone gain. The residual bone heights at the implant sites were between 0.5 mm and 10 mm (average ± SD: 3.9 ± 2.1 mm). The residual bone heights at the implant sites were between 0.5 and 5 mm in 75% of sinuses, and 25% of sinuses showed bone heights of 6 to 10 mm. Huge cysts (ranging from 17 mm to 30 mm wide) were observed in 6 maxillary sinuses. One maxillary sinus showed thickened sinus membrane (>5 mm) (Table 1). T1

Preparation of Fibrin-Rich Blocks With CGFs

Fibrin-rich blocks were prepared according to Sacco's protocol.[24] Before sinus grafting, 20 to 60 mL of patient's venous blood was taken from the patient's forearm, and the venous blood was divided into 2 to 8 glass-coated test tubes without anticoagulants. The blood in the test tubes was centrifuged at 2400 to 2700 rpm using a specific centrifuge with a rotor turning at alternated and controlled speeds for 12 minutes (Medifuge; Silfradent srl, Sofia, Italy); 2 to 6 pieces of fibrin-rich blocks were prepared using this specific centrifuge. The collected fibrin-rich blocks were characterized by 4 phases. The uppermost layer was represented by the serum (blood plasma without fibrinogen and coagulation factors), and the second layer was the fibrin buffy coat layer represented by a very large and dense polymerized fibrin block. The third layer was a liquid phase containing the CGFs, white line cells, and stem cells waiting for stimulation and to differentiate into specialized cell types. The lowest red layer represented platelet-rich coagulation. The red phase consisted of concentrated red and white blood cells, platelets, and clotting factors (Fig. 1, a). In this study, the second layer with the fibrin buffy coat and the third liquid phase were used as alteratives to bone substitutes for sinus augmentation.

Surgical and Prosthetic Procedures

Prophylactic oral antibiotics, Cefditoren pivoxil (Meiact; Boryung Parm., Seoul, Korea), 300 mg three times per day, were used routinely, beginning 1 day before the procedure and continuing for 7 days. Surgery was performed under local maxillary block anesthesia using 2% lidocaine with 1:100,000 epinephrine. Flomoxef sodium (Flumarin; Ildong Pharmaceutical Co., Korea, 500 mg intravenously) was administered 1 hour before surgery. Maxillary sinus floor elevation via the lateral approach was completed on all patients. The full thickness of mucoperiosteal flap was elevated to expose the lateral wall of the maxillary sinus. The piezoelectric saw, with a thin blade (S-Saw; Bukboo Dental Co., Daegu, Korea), connected to piezoelectric device (Surgybone; Silfradent srl), was used with copious saline irrigation to create the replaceable rectangular bony window at the lateral wall of the maxillary sinus. The anterior vertical osteotomy was made 2 mm distal to the anterior vertical wall of the maxillary sinus and the distal osteotomy was made approximately 20 mm away from the anterior vertical osteotomy. The height of the vertical osteotomy was approximately 10 mm. The anterior and inferior osteotomy lines were tilted to the inside of the maxillary sinus lateral wall, and then superior and posterior osteotomies perpendicular to the sinus wall were made. This design of osteotomy facilitated the precise replacement of the bony window as a barrier over the inserted fibrin-rich blocks in the maxillary sinus (Fig. 1, b and c). The bony window was detached carefully to expose the sinus membrane. The sinus membrane was carefully dissected from the sinus floor walls with a flat blunt-edged sinus membrane elevator. Dissection of the sinus membrane was continued to reach the anterior and medial walls of the sinus cavity. The height of exposed medial wall was parallel to the superior osteotomy line of the lateral window. F1 AQ: 2

After elevation of sinus membrane, a 1-step, undersized osteotomy was used to obtain initial stability of the implant at implant sites with low bone height. To verify the effect of the fibrin-rich block with CGFs, and to exclude the effect of the implant system, 11 kinds of implant systems with 4 different implant surfaces were placed in this study. A total of 113 implants with 4 different surfaced implant systems were placed. Twenty-eight resorbable blast media-surfaced implants (10 Dentis Implants [Dentis Inc., Daegu, Korea] and 18 SybronPro

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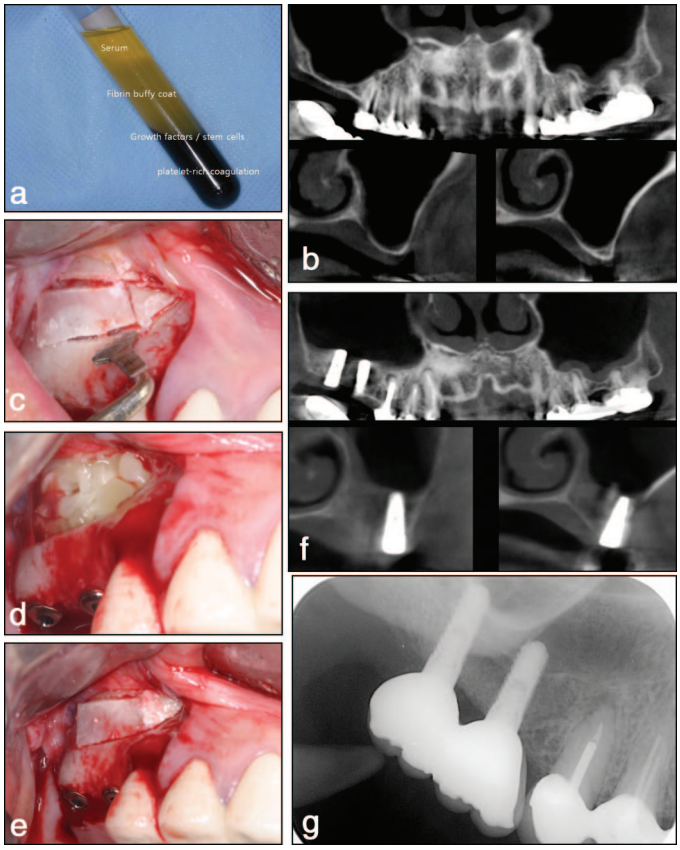

Fig. 1. a, A fibrin-rich block with concentrated growth factors made by a specific centrifugation (Medifuge, Silfradent srl). The second and third layers were utilized for sinus augmentation. **b**, Cone-beam computed tomogram showing 1 to 2 mm bone height at the right maxillary second (left) and first molar (right), respectively (from patient number 50). **c**, The piezoelectric saw, connected to piezoelectric device (Surgybone, Silfradent srl), was used to create the replaceable lateral window of maxillary sinus in all cases. **d**, After careful elevation of the sinus membrane, 4 pieces of fibrin-rich block were inserted into the new compartment between the elevated membrane and the sinus floor. Two tapered design implants (Dentis Implants; Dentis Inc.) were placed simultaneously after a 1-step down osteotomy. The initial stability was good. **e**, The bony window was repositioned with stability to seal the window. **f**, Cone-beam computed tomographic scans revealed new bone consolidation along the implant body at the right maxillary second (left) and the first molar (right), respectively, after 18 weeks healing. Implants were uncovered at this stage. **g**, Radiogram after 5 months loading. Note the newly formed bone in the sinus.

XRT implants [Sybron Implant Solutions, Grendore, CA]) were placed. Forty-seven hydroxylapatite-coated implants (14 Tapered screw vent implants [Zimmer Dental Inc., Carlsbad, CA]; 31 Legacy implants [Implant Direct LLC, Calabasas Hills, CA]; and 2 Bio-tite implants [Dio Implant Co., Busan, Korea]) were placed. Thirty-four sand-blasted, large grit, acid-etched surface implants (MIS Implants Technologies Ltd., Shlomi, Israel) were placed. Four sintered porous-surfaced implants (Endopore implants; Sybron Implant Solutions) were placed.

Two to six pieces of fibrin-rich blocks with CGFs were inserted in the new compartment between the elevated sinus membrane and the sinus floor (Fig. 1, d). The bony portion of the lateral window was repositioned to prevent soft tissue sinus cavity ingrowths and to promote new bone formation from the lateral wall of the maxillary sinus (Fig. 1, e). Flaps were sutured using interrupted mattress PTFE sutures (Cytoplast; Osteogenic Biomedical, TX) to achieve passive primary closure. Patients were instructed not to blow their noses for 2 weeks after surgery and to cough or sneeze with an open mouth. Antibiotic therapy was continued postoperatively for 7 days, and the sutures were removed 10 days postoperatively. After sinus augmentation, plain panoramic radiographs and cone-beam computed tomograms (Combi; Pointnix Co., and i-Cat; Imaging Sciences) were made immediately after surgery. An average 21.4 weeks (SD: ±5.6) healing period was allowed for new bone consolidation and the osseointegration of implants. Plain panoramic radiograms and dental cone-beam computed tomograms were obtained to assess the new bone formation around the implants before the implants were uncovered (Fig. 1, f). Bone biopsies were taken in 5 cases through the repositioned lateral window to verify new bone formation in the sinus during the uncovering. Implants were loaded with provisionals for an average 6 weeks to contour the soft tissue profile around the implant before the final prosthesis was delivered. In the maxillary sinuses with huge cysts, cystic fluid was aspirated with a syringe or suctioned through the stab incision area made by the surgical blade in the sinus membrane. And the same sinus augmentation procedure using fibrin-rich blocks with CGFs was performed after removal of cysts (Fig. 2, a–i).

Histologic Preparation

Five bone biopsies were harvested from the repositioned lateral window during the uncovering procedure after an average of 5 months healing period. Biopsy specimens were immediately fixed in 4% formaldehyde for 24 hours at 4°C and decalcified in 10% formic acid for 3 days. After dehydration in an ascending alcohol series, the biopsies were embedded in paraffin, and 5-μm thick sections, parallel to the longitudinal axis of the biopsy specimen, were prepared using a microtome. Sections were stained with Mayer's hematoxylin and eosin stain and Masson's Trichrome stain, and the specimens were evaluated to verify newly formed bone and soft tissue changes under light microscopy. The specimens were photographed using the AxioCam MRc5 (Carl Zeiss, Ger-

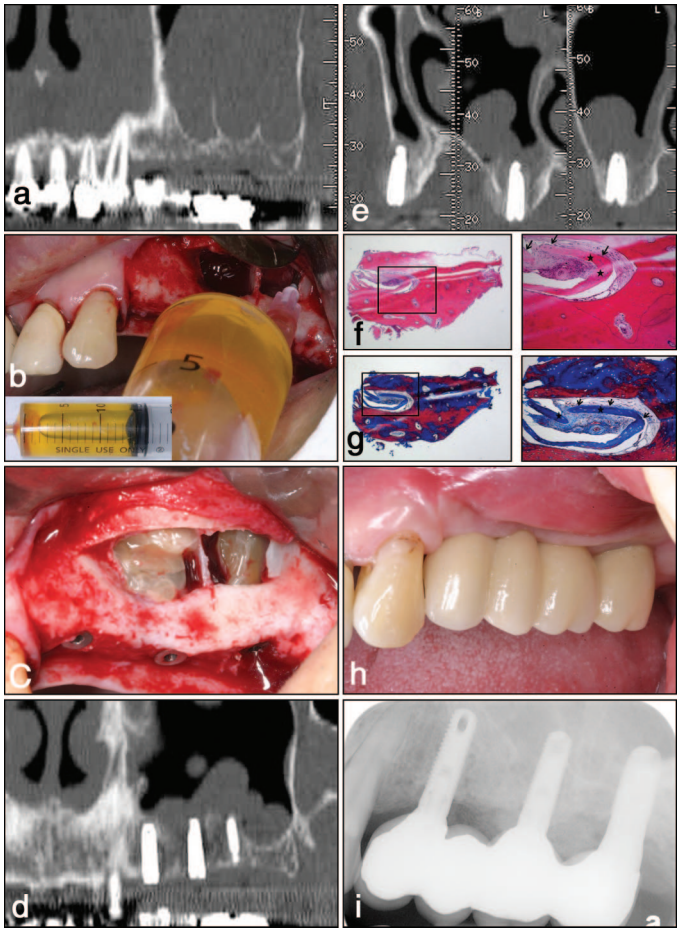

Fig. 2. a, Cone-beam computed radiogram showing approximately 30-mm wide mucous retention cyst in the sinus. High septum is seen in the tomographic scan. The residual bone was 3 mm and 2 mm at the left maxillary first and second molar respectively (from patient number 1). **b**, Approximately 15 mL of cystic fluid was aspirated with an 18-G needle and syringe after making 2 replaceable bony windows. **c**, Two pieces of fibrin-rich block were inserted into new anterior and posterior compartments, respectively, after membrane elevation. Three tapered design implants (Tapered screw vent implant; Zimmer Dental Inc.) were placed. Two bony windows were replaced to seal the lateral window. **d** and **e**, Cone-beam computed tomographic scans showing new bone consolidation around implants after 4 months of healing. Resized cyst and new bone formation is seen in the sinus. **f**, Bone biopsy was performed through the well-healed bony window after 4 months healing. Histologic examination shows dense and mature new bone (asterisks) and osteoblasts (arrow) next to the replaced bony window in hematoxylin and eosin stain. This indicates active new bone formation in the sinus (magnification, ×12.5 [left] and ×100 [right]). **g**, Active new bone formation (blue color) is seen in Masson's Trichrome stain (magnification, ×12.5 [left] and ×100[right]). **h** and **i**, Clinical and radiographic view of final prosthesis 7 months after loading.

many) interfaced with the Axiophot Photomicroscope (Carl Zeiss).

RESULTS

After sinus grafting, no significant postoperative complications developed in any augmented sinus during the healing period. After an average of 5 months healing period, plain panoramic radiograms and cone-beam computed tomograms showed newly formed bone along implant bodies and around implant apices in all cases except for 1 augmented sinus that obtained a large membrane perforation during sinus membrane elevation.

Membrane perforation occurred in 10 cases (16.4% of perforation rate). One perforation was made during osteotomy with the saw insert, and the others developed during the elevation of the sinus membrane. Eight perforations showed small perforations (<5 mm wide). Five small perforated membranes were repaired with collagen membrane (CollaTape; Zimmer Dental Inc.) before fibrin-rich blocks insertion. The other 3 small perforated sites were not repaired with collagen membrane. No radiographic difference on new bone augmentation was seen between the 2 groups after an average of 5 months healing period. Large membrane perforations (>10 mm wide) were observed in 2 cases. One perforated sinus membrane was repaired with collagen membrane before inserting the fibrin-rich blocks. The postoperative cone-beam computed tomogram showed favorable bone reformation around the implant body in this patient. The other large perforation developed because the sinus membrane was fused to the periosteum in the extraction socket. This perforation site was not repaired with collagen membrane before the 2 pieces of fibrin-rich block with CGFs were inserted. The sinus showed partially formed new bone along the implant in radiograms. The new compartment between the elevated sinus membrane and sinus floor could not contain a blood clot or fibrin-rich blocks in this case, so only partial bone augmentation was achieved. However, clinically, implant prostheses have been stable up to 9 months in function.

All repositioned lateral bony windows were well healed and fixed to the lateral wall of sinus in all cases at uncovering. The repositioned lateral bony windows acted as homologous barriers with stability to prevent soft tissue ingrowth into the sinus cavity. The success rate of implant was 98.2%, after an average of 10 months postloading. The criteria of Buser et al[25] were used to evaluate the osseointegration of implants. Two resorbable blast media-surfaced implants failed. One implant was removed at uncovering and another failed 3 months after loading. Even when implants failed, newly formed bone was evident in the sinus. Histologically, bone biopsies revealed no inflammatory reactions, all showed active new bone formation. The specimens revealed well-organized and mature lamellar bone. Osteoblasts

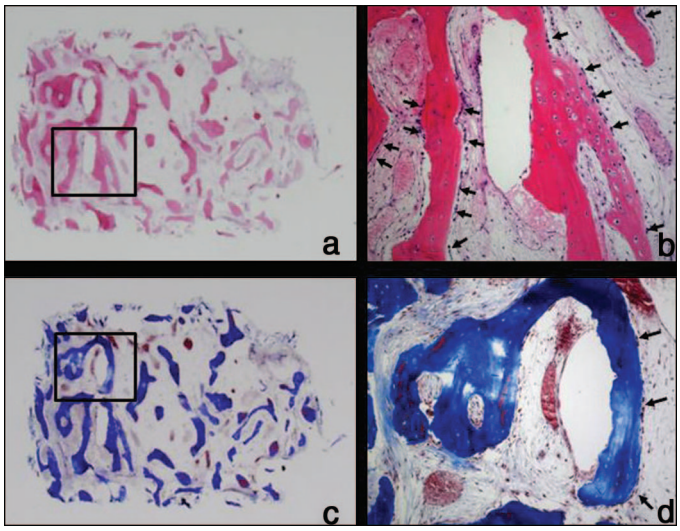

Fig. 3. Histologic finding from patient number 14. Active new bone formation is seen in hematoxylin and eosin stain (magnification, ×12.5 [**a**] and ×100[**b**]) and in Masson's Trichrome stain (×12.5 [**c**] and ×100 [**d**]). Abundant osteoblasts (arrows) are shown along newly formed bone. Red blood cells are shown in newly formed blood vessels.

were easily revealed at high magnification, and blood vessels were revealed in the marrow space (Fig. 3). F3

The residual bone height at the implant sites were between 0.5 and 10 mm (average ± SD: 3.9 ± 2.1 mm). The residual bone height at the implant sites were between 0.5 and 5 mm in 75% of the sinus grafts, and 25% of the sinuses showed 6 to 10 mm bone heights. Residual bone height did not affect the success rate of implant. Huge cysts (ranging from 17 to 30 mm high) were observed in 6 maxillary sinuses. The cystic fluid was aspirated or suctioned through the stab incision made in the sinus membrane before membrane elevation to facilitate membrane elevation. The cysts did not affect bone reformation in the maxillary sinus in this study.

DISCUSSION

Various studies have reported bone reformation in the maxillary sinus with bone grafting in humans and animals.[12–17] Palma et al[13] reported no histologic differences on bone reformation in the maxilla between membrane-elevated and grafted sites, regarding implant stability, bone-implant contacts, and bone area within and outside implant threads in animals. Sohn et al[14] reported favorable new bone formation in the maxillary sinus without bone grafting and clinical implant success with *in vivo* histologic evidence for the first time. Sohn et al[17] also reported that the fast absorbable gelatin sponge inserted loosely under the elevated sinus membrane acted as space maintainer for new bone formation in the maxilla as an alternative to bone fillers. Platelet aggregates, such as platelet-rich plasma and platelet-rich fibrin gel in CGFs, have been used to accelerate new bone formation associated with guided bone regeneration and sinus grafting for many years.[18–20] However, the effect of platelet-rich plasma on new bone formation in the sinus graft is debatable.[21] Fibrin-rich block can keep higher CGFs than platelet-rich plasma and can induce faster.[26,27] You et al[28] reported that platelet-rich fibrin gel can induce higher bone to implant contact than can platelet-rich plasma in bony defects around dental implants. Fibrin-rich gel is known to release growth factors, such as transforming growth factor-β1, platelet-derived growth factor, and vascular endothelial growth factor slowly, and accelerates new bone formation when combined with bone grafting in the maxillary sinus.[27,29,30] In addition, fibrin-rich blocks with CGFs as the sole material acted as an alternative to bone grafting and induced fast new bone formation in the sinus.[23] Compared with platelet-rich plasma or platelet-rich growth factors, fibrin-rich blocks with CGFs are simple to make and do not require any synthetics or biomaterials, such as bovine thrombin and calcium chloride, to make gel, so it is free from the risk of cross-contamination.

To our knowledge, studies on the effect of fibrin-rich blocks with CGFs alone as an alternative to bone grafting and functional survival rate of implant was not reported. Therefore, this study was designed to evaluate the effect of fibrin-rich blocks with CGFs alone on bone reformation in the maxillary sinus by clinical, radiographic, and histologic analyses with expanded data. Fast new bone formation in all the sinuses was apparent radiographically, and dense and mature new bone was seen in the sinus histology in this study. The resorbable or nonresorbable barrier membrane is necessary to prevent ingrowths of soft tissue into the sinus cavity.[31,32] Instead of resorbable or nonresorbable barrier membranes, the replaceable bony window was used to seal the lateral bony window in this study. According to the study by Sohn et al[15], new bone formation begins from the inner surface of the repositioned bony window early in the healing stage, but new bone formation was not shown from the collagen membrane over the bony window early in the healing phase. Replaceable bony windows offer more advantages over using resorbable or nonresorbable barrier membranes to seal the lateral bony window. Replaceable bony windows are not only homologous bony windows free from the risk of cross-contamination but also acts as osteoinductive substrates for accelerating new bone formation in the sinus. The ultrasonic piezoelectric device was effective in making the replaceable bony window. Compared with the rotary bur, piezoelectric bone cut provides highly controlled osteotomy and reduces the possibility of membrane perforation and induced minimal trauma to soft and hard tissue.[33–37] When creating the replaceable lateral bony window, a tilted osteotomy into the sinus cavity was required AQ:3–4

to prevent the replaceable bony window from dropping into the maxillary sinus cavity.[38] The replaceable bony windows made by the thin piezoelectric saw could be precisely repositioned because of the combination of the tilted osteotomy into the sinus, the highly controlled osteotomy, and the minimal bone loss during osteotomy.[38–41] Initial stability of implant was important to have successful osseointegration.[42] Regardless, 75% of implant sites had bone heights between 0.5 and 5 mm in this study, and the initial stability of the implants was stable. Initial stability of implants was achieved by a 1-step down undersized osteotomy and the placement of a tapered design implant. All implants were stable for an average of 10 months loading, thanks to stable initial stability.

CONCLUSION

According to this study, bone graft material may not be a prerequisite for sinus augmentation. Insertion of fibrin-rich blocks with CGFs as an alternative to bone grafting and simultaneous implantation showed successful new bone formation in the sinus, and this can be a predictable procedure for sinus augmentation.

Disclosure

The authors claim to have no financial interest in any company or any of the products mentioned in this article.

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AUTHOR QUERIES

AUTHOR PLEASE ANSWER ALL QUERIES 1

AQ1— Please confirm whether short title is OK as given.

AQ2— Please confirm whether the sentence "In this study, the second…" is OK as edited.

AQ3— Please confirm whether the edited sentence "Fibrin-rich gel is known…" is correct

AQ4— Please note that Ref. 29, duplicate of Ref. 27, has been deleted and subsequent references have been renumbered.

AQ5— Please check whether Ref. 24 is OK as given.

AQ6— Please confirm whether figure legends and artworks of Figs. 1 to 3 are OK as given.

AQ7— Please confirm whether affiliations are OK as given.

AQ8— Please confirm whether correspondence information is OK as given.