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Clinical, Radiographic, and Histological Evaluation of the Mineralized Plasmatic Matrix/Xenograft Mixture in Maxillary Sinus Floor Augmentation (A Randomized Controlled Clinical Trial)

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ABSTRACT

***Introduction*: Maxillary sinus pneumatization and alveolar ridge resorption following the extraction of posterior teeth make the installation of dental implants in the maxillary posterior region challenging. The direct sinus lift procedure proved to be a viable treatment option for such conditions. Aim of the study: to evaluate the mineralized plasmatic matrix/xenograft mixture in sinus elevation surgery.**

***Materials and Methods*: Eighteen patients were selected and randomly allocated into two groups; study group received a mineralized plasmatic matrix/xenograft mixture, while the control group received xenograft alone following sinus lifting.**

***Results*: The early wound healing index score showed a non-significant difference between both groups. Also, bone height was evaluated at the 6-month follow-up period, and there was a non-statistically significant difference. Core biopsies were taken for histological examination by H&E from both groups, revealing the presence of a more mature bone matrix in relation to the test group.**

***Conclusion*: The addition of mineralized plasmatic matrix to xenograft can speed up bone formation, thus reducing treatment duration.**

Keywords: Mineralized plasmatic matrix, piezosurgery, sinus lift, Xenograft.

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I. Introduction

After the loss of the posterior maxillary teeth and the remodeling of the socket, the residual bone will resorb in a vertical and horizontal manner, especially when pneumatization of the maxillary sinus occurs [1].

Several methods have been researched to overcome the vertical bone resorption, such as the use of tilted implants, short implants, zygomatic implants, guided bone regeneration, reconstruction, and sinus floor elevation by means of bone blocks and particulate bone grafts (autogenous bone, allograft, xenograft, alloplastic biomaterial) [2], [3].

Autogenous bone grafts are the gold standard grafting materials, offering the following advantages: osteogenic, osteoinductive, and osteoconductive [4]. The use of other substitute grafting materials has increased over the past few years due to their availability, ease of use, low resorption rate, and high success, especially in external sinus floor elevation [5]. Xenografts have shown promising results in terms of graft stability in maintaining the space and arresting the pneumatization of the maxillary sinus [6].

Platelet concentrates have been introduced into the field of maxillofacial surgery to optimize healing of tissues and bone [7]. Many studies have highlighted the advantage of mixing Platelet-rich fibrin with xenograft to optimize osseointegration of dental implants. Reference [8] reported that combining advanced platelet rich fibrin (A-PRF) with xenograft around immediate implants placed in the esthetic zone improved tissue healing, bone regeneration, and osseointegration of dental implants [8]. In sinus floor elevation, a PRF xenograft mixture sped up the healing time and favored the osseointegration of dental implants [6]. Reference [9] found that the APRF/xenograft mixture enhanced bone regeneration in comparison to conventional sinus floor elevation.

A randomized controlled clinical trial compared

mineralized plasmatic matrix (MPM) to bone grafts in extraction sockets, and the authors found the results were better for the MPM group in preserving the ridge [10]. Also, the mineralized plasmatic matrix was mixed with autogenous bone graft to repair alveolar defects with or without cleft palate. Furthermore, it was stated that the mineralized plasmatic matrix can positively affect implant treatment outcomes in terms of stability, graft loss, and density [11].

Therefore, the aim of this study was to evaluate clinically, radiographically, and histologically the effect of the mineralized plasmatic matrix (MPM) when mixing it with xenogenic bone graft in sinus floor elevation surgery.

II. Materials and Methods

This study was accomplished as a randomized controlled clinical trial following the consort guidelines. The study was carried out at the Oral Surgery Division, Faculty of Dentistry, Beirut Arab University, Lebanon, between January 2021 till August 2021. The institutional review board number (2019-H-0068-D-P-0332) was obtained prior to the start of the study. The study was completed in accordance with the Helsinki Declaration of 1975, revised in 2013. All the patients who participated in this trial were informed about all the steps and any complications that might arise during or after the procedure and signed an informed consent before the work began.

Sample size was estimated using the sample size calculator website; http://epitools.ausvet.com.au, by considering the means of bone-to-graft contact and the pooled variance of a similar study [12], and by adjusting the power of the study to 80% and regulating the alpha error to 5%. This generated a total of 16 patients; two patients were added to the final calculated sample size to avoid attrition and drop out from the sample that might occur throughout the follow-up period of the study, so a total of 18 patients of both genders with an age range of 40–60 years were included in the study.

The participants included eligibly in this trial were conveniently selected based on their need for sinus floor elevation, having less than 4 mm of residual bone height, and adequate bone width ≥6 mm. On the other hand, the exclusion criteria were patients with uncontrolled systemic conditions affecting bone healing and jeopardizing the surgery, patients with any pathological conditions related to the site of surgery, with chronic or acute infection in the maxillary sinus, pregnant females, heavy smokers, with psychological problems and patients suffering from a severely resorbed ridge that needs 3D bone reconstruction.

The selected sample was randomly allocated using a computer generator program (https://www.randomizer.org) into two equal groups: each consisting of nine patients. The study group had an external sinus lift procedure with an MPM/xenograft mixture, while the control group received xenograft solely following sinus lift surgery.

A. Pre-surgical Phase

A detailed intraoral examination was performed systematically on all patients, including their oral hygiene level, remaining dentition condition, and gingival biotype. Then, cone beam computed tomography (CBCT) was requested to assess the remaining bone width and height within the proposed surgical site. Also, the condition of the maxillary sinus was properly examined to guarantee that it is free of any pathological lesions, the presence or absence of sinus septa, and the level and pathway of the posterior superior alveolar artery for planning a complication-free lateral maxillary sinus augmentation surgery.

B. Surgical Procedure

On the day of surgery, patients with no history of penicillin allergy were asked to take, one hour before going into the surgery, 2 tablets of antibiotics (amoxicillin 875 mg and 125 mg clavulanic acid); in the case of penicillin allergy, patients were requested to take 2 tablets of Clindamycin 300 mg, and they were instructed to rinse their mouths with Chlorhexidine gluconate 0.2% mouthwash 30 minutes before the operation.

The entire surgical procedure was carried out under aseptic and sterile condition. All operations were performed under local anesthesia using Articaine HCI 4% with 1:100,000 epinephrine (Septanest-Septodont). The local anesthesia was administered through posterior superior alveolar, middle superior alveolar, and greater palatine nerve infiltration using an autoclaved metallic syringe and a short 30G needle.

After subjective and objective testing for the efficacy of the administered local anesthesia, a full thickness pyramidal flap was incised with a crestal incision, and two vertical releasing incisions placed away from the proposed window osteotomy using Bard Parker Blade Number 15c. Reflection of the full thickness mucoperiosteal flap was then performed using the molt No. 9 periosteal elevator to expose the alveolar crest and the lateral wall of the maxillary sinus (see Fig. 1a). The sinus lift procedure including, the window osteotomy and the elevation of the Schneiderian membrane, was completely accomplished by a piezosurgery device and specific piezoelectric sinus lift inserts (Piezosurgery White; Mectron, Italy). As an initial step, the osteotomy window was outlined as planned on the preoperative cone beam computed tomography using a 1 mm OT1 insert. Secondarily, the OT5 insert was used to finalize the osteotomy cuts until the shadow of the sinus membrane was clearly seen. The EL1 insert is then used to separate the Schneiderian membrane from the bony walls by 2 mm around the window frame. EL2, followed by EL3, is then inserted successively to separate the sinus membrane in the internal zones (see Fig. 1b). In areas where the membrane is tightly attached to the sinus walls, maxillary sinus lifting curettes of different shapes and sizes (Biomet 3i, USA) were used until it became completely detached from the lateral, medial, and inferior walls of the sinus (see Fig. 1c). Nine patients of the study group had the sinuses augmented using mineralized plasmatic matrix (MPM) mixed with xenograft (BEGO OSS – BEGO Implant Systems GmbH & Co. KG, Germany); on the other hand, in nine patients of the control group, xenograft alone was packed within the lifted sinuses.

MPM is prepared by withdrawing blood from the patient's antecubital vein and placing it in two 9 mL plastic tubes with no additives. The blood collected from the patient is immediately centrifuged for 15 minutes at 2700 rpm. After centrifugation, the outcome was two layers: a yellow plasma liquid on top of the tube separated from the red blood cells at the bottom (see Fig. 1d). A syringe was used to collect the

yellow portion, which was then placed into a sterile stainless-steel container containing the xenograft (BEGO OSS) (see Fig. 1e). The MPM was obtained after the entire mixture was stirred for a few seconds in a circular motion. In the raised sinus, the MPM-xenograft mixture was packed [13] (see Fig. 1f).

For both groups, after bone packing, the lateral window osteotomy was covered with a 20x30 cm BEGO porcine pericardium collagen membrane (BEGO Collagen Membrane – BEGO Implant Systems GmbH & Co. KG, Germany) (see Fig. 1g). Finally, the flap was repositioned to its original position and stabilized in its place using 4–0 prolene (Resolon, Resorba, Italy) suture material with simple interrupted sutures.

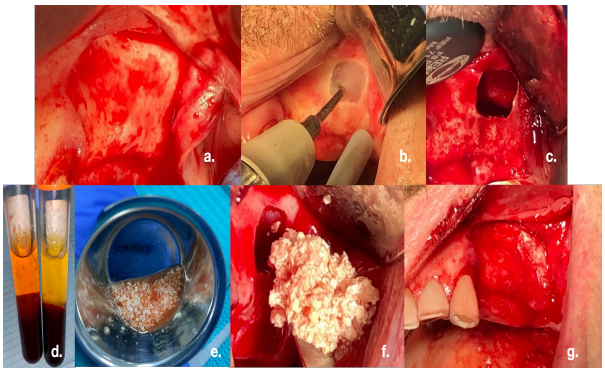

Fig. 1. (a) Mucoperiosteal flap refleted and exposure of the maxillary sinus lateral wall. (b) Piezosurgery assisted Schneiderian membrane elevation. (c) Schneiderian membrane completely elevated and separated from all sinus walls. (d) Plastic tubes after centrifuge showing the yellow plasma liquid. (e). MPM/Xenograft mixture. (f) Packing of the biomaterial into the lifted sinus. (g) Collagen membrane in place to cover the bone graft and the window osteotomy

C. *Post-surgical Phase*

The patients were directed to strictly follow the standard post-operative regimen including applying cold fomentations at the operation site every 5 minutes for the first 24 hours. The following day, the cold fomentations were replaced with warm ones for four days. The patients were encouraged not to blow their noses, not to drink via a straw, and not to sneeze too hard. Analgesics and anti-inflammatory medication (Ibuprofen 600 mg) were administered to all patients twice daily for 5 days, and the chlorhexidine mouthwash was continued from the 2nd postoperative day for the next 10 days. 14 days after the surgery, the sutures were removed.

D. *Follow up Phase*

Clinical healing was assessed on the 1st, 7th, and 14th postoperative days. The clinical signs of re-epithelization (CSR), clinical signs of hemostasis (CSH), and clinical indicators of inflammation (CSE) make up the early healing score (EHS) (CSI). CSR was scored with 0, 1, or 2 points, whereas CSH and CSI were scored with 0, 1, or 2 points. The EHS was created by adding the points from these parameters. The EHS for optimal wound healing was 10 points, with a score of 0 being the lowest possible. The worst score visible for each parameter was recorded. In the presence of suppuration, an EHS of 0 points was awarded, regardless of the evaluations for the three parameters [14].

E. *Histological Analysis*

Following a healing period of six months, a second surgery was done in which a full thickness mucoperiosteal flap was elevated at the augmented surgical field to insert dental implants. Before the sequential drilling for implant placement, a trephine bur with a 2.5 mm external diameter (Hager & Meisinger GmbH, Neuss, Germany) installed on the handpiece of the implant motor at 600 rpm, and a cylindrical bone specimen was harvested carefully with copious saline irrigation from the previously augmented surgical site. The specimens were preserved in a sterile glass tube containing 10% formalin solution and sent to the pathology lab for processing and histological examination and analysis. After complete decalcification, the specimens were embedded in paraffin according to standard protocols and were ready to be sectioned. Histologic sections of 5 microns (µm) were obtained using a microtome. The prepared specimens were copiously washed and then dehydrated by applying an ascending series of alcohol concentrations (70%, 80%, 96%, and 100%). The obtained sections were stained with Hematoxylin and Eosin stain (H&E) and mounted on the light microscope (Olympus BX60; Olympus Corp., Lake Success, NY, USA) to be examined. The histopathological specialist was blinded to the type of grafting material used in sinus augmentation within both groups of this study; this was done through slide coding.

F. *Radiographical Analysis*

All patients had two cone-beam computed tomography (CBCT) scans. One was the preoperative (baseline) CBCT, and the other was performed six months after augmenting the sinuses, and both were assessed by the same examiner. The pre-operative CBCT interpretation was performed using a software program (CS 9600, Carestream, Atlanta, USA). The point of greatest resorption of the bone was marked, and a line was taken from the middle of the crest to measure the residual bone height (RBH). The value obtained was added to the values of the residual bone height measurements of the adjacent mesial and distal slices of the CBCT, and their average was recorded as the average residual bone height. Six months after the external sinus lift procedure, a line was drawn from the center of the crest to the point of greatest augmented bone, and the value measured was the new residual bone height (NRBH). The values were also averaged with the measurements of the mesial and distal adjacent slices.

The IBM SPSS software package, version 24.0, was used to analyze the data that was entered into the computer (Armonk, NY: IBM Corp.). Numbers and percentages were used to describe qualitative data. The Kolmogorov-Smirnov test was employed to ensure that the distribution was normal. Range (minimum and maximum), mean, standard deviation, and median were used to characterize quantitative data. The significance of the acquired results was assessed at a 5% level.

III. Results

A. *Demographic Data*

The eighteen participants were divided into two equal groups randomly; the study group and the control group each included nine patients. The study group consisted of 5 females and 4 males ranging in age from 42 to 58 years with

a mean of 47.83 ± 5.42 years, whereas the control group consisted of 6 females and 3 males ranging in age from 44 to 52 years with a mean of 47.17 ± 6.51 years.

B. Clinical Results

All the surgeries were done with no intraoperative complications except for one case that belongs to the control group in which a small perforation of the Schneiderian membrane was encountered during its elevation. This perforation was immediately sutured using 6/0 vicryl suture (Ethicon, USA) material, and the operation was continued without any alteration of the pre-proposed surgical protocol.

Table I compares flap healing as measured by the early healing score (EHS) between the study and the control at various follow-up periods. There were no significant differences in mean EHS after 1, 7, and 14 days when comparing the control and study groups (P = 0.406, 0.861, and 1.00, respectively). There was also a non-statistical difference in each group upon comparison at different follow-up days (P = 0.055 (study), P = 0.259 (control)). The change from one to 14 days was statistically significant in the study and control groups (P< 0.0001 for both).

TABLE I: COMPARISON BETWEEN THE TWO STUDIED GROUPS ACCORDING TO EARLY WOUND HEALING SCORE

Early Wound Healing Score	DAY 1	DAY 7	DAY 14	P0
Study Group (n=9)				
Min. - Max	6-10	6-10	9-10	0.05
Mean ± SD.	8.33 ± 1.80	9.44 ± 1.33	9.89 ± 0.33	
Control Group (n=9)				
Min. – Max.	6 – 10	6 – 10	9 – 10	0.25
Mean ± SD.	9 ± 1.50	9.33 ± 1.32	9.89 ± 0.33	
P	0.406	0.861	1.000	

SD: Standard deviation, P0: p value for comparing between the two studied groups, P0: p value for comparing between the three studied periods, *: Statistically significant at P ≤ 0.05

TABLE II: COMPARISON BETWEEN THE TWO STUDIED GROUPS ACCORDING TO BONE RIDGE HEIGHT IN THE DEEPEST PORTION OF MAXILLARY SINUSES FLOOR

Bone quantity	Preoperative	6 months post op	P0
Study group (n = 9)			
Min. – Max.	2.30 – 3.40	10.0 – 15.8	<0.001*
Mean ± SD.	2.96 ± 0.39	11.41 ± 1.07	
Control group (n = 9)			
Min. – Max.	2.30 – 3.80	9.0 – 13.7	<0.001*
Mean ± SD.	3.02 ± 0.47	10.77 ± 0.96	
P	0.746	0.197	

SD: Standard deviation, p: p value for comparing between the two studied groups, P0: p value for comparing between the two periods, *: Statistically significant at P ≤ 0.05

C. Radiographic Results

Table II and Figs. 2a, 2b, and 3 show the comparison of bone height between study and control groups at different follow-up periods. Non-significant differences existed in mean ridge bone height preoperatively and after 6 months (P = 0.746 and 0.197, respectively). Preoperatively and after 6 months, the mean bone height in the study group was lower than that in the control group preoperatively but greater after 6 months. (Mean in study = 2.96 (preoperatively) and 11.41 (after 6 months), compared to mean in control = 3.02 (preoperatively) and 10.77 (after 6 months)). The change in ridge bone height before and after the intervention was statistically significant in both the test and control groups (P< 0.001 for both).

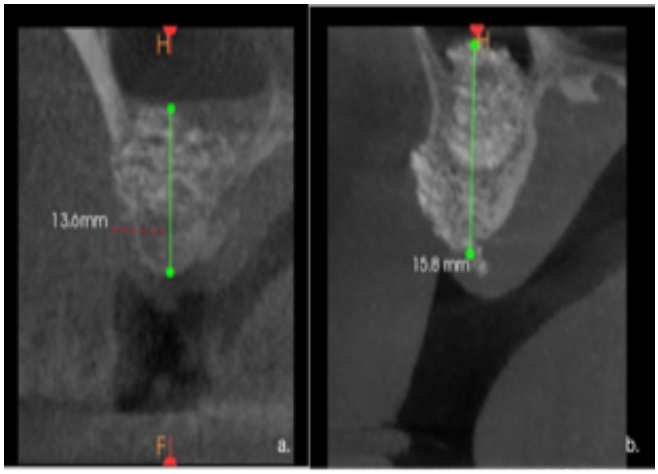

Fig. 2. (a) CBCT para-axial cut showing new bone height after 6 months. (Control group). (b) CBCT para-axial cut showing new bone height after 6 months (Study group).

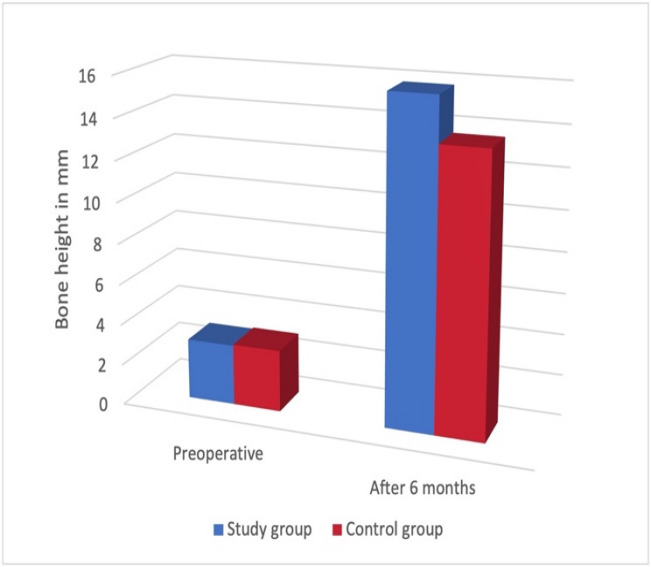

Fig. 3. Comparison between the two studied groups according to bone ridge height in the deepest portion of maxillary sinuses floor.

D. Histological Results

After a 6-month healing period, histological examinations of the specimens revealed that bone formation was present in all three groups, with some variances in the quantity and quality of the produced bone.

The newly generated bone trabeculae in the study group were seen to be adequately formed and lined by osteoblasts. Bone remodeling was indicated by well-vascularized marrow cavities filled with fibroblasts and some osteoclasts on the periphery. There was no evidence of inflammatory cells in the fibrotic tissues (See Fig. 4A).

The control group specimens displayed islands of freshly created bone trabeculae, osteocytes with an uneven organization, and lacunae that were quite large. In fibro-cellular connective tissue, fibroblasts, undifferentiated mesenchymal cells, and inflammatory cells fill the bone marrow gaps. The graft components were found beside the freshly produced bone, and they were clearly identifiable due to their staining (See Fig. 4B).

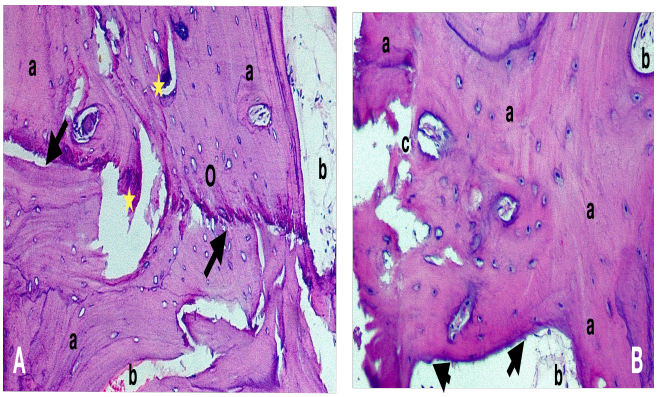

Fig. 4. A) Photomicrograph of the study group specimen showing well-formed bony trabeculae (a), lined by osteoblast (black arrows) and well vascularized marrow cavities filled with fibroblasts (b) and osteoclastic activity (c). (H&E x 100), B) Photomicrograph of the control group specimen revealing islands of newly formed bony trabeculae (a), osteoblasts (arrows), large osteocytes (o), the bone marrow spaces are filled by fibro-cellular CT rich in fibroblasts, undifferentiated mesenchymal cells and inflammatory cells (b), residual graft materials (*) (H&E x 100).

IV. Discussion

Several approaches and techniques for dealing with decreased alveolar bone height following maxillary posterior tooth extraction have been described in the literature. One of the most common and efficacious techniques is the external sinus lift, in which the space created between the sinus membrane and the floor of the sinus is filled with biomaterials to create a zone for new bone formation [15].

The sinus lift procedures performed in this clinical trial were achieved using a piezoelectric device and inserts in a way to decrease the probable intraoperative complications. This goes along with a systematic review that showed a statistical difference in favor of piezosurgery in sinus membrane perforation [16]. Furthermore, a meta-analysis comparing the rate of membrane perforation between conventional rotary instruments and piezosurgery discovered a highly statistical difference favoring piezosurgery in reducing this intraoperative complication [17]. On the other hand, several others found no advantage in using piezosurgery over conventional rotary instruments, and this could be attributed to the use of piezosurgery only for window preparation and not for membrane elevation [18], [19].

One perforation was encountered during this procedure, and it was managed by suturing the Schneiderian membrane. This technique agrees with a study that discussed several methods for managing perforation that occurred during external sinus lift, stating that suturing the membrane is a good alternative in that it preserves the osteogenic potential by making direct contact between the membrane and the bone graft, while also lowering the cost of the surgery [20].

The early wound healing score (EHS) [14] was selected to interpret the healing procedure within this study along with the early follow-up period due to its simplicity and accuracy in detecting any deviation from the normal healing cascade. This is in agreement with [21], the authors stated that all previous methods that assessed wound healing had limitations (relevant parameters are not considered, most indices start following wound healing 1 week post-surgically, previous indices are too complicated, there is an absence of objectivity, and some of the indices are not designed for all flap designs).

The present study showed non-significant differences existed when comparing the mean EHS between the control and study groups after 1, 7, and 14 days. These results do not match those of a study that showed a significant difference in healing between a xenograft/L-PRF mixture and xenograft alone [22]. This can be justified by the smaller sample size. While the current results are in accordance with a systematic review that compared xenograft/L-PRF mixture to xenograft in external sinus lift [23].

A cone-beam computed tomography was performed 6 months after sinus floor elevation to assess the bone gained after the surgery. Non-significant differences existed in mean ridge bone height between the control group and study group preoperatively and after 6 months. A significant difference was noticed in the same groups after 6 months; mean bone height was higher in the study group.

In a clinical study that assessed the mixture of xenograft particles with platelet-rich fibrin, the authors found that adding PRF to deproteinized bovine bone graft can be a foreseeable grafting technique, but with a gain in vertical bone height of 4 to 5 mm [6]. In the current study, a mean gain of 8.45 mm in vertical bone height was reordered in the study group, and this increased gain might be attributed to the consistency of the bone when mixed with the MPM, this mixture allows the bone particles to stick together, forming a strong, stable, and homogenous product.

Moreover, in a study comparing the MPM-autograft mixture to autograft alone in maxillary sinus floor elevation, they discovered a statistical difference in bone height between the study and control groups after 4 months. These dissimilar results could be justified by their use of autogenous bone graft solely in their control group, which has an increased resorption rate in contrast to the slow resorption rate of xenograft used in this study [24].

Xenograft was used in this study for the predictability and maintenance of the volume of the bone graft. In a recent 2-year prospective assessment of the volumetric changes and patient-reported outcome measures, it was shown that the use of bovine bone solely in sinus floor elevation surgery provided a concrete treatment option with good patient and clinical acceptance [25]. Furthermore, anorgnic bovine bone was compared to algae-derived hydroxyapatite in lateral sinus floor elevation, showing superior stability in the xenograft material group 6 months after the surgery [26]. Also, a comparison of three different biomaterials-the anorganic bovine bone, tricalcium phosphate, and tricalcium phosphate crosslinked with hydroxyapatite-in external sinus lift. Implants were inserted nine months after sinus lift, and they were loaded three months after placement. They concluded that the anorganic bovine bone had superior mechanical properties over the tested grafts [27].

The nature of the bone formed within the augmented sinus was investigated through a histological examination with the aid of a 2.5 mm core biopsy taken from all participants at the site of implant placement. The findings revealed newly formed bones of various maturities with little inflammatory response; more mature bones were observed in the study group. These results run parallel to a study that compared xenograft socket preservation to normal healing, the authors

noted in their core biopsy specimens superior trabecular bone formation without any inflammatory response [19]. Our histological results are similar to those revealed by [28]; superior bone maturation was noted when they combined platelet-rich growth factors (PRGF) with xenograft material over the xenograft alone in a 6-month clinical trial for maxillary sinus augmentation surgery.

Controversial findings were reported in the literature concerning the addition of PRF to bone substitutes in the sinus floor elevation procedure. An evaluation of the efficacy of PRF mixed with biomaterial in a meta-analysis concluded that the differences in new bone formation, survival rate, and percentage of residual bone graft were not statistically significant [29]. In addition, a comparison of the L-PRF and xenograft mixture to xenograft alone showed that the mixture did not improve the quantity of the newly formed bone around the graft materials [30]. The findings of this study are similar to an evaluation of a PRF/xenograft mixture in maxillary floor elevation. Also, a histological study on the effect of mineralized plasmatic matrix in the sinus lift procedure [13]. The authors compared MPM with beta-tricalcium phosphate histologically and found that MPM could accelerate bone maturation and thus reduce treatment time. These findings could be attributed to the stability of the MPM that binds to the biomaterial, forming a homogenous nesting of the grafting particles in it [31].

V. Conclusion

Within the limitations of this study, it can be concluded that the sticky character of the mineralized plasmatic matrix/xenograft mixture helps the graft particles to maintain their position with no seepage. The incorporated particles within the mixture maintain the desired space for bone formation. In addition, its use as a carrier material for xenografts could fasten bone maturation with improved bone formation, thus reducing treatment time. Furthermore, an MPM/xenograft mixture might improve bone height within the augmented maxillary sinuses. To generalize these findings, more research with a larger sample size is recommended.

Conflict of Interest

Authors declare that they do not have any conflict of interest.

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