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Evaluation of the Role of Platelet-Rich Fibrin (PRF) in the Management of Mandibular Bony Cysts after Surgical Enucleation

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Abstract

Background: **Cystic mandibular lesions may be epithelial or non-epithelial, odontogenic, or non-odontogenic, developmental, or inflammatory in origin. Clinically bony cysts are usually asymptomatic and are often accidentally discovered on routine radiological examination. PRF has been shown to act as a suitable scaffold for culturing human periosteal cells in vitro, which may be suitable for bone tissue engineering applications.** ***Aim:*** **to explore the clinical and radiographic effectiveness of autologous PRF in the treatment of intrabony cyst cavity after enucleation.** ***Subjects and Methods:*** **This randomized controlled clinical trial included patients with mandibular bony cysts as well as benign tumors of the mandibular surgery department at Suez Canal University Hospital and Suez Health Insurance Hospital. The study participants were randomly divided into two groups: i) the study group who underwent enucleation of the cysts then PRF was added and ii) the Control group who underwent enucleation of the cysts only.** ***Results:*** **In the control group, the mesiodistal length of the cyst at 6 months after enucleation was significantly lower than that length just after operation ($p<0.001$). However, there was no statistically significant difference in mesiodistal length of the cyst just after the operation and 2 months after enucleation. Meanwhile, in the PRF group, the mesiodistal length of the cyst just after the operation was significantly lower than the length at 2 and 6 months after enucleation ($p<0.001$). Patients who received PRF had significantly lower 6 months from baseline change in each mesiodistal length ($p=0.001$) and superior-inferior length ($p=0.002$) than patients in the control group.** ***Conclusion:*** **PRF promotes faster osseous regeneration in the Management of mandibular bony Cysts after Surgical Enucleation. The use of PRF in the management of cystic lesions seems to be a novel therapeutic approach promoting faster osseous regeneration.**

Keywords: *Platelet-Rich Fibrin (PRF), Mandibular Bony Cysts, Surgical Enucleation*

Introduction

Cystic mandibular lesions may be epithelial or non-epithelial, odontogenic or non-odontogenic, developmental, or inflammatory in origin. Clinically bony cysts are usually asymptomatic and are often accidentally discovered on routine radiological examination. The radiographic picture is usually a unilocular radiolucent area with

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scalloped margins between the roots of teeth. They may be multilocular, associated with unerupted or impacted teeth, and several cysts may be present in the same patient. The overlying cortical bone may be seen as a thin shell of bone on an occlusal radiograph[1]. Platelet-rich fibrin (PRF) was first used specifically in oral surgery by Dohan et al. and is currently considered as a new generation of platelet concentrate. It consists of a matrix of autologous fibrin. and has several advantages over platelet-rich plasma (PRP), including easier preparation and not requiring chemical manipulation of the blood, which makes it strictly an autologous preparation[2,3]. Platelets' regenerative potential was reported in the 70's, when it was observed that they contain growth factors that are responsible for increase collagen production, cell mitosis, blood vessels growth, recruitment of other cells that migrate to the site of injury, and cell differentiation induction, among others[3]. Platelets contribute not only to the hemostatic process but also to wound healing through the release of growth factors (cytokines). These growth factors initiate and sustain wound repair& bone growth[2]. Some studies have demonstrated that PRF is a healing biomaterial with a great potential for bone and soft tissue regeneration, without inflammatory reactions and may be used alone or in combination with bone grafts, promoting hemostasis, bone growth, and maturation[4,5]. Multiple approaches have been used to resolve bone cyst defects, including autografts, demineralized freeze-dried bone allografts, bovine-derived xenografts, barrier membranes, and combinations of membranes and bone grafts. Although these regenerative materials are still used today, the introduction of biomimetic agents, such as enamel matrix derivatives, platelet-derived growth factor (PDGF) and bone morphogenic proteins, has given new promise for better outcomes in bone cyst treatment. PRF consists of an intimate assembly of cytokines, glycanic chains, and structural glycoproteins enmeshed within a slowly polymerized fibrin network and has been shown to act as suitable scaffold for culturing human periosteal cells in vitro, which may be suitable for bone tissue engineering applications[7]. The study aimed to explore the clinical and radiographic effectiveness of autologous PRF in the treatment of intrabony cyst cavity after enucleation.

Patients and Methods

Research design
Randomized controlled clinical trial.

Study population and place
Target population was patients with mandibular bony cysts. This study took place in plastic surgery units in 1) Surgery department, Suez Canal University Hospital, Ismailia, 2) Surgery department, Suez Health Insurance Hospital, Suez.

Inclusion criteria
the study included patients at any age of both genders with i) Cysts at any condition (including infection), ii) Small or medium sized cysts (2-5cm) or, iii) cysts of benign nature.

Exclusion criteria
patients with any of the following were excluded from the study: i) Patients with severe systemic diseases and/or with organ failure, ii) Large bony cysts (bone graft indicated), iii) suspicious cysts that may need further excision, iv) cases indicated for segmental mandiblectomy, v) keratocyst and malignant ameloblastoma.

Study tools/procedure
Patients fulfilling inclusion criteria were subjected to:

1- History taking
i) History of chronic illness e.g., diabetes, hypertension… etc. ii) History of blood disorders e.g., coagulopathy, hypoproteinemia, etc. iii) General examination

3- Careful local examination
i) Site and size of the mass. ii) State of surrounding bone, soft tissue. iii) Presence of inflammation e.g., osteomyelitis, pus discharge … etc. iv) Number of missing teeth.

4- Pre-operative Preparations
i) Routine laboratory investigations. ii) panorama X-ray: size, site, any unerupted teeth. iii) 3D CT facial bone. iv) Aspiration biopsy of suspicious cysts. v) Analysis of the cyst (dimensions, bone density) by (Digora for windows ™).

Preparation of PRF
The PRF was prepared following the protocol developed by Choukroun et al [8]. Intraoperativelly for each 1 cc bony defect (measured by CT software preoperative)10 cc blood, intravenous blood (by venipuncture of the antecubital vein) was collected in 15 mL sterile tubes without anticoagulant and immediately centrifuged at 3000rpm for 10 min. Blood centrifugation immediately after collection allows the composition of a structured fibrin clot in the middle of the tube, just between the red corpuscles at the bottom and acellular plasma [platelet-poor plasma (PPP)] at the top. PRF was easily separated from the red corpuscle base [preserving a small red blood cell (RBC) layer] using a sterile tweezers and scissors.

Procedure and Surgical technique
Intraoral antisepsis was performed with betadine solution to carry out extra oral antisepsis & preoperative general antibiotic intravenous dose was given. Following administration of general anesthesia in supine, extended neck position, nasal or oral tube, we made buccal gingival incision then reflected mucoperiosteal flap. Meticulous defect debridement was carried out. Autologous PRF of the required size was filled into the bony defect, the mucoperiosteal flaps was repositioned and secured in place using 4-0 absorbable Vicryl surgical sutures. The interrupted & continuous sutures were placed. The autologous PRF was prepared just before placement in the defect and was not stored, as the success of this technique entirely depends on the speed of blood collection and transfer to the centrifuge.

Post-operative care:
i) General antibiotics, ii) Local wound care (mouth wash, oralgel) and iii) Anti-inflammatory, anti-edematous

Follow-up
The patient was followed regularly during the following 6 months (weekly in first month and monthly afterwards) and more frequently in complicated cases. Data was collected immediately postoperative, at 2 and 6 months by local exam, panorama, 3D CT. Analysis of bone density and dimension was done by Digora for windows ™. Bone healing in the defect after treatment of lesions was evaluated radiographically. Patients were recalled at intervals of two weeks in the 1st two months then every two months for four months. A single standard occlusal radiograph was obtained during follow-up appointments. A panoramic radiograph will be ordered if the dimension of osseous defect was very large.

Assessment of bone healing
Pre- and Post-operative CT 3D facial bone and panorama x-ray were done to document the changes and allow hard-evidence comparison.

Evaluation
Two radiologists and two Plastic surgeons

evaluated the pre and postoperative radiological studies. All evaluators were blinded.

Statistical Analysis

Data was processed using SPSS-11 software. P value was used for testing relationships between variables. Confidence Interval (CI) was used to compare the results both groups. Presentation of data was done in tables and figures.

Results

Baseline characteristics of the studied groups were summarized in table 1. The mean age of both groups was comparable. Males formed about two third of the control group (66.1%) and about one half of the patients in the PRF group (56.5%). Meanwhile, in control group, one tooth was involved in the cyst in one third of the patients (33.3%) whereas 25% of the patients in the PFR group had one tooth involved in the cyst. Most cysts were located at symphysis or para-symphysis while only two cases had cysts at the body of the mandible. Table 2 shows reported complications by patients in both groups.

Table 1: Socio-demographic characteristics in both groups

Variables	Total (n=48)	Control Group (n=24)	PRF Group (n=24)	p-value
Age (years), mean ± SD	27.42 ± 9.22	27.54 ± 9.29	27.29 ± 9.35	0.793[a]
Gender, n (%)				
Male	29 (60.5%)	16 (66.1%)	13 (56.5%)	0.37[b]
Female	19 (39.5%)	8 (33.9%)	11 (43.5%)	
No. of teeth involved, n (%)				
1	14 (29.2%)	8 (33.3%)	6 (25%)	
2	13 (27.1%)	6 (25%)	7 (29.2%)	0.95[c]
3	15 (31.3%)	7 (29.2%)	8 (33.3%)	
4	6 (12.5%)	3 (12.5%)	3 (12.5%)	
Site of cyst, n (%)				
Symphyseal	19 (40)	9 (37.5)	5 (20.8)	
Parasymphyseal	19 (40)	15 (62.5)	17 (70.8)	0.9[c]
Body	2 (20)	0 (0)	2 (8.4)	

[a]=Mann Whitney U test. [b]=Chi-square test. [C]=Fisher's Exact test. Statistical significance at P < 0.05

Post-operative pain was reported in 20 patients (9 in control and 11 in PRF group). Meanwhile, three patients had post-operative infection (two patients in the control group and one in the PRF group). Overall, there was no statistically significant difference between patients who received and did not receive PRF in the incidence of their post-operative infections. There were no cases with reported Trismus, motor dysfunction or sensory dysfunction. Table 2 shows that there was no statistically significant difference in the mesiodistal length between control and PRF groups at 2 months after enucleation (p=0.21). However, patients who received PRF had significantly lower mesiodistal length than patients in the control group 6-month post-operatively (p=0.004). Table 3 shows that patients who received PRF had significantly lower superoinferior length than patients in the control group 2-month and 6-month post-operatively (p=0.034) and (p=0.019), respectively. Patients who received PRF had statistically significantly higher bone density (1240.5 ± 169.73) than

patients in who did not receive PRF (1021.9±347.54) 2month after enucleation (p=0.043). Likewise, patients in PRF group had statistically significantly higher bone density (1456.2±144) than patients in who did not receive PRF (1215.4±315.8) 6 month after enucleation (p=0.011) (Table 4). Table 5 shows the change in the mesiodistal length of the cyst over the three time points in each group of patients. In the control group, mesiodistal length of the cyst at 6 months after enucleation (2.53±1.74) was significantly lower than that length just after operation (3.03±1.93) (p<0.001). However, there was no statistically significant difference in mesiodistal length of the cyst just after operation (3.03±1.93) and 2 months after enucleation (2.98±1.96).

Table 2. Comparison between interventional and control regarding mesiodistal length at different time points

Mesiodistal length (mm)	**Total** (n=48)	**Control group** (n=24)	**PRF group** (n=24)	**p-value**
Immediate	3.10 ± 1.89	3.03 ± 1.93	3.17 ± 1.89	0.72 [a]
2-month post-intervention	2.59 ± 1.71	2.98 ± 1.96	2.20 ± 1.35	0.21 [a]
6-month post-intervention	1.98 ± 1.67	2.53 ± 1.74	1.43 ± 1.44	**0.004** [a]

Data are presented as mean ± SD, [a]=Mann Whitney U test. Statistical significance at P < 0.05

Table 3. Comparison between interventional and control regarding superio-inferior length at different time points

Superioinferior length (mm)	**Total** (n=48)	**Control Group** (n=24)	**PRF Group** (n=24)	**p-value**
Immediate	2.04 ± 1.01	2.14 ± 1.32	1.94 ± 0.54	0.93 [a]
2-month post-intervention	1.62 ± 0.83	1.88 ± 1.04	1.35 ± 0.45	**0.034** [a]
6-month post-intervention	1.11 ± 0.77	1.37 ± 0.92	0.85 ± 0.47	**0.019** [a]

Data are presented as mean ± SD, [a]=Mann Whitney U test. Statistical significance at P < 0.05

Meanwhile in the PRF group, mesiodistal length of the cyst just after operation (3.17±1.89) was significantly lower than that length at 2 and 6 months after enucleation (2.20±1.35) and (1.43±1.44) (p<0.001). Table 6 shows the change in the superoinferior length of the cyst over the three time points in each group of patients. In the control group, superoinferior length of the cyst at 6 months after enucleation (1.37± 0.92) was significantly lower than that length just after operation (2.14±1.32) (p<0.001) and 2 month after enucleation (1.88±1.04) (p=0.015). Likewise, in the PRF group, superoinferior length of the cyst at 6 months after enucleation (0.85±0.47) was significantly lower than that length just after operation (1.94±0.54) (p<0.001) and 2 months after enucleation (1.35±0.45) (p=0.004). on analyzing the change in the bone density over the three time points in each group. In the control group, bone density at 6 months after enucleation (1215.46±315.8) was significantly higher than that just after operation (869.3±363.2) (p<0.001) only. No significant difference was found in the bone density just after operation (869.3±363.2) and 2 months after enucleation (1021.9±347.5) (p=0.07). However, in the PRF group, bone density at 6 months after enucleation (1456.2±144) was significantly higher than that just after operation (976± 369.9) (p<0.001) and 2 months after enucleation

(1240.5±169.7) (p=0.002). Moreover, bone density at 2 months after enucleation was significantly higher than that just after operation (976±369.9) (p= 0.002).

Table 4. Comparison between interventional and control regarding bone density at different time points

Bone density (Hu)	**Total** (n=48)	**Control group** (n=24)	**PRF group** (n=24)	**p-value**
Immediate	922.69 ± 366.64	869.38 ± 363.2	976 ± 369.9	0.28 [a]
2-month post-intervention	1131.21 ± 292.24	1021.9 ± 347.54	1240.5 ± 169.73	0.043 [a]
6-month post-intervention	1335.88 ± 271.58	1215.46 ± 315.8	1456.29 ± 144	0.011 [a]

Data are presented as mean ± SD, [a]=Mann Whitney U test. Statistical significance at P < 0.05

Table 5. Comparison of mesiodistal length (mm) in the groups
(Immediate, 2 and 6 months after enucleation)

Variables	**Immediate**	**2-month post-intervention**	**6-month post-intervention**	**p-value**
Control group	3.03 ± 1.93	2.98 ± 1.96	2.53 ± 1.74	0.001 [a]
PRF group	3.17 ± 1.89	2.20 ± 1.35	1.43 ± 1.44	<0.001 [a]

Data are presented as mean ± SD, [a]=Friedman ANOVA Test, Statistical significance at P < 0.05

Table 6. Comparison of superioinferior length in the groups
(Immediate, 2 and 6 months after enucleation)

Variables	**Immediate**	**2-month post-intervention**	**6-month post-intervention**	**p-value**
Control group	2.14 ± 1.32	1.88 ± 1.04	1.37 ± 0.92	**<0.001** [a]
PRF group	1.94 ± 0.54	1.35 ± 0.45	0.85 ± 0.47	**<0.001** [a]

Data are presented as mean ± SD, [a]=Friedman ANOVA Test, Statistical significance at P < 0.05

Discussion

In the present study, the mean age of both groups (27.42 ± 9.22) was comparable. Males formed about two third of the control group (66.1%) and about one half of the patients in the PRF group (56.5%). Similarly, a study was conducted in the Department of Oral and Maxillofacial Surgery, Govt. Dental College and Hospital, Srinagar. 20 patients (13 males and 7 female) were diagnosed with cystic lesions based on clinical and radiographic findings with age groups ranging from 20 years to 55 years[9]. In the present study, there was no statistically significant difference between patients who received and did not receive PRF in the incidence of their post-operative infections, pain, or edema. Similarly, Gülşenet al., at 2017, reported that Using or not using PRF to reduce postoperative pain and edema in third molar surgery was equally successful[10]. In the present study there were radiological signs that confirm the effect of PRF. Similarly, Mitrea et al., 2015 reported that A-PRF speeds up the healing process, as shown in our case report in which A-PRF is effective in the healing of the bone defect resulting from cyst enucleation in a faster rate, both clinically and radiologically, so the healing time of cystic cavity was reduced to 3 months instead of 6 to 12 months. In the present study, the there was no statistically significant difference in the mesiodistal length between control and PRF groups at 2

months after enucleation, however, patients who received PRF had significantly lower mesiodistal length than patients in the control group 6-months post-operatively. Moreover, patients who received PRF had significantly lower superior-inferior length than patients in the control group 2-month and 6-month post-operatively. These results show that PRF helped in bone regeneration 2 and 6 months after the operation. Similarly, Eldibany et al., in 2014calculated the surface area and the bone density immediately post-operatively and at 6 and 9 months post-operatively to assess effect of PRF reported that the mean surface area/SD of the lesions immediately post-operatively was 487.5±32.0 mm^2, on the 6th month there was 31% size reduction of the surface area with a value of 336.3±57.6 mm^2, and on the 9th month the surface area was recorded as 238.8±56.5mm^2 with a 51% size reduction[11]. In the present study, it was also found that the rate of bone regeneration was also higher than that of the control group as it was found that in the PRF group, mesiodistal length of the cyst just after operation (3.17±1.89) was significantly lower than that length at 2 and 6 months after enucleation. Likewise, in the PRF group, superioinferior length of the cyst at 6 months after enucleation (0.85± 0.47) was significantly lower than that length just after operation (1.94±0.54) ($p<0.001$) and 2 months after enucleation. The difference in bone regeneration rates may be attributed to the different age groups and races in these different studies[11]. In the present study, Patients who received PRF had statistically significantly higher bone density (1240.5± 169.73) than patients who did not receive PRF (1021.9± 347.54) 2 month after enucleation ($p=0.043$). Likewise, patients in PRF group had statistically significantly higher bone density (1456.29 ± 144) than patients in who did not receive PRF (1215.46 ± 315.8) 6 month after enucleation ($p=0.011$). In the control group, there was no statistically significant difference in the bone density just after operation or 2 months after enucleation ($p=0.07$). However, in the PRF group, bone density at 6 months after enucleation (1456.29 ± 144) was significantly higher than that just after operation (976 ± 369.9) ($p<0.001$) and 2 months after enucleation (1240.5 ± 169.73) ($p=0.002$). Moreover, bone density at 2 months after enucleation was significantly higher than that just after operation. Similarly, Eldibany et al.,[11] reported that The mean bone density/SD was 153.95 ± 15.04 HU immediately post-operatively, which increased by 22.2% ore188.17 ± 17.33 HU by the 6th month and continued to increase by 50.8% reaching 226.9±33.1 HU by the 9th month. The increase in bone density was statistically significant throughout the different follow up periods[11]. Another study also reported that Follow-up radiographic examination by grayscale histogram study revealed progressive, predictable, and significant radiographic osseous regeneration and an increase in bone density. Radiographically, all patients showed that PRF promotes faster osseous regeneration within the 3rd postoperative month, and within 6th postoperative month, complete bone regeneration was seen [12].

Conclusion

The present study concluded that PRF promotes faster osseous regeneration in Management of mandibular bony cysts after surgical enucleation. The use of PRF in management of cystic lesions seems to be a novel therapeutic approach promoting faster osseous regeneration.

The study Limitations

The small sample size and performing the

study in one healthcare facility are two limitations in this study. It is favorable to perform further studies with larger sample sizes in more than one hospital to confirm these findings.

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