Review Article

Assessment of Platelet Rich Fibrin Combined With Bioactive Glass on Healing Of Bony Defect after Cyst Enucleation

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Abstract

The purpose of this study is to clinically and radiographically evaluate the osteoconductive effect of platelet-rich fibrin (PRF) combined with bioactive glass as graft material on repairing the surgically created bony defects following cysts enucleation. The study was conducted on twelve patients suffering from cystic lesions. The cystic lesions were surgically enucleated according to the standard techniques and the resulting surgical defects were grafted using bioactive glass. The patients were divided randomly into two groups of six patients each. The first group was grafted with bioactive glass along with platelet-rich fibrin (PRF) while the second group which is the control group was grafted using bioactive glass only. Data were collected and statistically analyzed by applying a T-test. The bioactive glass exhibits bioactive behavior, without escape or migration of the granules from the cystic defects. The addition of PRF to bioactive glass allograft accelerates the regenerative capacity of bone Comparing the two groups, the Independent sample t-test showed no statistically significant difference in the bone density between the two groups throughout the study period.

Introduction & Review

Surgical removal of cysts is applied by two clinical methods, either enucleation and marsupialization. Many materials help to increase the strength of the bone replacement material such as the bioactive glass. Bioactive glass is one of the bioactive ceramics, mainly used in the form of granules as bone fillers.**(**1,3**)**

Bone and bioactive ceramics are bonded together by the appetite layer found on the surface which is in contact with interstitial fluids. **(**4,5**)** The glass surface on the bioactive glass can stimulate the formation of the bone when it comes in direct contact with the bone. **(**6**)** The bioactive glass has a positive effect on the osteoblasts, and this effect is demonstrated by the calcium phosphate layer on the formation of the bone matrix. **(**7**)**

Recent studies have revealed new bone production on the bioactive glass granules that were found away from the deficient walls, this could reveal that the bone repair is not only achieved through the osteoconductive feature of the bone substitute material but also the cellular differentiation in the particles internal chamber, because there is no bond between the newly formed bone and the preexisting bone. It was found that there was active deposition on the particle surface. **(**8**)**

PRF was first developed in France by Choukroun **(**9**)** et al. for specific use in oral and maxillofacial surgery. It's a new generation of platelet concentrates, with simplified processing and without biochemical blood handling. **(**10**)** Fibrin sealing mimics the last phases of the coagulation cascade, where fibrinogen is converted to fibrin. This supports the natural wound healing process. Platelets contain potent growth factors that stimulate new tissue synthesis, e.g. platelet-derived growth factor (PDGF) PRF preparation. **(**11**)**

This technique requires neither anticoagulant nor bovine thrombin (nor any other gelling agent). It's centrifuged blood without any addition. To obtain PRF, a table centrifuge and a collection kit from Process are needed. **(**9**)**

PATIENTS AND METHODS

The present study was conducted on twelve patients suffering from cystic lesions. They were selected from the outpatient clinic; Oral and Maxillofacial Surgery Department, Faculty of Oral and Dental Medicine, Cairo University.

The cystic lesions were surgically enucleated according to the standard techniques and the resulting surgical defects were grafted using bioactive glass. The patients were divided randomly into two groups' six patients each. In the recent work cystic lesions of at least 2x1 cm size as measured on a digital panoramic x-ray were corrected to 1:3

- **Group I:** was grafted with bioactive glass along with platelet rich fibrin (PRF).
- **Group II:** The control group was grafted using bioactive glass only.

All the patients were entailed about the cyst enucleation and a bone substitute implantation in the bony cavity and they gave their approval to participate in the written consent.

Patients were informed about unfavorable conditions for cyst enucleation and given the necessary information about the procedure including its prognosis, potential hazards, and complications.

Criteria for patients' selection

- Patients were physically healthy and with no known history of systemic or local disease that might affect bone grafting and the healing process.

Pre-operative Evaluations

Medical & Dental Evaluation

a. Clinical Examination

Extra-oral & intra-oral examinations were carried out.

b. Radiographic Examination

Preoperative digital panoramic radiographs were obtained for each patient to:

- Determine the cyst dimensions and reveal the proximity of the cyst margins to the maxillary sinus and the nasal floor in the maxilla as well as the proximity to the inferior dental canal and its contents in the mandible.

Surgical Procedure

- Surgical access by enucleation was obtained through trans-oral flap design in all cases. **(Fig.1 A)**

In group No. I (PRF+ Bioactive glass)

- The PRF prepared as follows: blood samples were taken according to the PRF protocol without anticoagulant in 10 ml tubes which are immediately centrifuged.
- Circulating thrombin transforms it into fibrin. A fibrin clot is then obtained in the middle of the tube **(Fig.3 A).**
- PRF is then separated from the red corpuscles and the acellular plasma layers by a scissor or any sharp instrument and mixed with the bioactive glass **(Fig.3 B, C).**
- The mixture of bioactive glass and PRF is added to the bony cavity **(Fig.1 C).**

In group no. II (Bioactive glass only)

- Bioactive glass granules were mixed with saline and the mix was used to fill up the cavity **(Fig.2 C)**
- The mucoperiosteal flap was repositioned back and sutured in position using three zero black silk sutures.

Group 1:

Fig 1: A: The bony cavity after cyst enucleation. B: The bony cavity after being filled with PRF before adding the bioactive glass. C: The bony cavity after being filled with bioactive glass and PRF mixture.

Group 2:

Fig 2: A: The cyst lining separated from the surrounding bone. B: The bony cavity after roots apicectomy and trimming of sharp bony edges. C: Filling of the bony cavity with bioglass that was previously mixed with saline.

Fig3: A: platelet rich fibrin in the middle of the tube after being prepared in the middle of the tube. B: PRF after being separated from the other blood components. C: the bioactive glass being mixed with PRF in a metal mixer before adding it to the bony cavity.

Radiographic Evaluation

- The radiographic evaluation was performed for each Patient by obtaining a digital panorama. All digital radiographs were taken with the same machine and the same parameters, under the slandered instructions & recommendations.
- All radiographs were performed at the following intervals: immediate postoperative, 3 months, and 6 months.

Radiographic Image Analysis

- Panoramic images were analyzed by one radiologist. Each image was analyzed twice by the same

examiner at two different sessions with two weeks interval in between.

- Radiodensitometric analysis obtained by measurement of the relative bone density using the sigma view, Digora software.

Statistical Analysis

Statistical analysis was performed using STATA special edition version 10, Stata Corp., U.S.A. Data were represented as mean + standard deviation. Paired Student t-test was used to compare two variables within the same group. Independent samples t-test was used to compare variables between the two studied groups. The result was considered statistically significant if the p-value was less than 0.05.

Results

A total of 12 patients (4 males and 8 females) suffering from jaw cysts of almost (2x1cm) in dimensions. Patients underwent surgical enucleation of the cystic lesions and the bony cavities had been obliterated using Bioactive glass only in Group II (The control group), while Group I (The study group) was grafted with Bioactive glass and platelet-rich fibrin (PRF).

All patients were included for statistical analysis. Data were reported as mean + standard deviation. Patients age, gender, site, and cyst type were shown in the following tables and figures:

Descriptive Statistics

Age:

Group I: Table (1) represents patients' age of group I. Group I age ranged between 17 and 43 years old with mean age of approximately 32.3± 9.7 years old.

Table (1): Patients' age of group I

	Minimum	Maximum	Mean	Std. Deviation
Age (Years)	17.0	43.0	32.3	9.7

Group II: Table (2) represents patients' age of group II. Group II age ranged between 15 and 45 years old with mean of approximately 27.6±10.5 years old.

Table (2): Patients' age of the group II

	Minimum	Maximum	Mean	Std. Deviation
Age (Years)	15.00	45.00	27.6	10.5

There was no statistically significant difference between the two studied groups regarding the age P=0.64.

The study consisted of cyst lesions of different types and in both the maxilla and mandible. It was found that the maxilla is a more common site for the oral cysts with a percentage of 91.7% compared to the mandible which had a percentage of 8.3% only. All the cases of this study were maxillary cysts except one case only of a mandibular cyst.

All the cysts in this study were found to be radicular cysts except one case of a dentigerous cyst. The percentage of radicular cysts was 97.1% while the percentage of the dentigerous cysts was 8.3% only.

Radiodensity Results

Group I

The mean value of the bone density measured immediately postoperatively was 149.514 + 29.757HU. By the end of the third month, it was reduced to 138.2 + 3.49HU. While, after six months at the end of the follow-up period, it reached 146.93 + 33.22HU.

The percentage change of the bone density throughout the study was -7.56% and –1.7% by the end of the third and the sixth months respectively. There was no statistically significant difference in the mean values of the bone density three months postoperatively p= 0.12 as well as six months postoperatively p= 0.71 **(Table 5) (fig.4).**

Table 3: bone density group I.

	Min	Max	Mean	Std
Immediate	121.52	186.81	149.51	29.78
3 months	94.41	183.32	138.2	34.49
6 months	99.03	184.63	146.938	33.22
Percentage change at 3m	-22.31	-1.87	-7.56	15.82
Percentage change at 6m	-18.51	-1.16	-1.72	11.55

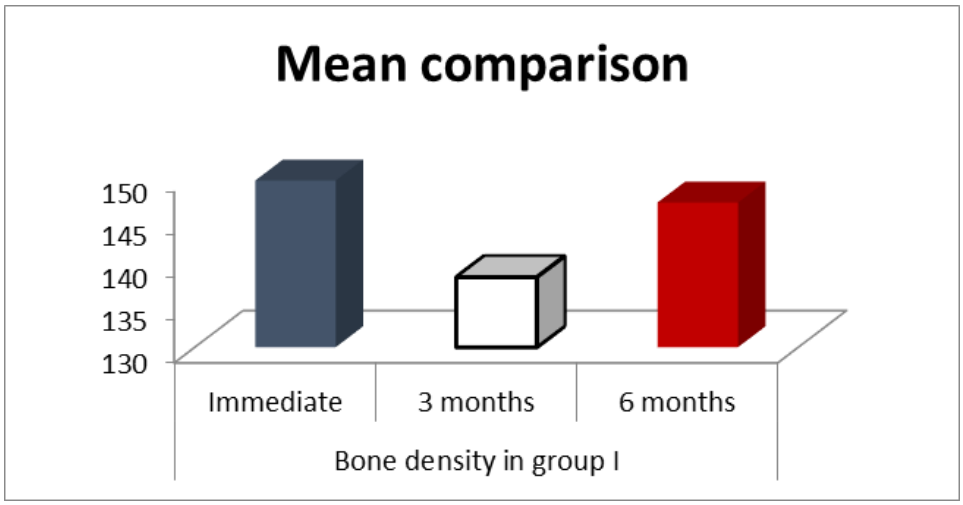

Fig.4: Bone density group II.

Group II

The mean value of the bone density measured immediately postoperatively was 131.78 + 21.99HU. Three months postoperative, it was reduced to 126.42 + 29.19HU. While by the end of the follow-up period in the sixth month it reached 138.05 + 16.36HU. The percentage change of the bone density at three months was -4.07%, where it was 4.76% at the sixth months postoperatively. There was no statistically significant difference in the mean values of the bone density three months postoperatively p= 0.73 as well as six months postoperatively p= 0.49 **(Table 4) (fig.5).**

Table 4: bone density group II

	Min	Max	Mean	Std
Immediate	105.77	151.65	131.78	21.99
3 months	88.66	152.94	126.42	29.19
6 months	111.01	150.78	138.05	16.36
Percentage change at 3m	-16.18	0.85	-4.07	32.74
Percentage change at 6m	4.95	-0.57	4.76	-25.60

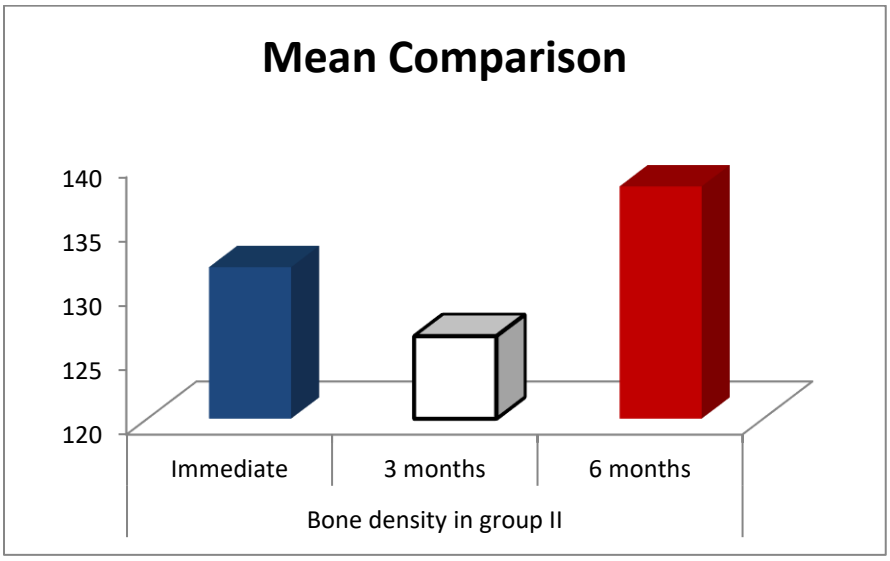

Fig.5: Bone density group II.

Comparing the two groups

Independent sample t-test showed no statistically significant difference in the bone density between the two groups throughout the study. p=0.5, 0.1, 0.1 immediate, three and six months postoperative respectively **(Table 5) (Fig.6).**

Table 5: Comparing bone density of the two groups.

	Immediate		3 month		6 month	
	Mean± STD	P value	Mean ±STD	P value	Mean ±STD	P value
Group I	149.51±13.31	0.31	138.2±15.42	0.58	146.94±14.86	0.61
Group II	142.±9.84		126.42±13.05		138.05±7.31	

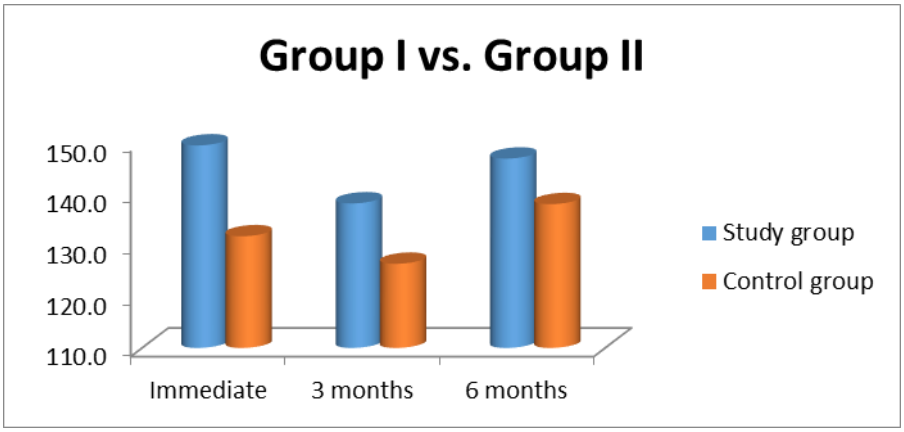

Fig.6: comparing bone density of the two groups.

Discussion

Cauley et al., (2003)12, reports concluded that jaw cysts were observed to be affecting both males and females constantly. However, In the present study females were more affected than males, unlike what was found in the other studies by Jones et al., (2006)13, Avelar et al., (2009)14, and Açikgöz et al., (2012)15, who concluded that males are usually more affected than females because men customarily have worse oral hygiene habits and are more susceptible to trauma than women.

According to the location & type of the cystic lesion, our findings reported 91.7% of radicular cystic lesions in the maxilla, except one case was located in the mandible. All the cystic lesions were found to be radicular cysts except one case was a dentigerous cyst. In agreement with Bodner et al (2011)16, a retrospective study of 27 cystic jaw lesions in edentulous patients showed that the maxilla was more affected than the mandible, with radicular/residual cysts being the most common. Also, El-Gehani et al., (2008)17, reported that the maxilla was found to be more affected by cystic lesions than the mandible with a ratio of (1.3:1); especially the anterior part of the maxilla, which coincides with our findings.

The prevalence of odontogenic cysts was reported to be (54.7%) radicular as reported by the findings of Açikgöz et al., (2012)15, which were in agreement with our findings reported (100%), radicular cysts were the most common type. However, there was a disagreement with the above-mentioned studies, in the work done by Avelar et al (2009)14, who reported that the mandible was the most prevalent site by (56%). Regarding the ethnic background, almost 40% of the patients were of African descent, which was in agreement with the recent study, where all the subjects were African.

Bioactive glasses have high potential as scaffold materials as they stimulate bone cells to produce new bone, they are degradable in the body and they bond to bone. (Jones et al., 2007, Hench et al., 1993 & Oliveira et al., 1995)18-20. Bioglass is a scaffold that is thought to be required for three-dimensional tissue growth, our findings were in agreement with Jones's study as the application of bioactive glass in the three-walled cystic defects stimulated the bone cells to produce new bone.

Platelet-rich fibrin matrix represented a simple and effective means of accelerating new bone growth in a variety of oral and dental applications without the disadvantages of barrier membranes, non-vital graft materials, or exogenous thrombin associated with other PRP systems9, 21.

The combined use of PRF and (β-TCP or demineralized bone matrix) for bone augmentation in the treatment of periapical defects was an alternative for faster healing than using tricalcium phosphate or Osseograft alone 22, 23 However, the results gained in the present study have shown no statistically significant differences between using bioactive glass alone or when combined with platelet-rich fibrin. Zhao et al., (2012)24, reported that the combination of PRF and bioactive glass is an effective modality of regenerative treatment for radicular cysts at 4 months postoperatively. In the present study, clinical & radiographic assessment at 6 months post-operatively has shown a promising approach for augmenting cystic defects, whereas, no statistically significant difference was reported with the use of bioactive glass alone Bioactive glass particles mixed with saline were applied after cyst enucleation to fill intrabony cystic defects in the present study.

Upon implantation of the bioactive glass particles inside the intrabony defect, the material seemed to be coherent in the defect, easy to be manipulated and has a hemostasis effect. This is by the results stated by Abd-el azym and El Sherbiny, (1999)25 which proved the coherence of the glass inside the bony defect.

The test group patients were grafted with platelet-rich fibrin (PRF) along with bioactive glass.
It is hypothesized that the PRF has a natural fibrin framework that can protect growth factors from proteolysis according to Dohan et al., (2006)26. It is organized as a dense fibrin scaffold with a specific slow release of growth factors27.

The target of this study was to evaluate clinically and radiographically the efficacy of filling cystic defects with bioactive glass in combination with or without PRF. During the whole follow-up period, there were no signs of mucosal dehiscence, infection, or graft rejection were detected. Wound stability and infection control were of prime importance. This goes with the results stated by Nasr (2000)28.

The findings of the present study using direct digital radiography to measure the changes in the density of the grafted cystic bony defects in both groups through the specific follow-up periods: immediately, three then six months post-operatively. Direct digital radiography made both qualitative and quantitative visualization of bone density changes easy to be detected.29, 30.

As proven to be a more accurate, sensitive, and reliable alternative technique to routine x-rays, in the present study. Also, it offers a lower level of irradiation to the patient and decreases the time consumption for both the patient and operator.

Radiodensitometric analysis was obtained by measurement of the relative bone density using Digora software. The computerized image analysis system was found to be an appropriate tool in detecting changes in bone density as it provides numeric values for the progression of the healing process. This goes with the present study & the results confirmed by Delano et al., (2001)31 and Yoshioka et al., (2002)32.

Postoperative digital orthopantomography was taken immediately, 3 months than 6 months postoperatively to evaluate the bone density changes in the grafted former cyst cavity. Radio density measurement throughout the study showed a decrease in bone density after three months in both groups. This decrease in density was due to the formation of a soluble silica layer that is readily absorbed and excreted from the body. Also, excavation of the granule core by phagocytosis and early osteoid

formation within the excavated chambers. That was coincident with the studies of Gaisser et al., (2002)33.

In both groups, the radiodensity raised again at the 6th month radiographic assessment. That increase in radiodensity was thought to be because of new bone formation after the invasion of osteoblasts as a result of the osteostimulatory effect of bioactive glass which is coincident with the studies of Schepers et al., (1991)34, Schepers et al., (1997)35, Furusawa et al., (1998)36, and Froum et al., (2002)37.

Comparing the two groups, the Independent sample t-test showed no statistically significant difference in the bone density between the two groups throughout the study. p=0.5, 0.1, 0.1 immediate, three and six months postoperative respectively. There are no many studies to compare these results with, however, Zhao et al., (2012)24, found out after grafting two cases of radicular cysts and bioactive and a follow-up of 7 months that PRF can improve periapical osseous healing as the fibrin matrix can guide the healing processes, but no statistical data was available to compare with. From the results gained in the recent study, bioactive glass can be used alone to augment the 3-walled cystic defects.

Conclusion

From the results of this study it could be concluded that:

1. The bioactive glass exhibits bioactive behavior, without escape or migration of the granules from the cystic defects. The formation of hydroxycarbonate apatite transformed, remodeled, and replaced by newly formed osseous tissue.

2. The addition of PRF to bioactive glass allograft accelerates the regenerative capacity of bone. Utilizing bioactive glass in conjunction with platelet-rich-fibrin membranes may be a reliable choice for osseous regeneration in cases of bony defects.

3. Platelet-rich fibrin matrix acts as a membrane with the property of healing benefits. Platelet-rich fibrin is an autologous preparation and found to be clinically effective and economical than any other available regenerative materials. It is cheap, easy manipulative as a bone defect filler.

4. The direct digital radiography system used in this study (digital system) proved to be an appropriate tool in assessing the density of the cystic bony defects. Direct digital radiographs can be used reliably in tracing the healing process in the cystic bony defects of the jaws.

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