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EFFECT OF BONE GRAFT MATERIAL IN COMBINATION WITH AUTOLOGOUS GROWTH FACTORS ON BONY REGENERATION FOLLOWING MANAGEMENT OF MAXILLARY ODONTOGENIC CYSTS

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ABSTRACT

Objectives: the purpose of this study was to compare the outcomes of Resorbable bioactive glass UNIGRAFT® alone in comparison with those combined with autologous platelets rich fibrin (PRF) on the bone regeneration after treatment of maxillary odontogenic cysts.

Patients and Methods: A total of twelve patients suffering from large maxillary odontogenic cysts were randomly assigned into two groups, each group were formed of six patients. Enucleation with peripheral ostectomy was done. The bony defects were grafted by application of Resorbable bioactive glass (Unigraft; Unicare Biomedical, Laguna Hills, CA) UNIGRAFT® alone in group (I) while in group (II) UNIGRAFT® mixed with Platelet Rich Fibrin.

Clinical assessment was performed in the postoperative follow up including, Pain and swelling scores which was measured using VAS at 1 weeks. Radiographic examination measuring the bone density of the bony defects using cone beam computerized tomography (CBCT) at 3 and 6 months post-operative follow up.

Results: all cases were healed without any signs of postoperative complications. Results showed that after 3 and 6 months, group (II) had significantly higher values than group (I) ($p<0.05$). Within both groups, there was a significant difference between densities measured at different intervals, with value measured after 6 months being higher significant than pre-operative value ($p<0.05$).

Conclusion: UNIGRAFT® mixed with PRF improved the bone quality rather than UNIGRAFT® alone.

KEYWORDS: Odontogenic Cyst, PRF, bone substitutes, Uni-Graft ®

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INTRODUCTION

In the oral and maxillofacial regions, jaw cysts are a prevalent pathology. The site of odontogenic jaw cysts depends on their origin and rate of growth. Management of odontogenic cysts with various surgical procedures have been described such as enucleation [1,2] and marsupialization, decompression, cystectomy and curettage which represented the standard techniques used for removing large odontogenic cyst [3-4-5]

The resulted bony defects following enucleation of cysts and cyst-like lesion can be left for spontaneous bone healing or it may need a grafting material to fill the defect. [6]

Bone graft materials have been commonly used along with growth factors and/or barrier membranes in situations such as periodontal regeneration therapies and guided bone regeneration procedures [7]

Choukroun et al. [8] was first described the Platelet-rich fibrin (PRF) which is a second-generation platelet concentrate that allows to obtain fibrin membranes enriched with various factors such as platelets and growth factors. The PRF clot forms a strong natural fibrin matrix, which concentrates almost all the platelets and leucocytes of the anticoagulant free blood harvest [9,10]

The aim of this study was to compare the outcomes of Resorbable bioactive glass UNIGRAFT® alone in comparison with those combined with autologous platelets rich fibrin (PRF) on the regenerated bone after treatment of maxillary odontogenic cysts.

PATIENTS AND METHODS

Twelve patients with large maxillary cystic lesions were selected from the outpatient clinic of the Oral and Maxillofacial Surgery Department, Faculty of Dentistry of both October 6 University and Future University.

Ethic approval

The study was approved by Research Ethics Committee at Faculty of Dentistry, October 6 University, Giza, Egypt, with approval number: **RECO6U/16-2020** obtained in its meeting held on 7 December 2020.

Sample size calculation:

Sample size calculated depending on a previous study. According to this study, the minimally accepted sample size was 6 per group, when the response within each subject group was normally distributed with standard deviation 2.7, the true mean difference was 5, when the power was 80 % & type I error probability was 0.05.

Eligibility criteria

The patients were selected according to the following criteria:

Inclusion criteria:

1. Age range was 25- 60 years old.
2. A maxillary cyst larger than 3 cm in size in any dimensions.
3. Free medical history

Exclusion criteria:

The presence of any medical condition that may affect bone regeneration was considered as exclusion criteria.

Study design:

Thorough preoperative clinical and radiographic examination was carried out for all patients. Cone beam computerized tomography (CBCT) was taken for all patients to identify cystic outlines preoperatively and at the consolidation of the follow up period. (Figures 1,6,8)

Teeth related to the cystic lesion were evaluated carefully in terms of vitality and restorability. They were either endodontically treated preoperatively or planed for extraction during surgery if they lack enough bony support.

Patients Grouping:

Selected patients were randomly divided into two equal groups:

Group (I): Six patients (4 males and 2 females) had undergone enucleation of the cystic lesion with peripheral ostectomy, then application of UNIGRAFT® (Unigraft; Unicare Biomedical, Laguna Hills, CA) Resorbable bioactive glass**.** ***Group (II):*** Six patients (3 males and 3 females) had undergone enucleation of the cystic lesion with peripheral ostectomy, then application of UNIGRAFT® mixed with PRF to form sticky bone.

Surgical technique for both groups:

A muco-periosteal flap was elevated to gain access to the cystic cavity. Careful dissection was done to separate the cystic lining from the mucoperiosteal layer and overlying mucosa in cases where the cystic lesion perforated the overlying buccal plate of bone, (figure 2). Grasping the cystic lesion with Allis Forceps to complete the enucleation procedure, apicectomies were done to the previously endodontic treated teeth then peripheral ostectomy was completed to cystic cavity using dome shape bur. the cavity was then irrigated with saline, (figure 3,7)

Group (I)

After completing the surgical removal of the cystic lesion and peripheral ostectomy was done, application of UNIGRAFT in the defect area.

Group (II)

PRF preparation

Blood samples were taken from patients' antecubital vein into 10-ml glass-coated plastic tubes (Vacutainer; Becton, Dickinson and Company, Franklin Lakes, NJ, USA) without the addition of any anticoagulant and centrifuged at 3000 rpm for 12 minutes.

Three parts were founded in the tube, the upper part contained acellular plasma, the middle part contain the fibrin clot and the bottom part contained red corpuscles. The fibrin clot was separated easily from the lower part of the centrifuged blood. The PRF clot was pressed gently into a membrane with sterile dry gauze.

UNIGRAFT / PRF mixing:

We collected the middle plasma rich layer that contains fibrin leukocytes and mesenchymal cells. UNIGRAFT® Resorbable bioactive glass was added to the fibrin mix along with few drops of the patient blood for sticky bone formation. The mixture was allowed to set for few minutes, thus allowing the coagulation cascade and polymerization to take place.

UNIGRAFT® mixed with the minced PRF and were carried and packed into the defects. (Figures 4, 5, 9) Watertight closure of wound was done using 4-0 Vicryl sutures.

® (Unigraft; Unicare Biomedical, Laguna Hills, CA) Resorbable bioactive glass

Postoperative care:

Patients were instructed with adequate postoperative instructions along with oral hygiene measures. Analgesics and antibiotics were prescribed, and the patient was advised to use chlorhexidine mouthwash for a week. The sutures were removed after 7 days whenever healing was prompt. Prescription of ***Augmentin ©*** 1gm b.i.d for 5 days. For postoperative pain they received ***Brufen*** 400 mg, dexamethasone 8 mg I.M once every 12 hours for 3 days to decrease postoperative edema

Clinical assessment was performed in the postoperative follow up including, Pain scores which was measured using VAS at 1 weeks. The wound sites were carefully examined for signs of healing and any signs of infection. Radiographic examination measuring the bone density of the bony defects using cone beam computerized tomography (CBCT) at 3 and 6 months post-operative follows up.

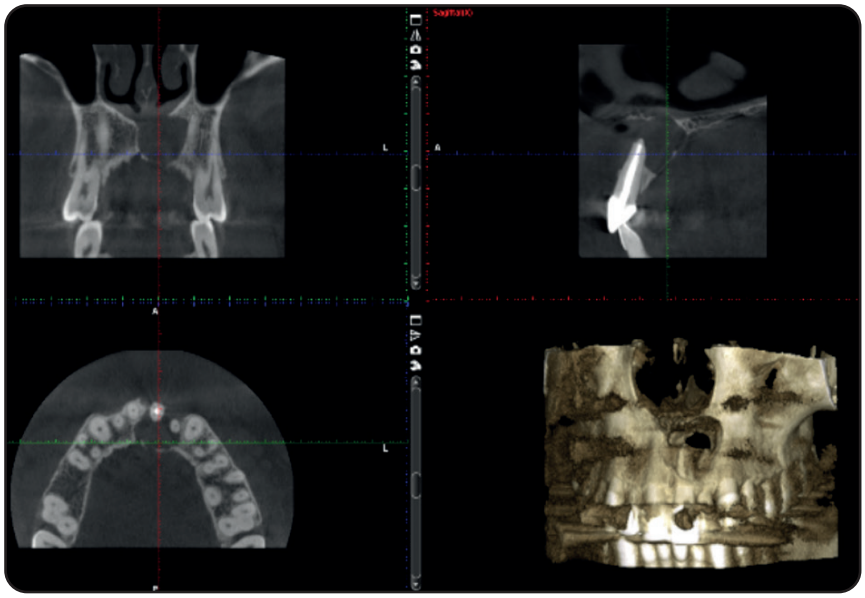

Fig. (1): preoperative CBCT showing the cystic lesion over the maxillary anterior region of patient number 1 group I

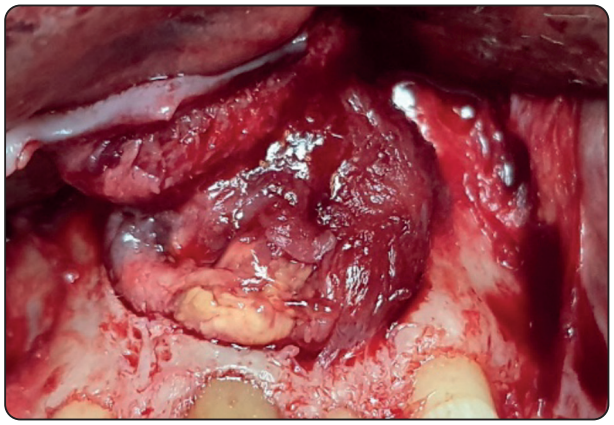

Fig. (2): Clinical photograph showing maxillary cystic lesion in patient number I group I

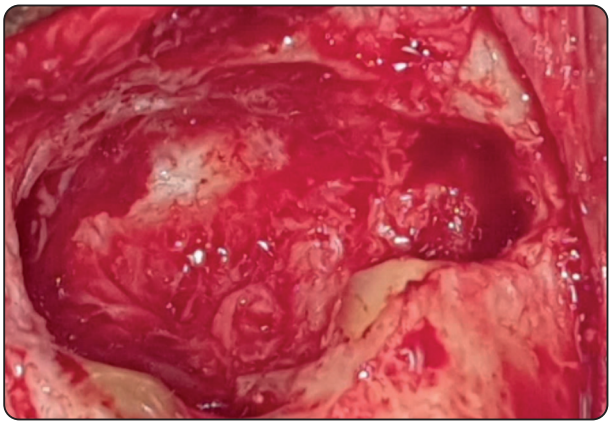

Fig. (3): Clinical photograph showing complete removal of maxillary cystic lesion in patient number I group I and apicectomies of the involved teeth with peripheral ostectomy

Fig. (4): Clinical photograph showing the UNIGRAFT®

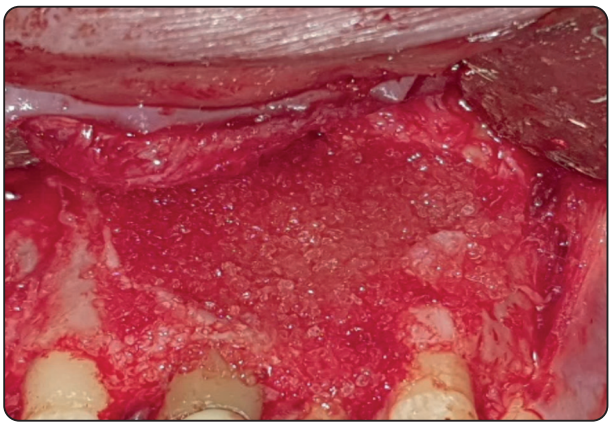

Fig. (5): Clinical photograph showing the cystic cavity filled with the UNIGRAFT® in patient number 1 group I

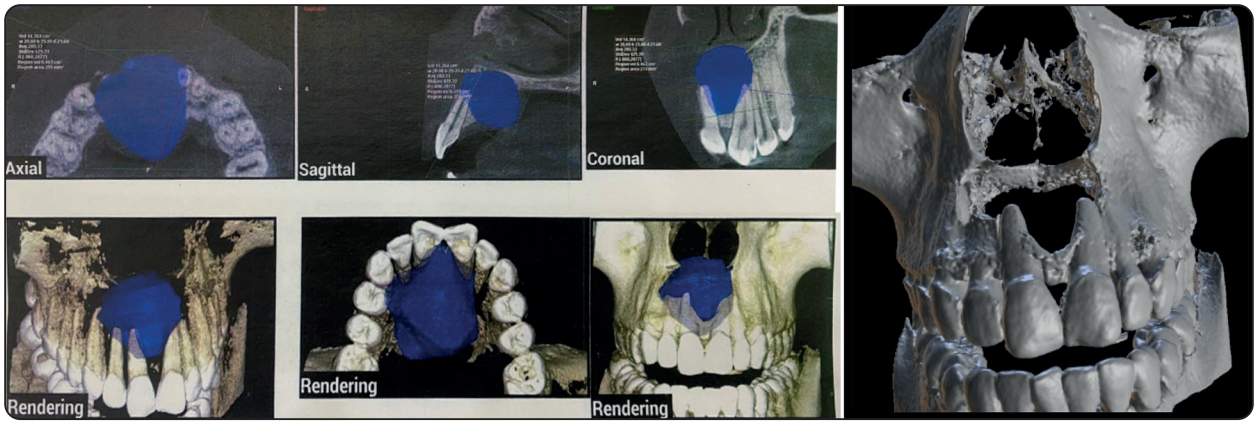

Fig. (6): CBCT of the patient number 1 group II showing the cystic lesion over the maxillary anterior region

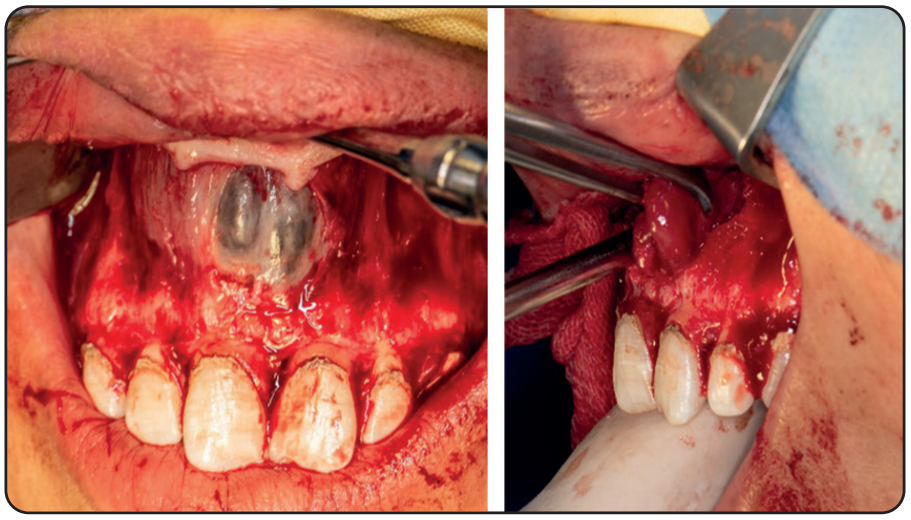

Fig. (7): Clinical photograph (front and side views) showing removal of maxillary anterior cystic lesion in patient number 1 group II

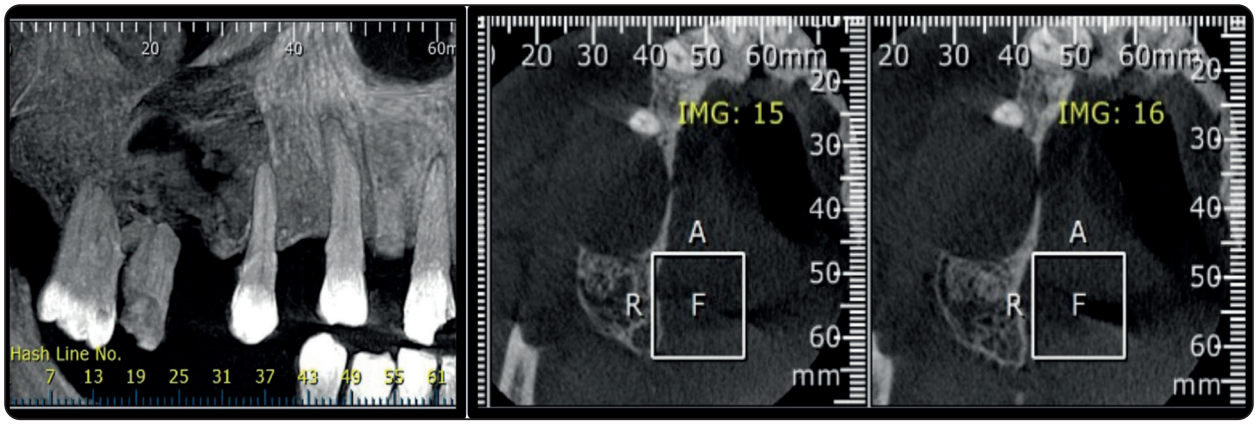

Fig. (8): CBCT of the patient number 2 group II showing the cystic lesion over the maxillary posterior region

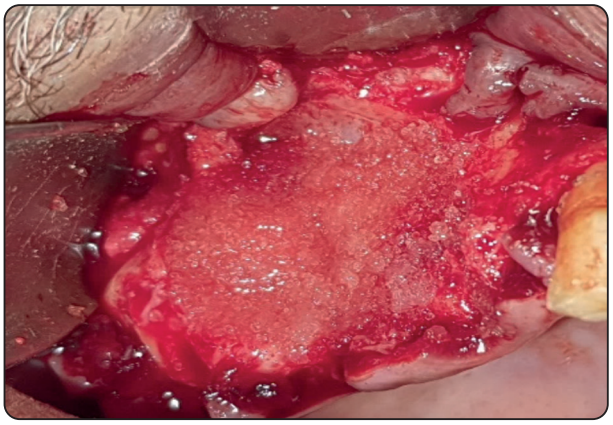

Fig. (9): Clinical photograph showing maxillary posterior cystic cavity filled with the UNIGRAFT® mixed with the PRF in patient number 2 group II

RESULTS

This study was conducted on twelve patients with large maxillary cystic lesions more than 3 cm in any dimensions. The age range of the patients was from 25 to 60 years old. The mean age range was 28.5 in group I and 29.8 in group II.

Follow up:

Statistical Analysis:

Categorical data were presented as frequency and percentage values and were analyzed using Fisher's exact test. Numerical data were presented as mean and standard deviation (SD) values. Shapiro-Wilk's test was used to test for normality. Data were non-parametric and were analyzed using Mann-Whitney U test for intergroup comparisons and Freidman's test followed by Nemenyi post hoc test for intragroup comparisons. The significance level was set at $p<0.05$ within all tests. Statistical analysis was performed with R statistical analysis software version 4.1.3 for Windows*.

Demographic data:

Results of intergroup comparisons of cyst type presented in table (1), showed that there was no significant difference between both groups (p=1), with majority of cases having periapical cysts.

TABLE (1): Intergroup comparison of cyst type

Cyst type		Group (I)	Group (II)	χ^2	p-value
KCOT	**n**	0	0		
	%	0.0%	0.0%		
Dentigerous cyst	**n**	2	1		
	%	33.3%	16.7%		
Periapical cyst	**n**	4	5	**0.00**	**1.000**
	%	66.7%	83.3%		
Residual cyst	**n**	0	0		
	%	0.0%	0.0%		
Unicystic ameloblastoma	**n**	0	0		
	%	0.0%	0.0%		

Clinical examination:

During the first month patients were recalled every week. Then once every month till the end of the follow up period. The wound sites were carefully examined for signs of healing and any signs of infection. No signs of infections or wound dehiscence in all patients for both groups.

Pain (VAS scores)

Post-operative pain was evaluated using a visual analogue scale (VAS) that ranged from 0 = "no pain" to 10 = "the worse possible pain."

Results of inter and intragroup comparisons of VAS presented in table (2), showed that at all intervals, there was no significant difference

* Core Team (2022). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL https://www.R-project.org/.

between both groups (p>0.05). Within both groups there was a significant difference between values measured at different intervals (p<0.001). Post hoc pairwise comparisons showed value measured at day 1 to be significantly higher than values of other intervals except for day 3 (p<0.001). In addition, they showed value measured at day 3 to be significantly higher than value measured at day 7 (p<0.001). (Figure 10) (table 2)

TABLE (2): Inter and intragroup comparisons of VAS

Interval	VAS (Mean±SD)		U-value	p-value
	Group (I)	*Group (II)*		
Day 1	7.83±1.47^{A}	8.17±1.17^{A}	**21.00**	**0.680**
Day 3	5.00±0.89^{AB}	6.00±1.41^{AB}	**26.00**	**0.215**
Day 5	3.17±1.17^{BC}	3.03±0.03^{BC}	**15.00**	**0.677**
Day 7	0.83±0.75^{C}	1.00±0.89^{C}	**20.00**	**0.798**
Q-value	**18.00**	**18.00**		
p-value	**<0.001***	**<0.001***		

Different superscript letters indicate a statistically significant difference within the same vertical column; *significant (p<0.05)

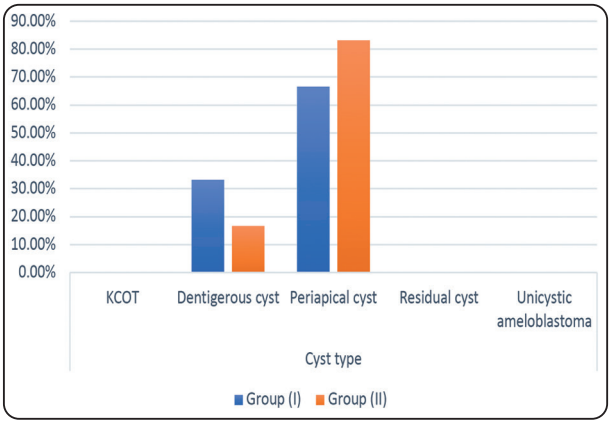

Fig. (10): Bar chart showing cyst type for both groups

Similarly, in Group II, there was a statistically significant change in pain scores by time (*P*-value <0.001, Effect size = 0.851). Pair-wise comparisons between the time periods revealed that there was a statistically significant decrease in pain scores from 1 day to 3 days as well as from 3 to 7 days.

Radiographic examination:

Cone beam computed tomography CBCT were taken at the following intervals preoperative, 3 and 6 months postoperative of the follow up period to evaluate the amount of bone regeneration. (Figure 11)

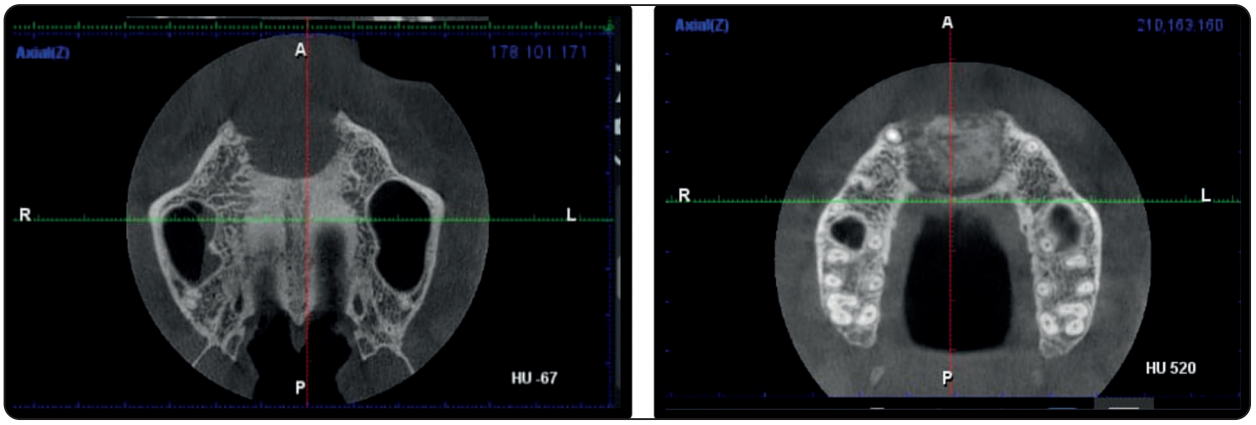

Fig. (11): a) preoperative CBCT showing the bone density in HU (67), b) postoperative CBCT showing the bone density in HU (520) in patient No 1 Group II

Bone density:

Results of inter and intragroup comparisons of bone density presented in table (3), showed that after 3 and 6 months, group (II) had significantly higher values than group (I) ($p<0.05$). Within both groups, there was a significant difference between densities measured at different intervals, with value measured after 6 months being significantly higher than pre-operative value ($p<0.05$). (Figure 12)

TABLE (3): Inter and intragroup comparisons of bone density (HFU)

Interval	Bone density (HFU) (Mean±SD)		U-value	p-value
	Group (I)	Group (II)		
Pre-operative	15.50±46.66^{B}	54.00±46.24^{B}	26.00	0.240
After 3 months	451.33±51.54^{AB}	565.67±44.42^{AB}	34.50	0.010*
After 6 months	494.44±13.32^{A}	646.67±34.88^{A}	36.00	0.005*
Q-value	9.33	12.00		
p-value	0.009*	0.002*		

Different superscript letters indicate a statistically significant difference within the same vertical column; *significant (p<0.05)

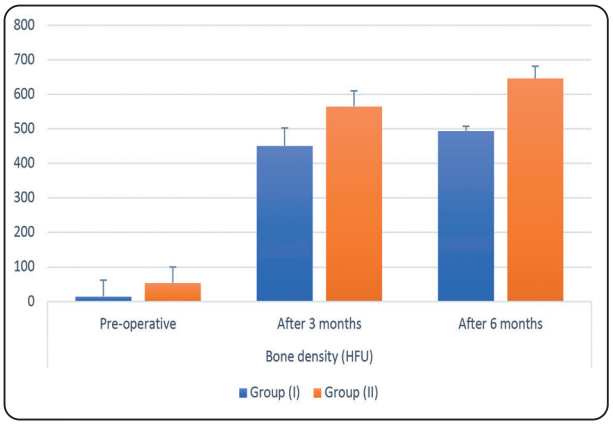

Fig. (12): Bar chart showing mean and standard deviation values of bone density

Intraoperative and postoperative complications:

Minimal amount of bleeding was noticed intraoperatively. Proper wound healing was noticed without wound dehiscence in both groups. No post-operative infections were noticed during the follow up period.

DISCUSSION

Cystic lesions may affect any sites of the jaws during any period of life. Usually, they remain asymptomatic till they result in large bony defects. The resulting bony cavity following complete cystic enucleation can be left for spontaneous healing as reported by many studies. [11,12] However, it is well documented in the literature that critical size defects will not show complete bone regeneration without grafting. [13,14] An animal experimental study by ***Schlegel et al***, showed that mono-cortical defects with 10x10mm dimensions had incomplete bone regeneration even after 52 weeks. [15] Therefore such defects need to be grafted following cystic enucleation. Moreover, many grafting materials were described in the literature for defect filling ranging from autografts, xenografts, allografts as well as synthetic bone substitutes. [16-17-18-19-20]

Platelet Rich Fibrin is considered as a natural fibrin-based biomaterial to guide cell migration. It's prepared as Choukroun's described without the addition of thrombin. it has a natural fibrin framework that can protect growth factors from proteolysis. [9,21] organized as a dense fibrin scaffold, facilitate mineralized tissue formation due to osteoconductive and/or osteoinductive properties [22] with a specific slow release of growth factors that are active for longer period and highly effective in stimulating tissue regeneration, such as platelet-derived growth factor and transforming growth factor. [9,21, 23]

Our study was in accordance with those done by **Yilmaz et al** who had compared the healing effects of β-TCP with or without PRF in bone defects of pig's tibiae. The results of their study were a statis-

tically significant higher difference in bone density measurement of the newly regenerated bone when used together. Similar to the results of this study according to the bone density measurements. [24]

Our study was in coincidence with **Saluja et al** and **Gupta et al** who announced that PRF was considered one of the most promising biomaterials for its easy technique and the wide use in different surgical applications. It has been used as fragments mixed with different types of bone grafting materials to improve both bone regeneration and bone quality. [25,26]

Zhang et al evaluated the efficacy of mixing PRF in combination with FDBA to accelerate bone regeneration in a maxillary sinus lifting surgery before implant insertion. The results showed acceleration in bone regeneration rate, a reduction in maturation time of FDBA and a decrease in implant placement time (placed after 4 months rather than 8 months). This was in agreement with our study as regarding bone regeneration and density improvement. [27]

Our study was in acceptance with the study of **Jayalakshmi et al**. They used b-TCP allograft in combination with PRF for augmentation of a periapical bony defect after enucleation of a periapical cyst in the anterior part of the maxilla. The results of their study showed that the combination of b-TCP allograft and PRF had promoted the regenerative capacity of bone. [28]

CONCLUSION

UNIGRAFT® mixed with PRF improved the bone quality rather than UNIGRAFT® alone.

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