STUDY OF THE EFFECT OF THE COMBINATION OF PLATELET-RICH FIBRIN (PRF) AND ALLOGENOUS BONE GRAFT AROUND IMMEDIATE IMPLANTS

Shaimaa A. Zaki[1] *BDS,* Sherif S. Mohamed[2] *PhD,* Ahmed M. Hommos[3] *PhD,* Adham A. El Ashwah[4] *PhD*

ABSTRACT

INTRODUCTION: Following the immediate implant placement, there is a gap called jumping space which increases the risk of implant failure.

OBJECTIVES: The aim of the study was to evaluate the clinical and radiographic efficiency of platelet-rich fibrin membrane (PRF) combined with bone graft surrounding immediate implants in fresh extraction sockets.

MATERIALS AND METHODS: A clinical and radiographic study was carried out on ten fresh extraction sockets with age range from 20 to 50 years. Sockets were occupied by immediate endosseous implant and grafted with allogenous bone graft and PRF. After placement all implants were evaluated clinically after 6 months (modified sulcus bleeding index, probing pocket depth and degree of mobility) and radiographically to evaluate marginal bone loss.

RESULTS: There was less pain, edema, bleeding and probing depth in the study group than in the control group but the difference among them was not statistically significant ($P > 0.05$). There was significantly more bone density and less marginal bone loss in the study group than in the control group on the sixth postoperative month ($P < 0.05$).

CONCLUSIONS: It is clear that PRF is biocompatible and can improve both soft tissue healing and bone regeneration after immediate implant placement.

KEYWORDS: Immediate implant, PRF, bone graft.

1- B.D.S. Faculty of Dentistry Alexandria University
2- Professor of Oral and Maxillofacial Surgery, Faculty of Dentistry Alexandria University
3- Professor of Periodontology, Oral Medicine, Diagnosis and Radiology, Faculty of Dentistry Alexandria University
4- Assistant Professor of Oral and Maxillofacial Surgery, Faculty of Dentistry Alexandria University

INTRODUCTION

Dentists are constantly seeking improvements in surgical and prosthetic techniques to reduce treatment time in dental implant therapy (1).

The current implant surfaces have improved bone-implant unions and accelerate bone healing mainly by reducing the osseointegration period and accelerating prosthetic rehabilitation (1).

Tooth loss always leads to atrophic changes of the alveolar ridge and the key processes of postextraction bone modeling and remodeling have been well documented in both animal and human studies (2). Human reentry studies showed horizontal bone loss of 29 to 63% and vertical bone loss of 11 to 22% during the first 6 months after tooth removal (3). This three-dimensional resorption process at the postextraction sites may result in significantly narrowed ridges with reduced vertical height and lingual/palatal shifting of their long axes, rendering the subsequent correct placement of endosseous implants difficult or even impossible (4).

Schropp et al. (5) analysed postextraction alveolar bone changes using standardized radiographs and study casts. The results showed that most alveolar bone changes occurred in the first 12 months following extraction, with a 50% reduction in the alveolar ridge thickness (5–7 mm). In addition, two-thirds of this bone loss occurred within the first 3 months after extraction.

Immediate implants were first described by Schulte and Heimke in 1976 (6) in a clinical report, followed by histologic studies that confirmed the procedure as successful (7). They are designed to prevent bone resorption following extraction. With this method, the ridge dimension and height are maintained and a number of surgical procedures omitted, shortening the healing period (8).

One problem that remains unresolved with this procedure, however, is that, due to the discrepancy in size and form between the extraction socket and the implant, there is usually a space left in the area surrounding the coronal portion of the implant, called "jumping distance (9), however, the diastasis observed between bone and implant after dental extraction may influence osseointegration. So, autogenous bone grafts and/or biomaterials have been used in those gaps to correct bone defects and provide appropriate stability (10).

Bone grafting to augment skeletal healing has become one of the most common surgical techniques. However, the morbidity and limited availability associated with auto grafts, as well as the potential for disease transmission, immunogenic response and variable quality associated with allograft have led to wide variety of alternative materials. Characteristics of an ideal bone grafts substitute consist of a product that induces bone formation and is nontoxic, non-carcinogenetic, readily available, and easy to use (11).

Development of the bioactive surgical additives is one of the great challenges of clinical research which has been used to regulate inflammation and increase the speed of healing process (12).

A wide range of intra- and extraarticular events and various signaling proteins mediate and regulate the healing process of both hard and soft tissues, respectively. But understanding this entire process is still incomplete; however, it is known that platelets play a crucial role not

only in hemostasis, but also in the wound healing process (13).

In 1974, platelets regenerative potentiality was introduced, and Ross et al. (14) were the first to describe a growth factor from platelets. It has been shown in several studies that bone regenerative procedures may be enhanced by the addition of specific growth factors (15).

PRF represents a new revolutionary step in the platelet gel therapeutic concept (12). Unlike other platelet concentrates, this technique does not require any gelifying agent, but no more than centrifugation of the natural blood without additives (16). Choukroun et al., (17) developed the PRF in 2001 in France and the production protocol of PRF attempted to accumulate platelets and released cytokines in a fibrin clot.

This biomaterial presents a specific biology which offers several advantages including promoting wound healing, bone growth and maturation, graft stabilization, wound sealing and hemostasis, and improving the handling properties of graft materials. PRF can also be used as a membrane. Clinical trials suggest that the combination of bone grafts and growth factors contained in PRF may be suitable to enhance bone density (18).

This study was to evaluate if platelet rich fibrin has an effect on healing of hard and soft tissues of peri-implant defects in cases of immediate implant placement.

MATERIALS AND METHODS

I- Study design

This study was a clinical trial on 10 patients selected from the out-patient clinic of Oral and Maxillofacial Surgery Department, Faculty of Dentistry, Alexandria University.

The patients were randomly allocated:

Group A: (Study group)

Five patients in need for extraction of single rooted tooth (width of the socket at the coronal third > 2mm), underwent immediate implant placement with PRF combined with allogenic bone graft.

Group B: (Control group)

Five patients in need for extraction of single rooted tooth (width of the socket at the coronal third > 2mm); underwent immediate implant placement with bone graft. Without PRF.

The participating patients in this study were chosen according to the following criteria:

II- Inclusion criteria

Presence of non-restorable single rooted tooth (maxillary or mandibular) due to trauma, caries, root resorption, root fracture, endodontic or periodontal failure, age ranging from 20-50 years, sufficient bone volume, good oral hygiene, nonsmokers and the remaining space between the socket and the fixture equal to or more than 2mm at the coronal third of the socket.

III- Exclusion criteria

Extreme bone atrophy, active infection {peridontitis or mucosal infection}, patients on chemotherapy or radiotherapy, alcohol or drug abuse, patients who have systemic disorders {uncontrolled diabetes mellitus, autoimmune disease, …etc}, pregnant patients, patients with bone diseases and presence of periapical pathology affecting the neighboring teeth.

IV- Informed consent

Informed consents were taken from all patients after explaining all the procedures to the patients including all benefits and side effects in simple and easy way, also the patients have the right for withdrawal at any time.

Materials

1- The Implant system

Conventional, two pieces, screw-type titanium dental implants (Dentis S-clean, DENTIS, Daegu, Korea) were used.

Implant surface treatment: resorbable blasting media (blasting with Beta Tricalcium phosphate (BTCP), Hydroxy Apatite (HA) and Calcium pyrpophosphate), then all these material subsequently removed using a cleaning process.

2- Bone graft material (Genesis synthetic bone graft substitute, Dio implant, Busan, Korea).

Genesis synthetic bone graft substitute.

3- Armementerium of the PRF preparation

i- Centrifuge device

A table centrifuge (Centrifuge Model 800, Xiangshui FADA medical apparatus factory, China) was used to separate out blood component.

ii- Glass centrifuge tubes (The laboratory test tubes available in the market no specific trademark).

iii- Set of blood sample collection: Tourniquet, sterile plastic syringe 10 CC.

Platelet-Rich Fibrin (PRF)

Platelet-rich fibrin (PRF) was prepared by centrifugation of 10 ml of whole blood of the patient in a table centrifuge at 3000 revolutions per minute (rpm) for 10 minutes (19). The resultant product consisted of the following three layers:

- Top most layer consisting of a cellular platelet poor plasma (PPP).
- PRF clot in the middle.
- RBCs at the bottom.

A fibrin clot was then obtained in the middle of the tube, just between the red corpuscles at the bottom and a cellular plasma at the top. PRF was then separated from PPP and RBC layer, ready for application in the peri-implant defect.

Methods

A- Preoperative phase

All patients were evaluated by proper history taking and through clinical and radiographical examination:

Preoperative preparation

Phase I therapy was carried out for all patients including scaling and gingival treatment.

i- Clinical examination of the remaining root or tooth in need for extraction to ensure absence of infection and presence of four intact socket walls (Figure 1).

ii- Radiographic examination of tooth indicated for extraction by using digital periapical radiograph to evaluate the recipient site (Figure 2).

The standardized periapical radiographs will be taken by the Rinn- XCP (Rinn corp. Elgin, IL, USA) film holder with a personalized bite registration record, made from putty rubber base impression material, for extension cone paralleling technique.

All exposures were done with the same dental x-ray machine at the same kilovoltage, milliampere, exposure time and the same periapical X-ray sensor.

B- Surgical phase

Oral cavity was prepared by scrubbing the surgical site using Betadine: Povidone – iodine, 7.5% (0.75% available iodine) the Nile Comp. for Pharmaceuticals and Chemical Industries, Alexandria, Egypt, nerve block or infiltration anaesthesia was administrated Mepivacaine 31.36 mg/1.8 ml (Mepecain-L, Alexandria Co. for pharmaceuticals & Chemical Industries, Alexandria, Egypt) or both.

Atraumatic extraction of the tooth or remaining root using periotome, then sequential drilling with copious irrigation was carried out till the desired dimensions (2-3 mm apical to the apical part of the socket to get proper primary stability).

Figure 1: This picture shows case I preoperatively.

Figure 2: Preoperative X-ray shows horizontal tooth fracture.

The sealed sterile implant package was opened and the implant was guided into its position with light stable finger pressure. Ratchet wrench was used to complete installation of implant till bone level. The smartpeg was attached and screwed to the implant to determine the value of primary stability by using Resonance Frequency Analysis Device (Osstell ISQ, Osstell, Gothenburg, Sweden) (Figure 3).

Osstell was used to measure the primary stability at two different sites, buccolingually/or buccopalatally and mesiodistally, the smartpeg then was detached and finally, the cover screw was attached to the implant top by the aid of its driver.

A sample of 10 C.C of venous blood was withdrawn from the patient (in study group) and centrifuged without delay at 3000 rpm (round per minute) for 10 minutes.

Bone graft material (betatricalcium phosphate) mixed with PRF was applied and condensed around the dental implant filling the gap between the fixture and the walls of the socket (in the study group) but bone graft alone was applied and condensed around the dental implant filling the gap between the fixture and the walls of the socket (in the control group). Tension free Closure of the wound was achieved using 3/0 black silk sutures.

Figure 3: A: Osstell reading labiopalatally, **B:** Osstell reading mesiodistally.

Prosthetic phase

After 6 months' porcelain fused to metal crown restorations were placed after radiographic evaluation and determining their final stability (Figures 4 - 6).

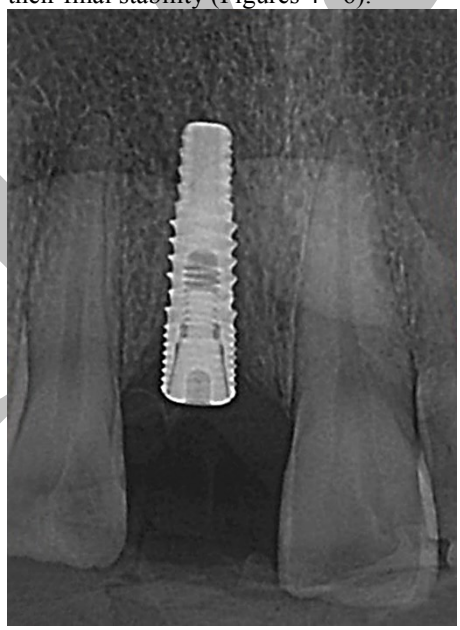

Figure 4: 6 months' postoperative x-ray.

C- Postoperative phase

I- Postoperative instructions

i- No pressure on the surgical site.
ii- Cold fomentation for the first 24 hours.
iii- Mouth wash on the next day.
iv- Avoid chewing solid food.
v- Oral hygiene recommendation.
vi- Sutures were removed one week after surgery.

II- Postoperative medications

All patients received:

i- Antibiotic tablets for 7 days, 1 tablet every 12 hours {Amoxicillin 875+ clavulenic acid 125} (Augmentin 1 g, GlaxoSmithkline, Hungary).

ii-Analgesic and anti-inflammatory (50 mg diclofenac potassium): (Cataflam, Novartis Pharma, Cairo, Egypt) non-steroidal anti-inflammatory drugs for 5 days, 1 tablet every 12 hours.

iii- Mouth wash, chlorohexidine HCL (0.12%) (Hexitol, The Arab Drug Company, Cairo, A.R.E).

III- Postoperative follow up

Clinical evaluation

Postoperative healing

1- Wound was inspected clinically on the second day.

2- Healing was evaluated clinically on the second day, after 45 days and after 3 months for soft tissue dehiscence, bleeding, inflammation and infection.

Postoperative pain, swelling or infection

Pain was evaluated on the second day, after 45 days and after 3 months through Visual Analougue Scale (20) as follows:

0= No pain.

1= Mild pain: It is easily tolerated.

2= Moderate pain: It is causing discomfort but bearable.

3= Severe pain: It is causing discomfort, hardly tolerated and unbearable.

The presence of pain, tenderness, infection or swelling may indicate the presence of peri-implant disease and possible accelerated bone loss.

Postoperative edema

Edema was evaluated by inspection.

Each patient was evaluated clinically and radiographically:

a) Clinical evaluation

1- Presence of pain, tenderness and discomfort.

2- Gingival condition around the implant for presence of any inflammation.

Modified sulcus bleeding index (MSBI)

Clinical signs and symptoms of inflammation of peri-implant mucosa was graded using criteria of MSBI by Mombelli et al (21).

The tissues surrounding each implant was divided in to 2 gingival scoring units (mesial and distal) and a periodontal probe was used to assess the bleeding tissues after 3 and 6 months.

The following scores demonstrates the criteria for recording modified sulcus bleeding index:

Score Clinical interpretation

1. No bleeding.
2. Isolated bleeding spot.
3. Blood forms a red line mucosal margin.
4. Heavy or profuse bleeding.

3- Peri-implant probing depth

It refers to the distance from the gingival margin to the bottom of the sulcus. Probing in the peri-implant sulcus will be made with light force to avoid undue tissue damage and over extension in to the healthy tissues.

4- Implant stability

a) Stability of all implants was determined at base line and 6 months later using osstell.

b) Radiographic evaluation (Figure 5 and 6)

Periapical film also was used immediately after implant placement and after 3 and 6 months to evaluate bone density to evaluate:

1- Bony density and osseointegration around implant.

2- Marginal bone level.

3- Periimplantitis if present.

1) Exposure technique of radiographs

The digital periapical radiographs were taken by the Rinn XCP film holder with a personalized bite registration record, made from putty rubber base impression material, for extension cone paralleling technique.

The film holder consisted of a bite block, directing rod and a guide ring.

The bite block contains a slot into which the X-ray sensor was inserted.

To ensure accurate repositioning of the film during each radiograph, a putty rubber base impression material was folded around the bite block. And then a bite registration was obtained for each side in closed mouth position so the teeth indentations were used for further orientation of the film holder.

The guide ring was slided close to the patient's face, and the X-ray tube was positioned flushing with the ring and the exposure was done.

All exposures were done with a dental X-ray machine (MINRAY™, Soredex, Tuusula, Finland) at 70Kv and 10mA with similar exposure time (0.02-3.2 seconds), standardized periapical X-ray sensor (DIGORA™ Toto, Soredex, Tuusula, Finland) and the same printer (Kodak, (dry view) 5800 laser imager, New York, U.S.A).

The digital radiographic imaging was analyzed with the aid of x-ray analysis software: Image J software (Image J 1.31; public image processing domain software, Bethesda, Maryland, USA) from the National Institute of Health (USA) (22).

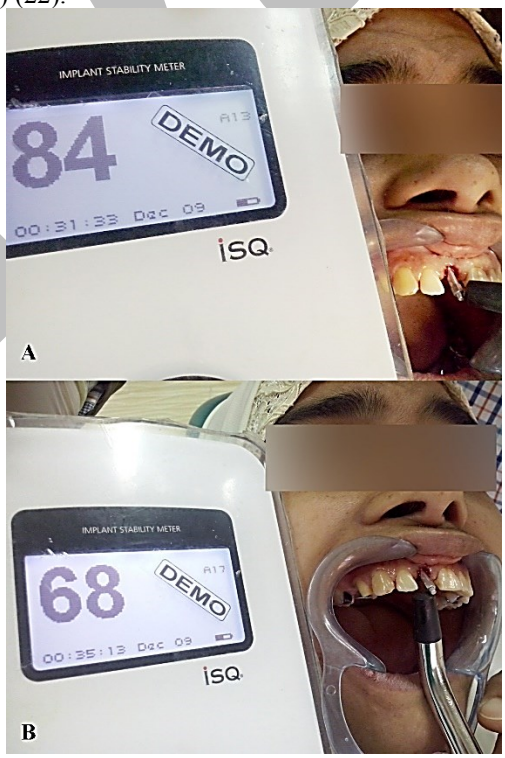

Figure 5: A: Osstell reading mesiodistally after 6 months, **B:** Osstell reading labiopalatally after 6 months.

Image analysis

I- Measurements of the bone density around the implant

Image J software was used to evaluate radiographic bone density mesial and distal to each implant.

II- Assessment of marginal bone level around the implants

Marginal bone level (MBL) was defined as the distance between a reference point (the implant shoulder) and the first marginal bone-to-implant contact level (23).

Marginal bone level was determined on both mesial and distal implant surfaces using the linear measurement system supplied by the specially designed Image J software.

Figure 6: A: Abutment in place, **B:** Porcelain crown restoration.

RESULTS

I-Clinical follow up

A. Post-operative pain

There was less pain in the study group than in the control group: the mean post-operative pain scores for the study group on the second day was 1.0 ± 0.0 while the mean post-operative pain scores for the control group on the second day was 1.40 ± 0.55. The difference was not statistically significant on the second day. After 45 days and after 3 months (p=0.134, 1.000, 1.000 respectively).

B. Post-operative edema

There was less edema in the study group than in the control group by inspection.

II-Clinical evaluation

A. Modified sulcus bleeding index (MSBI)

There was less bleeding in the study group than in the control group. On the sixth month, the mean MSBI scores for the study group was 1.0±0.0. While the mean MSBI scores for the control group was 1.40 ± 0.89. The difference was not statistically significant (p=0.317).

B. Peri-implant probing depth

There was less probing depth in the study group than in the control group. On the sixth month, the mean Peri-implant probing depth scores for the study group was 0.98±0.24. While the mean Peri-implant probing depth scores for the control group was 1.35±0.42.

The difference was not statistically significant (p=0.120).

III-Radiographic evaluation

A. Bone density

Table (1) shows the comparison among the study and control groups as regards bone density.

Starting from the first to the sixth month post operatively, there was slightly denser bone in the study group than in the control group. The difference among the two groups was not statistically significant immediate post-operative and after 3 months (p=0.822, 0.987 respectively), but it was statistically significant after 6 months (p=0.035*). After 6 months the mean bone density scores was 120.62 ± 5.99 for the study group while the mean bone density scores were 98.38±18.73 for control group.

Table 1: Comparison between the two studied groups according to bone density.

	BD		
	Immediate Postoperative	**3 months**	**6 months**
Study			
Min. – Max.	71.81 – 115.16	74.42 – 125.11	115.02 – 128.0
Mean ± SD.	83.87 ± 17.69	92.11 ± 19.33	120.62 ± 5.99
Median	77.20	88.34	119.19
Sig. bet. periods	p_1=0.012*, p_2= 0.004*, p_3= 0.014*		
Control			
Min. – Max.	69.44 – 115.61	74.26 – 121.98	80.0 – 127.58
Mean ± SD.	81.11 ± 19.78	91.90 ± 18.62	98.38 ± 18.73
Median	70.35	88.62	99.19
Sig. bet. periods	p_1= 0.013*, p_2= 0.007*, p_3= 0.004*		
t	0.232	0.017	2.528*
p	0.822	0.987	0.035*

t: Student t-test

Sig. bet. periods were done using Post Hoc Test (LSD) for ANOVA with repeated measures

p_1: p value for comparing between Immediate Postoperative and 3 months

p_2: p value for comparing between Immediate Postoperative and 6 months

p_3: p value for comparing between 3months and 6 months

*: Statistically significant at $p \leq 0.05$

B. Marginal bone level

Table (2) shows the comparison among the study and control groups as regards marginal bone level which has been measured from a reference point (the implant shoulder) and the first marginal bone-to-implant contact level.

There was less marginal bone loss in the study group than in the control group, the difference was statistically significant after 3 and 6 months (p=0.007* and 0.001* respectively) After 6 months the mean marginal bone level scores was 0.35 ± 0.05 for the study group while the mean marginal bone level scores were 0.52±0.05 for the control group.

IV- Implant stability (ISQ)

There was higher osstell reading score in the study group than in the control group, the difference was not statistically significant at the day of surgery (p=0.721), but it was statistically significant after 6 months (p=0.032*). After 6 months the mean osstell reading scores was 79.0±2.65 for the study group while the mean osstell reading scores after 6 months was 71.40±6.02 for the control group.

DISCUSSION

This study was conducted on ten patients selected from the Outpatient Clinic of the Oral and Maxillofacial Surgery Department, Faculty of Dentistry, Alexandria University. Each

one had a single rooted tooth indicated for extraction. Beta-tricalcium phosphate (β-TCP), is a synthetic alloplastic material was placed around the immediately placed dental implants.

Table 2: Comparison between the two studied groups according to marginal bone.

	MB		
	Immediate Postoperative	**3 months**	**6 months**
Study			
Min. – Max.	0.0 – 0.0	0.12 – 0.17	0.30 – 0.42
Mean ± SD.	0.0 ± 0.0	0.14 ± 0.02	0.35 ± 0.05
Median	0.0	0.15	0.37
Sig. bet. periods	p_1 <0.001*, p_2 <0.001*, p_3= 0.001*		
Control			
Min. – Max.	0.0 – 0.0	0.18 – 0.27	0.44 – 0.58
Mean ± SD.	0.0 ± 0.0	0.23 ± 0.04	0.52 ± 0.05
Median	0.0	0.25	0.51
Sig. bet. periods	p_1 <0.001*, p_2 <0.001*, p_3 <0.001*		
t	-	4.107*	5.103*
p	-	0.007*	0.001*

t: Student t-test
Sig. bet. periods were done using Post Hoc Test (LSD) for ANOVA with repeated measures
p_1: p value for comparing between Immediate Postoperative and 3 months
p_2: p value for comparing between Immediate Postoperative and 6 months
p_3: p value for comparing between 3months and 6 months
*: Statistically significant at $p \leq 0.05$

Akimoto et al. (24) demonstrated that the diameter of the bone defect influences the percentage of bone/implant contact, which hints to the potential usefulness of inserting biomaterial for filling of those defects.

In the year 1983, Eriksson and Albrektsson (25) conducted an experiment on the rabbit tibia to evaluate the effects of heat production on bone regeneration. They found that heating the implants in the rabbit tibia to a temperature of 50ºC for 1 min was enough to cause 30% of the bone to be resorbed.

Various studies have been conducted on PRF and its clinical application in various disciplines of dentistry. PRF is used for continuity defects, sinus lift augmentation, horizontal and vertical ridge augmentations, ridge preservation grafting, periodontal defects, cyst enucleation, healing of extraction wounds, endodontic surgeries and to treat gingival recession (26).

All these studies showed that PRF is a healing biomaterial for both soft and hard tissue because of the presence of various growth factors (26).

This study was conducted to evaluate the effect of PRF on peri-implant hard and soft tissues in cases of immediately placed dental implants.

The PRF was freshly prepared and used without delay to exert maximum beneficial effect and glass tube was used to prepare PRF, as silica behaves as clot activator and necessary to start the polymerization process. The same centrifuge machine was used throughout the study for the preparation of PRF. In this study intra-oral digital periapical radiographs were used for the assessment of bone level were obtained by using paralleling technique to minimize distortion and standardized by using occlusal putty jig.

Regarding the post-operative pain, the present study showed less pain in the study group than in the control group on the second postoperative day, but the difference was not significant.

This finding is in agreement with Krumer N et al (2015) (27), who conducted a study to evaluate the treatment outcome after impacted third molar surgery with the use of PRF. They concluded that the application of PRF lessened the severity of immediate post-operative sequelae.

Minimal post-operative edema was observed in both study and control groups on the second post-operative day, and this finding may be due to the flapless technique used.

When soft tissue flaps are reflected for implant placement, the blood supply from the soft tissue to the bone (supraperiosteal blood supply) is also removed, leaving only poorly vascularized cortical bone. The preservation of bone vascularization through use of the flapless (FL) technique may help to optimize bone regeneration around implants, while full-thickness flaps (FTs) demonstrate high bone resorption after surgery (28).

Moreover, this approach was selected in order to minimize patient morbidity, surgical time, and cost, but mostly in an attempt not to displace the mucogingival junction.

The argument of implementing flapless techniques when possible is also supported by the conclusions of a systematic review by Wang and Lang (29).

In the year 2014, Kulkarni et al. (30) stated that PRF is an excellent material for enhancing wound healing. The use of PRF dressings may be a simple and effective method of reducing the morbidity associated with donor sites of autogenous free gingival grafts. Yelamali and Saikrishna (31) found better and faster wound healing and bone formation with PRF, and also he stated preparation of PRF is simpler than PRP.

On the seventh post-operative day, sutures were removed, good gingival healing was found, no signs of infection or inflammation and no wound dehiscence were found in all patients. All patients continued the follow up period without signs of infection, gingivitis, or peri-implantitis.

As regards peri-implant probing depth, there was a decrease in probing depth in study group than in control group. This in agreement with Chang et al., (32) who stated that PRF releases growth factors which promote periodontal regeneration.

Regarding to the bone density and marginal bone level from the first to the sixth post-operative months, there was an increase in bone density in both study and control groups, but this increase in bone density was greater in the study group than in the control group on the sixth post-operative month. The difference between the two groups was statistically significant.

Also, there was decrease in marginal bone loss in the study group than in control group on the sixth post-operative month. This is in agreement with Choukroun et al (26) who evaluated the potential of PRF in combination with freeze-dried bone allograft (FDBA) to enhance bone regeneration in human sinus floor elevation. Nine sinus floor augmentations were performed. In 6 sites, PRF was added to FDBA particles (test group), and in 3 sites FDBA without PRF was used (control group). Four months later for the test group and 8 months later for the control group, bone specimens were harvested from the augmented region during the implant insertion procedure. The histological results revealed that bone maturation in PRF group at 4

months of healing was similar to that in the control group at 8 months. Thus they concluded that sinus floor augmentation with FDBA and PRF leads to a reduction of healing time prior to implant placement.

Toffler et al. (33) have reported a positive effect of PRF on bone regeneration in a graft. When platelet products are added to different kinds of graft materials, a more predictable outcome is derived after bone augmentations.

Tatullo et al. (34) conducted histological and clinical evaluations of 60 patients who underwent surgery before implant surgery. The experimental group received bovine bone graft material combined with PRF, whereas the control group received only bovine bone graft material. The results revealed that PRF led to the production of new bone, even at 106 days.

On the other hand, Zhang et al (35) conducted histological and clinical evaluations of 10 patients who underwent sinus lifting. As a test group, six sinus floor elevations were grafted with a Bio-Oss and PRF mixture, and as control group, five sinuses were treated with Bio-Oss alone. Their results revealed that there was no difference in the new bone between the group receiving only bovine bone graft (Bio-Oss) and that receiving PRF in combination with bovine bone graft 6 months after sinus-lifting surgery.

In this study all implants remained unloaded for 6 months.

This agrees with Quirynen et al. (36) who concluded that the incidence of implant failure is significantly higher when combining immediate implant insertion with immediate loading.

From this study, it is clear that PRF is considered a good material for bone fill and therapeutic agent of choice in the treatment of bone defects.

CONCLUSIONS

From the results of this study we can conclude the following:

- It is clear that PRF is biocompatible and can improve both soft tissue healing and bone regeneration.
- PRF is an effective and stable treatment option to treat osseous defects around an immediately placed dental implants.

CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest.

REFERENCES

1. Albrektsson T, Sennerby L, Wennerberg A. State of the art of oral implants. Periodontal 2000. 2008; 47: 15-26.
2. Araújo MG, Lindhe J. Ridge alterations following tooth extraction with and without flap elevation: an experimental study in the dog. Clin Oral Implants Res. 2009; 20: 545-9.
3. Tan WL, Wong TLT, Wong MCM, Lang NP. A systematic review of post-extractional alveolar hard and soft tissue dimensional changes in humans. Clin Oral Implants Res. 2012; 23: 1-21.
4. VittoriniOrgeas G, Clementini M, De Risi V, de Sanctis M. Surgical techniques for alveolar socket preservation: a systematic review. Int J Oral Maxillofac Implants. 2013; 28: 1049-61.
5. Schropp L, Wenzel A, Kostopoulos L, Karring T. Bone healing and soft tissue contour changes following single-tooth extraction: a clinical and radiographic 12-month prospective study. Int J Periodont Restor Dent. 2003; 23: 313-23.
6. Shulte W, Heimke G. The Tubinger immediate implant. Quintessenz 1976; 27: 17-23.
7. Anneroth G, Hedstrom KG, Kjellman O, Kondell PA, Nordenram A. Endosseus titanium implants in extraction sockets. An experimental study in monkeys. Int J Oral Surg. 1985; 14: 50-4.
8. Covani U, Cornelini R, Calvo JL, Tonelli P, Barone A. Bone remodeling around implants placed in fresh extraction sockets. Int J Periodontics Restorative Dent. 2010; 30: 601-7.
9. Botticelli D, Berglundh T, Buser D, Lindhe J. The jumping distance revisited: an experimental study in the dog. Clin Oral Implants Res. 2003; 14: 35-42.
10. Santos PL, Gulinelli JL, Telles Cda S, Betoni Júnior W, Okamoto R, Chiacchio Buchignani V, et al. Bone Substitutes for Peri-Implant Defects of Postextraction Implants. Int J Biomater. 2013; 2013: 307136.
11. Schepers S, Barbier P, Ducheyne L. Bioactive glass particles as a filler for bone lesions. J Oral Rehabil. 1991; 18: L439-52.
12. Dohan DM, Choukroun J, Diss A, Dohan SL, Dohan AJ, Mouhyi J, et al. Platelet-rich fibrin (PRF): A second-generation platelet concentrate. Part I: Technological concepts and evolution. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2006; 101: e37-44.
13. Gassling VL, Açil Y, Springer IN, Hubert N, Wiltfang J. Platelet-rich plasma and platelet-rich fibrin in human cell culture. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2009; 108: 48-55.
14. Ross R, Glomset J, Kariya B, Harker L. A platelet-dependent serum factor that stimulates the proliferation of arterial smooth muscle cells in vitro. Proc Natl Acad Sci USA. 1974; 71: 1207-10.
15. Nevins M, Giannobile WV, McGuire MK, Kao RT, Mellonig JT, Hinrichs JE, et al. Platelet-derived growth factor stimulates bone fill and rate of attachment level gain: Results of a large multicenter randomized controlled trial. J Periodontal. 2005; 76: 2205-15.
16. Marx RE, Carlson ER, Eichstaedt RM, Schimmele SR, Strauss JE, Georgeff KR. Platelet-rich plasma: Growth factor enhancement for bone grafts. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 1998; 85: 638-46.
17. Choukroun J, Dohan DM, Diss A, Dohan SL, Dohan AJ, Mouhyi J, et al. Platelet-rich fibrin (PRF): a second-generation platelet concentrate. Part I: technological concepts and evolution. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2006; 101: e37-44.
18. Anitua E, Andia I, Ardanza B, Nurden P, Nurden AT, Autologous platelets as a source of proteins for healing and tissue regeneration. Thromb Haemost. 2004; 91: 4-15.
19. Hiremath H, Saikalyan S, Kulkarni S, Hiremath V. Second generation platelet concentrate (PRF) as a pulpotomy medicament in a permanent molar with pulpitis: a case report. Int Endod J. 2012; 45: 105-12.
20. Chang JD, Bird SR, Bohidar NR, King T. Analgesic efficacy of rofecoxib compared with codeine\ acetaminophen using a model of acute dental pain. Oral Surg Oral Med Oral Path Oral Radiol Endod. 2005; 100: 74-80.
21. Mombelli A, Lang NP. Clinical parameters for the evaluation of dental implants. Periodontal. 2000 1994; 4: 81-6.

22. Abramoff MD, Magelhaes PJ, Ram SJ. Image Processing with Image J. Biophotonics Int. 2004; 11: 36-42.
23. Dias DR, Leles CR, Lindth C, Ribeiro-Rotta RF. The effect of marginal bone level changes on the stabilityof dental implants in a short-term evaluation. Clin Oral Impl Res. 2015; 26: 1185-90.
24. Akimoto K, Becker W, Persson R, Baker DA, Rohrer MD, O'Neal RB. Evaluation of titanium implants placed into simulated extraction sockets: a study in dogs. Int J Oral Maxillofac Implants. 1999; 14: 351-60.
25. Eriksson AR, Albrektsson T. Temperature threshold levels for heat-induced bone tissue injury: a vital-microscopic study in the rabbit. J Prosthet Dent. 1983; 50: 101-7.
26. Choukroun J, Diss A, Simonpieri A, Girard MO, Schoeffler C, Dohan SL, et al. Platelet rich fibrin (PRF): a second-generation platelet concentrate. Part V: histologic evaluations of PRF effects on bone allograft maturation in sinus lift. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2006; 101: 299-303.
27. Kumar N, Prasad K, Ramanujam L, K R, Dexith J, Chauhan A. Evaluation of treatment outcome after impacted mandibular third molar surgery with the use of autologous platelet rich fibrin: a randomized controlled clinical study. J Oral Maxillofac Surg. 2015; 73: 1042-9.
28. Jeong SM, Choi BH, Li J, Kim HS, Ko CY, Jung JH, et al. Flapless implant surgery: an experimental study. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2007; 104: 24-8.
29. Wang RE, Lang NP. Ridge preservation after tooth extraction. Clin Oral Implants Res. 2012; 23: 147-56.
30. Kulkarni MR, Thomas BS, Varghese JM, Bhat GS. Platelet-rich fibrin as an adjunct to palatal wound healing after harvesting a free gingival graft: A case series. J Indian Soc Periodontol 2014; 18: 399-402.
31. Yelamali T, Saikrishna D. Role of platelet rich fibrin and platelet rich plasma in wound healing of extracted third molar sockets: A comparative study. J Maxillofac Oral Surg. 2015; 14: 410-6.
32. Tsai CH, Shen SY, Zhao JH, Chang YC. Platelet-rich fibrin modulates cell proliferation of human periodontally related cells in vitro. J Dent Sci. 2009; 4: 130e5.
33. Toffler M, Toscano N, Holtzclaw D, Corso MD, Dohan DM. Introducing Choukroun's platelet rich fibrin (PRF) to the reconstructive surgery milieu. J Implant Adv Clin Dent. 2009; 1: 22-31.
34. Tatullo M, Marrelli M, Cassetta M, Pacifici A, Stefanelli LV, Scacco S, et al. Platelet Rich Fibrin (P.R.F) in reconstructive surgery of atrophied maxillary bones: Clinical and histological evaluations. Int J Med Sci. 2012; 9: 872-80.
35. Zhang Y, Tangl S, Huber CD, Lin Y, Qiu L, Rausch-Fan X. Effects of Choukroun's platelet rich fibrin on bone regeneration in combination with deproteinized bovine bone mineral in maxillary sinus augmentation: a histological and histomorphometric study. J Craniomaxillofac Surg. 2012; 40: 321-8.
36. Quirynen M, Van Assche N, Botticelli D, Berglundh T. How does the timing of implant placement to extraction affect outcome? Int J Oral Maxillofac Implants. 2007; 22: 203-23.