SOFT TISSUE AND BONE REGENERATION OF RESIDUAL BONE DEFECT AFTER ERADICATION OF JAW CYSTS IN THE PRESENCE AND ABSENCE OF ALBUMIN PLATELET-RICH FIBRIN (A RANDOMIZED CONTROLLED CLINICAL TRIAL)

Mohamed Magdy Elsayed Mohamed Shokry[1]* *BDS*,
Lydia Nabil Fouad Melek[2], Tasneem Ahmed Amer[3]

ABSTRACT

INTRODUCTION: Platelets are crucial to the healing process of wounds. Accordingly, the orientation towards using platelet concentrates in healing has become familiar. Thus, a new material has been evoked known as albumin platelet-rich fibrin (Alb-PRF), which remains stable for up to 4 months and allows growth factors to be released for a long time, promoting the healing of both soft and hard tissues at the injured areas.
OBJECTIVE: to demonstrate how Alb-PRF affects soft and hard tissue recovery following the eradication of jaw cysts.
MATERIALS AND METHODS: This study contained 20 participants, divided equally into 2 groups. The study group was managed with cyst eradication followed by Alb-PRF application, while the control group was managed with cyst eradication and primary closure of the wound. According to the healing Landry index, soft tissue healing was evaluated on the 7th and 14th days. A postoperative immediate and post-6-month CBCT were performed to measure the 3-dimensional volumetric analysis of the bone defect after cyst eradication.
RESULTS: On the 7th and 14th days after the surgery, the difference was not statistically significant in soft tissue healing between both groups, P1 = 0.739 and P1 = 0.393, respectively. The change in the 3-dimensional volumetric analysis of bone defect after cyst eradication revealed that, six months later, there was no statistically significant difference between the two groups (t = 1.601, P1 = 0.130).
CONCLUSION: According to this study, the soft and hard tissues healed properly using Alb-PRF or natural blood clots after jaw cyst eradication.
KEYWORDS: 3-dimensional volumetric analysis, Alb-PRF, Soft tissue healing, CBCT.
RUNNING TITLE: Alb-PRF's Impact on Tissue Healing

1 BDS, Master's degree candidate, Resident doctor at the Oral and Maxillofacial Surgery Department, Faculty of Dentistry, Alexandria University, Egypt. Institution: Faculty of Dentistry, Alexandria University, Alexandria, Egypt.
2 PhD Oral and Maxillofacial Surgery, Professor of Oral and Maxillofacial Surgery, Faculty of Dentistry, Alexandria University, Egypt. Institution: Faculty of Dentistry, Alexandria University, Alexandria, Egypt.
3 PhD Oral and Maxillofacial Surgery, Lecturer of Oral and Maxillofacial Surgery, Faculty of Dentistry, Alexandria University, Egypt. Institution: Faculty of Dentistry, Alexandria University, Alexandria, Egypt.

*** Corresponding Author:**
E-mail: m.shokry.dent.pg@alexu.edu.eg,
m_magdy_shokry@hotmail.com.

INTRODUCTION

Cysts are benign pathological spaces with an epithelial lining that frequently arise in the head and neck regions. Depending on their epithelial nature, jaw cysts are categorized into two groups: odontogenic and non-odontogenic. Odontogenic cysts occur more regularly than non-odontogenic cysts(1). The prevalence of jaw cysts is more frequent in males than females, 1.6:1(2). Pain, swelling, and discomfort are the usual characteristics of jaw cysts, however, the cyst growth may cause bone resorption and luxation of the teeth. Nevertheless, the jaw cysts can be asymptomatic without any complaints, so they can be noted by chance at routine roentgenographic examination(3). The clinical and radiographic examinations are necessary to diagnose jaw cysts, where inspection for jaw enlargement, palpation for any alteration in bone contour or any crepitus, hot and cold test for the teeth, evaluation of tooth mobility, needle aspiration to detect intra-cystic fluid content, and the appearance of a well-defined radiolucency surrounded by a corticated rim radiographically are important before surgical intervention to treat cysts(4).

There are two conventional strategies to treat cysts. The first one is enucleation, Partsch II cystectomy, which involves the removal of the cyst completely through a surgical procedure for a cyst < 5 cm, while the other strategy is marsupialization, Partsch I cystotomy, a conservative procedure used with large cysts > 5 cm, which involves decreasing the intra-cystic pressure through a passive drain to get a small sized cyst followed by enucleation[5,6].

Healing of soft and hard tissues after cyst enucleation is a critical issue, whereas wound healing is a complex procedure involving successive events on cellular and molecular levels. These events are categorized into four stages: platelet plug and blood clot formation, release of inflammatory mediators, proliferation, and tissue remodeling[7,8]. Wound healing phases are significantly influenced by platelets. They accumulate in clusters, forming platelet plugs and blood clots upon activation[7]. They release essential growth factors, angiogenic factors, cytokines, and inflammatory mediators in charge of attracting and triggering immune cells participating in the healing stages[9].

Accordingly, the orientation towards using platelet concentrates in wound healing has become familiar in the regeneration field. Thus, the first generation of platelet concentrate, platelet-rich plasma (PRP), was developed in 1998[10]. PRP is an autologous byproduct of blood. To produce PRP, blood samples are subjected to dual centrifugations and activation using anticoagulants, bovine thrombin, and calcium chloride [11,12]. Upon the production of PRP, the release of growth factors from platelets begins and lasts for a short period of nearly 10 minutes[13]. However, the presence of anticoagulants during the PRP preparation which prevents the formation of natural blood clots, the difficulty in PRP preparation protocol, and the release of growth factors for a short period led to the upcoming generation of platelet concentrations known as platelet-rich fibrin (PRF) which Choukroun et al. initially described in 2001. [13,14].

PRF is a dense clot rich in platelets, white blood cells, growth factors, and cytokines. PRF releases growth factors during seven days. These growth factors are found within the α-granules of platelets and are responsible for the wound-healing cascade[15]. The high concentration of neutrophils and macrophages in PRF is responsible for preventing infection and removing any necrotic tissues at injured sites. Macrophages are also responsible for secreting growth factors such as transforming growth factor beta 1, platelet-derived growth factors, and vascular endothelial growth factors, needed in wound healing and angiogenesis[16]. However, one of the drawbacks of PRF is the fast resorption rate, whereas it can resorb within 2 weeks, thus leading Kawase et al. to use heat treatment to prolong the degradation rate of PRF.

Accordingly, the change of PRF preparation protocol has been evoked to change the properties of control PRF producing a new autologous material known as Alb-PRF which remains stable for a long time up to 4 months due to the presence of albumin gel which gives a chance for growth factors to be released for a long time to enhance repair and renewal of both soft and hard tissues at wounded sites[17].

Nowadays, the recommendation is oriented towards the use of 3-dimensional radiographic cone beam computed tomography (CBCT) to detect and illustrate any hard tissue defect in a 3D view, which is more accurate than a 2D radiograph[18].

This study aimed to demonstrate how Alb-PRF affects soft and hard tissue recovery following the eradication of jaw cysts using CBCT.

MATERIALS AND METHODS

A 1:1 allocation ratio was used in this randomized controlled clinical experiment. It was reported according to the CONSORT guidelines[19]. The Faculty of Dentistry's Institutional Review Board of the Research Ethics Committee at Alexandria University in Egypt approved this study. These study activities followed the Declaration of Helsinki for human subjects. Written informed consent was signed by each participant before the surgery. 80% research power and a 5% alpha error were assumed for estimating the sample size. The mean (SD) percent reduction in the 3-dimensional analysis of lesions after 6 months was calculated to be 99.61% (1.06%) after cyst eradication without filler materials[20] and 43.79% (39.84%) for the albumin platelet-rich fibrin group[21]. The minimum sample size was determined to be nine patients per group, but it was increased to ten patients per group based on the difference between the two independent means using the highest SD=39.84% to obtain sufficient power. Total sample size, as determined by Rosner's approach[22] and Brant's sample size calculator at the University of British Columbia[23], is equal to the number per group x number of groups = 10 x 2 = 20 patients.

Participants' eligibility

The participants were selected from the Oral and Maxillofacial Surgery Department of the Faculty of Dentistry, Alexandria University, from May 2022 to March 2023. Participants with a jaw cystic cavity volume more than $1cm^3$[5], those without a gender preference, those who committed to attending follow-up appointments for at least six months after surgery, and those whose conditions require surgery under local or general anesthesia were included in this study, while those who have previously received chemotherapy or radiation therapy, those who have a low platelet count, those who are on anticoagulant medication, those who were unable to attend follow-up appointments, or medically compromised participants were excluded[24,25].

Participants allocation

This study contained two groups

- The study group included 10 participants who had been managed with cyst eradication and had filled the cystic cavity with Alb-PRF.
- The control group included 10 participants who had been managed with cyst eradication and primary closure of the wound.

Materials

- A centrifuge machine.
- A warm water bath.
- Plastic centrifuge tubes.
- 2 syringes of 3 ml with a Luer lock.
- 3-way stopcock.

Methods

I. Preoperative assessment

Full personal data were obtained from the participants. The medical history, dental history, and chief complaint were recorded. Then the clinical examination was performed to determine the color of the mucosa, the presence of any fistula, and to assess any swelling or any alteration in bone contour. Aspiration examination was performed to determine the color and consistency of the cystic fluid. Cone beam computed tomography (CBCT) was performed preoperatively (T0) to evaluate the cystic cavity's extension and size.

II. Surgical procedure

Cyst enucleation

All the necessary laboratory investigations were performed preoperatively. The surgical procedure was performed under local or general anesthesia, depending on the size of the cystic lesion, its extension, and the condition of the participants. Using blade No. 15, a mucoperiosteal flap was performed and then reflected with a periosteal elevator to reveal the bone, which was removed to get access to the cystic cavity to be easily enucleated. The apices of the involved teeth were removed, and a retrograde filling was applied while the badly destructed teeth were extracted.

Albumin platelet-rich fibrin preparation[17,26]

10 ml of venous blood was withdrawn in a plastic centrifuge tube and centrifuged at 700 g for 8 min. **(Fig. 1)**. Then the pure plasma layer, without platelets, was withdrawn and heated in a warm water bath at 75°C for 10 min. to get albumin gel **(Fig. 2)**, which was mixed with the growth factors-rich layer of PRF using 2 syringes of 3 ml. with luer lock and 3-way stopcock to get albumin platelet-rich fibrin (Alb-PRF) **(Fig. 3)**.

The Alb-PRF was applied in the study group **(Fig. 4.A)**, while the control group was empty **(Fig. 5.A)**.

III. Post-operative phase

All the participants were instructed to apply ice packs postoperatively on the day of the surgery. A soft diet rich in proteins and high calories was recommended, while hot drinks were avoided for 2 weeks postoperatively. The postoperative medication was prescribed, where a broad-spectrum antibiotic, 125 mg clavulanic acid, and 875 mg amoxicillin (Clavimox 1 g: Pharco Co., Egypt) was prescribed every 12 hours for 5 days. Antiedematous, anti-inflammatory medication, chymotrypsin 300 E.A.U and trypsin 300 E.A.U (Alphintern tab.: Amoun Co., Egypt) were prescribed every 8 hours for 5 days. A diclofenac potassium, a nonsteroidal anti-inflammatory drug (Cataflam 50 mg: Novartis, Switzerland), was prescribed every 8 hours for 5 days. Chlorhexidine mouthwash (Hexitol 125 mg: The Arab Drug Co., Egypt) was prescribed every 12 hours for 1 week postoperatively.

IV. Follow-up phase

Clinical evaluation

Soft tissue healing was assessed on the 7th and 14th days using the healing Landry index described by Landry et al[27] **(Fig. 6)**.

Radiographic evaluation

Postoperative immediate CBCT (T1) and post-6-month CBCT (T2) were performed to detect and measure the 3-dimensional volumetric analysis of bone defect after cyst eradication, where T1 and T2 mean values were compared

Measuring the 3-dimensional volumetric analysis of the bone defect

Using CBCT and an On-demand 3D viewer, the bone cavity was cropped in different sections: sagittal, coronal, axial, and 3d sections. Using the segmentation tools, the bone cavity was segmented manually, and then the fine-tuning was changed to get the 3d bone cavity. After that, the 3d volumetric analysis was measured in cubic centimeters automatically **(Fig. 4. B, C, D)** and **(Fig. 5. B, C, D)**.

V. Data analysis through statistical methods

IBM SPSS software package version 20.0 (Armonk, NY: IBM Corp) was used to examine the data that was fed into the computer. Qualitative data were described using numbers and percentages. The Shapiro-Wilk test was used to verify the normality of distribution. Quantitative data were described using range (minimum and maximum), mean, and standard deviation. The significance of the obtained results was judged at the 5% level. Student t-tests and Paired t-tests were used for normally distributed quantitative variables to compare two study groups and two periods, respectively, while the Mann-Whitney test and Wilcoxon signed ranks test were used for abnormally distributed quantitative variables to compare two study groups and two periods, respectively.

Figure 1: A) A plastic centrifuge tube containing blood samples following centrifugation at 700 g for 8 minutes with the pure plasma layer on the top, followed by the growth factors-rich layer of PRF in the middle, followed by the red blood cells layer at the bottom. B) A centrifuge machine.

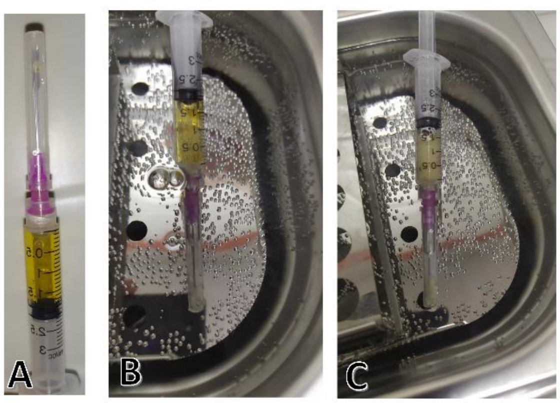

Figure 2: A) The pure plasma layer, which was withdrawn and, B) heated in a warm water bath at 75℃ for 10 minutes to get, C) the albumin gel.

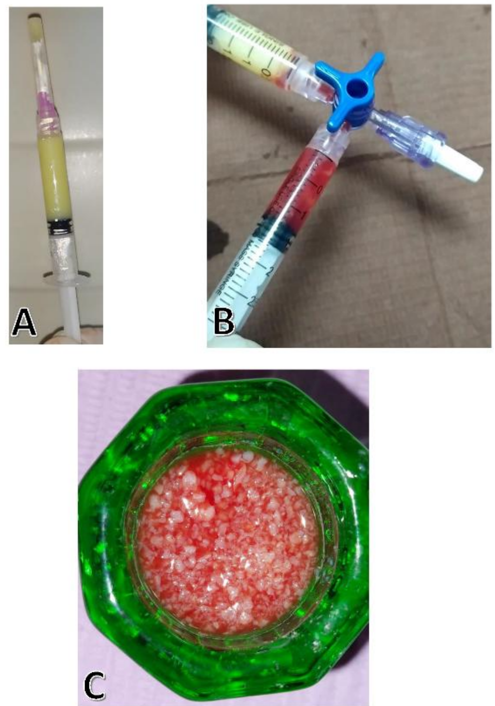

Figure 3: A) The albumin gel, B) The albumin gel was mixed with the growth factors-rich layer of PRF using 2 syringes of 3 ml with a Luer lock and a 3-way stopcock to get C) the albumin platelet-rich fibrin (Alb-PRF).

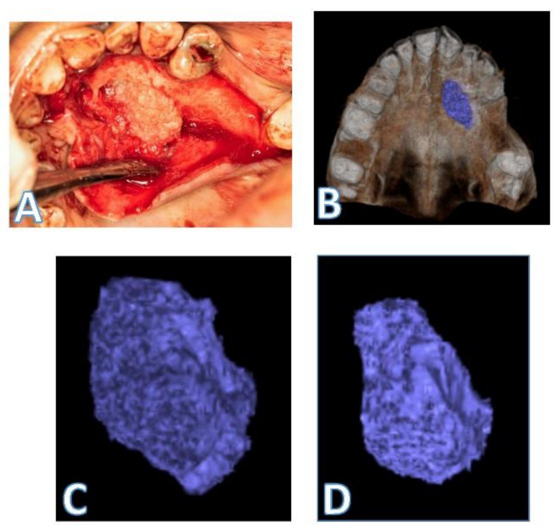

Figure 4: A) The Alb-PRF was applied after cyst eradication in the study group. B) 3d view of CBCT (T1) showing the bone defect from axial view postoperatively immediately in the study group. C) The bone defect from axial view after segmentation postoperatively, immediately compared to D) the segmented bone defect from axial view post-6 months (T2) in the study group.

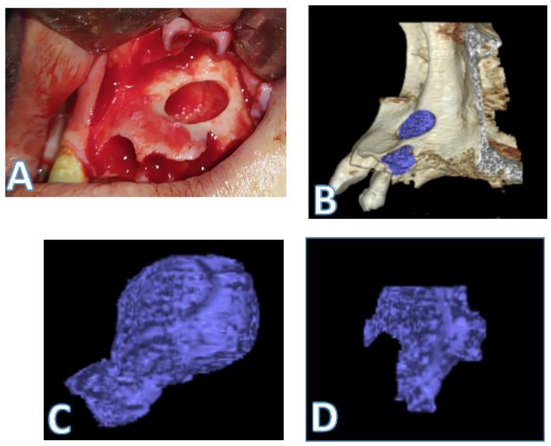

Figure 5: A) Cyst eradication and primary closure without filler materials in the control group. B) 3d view of CBCT (T1) showing the bone defect from the sagittal view postoperatively, immediately in the control group. C) The bone defect from the sagittal view after segmentation postoperatively, immediately compared to D) the segmented bone defect from the sagittal view post 6 months (T2) in the control group.

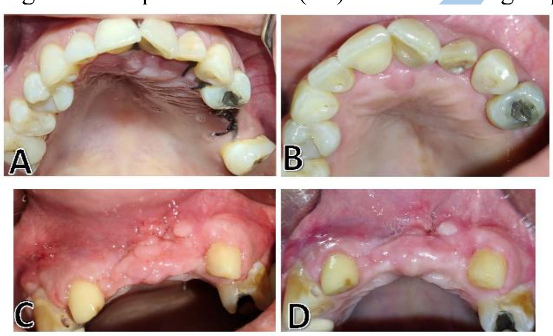

Figure 6: A) and B) Clinical photos showing the soft tissue healing after the 7th day and 14th day from the surgery, respectively, in the study group. C) and D) Clinical photos showing the soft tissue healing after the 7th and 14th days from the surgery, respectively, in the control group.

RESULTS

This study involved 20 participants, 9 males and 11 females. They were equally split up into two groups, the study group and the control group. The study group's mean age was 33.8 years, whereas the control group's was 30.3 years.

- The soft tissue healing

The healing Landry index[27] was used to perform soft tissue healing. In the study group, the healing Landry index ranged from 2 to 4, with a mean of 2.90 ± 0.74 on the 7th day, while it ranged from 3 to 5, with a mean of 4.10 ± 0.88 on the 14th day. The study group's soft tissue healing increased statistically significantly after 14 days ($P^* = 0.003$). **Table (1)**

In the control group, the healing Landry index ranged from 1 to 4, with a mean of 2.70 ± 0.82 on the 7th day, while it ranged from 2 to 5, with a mean of 3.70 ± 0.82 on the 14th day. The control group's soft tissue healing increased significantly after 14 days. ($P^* = 0.002$). **Table (1)**

When contrasting the study group with the control group regarding soft tissue healing after 7 and 14 days from the surgery day, the two groups did not differ significantly ($U = 45.0$, $P_1 = 0.739$) and ($U = 38.0$, $P_1 = 0.393$), respectively. **Table (1)**

Table (1): Comparison between the study and the control groups according to soft tissue healing on the 7th and 14th days using the healing Landry index.

Soft tissue healing (Landry Index)	The study group (n = 10)	The control group (n = 10)	U	P_1
7th Min.- Max. Mean ± SD	2.0 – 4.0 2.90 ± 0.74	1.0 – 4.0 2.70 ± 0.82	45.0	0.739
14th Min.- Max. Mean ± SD	3.0 – 5.0 4.10 ± 0.88	2.0 – 5.0 3.70 ± 0.82	38.0	0.393
P^*	0.003^*	0.002^*		

SD: **Standard deviation** U: **Mann Whitney test**

p_1: p-value for comparing between the study groups

p^*: p-value for **Wilcoxon signed ranks test** for comparing between the **7th** and **14th** days

*: Statistically significant at $p \le 0.05$

- The 3-dimensional volumetric analysis of the bone defect after cyst eradication

In the study group, the minimum value of 3-dimensional volumetric analysis of bone defect was 1.1 cc, while the maximum value was 2.7 cc, with a mean of 2.1 ± 0.7 cc immediately postoperatively. However, after 6 months, the minimum value of 3-dimensional volumetric analysis of bone defect was 0.4 cc, while the maximum value was 1.9 cc, with a mean of 1.0 ± 0.5 cc. A statistically meaningful decrease was seen in the 3-dimensional volumetric analysis of bone defect after 6 months in the study group ($P^* < 0.001$). **Table (2)**

Table (2): Comparison between the study and the control groups according to 3-dimensional volumetric analysis of bone defect postoperative immediate and post-6 months.

3-dimensional volumetric analysis (cc)	The study group (n = 10)	The control group (n =10)	t	P_1
Postoperative immediate Mean ± **SD**	2.1 ± 0.7	1.6 ± 0.5	1.7	0.1
Post 6 months Mean ± **SD**	1.0 ± 0.5	0.9 ± 0.6	0.5	0.6
P*	< 0.001*	< 0.001*		
Decrease Mean ± **SD**	1.0 ± 0.4	0.8 ± 0.3	1.601	0.130

SD: **Standard deviation** t: **Student t-test**

p_1: p-value for comparing between the study groups

p^*: p-value for **Paired t-test** for comparing between **Postoperative immediate** and **Post 6 months**

*: Statistically significant at $p \leq 0.05$

In the control group, the minimum value of 3-dimensional volumetric analysis of bone defect was 1.1 cc, while the maximum value was 2.5 cc, with a mean of 1.6 ± 0.5 cc immediately postoperatively. However, after 6 months, the minimum value of 3-dimensional volumetric analysis of bone defect was 0.2 cc, while the maximum value was 2.2 cc, with a mean of 0.9 ± 0.6 cc. A statistically meaningful decrease was seen in the 3-dimensional volumetric analysis of bone defect after 6 months in the control group ($P^* < 0.001$). **Table (2)**

According to the change in the 3-dimensional volumetric analysis of bone defect after 6 months in both groups, the minimum value of difference was 0.5 cc, while the maximum value was 1.6 cc, with a mean difference of 1.01 ± 0.43 cc in the study group. The minimum value of the difference was 0.4 cc, while the maximum value was 1.3 cc, with a mean difference of 0.75 ± 0.28 cc in the control group. After six months, there was no discernible statistically significant difference between the two groups, but the study group's 3-dimensional volumetric analysis of bone defect changed more than the control group's. ($t = 1.601$, $P_1 = 0.130$). **Table (2)**

DISCUSSION

Both soft and hard tissue healing after cyst eradication is a critical issue to restore function and aesthetics to the tissues. Whether spontaneous or assisted by adjunctive material, wound healing is a complex procedure involving successive events on cellular and molecular levels. These events are categorized into 4 stages: platelet plug and blood clot formation, release of inflammatory mediators, proliferation, and tissue remodeling[7,8].

This study aimed to demonstrate how Alb-PRF affects soft and hard tissue recovery following the eradication of jaw cysts using CBCT.

In this study, the healing Landry index, as defined by Landry et al., was used to evaluate soft tissue healing[27]. The mean healing score was 2.90 ± 0.74 on the 7th day while it was 4.10 ± 0.88 on the 14th day in the study group, which shows that the healing of soft tissues has improved statistically significantly after 14 days from the surgery day when using Alb-PRF ($P^* = 0.003$). Alb-PRF has a slow degradation rate due to the heat treatment of the pure plasma layer and the production of albumin gel. Alb-PRF can release several growth factors, WBCs, cytokines, and inflammatory mediators that participate in wound healing to restore soft and hard tissues[17,26]. A research by Javid et al. compared L-PRF to Alb-PRF after tooth extraction and revealed positive effects for Alb-PRF on the closure of wounds and regeneration of both soft and hard tissues[28].

On the other hand in this study, the mean healing score was 2.70 ± 0.82 on the 7th day while it was 3.70 ± 0.82 on the 14th day in the control group, which shows that, 14 days following the surgery day, spontaneous soft tissue healing has improved statistically significantly ($P^* = 0.002$). However, in this study, statistically, the study and the control group did not differ in any way concerning soft tissue recovery between 7 and 14 days following the day of surgery ($U = 45.0$, P_1 0.739), and ($U = 38.0$, $P_1 = 0.393$) respectively. Similarly, Ritto et al. used the modified Landry et al.'s healing index for assessing soft tissue healing after the lower third molar had been extracted and revealed no statistically significant distinction between the L-PRF and the control group ($P > 0.05$)[29]. Al Hamed et al. revealed similar conclusions to this study, whereas the PRF and the control group did not differ statistically significantly regarding soft tissue healing, according to their findings, where the mean healing index score was 4.52 ± 0.74 in the PRF group while it was 4.20 ± 0.95 in the control group ($P = 0.187$)[30]. On the contrary, a study by Afat et al. demonstrated how one of the platelet concentrates affected the repair of soft tissue following the extraction of the mandibular third tooth. They revealed a statistically significant impact of L-PRF on the healing of mucosa on the 7th and 14th days[31]. Similarly, Singh et al. demonstrated that the PRF and the control groups differed statistically significantly in terms of soft tissue healing after tooth extraction using the healing index described by Landry et al., Turnbell, and Howley, whereas the mean healing index value on the 1st day after the surgery was 3.4 and 2.9 in the PRF and the control group respectively. However, on the 3rd day, the mean healing index was 4 and 3.2 in the PRF and the control group, respectively, while it was 4.8 and 4.3 on the 7th day in the PRF and the control group, respectively[32]. Daugela et al. used a modified wound healing index on days 1, 3, 7, and 14 postoperative to evaluate soft tissue recovery following the removal of the lower third molar, whereas the L-PRF group's wound healing was superior to that of the control group, demonstrating a difference between the two groups that is statistically significant[33].

In this study, CBCT was used to illustrate the healing of hard tissue, where a 3-dimensional volumetric analysis of the bone defect after cyst eradication could be viewed. The Orthopantomogram (OPG), a 2-dimensional view, was used in previous studies to demonstrate the volume of osseous lesions[34,35], and this was not accurate, as volume should be viewed and measured in 3 dimensions. Accordingly, Abdel-Ghany H. and associates carried out a study and used CBCT to measure the volume of the cystic lesion in 3D[36]. Similarly, Schloss et al showed that CBCT is better than 2D radiograph in demonstrating the volume of osseous lesions[18].

In this study, the study group's hard tissue healing improved statistically significantly after six months ($P^* < 0.001$), whereas the mean of 3-dimensional volumetric analysis of bone defect postoperatively immediately was 2.1 ± 0.7, while it was 1.03 ± 0.50 after 6 months. That illustrates how Alb-PRF affects the repair of hard tissues, where the long-term growth factor release, the presence of essential cytokines and inflammatory mediators, the presence of white blood cells, and the slow degradation rate of Alb-PRF participate in wound healing[17,26]. In this regard, Javid et al. showed favorable effects of the Alb-PRF on soft and hard tissue healing after the removal of the lower third molar[28]. Similarly, Salman Shams et al. reported using the PRP gel as a filler material after cyst enucleation when they revealed that the mean bone fill after 6 months was 95.95%[37].

Conversely, the control group experienced a statistically significant improvement in spontaneous hard tissue healing after 6 months ($P^* < 0.001$), where the mean of 3-dimensional volumetric analysis of bone defect postoperatively immediately was 1.6 ± 0.5, while it was 0.9 ± 0.6 after 6 months. Similarly, Vitale et at. evaluated the spontaneous healing of bone after mandibular cyst enucleation using a CT scan and reported a 90% filling of the residual cavity with the regenerated bone after 6 months, where the mean volume of the cystic cavity was 11.82 cc preoperatively, while it was 1.49 cc after 6 months[20].

In this study, no change that is statistically significant was seen between the study and the control group in hard tissue healing ($t = 1.601$, $P_1 = 0.130$). This illustrates the effect of natural blood clots and primary closure in wound healing spontaneously. The presence of blood clots, intact bone plates to preserve it, periosteum, and endosteum are essential in the spontaneous healing of wounds. Upon cyst enucleation, platelets gather, forming platelet plugs and blood clots which act as scaffolds for the accumulation of inflammatory cells, which will release, besides platelets, essential growth factors participating in wound healing. These growth factors will bind to their receptors found on cell membranes, to activate signals which orient genes functioning in wound healing[38]. In the view of this study, no statistically significant distinction was found between CGF, PRF, and spontaneous blood clots in hard tissue healing after 6 months according to You et al.[39]. However, Singh et al. revealed that the PRF group's mean bone density was greater than the control group's following tooth extraction using grayscale in a follow-up session after 3 months. Still, the limitation of this study was that they used intraoral periapical (IOPA) radiographs to evaluate the bone density[32]. Ritto et al. conducted a study to evaluate the effect of L-PRF on hard tissue healing following the extraction of the lower third molar using CBCT and the ITK-SNAP software. They found that the L-PRF and the control sides differed significantly in bone density after 3 months, where the mean bone density in the L-PRF side exceeded that of the control group ($P = 0.007$)[29].

The brief follow-up period and the tiny sample size are considered limitations for this study, thus, further clinical trials with a large number of participants and a prolonged follow-up are advised.

CONCLUSION

According to this study, the soft and hard tissues healed properly using either Alb-PRF or natural blood clots after jaw cyst eradication, where wound healing primarily depends on the release of growth factors, essential cytokines, and inflammatory mediators. Thus, the autologous bio-filler material, Alb-PRF, or the natural blood clot, will enhance the regeneration and healing of soft and hard tissues.

Conflict of interest

The authors declare that they have no conflict of interest.

Funding statement

The authors received no specific funding for this work.

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