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EFFECTIVENESS OF PLATELET RICH FIBRIN (PRF) AS A SOLE GRAFT MATERIAL VERSUS NANO-CRYSTALLINE HYDROXYAPATITE IN MAXILLARY SINUS AUGEMENTATION WITH IMPLANT PLACEMENT SIMULTANEOUSLY : A RANDOMIZED CONTROLLED CLINICAL TRIAL

Saleh Ahmed Bakry* *and* Waleed Nour El Din**

ABSTRACT

Aim: The aim of this study was to evaluate the effectiveness of platelet rich fibrin (PRF) as sole graft material versus Nano crystalline hydroxyapatite in maxillary sinus augmentation with implant placement simultaneously.

Patients and Methods : This was a randomized controlled clinical trial conducted on 18 patients suffering from atrophied maxillary ridge (less than 5mm in bone height) for implantation indicating the need for maxillary sinus floor augmentation before implant placement. **Group (A)** received sinus augmentation with nano crystalline hydroxyapatite with immediate implantation (**Nano bone** ARTOSS GmbH hydroxyapatite particles) and **Group (B)** received sinus augmentation with PRF as sole graft material with immediate implantation. All patientswere followed up for 6 months recording the progress of the healing both clinically and radiographically via CBCT and to evaluate the new bone formation.

Results: Surgeries went uneventful in patients of both groups. No notable complications occurred during the surgical procedures and the healing period of the two groups. Radiographic results after 6 months showed that there was no statistically significant difference between the two groups. The highest mean value was found in **(Group B)** while the least mean value was found in **(Group A).** All implants were clinically stable at the time of abutment insertion, 6 months after sinus augmentation.

Conclusions : The use of the PRF as a sole graft material in maxillary sinus augmentation proved to be a successful material that offers sufficient amount of natural bone in the sinus that cover all the surface of the inserted implant.

KEYWORDS: PRF, Maxillary sinus augmentation, Hydroxyapatite graft material.

* Associate Professor, Oral Surgery Department, Faculty of Dentistry, Cairo University, Egypt
** Master Student, Oral Surgery Department, Faculty of Dentistry, Cairo University, Egypt

INTRODUCTION

The pneumatization of the maxillary sinus through the person lifetime in addition to the extraction of the posterior maxillary teeth limit the uses of dental implant in this critical area of the jaw due to the little amount of vertical bone volume available for implant placement. [1-6]

The elevation of the sinus membrane was described firstly by ***Tatum***[2] ***and by Boyne et al***[7]. They utilized iliac autogenous bone graft for sinus augmentation .Bone grafts can be classified into human bone and bone substitutes. This can be further classified by ***Nasr et al 1999***[8]into autograft, allografts, xenografts, and alloplasts.

HA biomaterials are complex calcium phosphates in their chemical composition {Ca10(PO4)6(OH)2}. There are different forms of HA biomaterials like HA cement, nonporous hydroxyapatite, porous hydroxyapatite and nano sized hydroxyapatite. HA are biocompatible material with minimum inflammatory response when used within the human tissues.[9, 10]

Nano-sized hydroxyapatite have other unique properties due to its small size and large specific surface area. Thus, leads to an increase in osteoblasts adhesion and protein adsorption on the Nano-sized ceramic . The rate of resorption of Nano-bone is twelve weeks that represents why bone healing is faster in the first three months postoperative due to high rate of bone graft resorption and newly bone formation.[11]

PRF was introduced in 2001 by ***Choukron et al***[12] as an autologous leukocyte and platelet-rich fibrin biomaterial .***Naik B et al***[13] proved by their study that the PRF contain fibrin network and platelets that release growth factor and cytokines which stimulate angiogenesis and play an important role in organization and maturation of clot formation and have the ability of inflammation resistance.

PRF can induce osteoblasts proliferation through stimulating the phosphorylated extracellular signal regulated protein kinas (P-ERK) and stimulate the production of osteoprotegrein (OP)[14-16] PRF was used as scaffold for human cell proliferation, reporting superiority over collagen scaffold as result of its microstructure and growth factor bioavailability in it[17-19]**.** For all the advantages of PRF in hemostasis, stimulation of cellular migration and proliferation, simplicity in technique (no anticoagulant used) it is used in dentistry in several branches. [15] The purpose of the present study is to evaluate the effectiveness of platelet rich fibrin (PRF) as sole graft material versus Nano crystalline hydroxyapatite in maxillary sinus augmentation with implant placement simultaneously.

PATIENTS AND METHODES

Study Design

This was a randomized controlled clinical trial conducted on 18 maxillary sinuses in 18 patients(10 males and 8 females). The sinus was randomly divided into 2 groups according to the graft materials. **Group A** received sinus augmentation with nano crystalline hydroxyapatite and placing implants simultaneously (**Nano bone** ARTOSS GmbH hydroxyapatite particles) and **Group B** received sinus augmentation with PRF as sole graft material and implants placement simultaneously. The study was conducted in Faculty of Dentistry, Cairo University.The Ethics Committee of the Faculty of Dentistry, Cairo University approved the protocol, and a detailed informed written consent including the details of surgery and the possible complications was obtained from all patients.

Eligibility Criteria

The selected patients suffered from atrophied maxillary ridge with insufficient bone height (less than 5mm in bone height) for implant placement seeking for maxillary sinus floor augmentation before implant placement.

The patients included in the study fulfilled the following criteria

Inclusion criteria

- All patients were asking for implant placement in the maxillary posterior region.
- No systemic diseases which could affect the result of the treatment based on modified Cornell medical index. [19]
- The height of the alveolar bone remaining in the maxillary posterior region should be ranging from 3-5 mm.

Exclusion criteria:

- Patient under steroid therapy
- Any maxillary sinus disease that could contraindicated the surgical procedure or interfere with normal bone.
- Previously operated sites of the maxilla.

Randomization

This study was a randomized clinical controlled trial. Patients were randomly assigned into two equal groups: **group (A)** and **group (B)** according to the website (http//www.random.org.eg).

Preoperative Preparation

At the initial visit, all patients underwent a clinical and occlusal examination including: the condition of covering mucoperiosteum, measuring the inter arch space and finally, measuring the width of the alveolar bone. Preoperative dental cone beam computed tomography scans were taken for each patient to obtain data concerning the residual alveolar bone height and to detect any remaining roots or localized bony pathosis and to be used as a document for the comparison of the bone quantity before and after the surgery **(Figure 1).**

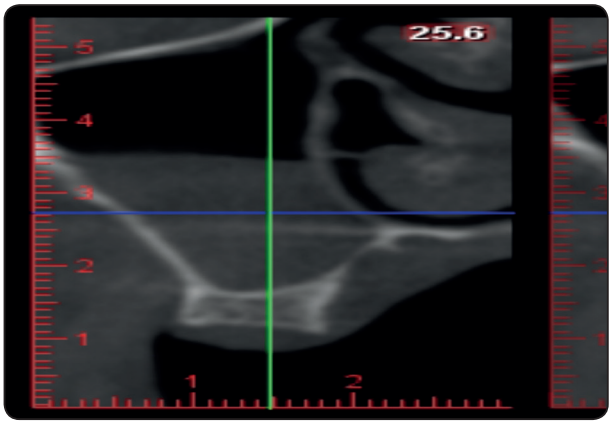

Fig. (1): Preoperative CBCT show the residual ridge height

Surgical method

All surgical procedures were performed under local anesthesia (Articane 4 % with 1: 100 000 epinephrine, Ubistesin™ forte, 3M ESPE, Germany). Maxillary sinus floor elevation was performed using lateral window approach. Three-line pyramidal flap was used to expose the area of interest and to ensure proper closure of the flap over intact bone. Reflection of the mucoperiosteal flap was performed to expose the lateral wall of the maxilla. No.8 diamond round bur was used on a handpiece at approximately 1,000 rpm to determine the outline of the osteotomy on the lateral wall of the maxillary sinus. The osteotomy was carried through the cortical bone without tearing the antral membrane. Once the osteotomy was completed, the underlying Schneiderian membrane with its dull gray color was seen. The osteotomy with the membrane attached to it were infractured with gentle tapping to get a cleavage between the membrane and the medial surface of the lateral wall of the antrum.

Membrane elevation was started from inferiorly followed by elevation of the membrane from the medial surface of the lateral wall of the sinus around the borders of the window. The membrane was carefully elevated from the lateral wall and floor of the maxillary sinus resulting in a space bordered medially by the medial wall of the sinus and the antral

membrane, upward with the hinged lateral wall and antral membrane. Sequential drilling was performed till reaching the appropriate drill size for proper implant placement. Dental implants (ANKYLOS DENTSPLY GmbH) were placed according to the preoperative plan guided by the CBCT.The grafting materials packed in the sinus cavity under the lifted membrane especially in the posterior and anterior parts and a resorbable collagen membrane (Biocollagen, Bioteck, Italy) was positioned to cover the graft material and the lateral window. The mucoperiosteal flap was repositioned and sutured with 000 vicrylsuture material.

For **group A ,** the maxillary sinus was augmented with Nano crystalline hydroxyapatite (Nano bone ARTOSS GmbH hydroxyapatite particles) **(Figure 2)**and placing implants simultaneously .For **group B,** the PRF was performed by collection of ablood (2 tubes of 10 ml each) from the antecubital vein. The blood sample was quickly centrifuged at 3,000 rpm for 10 minutes at room temperature. The PRF clot was removed from the tubeafter centrifugation, the RBC base separated from it, and placed in a sterile metalcup**(Figure 3).**Then, the maxillary sinus was augmented with PRF as sole graft material (**Figure 4)**and placing implants simultaneously.

Postoperative care:

1. Patients were instructed to avoid any negative or positive pressure on the nasal cavity (e.g., drinking using straw, blowing nose, breathing down and spitting) for the first 24 hours after the surgery.
2. Postoperative medication regimen included:

- Non-steroidal anti-inflammatory analgesic (Diclofenac potassium 50mg, Catafast 50 mg tablets, Novartis Pharma AG, Cairo, Egypt.) was prescribed three times daily.

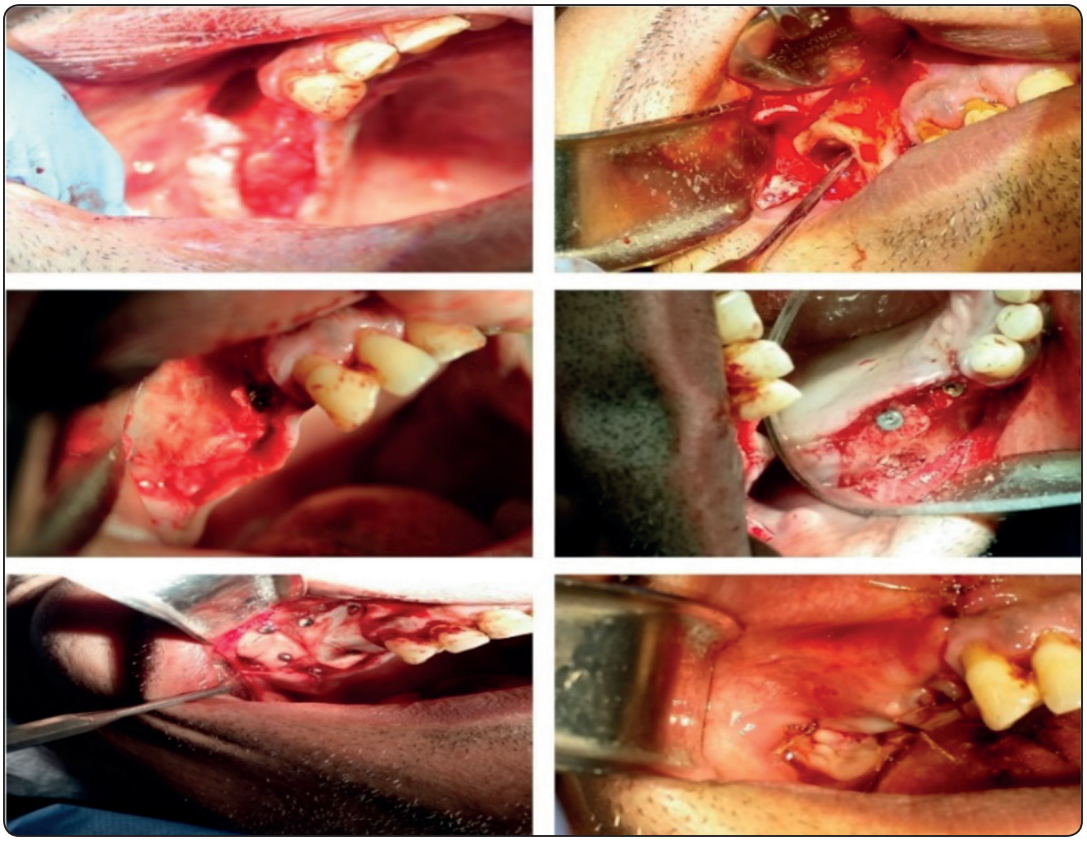

Fig. (2): Sinus augmentation and simultaneous implant placement for Group A using Nano HA particles

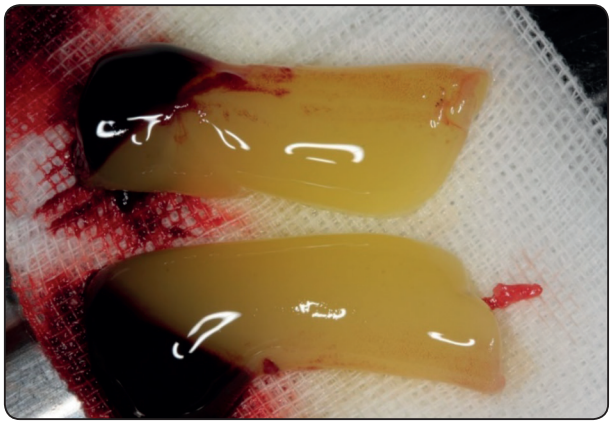

Fig. (3): Photograph showing the separation of the PRF from the blood sample

- Antibiotic (clindamycin 300 mg, Clindam 300 mg capsules, Sigma pharmaceutical industries, Egypt) was prescribed three times daily for five days.
- Nasal decongestants: Xylometazoline hydrochloride 0.1 % nasal drops (Otrivin, Glascosmithkline, Egypt) every 8 hours for 3 days.
- Chlorohexidine Gluconate 0.1% mouth wash (Antiseptol, Kahira Pharma Co, Cairo, Egypt.) every 8 hours for two weeks.

Postoperative follow up & assessment

Clinical assessment

Patients were clinically assessed on regular bases with the following intervals: 48 hours, 1 week, 2 weeks, 1month and on monthly basis till six months postoperative after first stage surgery.

The intra oral wounds were evaluated for any signs of bleeding, hematoma, infection or wound dehiscence. Patients were questioned and examined for any signs and symptoms of sinusitis.

Radiographic assessment

Radiographic follow up was achieved by CBCT scan postoperatively and 6 months later to evaluate the new bone formation**(Figure 5, 6).**

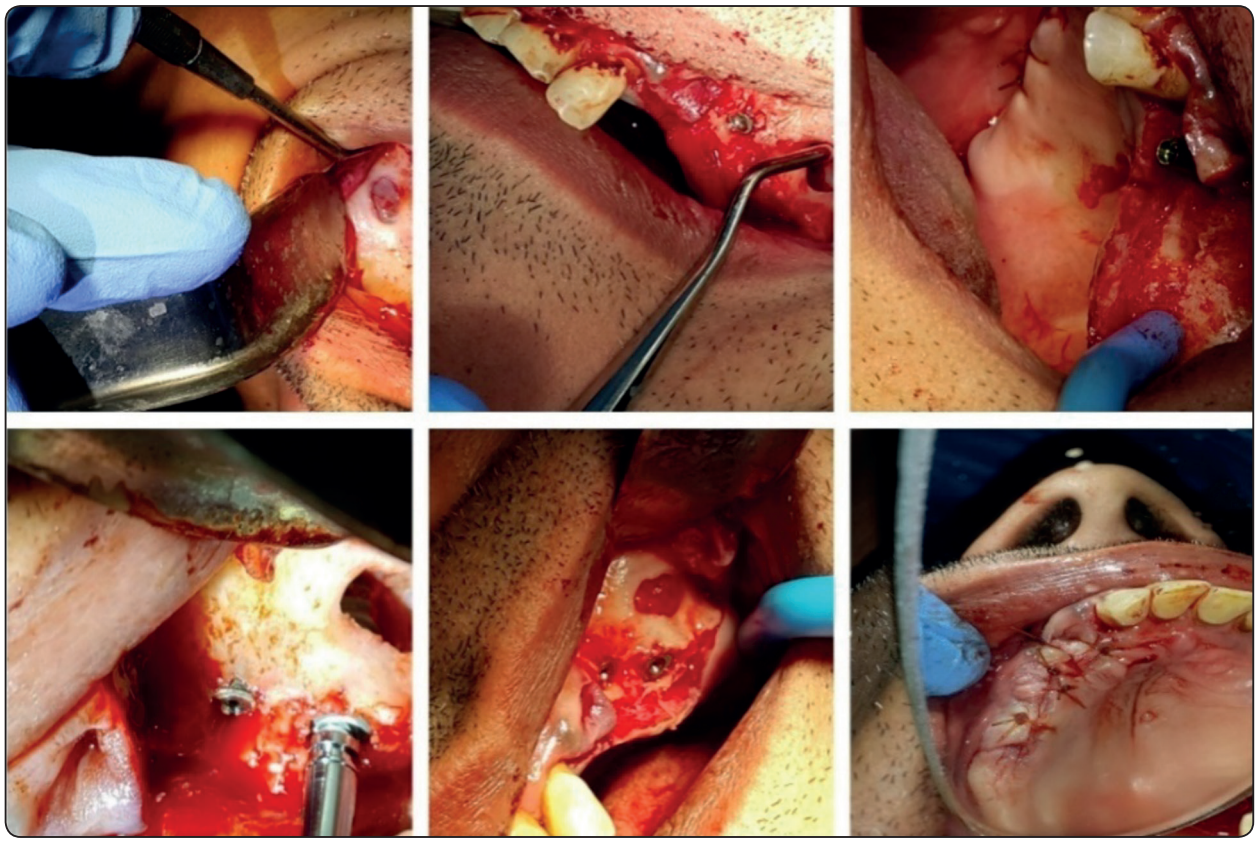

Fig. (4): Sinus augmentation and simultaneous implant placement for Group B using PRF.

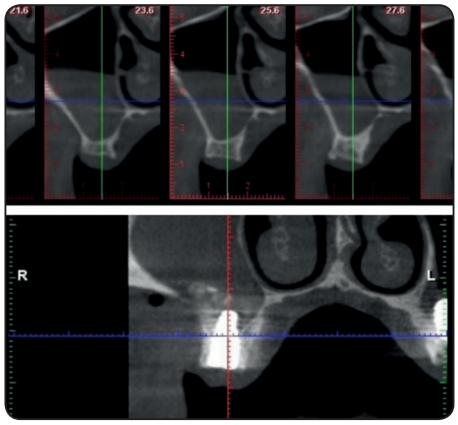

Fig. (5): CBCT preoperatively and 6 months postoperatively for Group A

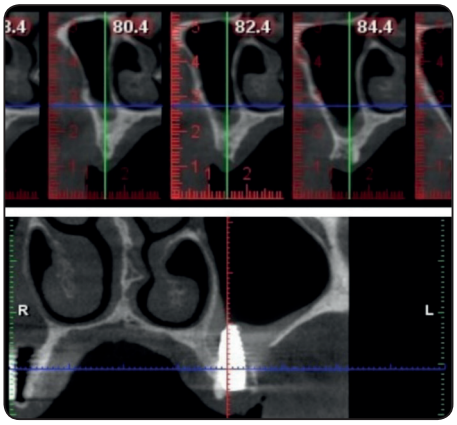

Fig. (6): CBCT preoperatively and 6 months postoperatively for Group B

Data Management and Analysis

The mean and standard deviation values were calculated for each group in each test. Data were explored for normality using Kolmogorov-Smirnov and Shapiro-Wilk tests, data showed parametric (normal) distribution.

Independent sample t-test was used to compare between two groups in non-related samples. Paired sample t-test was used to compare between two groups in related samples. The significance level was set at $P \leq 0.05$. Statistical analysis was performed with IBM® SPSS® Statistics Version 20 for Windows.

RESULTS

This study was conducted on Eighteen (10 males and 8 females) patientswith eighteen sinus lifting procedures and 18 implants simultaneously. The mean residual bone height between the sinus floor and alveolar crest was 4.03 ± 0.49 mm (range, 3.1 to 4.85 mm) preoperative and 11.99 ± 0.93 mm (range, 10.1 to 14.1 mm) postoperative. There was no bucco-lingual bone deficiency interfere with the implant placement in all cases. The mean density of the newly gained bone around the implants was 571 ± 111.92 HU (range, 375 to 713 HU). At the time of abutment insertion all implants were clinically stable, 6 months after sinus lifting procedure.

Bone Quantity Results (Table 1, Figure 7):

A. Preoperative:

There was no statistically significant difference between (Group A) and (Group B) where (p=0.842). The highest mean value was found in (Group A) while the least mean value was found in (Group B).

B. After 6 months

There was no statistically significant difference between (Group A) and (Group B) where (p=0.308). The highest mean value was found in (Group B) while the least mean value was found in (Group A).

TABLE (1): The mean, standard deviation (SD) values of Bone quantity of both groups.

Variables	Bone quantity				
	Group A		Group B		p-value
	Mean	SD	Mean	SD	
Preoperative	4.03	0.49	3.99	0.44	**0.842ns**
After 6 months	11.99	0.93	12.42	0.85	**0.308ns**
p-value	**<0.001***		**<0.001***		

Significant (p<0.05) ***Non-significant (p>0.05)***

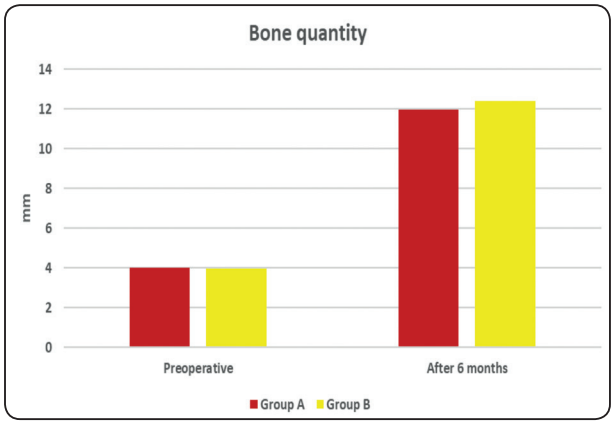

Fig. (7): Bar chart representing bone quantity results

Bone Quality Results After 6 Months (Table 2, Figure 8):

There was no statistically significant difference between (Group A) and (Group B) where (p=0.0.4753).The highest mean value was found in (Group A) while the least mean value was found in (Group B).

TABLE (2): The mean, standard deviation (SD) values of Bone quality of both groups.

	Group A		Group B		p-value
	Mean	SD	Mean	SD	
Bone density	571.89	111.93	531.56	108.73	0.4753 NS

Significant (p<0.05) *Non-significant (p>0.05)*

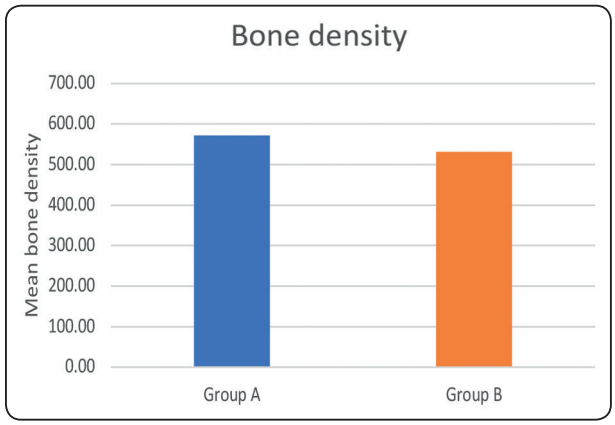

Fig. (8): Bar chart representing bone density results

DISCUSSION

PRF is used as a natural and optimized blood clot for protection of the sinus membrane or improvement of the bone graft maturation during a sinus augmentation procedure.[20-22]It was surveyed that while using allograft in combination with PRF in equal volume during sinus lifting procedure is able to produce potentially mature bone suitable for implant placement after 4 months rather than a sole allograft after 8 months.[23]

Lately,in maxillofacial surgery, the utilization of autogenous platelet concentrates plays a role in bone regeneration enhancement. [24] The utilization of platelet-rich plasma (PRP) was first reported in oral surgery procedures. [25] The use of PRP have many disadvantages as it contains synthetic or anticoagulant materials. While developingof the PRF by ***Choukron et al***[12] does not require heterogeneous agents. PRF is more preferable to PRP as PRF is safer, cheaper and has less time for production. [25, 26] Moreover, PRF contains more growth factors as a biological activator than PRP and those growth factors has more impact on proliferation and differentiation of the human cells.[14]The current study showed that both groups reported a significant improvement in new bone formation compared to baseline in both groups with no significant difference between groups.

This result was in accordance with ***Zhang et al***[27], ***Bolukbasi et al***[28] ***and Tatullo et al***[29] Who compare between PRF in addition to Bio-oss versus Bio-oss alone. They found no statistically significant difference after 6 months, concluded that PRF does not play a role in the acceleration ofBio-Oss maturation.

However, in a study made by ***Choukroun et al***.[23], they performed maxillary sinus augmentation by PRF in addition with freeze-dried bone allograft. They concluded that the histological evaluation of the study showed sufficient new bone formation. Moreover, the PRF with the graft material could

decrease the healing time. These results were in accordance to our results, that the utilize of the PRF as sole graft material could be replaced the need of bone graft material in case of sinus lift or at least, the utilize of the PRF in combination with graft materials decrease the amount need from it.

In the current study, theutilize of PRF membranes promote the healing of the sinus membrane; stimulate new bone formation through the stimulation of the periosteum like effect of the membrane and finally played a major role in the stabilization of the bone volume around the implant end. This result was in accordance with ***many authers***[30-35] who reported that PRF can be used safely as a sole graft material that offers sufficient amount of natural bone in the sinusand cover all the surface of the inserted implant. In this study, all implants in both groups achieved primary stabilitywith no statistically significant difference in new bone level between **(Group A)** and **(Group B)** where (p=0.244).

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