Acta Scientific Dental Sciences (ISSN: 2581-4893)

Volume 2 Issue 7 July 2018

Research Article

Comparison of Prf Versus Collagen Membrane on Healing of Socket and Bone Formation (Randomized Split Mouth Design)

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Received: April 18, 2018; **Published**: June 05, 2018

Abstract

Purpose: is to evaluate the effect of platelet rich fibrin (PRF) on socket healing following extraction of mandibular molars

Materials and Methods: This study was conducted as a randomized controlled clinical trial, split mouth design. A total of ten patients, seeking removal of bilateral mandibular molars (20 extraction sockets), were selected to contribute in this study. The selected sample was randomly allocated into two equal groups. Atraumatic extraction of a lower molar has been performed, after an envelope flap was reflected, a PRF membrane was packed over the extraction socket (study site S) where on the control site (C), a collagen membrane was packed to cover the extraction socket of the contralateral side. In both sides, the flap was closed gently by figure of eight sutures.

Results: Clinically, swelling values were recorded at 1st, 2nd and 7th days postoperatively, the values of the side S are less than the values of the side C, but these differences were not statistically significant.

Pain values were recorded at the first 5 days postoperatively. Less pain sensation in the side S in comparison with side C, but these differences were not significant. The pain in the side S was relieved faster than side C.

Radiographic findings showed that the bone density increased in both groups at 1, 3 and 6 months, with no significant difference between these two groups, even though the bone density increases more in the sockets treated with PRF

Conclusions: Within the limitations of this study, it could be concluded that PRF membrane could be used effectively as a socket preservation aid, but it has no effect on hard tissue healing and bone density when compared with collagen membrane. PRF preparation is a technique sensitive, that should be operated carefully, yet it is an easy procedure that have a beneficial clinical and economic effects.

Keywords: Platelet Rich Fibrin (Prf); Collagen Membrane; Extraction Socket; Bone Healing

Introduction

The healing process is a normal biochemical, mechanical, cellular and molecular response of the body in order to restore the tissue integrity and is an essential defense response to maintain the organism vitality and continuity [1].

A cascade of mechanisms that is correlated and controlled by several factors consist the normal wound healing that could be typically broken down into three distinct overlapping phases: inflammatory, proliferative, and remodeling [2].

The healing of an extraction socket is a specialized example of healing by secondary intention [3], where blood fills the socket and both intrinsic and extrinsic pathways of the clotting cascade are activated, then a series of body reaction in both bone and epithelium occur in the organized clot in order to have finally a healed wound [4].

With time, optimizing wound healing becomes an interest [4], several methods are used to achieve this goal. But understanding this entire process still incomplete; however, it is known that platelets play a crucial role not only in homeostasis, but also in the wound healing process [5]. In modern dentistry, ridge preservation after tooth extraction becomes an essential matter to study and to find new techniques to play a role in preservation of bone and soft tissue, that will be altered after extraction which leads to dimensional changes and loss of important factors for future replacing of missing tooth and proper ridge contour [6].

Collagen materials have been utilized in medicine and dentistry because of their proven biocompatibility and capability of promoting wound healing [7], it is beneficial to use collagen membrane placement which is effective in inhibiting epithelial migration [8].

On the other hands, platelets isolated from peripheral blood act as a natural source of growth factors, several uses of platelets and other blood components has been described in treatment and healing of bleeding condition. Various materials and techniques have been developed to facilitate bone healing process and reduce its healing period.

With time, several platelets concentrates have been used in medicine, like PRP (platelet rich plasma) and PRF (platelet rich fibrin). PRF represents a new revolutionary step in platelet gel therapeutic concept because of its matrix in addition to its components [9]. It is believed that (PRF) or leucocytes and platelet rich plasma (L-PRF) is a second generation of (PRP) where autologus platelets and leucocytes are present in a complex fibrin matrix [10] to accelerate the healing of soft and hard tissue.

In recent studies, it is pointed out that, platelet-rich fibrin (PRF) which is derived autogenously from the own blood of the individuals, increase regeneration and accelerate the healing of the wound, due to the consisting various growing factors [11].

Several use of PRF has been described in medicine and dentistry, profiting of its vital characteristics. Recently platelet rich fibrin is employed to accelerate soft and hard tissue healing and to provide a better-healed recipient site for accelerated, early implant placement which is known as "accelerated-early" implant placement protocol which is a revolutionary bioengineered protocol benefiting from the biological PRF characteristics [12].

On the light of the above information, this study was conducted in order to evaluate the use of PRF membrane for socket preservation. This study hypothesized, that there is no difference in term of both soft and hard tissue healing of the extraction socket, when using either PRF or collagen membrane.

Materials and Methods

I-Materials

Study design

This study was carried out as an experimental study, randomized controlled clinical trial, (-split mouth design. A total of ten patients, seeking removal of bilateral mandibular molars (20 extraction sockets), were selected, fulfilling the following inclusion and exclusion criteria [13].

Inclusion criteria

Healthy male patients seeking extraction of bilateral molars, with a stable periodontal condition and without periapical infection, aged between 18 - 35, with no history of aspirin intake or other medications that might interfere with coagulation.

Exclusion criteria

1. Smoker, alcoholic
2. Diabetic, asthmatic patients suffering from heart or liver diseases.
3. Undergoing chemotherapy or radiotherapy.
4. Osteoporotic or suffering from bone abnormalities that may interfere with bone healing.

The Ethical Committee (Institutional Review Board, IRB number: 2017H-0050-D-M-0206) gave the ethical clearance before the study began, selected patients were informed about the nature of the study, and informed consent was obtained.

The selected sample was randomly allocated into two equal groups according to the site of operation; the study site with PRF membrane (S), and the control site with collagen membrane (C) of the selected sample enrolled in this study were assigned randomly through a computed generated randomized table. Because this is a split mouth study design, each patient underwent two operations for removal of their bilateral mandibular molars in the same day.

II-Methods

A pilot study was done prior to the work by conducting 4 operations for 2 patients. It included interpretation of radiographs, to standardize the selected cases, and ping the technical steps of the grafting of the Collagen membrane and PRF membrane to gain examiner reliability.

All patients were assessed and evaluated by proper history taking and thorough clinical and radiographic examination. Digital panoramic X-ray were done for all patients preoperatively, and a standardized periapical radiograph by the use of customized Rinn XCP, that should be used each time when periapical x-ray should be done.

For both sites, a full thickness flap was made by an incision using no.15c surgical blade mounted on Bard Parker handle no.3, the incision was directed anteriorly and posteriorly around the neck of the neighboring teeth if present, the flap was then gently reflected with a molt no.9 periosteal elevator, then the periosteal membrane is dissected horizontally at the depth of the flap to secure a tension free closure of the flap. The flap helped to expose the buccal aspect of the bone to ensure that no bone deterioration occurred, and to ensure that it was covered by the membranes, a little reflection of the flap was performed lingually, to let the membrane edges slide below the flap edges.

Then the atraumatic extraction of both lower molar teeth was performed in the same session, using curved periotome (Hu Freidy, USA), lower full crown extraction forceps (Zeffiro, Italy), and curved apexo elevators (Zeffiro, Italy).

For PRF study side (S): preparation of PRF was performed according to Dohan., et al. blood samples were collected from the patients. For each patient, the blood sample (4 tubes of 10 ml) was obtained from an antecubital vein [14]. The blood was taken without anticoagulant for PRF production (Figure1).

The blood collection was performed quickly, and the tube were immediately centrifuged at 3,000 rpm for 10 minutes with a specific table centrifuge (Champion, USA) at room temperature. After centrifugation, the PRF clot was removed from the tube using sterile tweezers, separated from the RBC base using scissors (Figure 2

and 3), and placed in a sterile metal cup (Figure 4).

Figure1: Collected Blood.

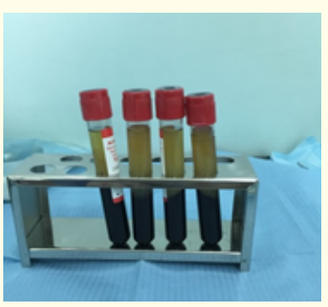

Figure 2: PRF clots after centrifugation.

Figure 3: PRF Clot Removal.

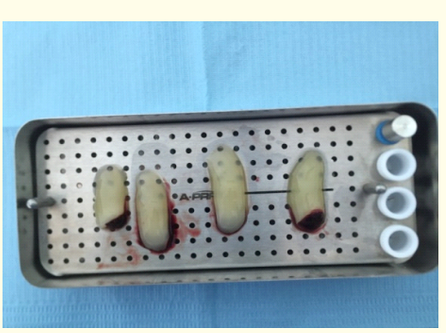

Figure 4: PRF clot on the metal cup.

Each PRF clot started to release its serum (PRF-clot exudate) and was ready for compression into the membrane.

The four clots were emptied from their serum by compressing them with a metal spoon forcible exudate extraction in the PRF Box. All membranes underwent a final compression on sterile woven gauzes to flush out a maximum of fluids; The dehydration facilitated fixation and processing for grafting in the extraction socket (Figure 5).

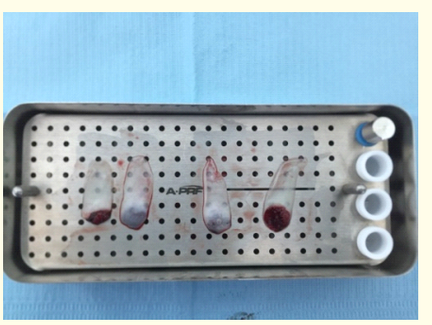

Figure 5: PRF membrane after compression.

After extraction was performed, cover the extraction socket was covered by the PRF membrane, applying the edges of the membrane 2 mm below the edges of the flap (Figure 6), a figure of eight suture is then performed to close the flap over the graft (Figure 7).

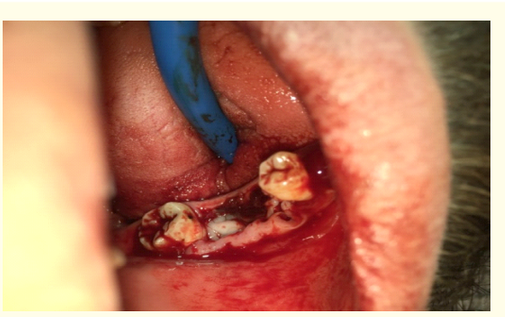

Figure 6: PRF membrane inserted over the extraction socket.

Figure 7: Figure of Eight Suture.

For the control site (C): Preparation of collagen membrane (pericardium) (Osteobiol, Italy). The membrane was trimmed to fit the defect. The membrane was wetted in sterile 0.9% saline solution until it became soft and flexible.

After extraction was done in the same manner of the study site, grafting of collagen membrane, and suturing using a 3 - 0 silk suture material was done (Figure 8 and 9).

Figure 8: Collagen Membrane Inserted Over the Extraction Socket.

Figure 9: Figure of Eight Suture.

A-Clinical evaluation

Postoperative pain

Postoperative pain was assessed using a four-point Category Rating Scale. Accordingly, pain was recorded as: "0-no pain" (participant experiences no discomfort), "1-mild pain" (almost unnoticeable pain), "2-moderate pain" (noticeable pain, but participant can still engage in routine daily activities), "3-severe pain" (very noticeable pain which disturbs the patient's daily routine). For each participant, the appropriate score was recorded in the data sheets on a daily basis for 5 days [15].

Postoperative edema

Measurement of edema (facial width), called tape measuring technique, was performed by the use of a measuring tape to measure facial width and swelling in one-dimension only. The reference points were the tip of tragus of left and right ears, with lip junction. Change of swelling was calculated as follows:

facial swelling = postoperative values - preoperative values at baseline

B-Radiographic evaluation

The radiographic evaluation was performed at the following intervals: immediate postoperative (T0), 1 month (T1) and 3 months (T2), 6 months (T3).

The radiographs that were used

Standardized digital periapical x-rays were used for measurement of bone density using XCP film (sensor) holder and Image J software. A standardized sized square (33 x 33 pixels) was inserted in the center of the extracted socket, which is determined by identification the intersected point between 2 straight lines: a horizontal line extending from the distal wall of the socket of the mesial root to the mesial wall of the socket, and a vertical line extending from the alveolar bone crest to the apex of the socket. The bone density within this square was measured by selecting Region of Interest (ROI), from tools and then the given data were analyzed in terms of pixels. The same square was drawn for all patients the bone density was measured and the results were subjected to statistical analysis.

Statistical analysis

The variables included in the study were tested for normality using Kolmogrov Smirnov test. Descriptive statistics were calculated as means and standard deviations because they were normally distributed variables (swelling, pain, bone density) and t-test was performed.

Significance level was set at 5% level. Statistical analysis was performed, using SPSS version 21.0.

Results

This study was carried out as a randomized controlled clinical trial, split mouth design. Ten male patients of age between 18 and 35 (mean of age 26.8 ± 4.3 years) participated in this study, all patients were seeking extraction for bilateral lower molars due to several causes, the most causative factor of extractions was the failure of previous root canal treatment (Figure 10). The sides of experiments (Figure 11), extraction and grafting of membranes were selected randomly.

Postoperative swelling

The comparison of facial swelling between side S and side C during day1, shows that the side S enlarged more than side C, but this was not a significant difference as $p = 0.5987$ (significance: $p < 0,05$).

The comparison of facial swelling between S and C during day 2, shows that the side S enlarged more than side C, no significant difference as $p = 0.5074$.

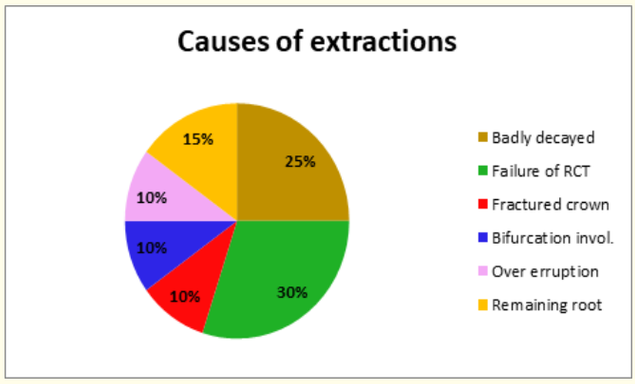

Figure 10: Pie chart showing the distribution of causes of extractions.

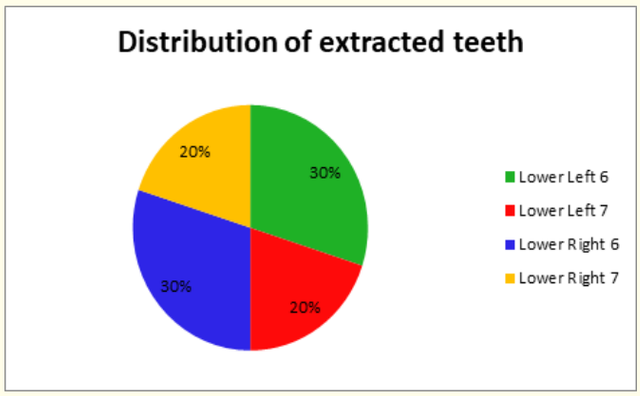

Figure 11: Pie chart showing the distribution of extracted teeth according to the side.

The comparison of facial swelling between S and C during day 7, shows that the side S enlarged more than side C, yet no significant difference as P = 0.9406.

These results showed that there is no significant effect of PRF on facial swelling, in comparison with collagen membrane, even though the side with PRF has enlarged less than the other side but this difference is not statistically significant.

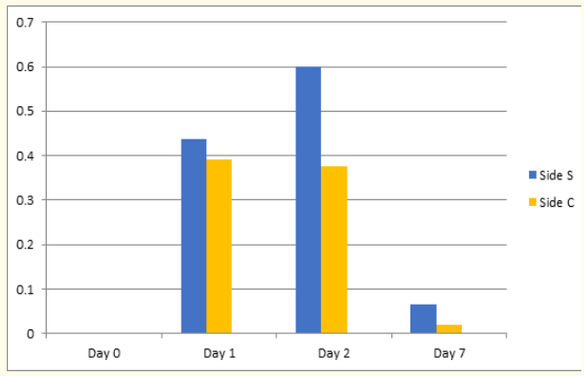

Figure 12: The mean value of facial swelling of side S and side C during different periods.

Sides	Day 0		Day 1		Day 2		Day 7	
	S	C	S	C	S	C	S	C
Mean	0	0	0.436 ± 0.19	0.39 ± 0.12	0.6 ± 0.18	0.375 ± 0.22	0.065 ± 0.06	0.02 ± 0.03
P*			0.598		0.507		0.940	

Table 1: Shows the comparison of change in swelling between side (S) and side (C) at different follow up periods, at baseline, day 1, day 2 and day 7.

Pain

The comparison of pain sensation, between S and C in day 1, shows that the pain is lesser in the side S, but this difference is not statistically significant as p = 0.95729 (significance p < 0.05).

The comparison of pain sensation, between S and C in day 2, shows that the pain is lesser in the side S, but this difference is not statistically significant as p = 0.9109 (significance p < 0.05).

The comparison of pain sensation, between S and C in day 3, shows that the pain is lesser in the side S, but this difference is not statistically significant as p = 1 (significance p < 0.05).

The comparison of pain sensation, between S and C in day 4, shows that the pain is lesser in the side S, but this difference is not statistically significant as p = 0.6886 (significance p < 0.05).

The comparison of pain sensation, between S and C in day 5, shows that the pain is lesser in the side S, but this difference is not statistically significant as p = 0.9841 (significance p < 0.05).

Sides	Day 0		Day 1		Day 2		Day 3		Day 4		Day 5	
	S	C	S	C	S	C	S	C	S	C	S	C
mean	0	0	0.5 ± 0.52	0.9 ± 0.31	0.8 ± 0.63	1.2 ± 0.42	0.9 ± 0.31	1.8 ± 0.42	0.7 ± 0.67	0.9 ± 0.31	0.1 ± 0.31	0.7 ± 0.67
P*			0.9572		0.9109		1		0.688		0.984	

Table 2: shows the comparison of pain sensation measured by a four-point Category Rating Scale (CRS) scores at day 1, 2, 3, 4 and 5.

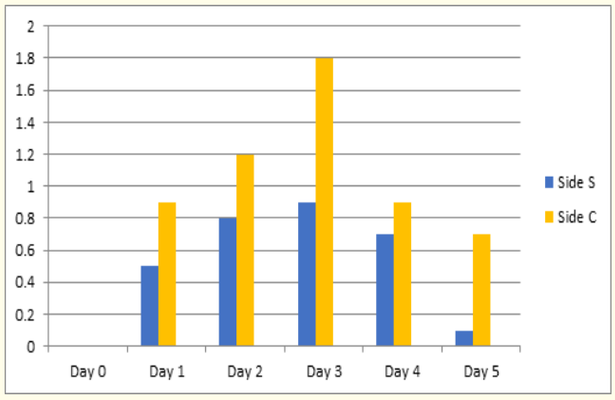

Figure 13: Comparison between the means of pain sensation during 1, 2, 3, 4 and 5 days.

Radiographic evaluation

Table 3 shows the percentage of increase of bone density (BD) from the baseline period (T0) to each period of the study; after one month (T1), after three months (T2) and after six months (T3). The values were calculated using the following formula:

Percentage of increase at T(x) =

$$\frac{\text{Value of BD at T(x) - Value of BD at T (0)}}{\text{Value of BD at T (0)}} \times 100$$

*where x is the number of period related to the needed value

The calculated values showed the percentage of increase bone density at the extraction socket at a selected period. The comparison between the values show the following:

- At T (1), after one month of the surgery, the BD in the side S increase by 9.67%, in the side C the BD increase by 10.79%. The BD in the side C increased more than the side S, but this difference is not significant statistically as P=0.5757.
- At T (2), after three months of the surgery, the BD in the side S increase by 40.04%, in the side C the BD increase by 32.77%. The BD in the side S increased more than the side C, but this difference is not significant statistically as P=0.6866.
- At T (3), after six months of the surgery, the BD in the side S increase by 58.96 %, in the side C the BD increase by 45.66%. The BD in the side S increased more than the side C, but this difference is not significant statistically as P=0.7827.

The present study shows that the PRF enhances and favors a rapid bone healing, in comparison with the effect of collagen membrane, as the bone density increased in the socket treated with PRF more than the socket treated with collagen membrane, during the same period, but this difference is not statistically significant. The effect of PRF is prolonged in comparison with the collagen membrane as the effect appears after three months, at the beginning the effect was approximately similar, and continues to six months.

No	T0		T1		T2		T3	
	S	C	S	C	S	C	S	C
Mean			9.67 %	10.79 %	40.04 %	32.77 %	58.96 %	45.66 %
pttst			0.57		0.41		0.28	
p			0.5757		0.6866		0.7827	

Table 3: The percentage increase of bone density from T0 to each period of T1, T2 and T3.

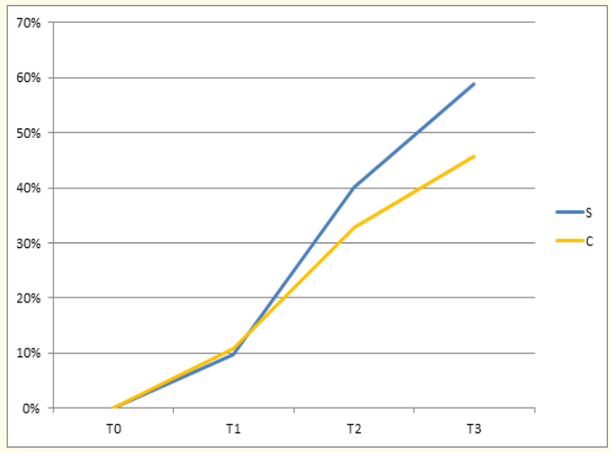

Figure 14: Chart line showing the mean of percentage increase of bone density from T0 to each of periods T1, T2 and T3.

Discussion

A proper rapid wound healing with the best acceptable soft and hard tissue results are essential in modern dentistry. This insists us to find new therapies, biomaterials and bioactive surgical additives in order to improve success and predictability of patient outcomes in terms of soft and bone tissue healing and regeneration [16].

The healing of extraction wound has been studied extensively histologically, radiographically [17]and clinically. It is currently understood that during the first 8 weeks following the extraction there is marked osteoclastic bone resorption that takes place on the surface of the residual ridge particularly the coronal part of the buccal bone wall and there is reduction of buccal crest in both the vertical and horizontal planes [17].

It is believed that preservation of extraction socket prior to implant surgery, is essential to maintain the soft and hard tissue needed for future treatment in both function and esthetic and minimizes the need for future augmentation procedures [18].

Many different ridge preservation techniques have been proposed and studied, in order to achieve the needed goal of performing it, which are essential in esthetic regions and regions close to the anatomic structures and which need the best bone and soft

tissue quantity and quality to achieve a successful final treatment [19].

The use of membranes from various materials are one of current methods to preserve the extraction socket and prevent ridge resorption [20]. Benefiting from mechanical and physiologic characteristics, membranes prevent ingress of soft tissue which permits a maximal bony healing of extraction socket [21].

In this study, two types of membranes have been used, Collagen membrane as a control and PRF as a study group. The clinical effects (pain and edema) and radiographic effects (bone density) were compared, in order to have an idea about the effect of the PRF membrane on the healing socket, using the mechanical effect of the fibrin inside to be a barrier of soft tissue invasion to the extraction socket during the healing period, and the matrix characteristics that maintain concentrated the cytokines and other factors that are essential for wound healing in order to promote a better healing for both soft and hard tissue.

Platelet Rich Fibrin (PRF), a patient blood-derived and autogenous living biomaterial, is increasingly being investigated and used worldwide by clinicians as an adjunctive autologous biomaterial to promote bone and soft tissue healing and regeneration. The gold standard for in vivo tissue healing and regeneration requires the mutual interaction between a scaffold (fibrin matrix), platelets, growth factors, leukocytes, and stem cells [22].

These key elements are all active components of PRF, and when combined and prepared properly are involved in the key processes of tissue healing and regeneration, including cell proliferation and differentiation, extracellular matrix synthesis, chemotaxis and angiogenesis (neo-vascularization) [23].

Platelet-rich fibrin was prepared for each patient according to the protocole determined by Dohan., *et al*. the collected blood should be immediately centrifuged and at room temperature, which is essential and critical, the success of this technique entirely depends on the speed of blood collection and transfer to the centrifuge, because the blood samples start to coagulate almost immediately upon contact with the tube glass [14]. If the duration required to collect blood and launch centrifugation is overly long, failure will occur, the collected blood samples in 10-ml tubes was centrifuged at 3000 rpm for 10 minutes.

At the end of centrifugation, the PRF clots were removed from the tubes, and inserted in a special device, PRF box, which is essential because it minimizes the damage of platelets contained in the PRF membranes and minimizes the lost or degradation of growth factors in the PRF membranes [24].

A good dehydration of the PRF membranes, was performed to gain a good adaptation over the extraction socket, that was the result of atraumatic extraction procedures, that was performed in both sides at the same visit.

A full thickness envelope flap was done, the advantage of this flap is the avoidance of vertical incision and easy reapproximation to original position, lower chance of dihescence, less traumatic to the tissue, maintains blood supply, extended from the distal aspect of the distal tooth if present, to the mesial aspect of the mesial tooth [25].

The atraumatic extraction was done by the use of curved periotomes, that were used to severe the periodontal ligaments around the teeth to be extracted in order to decrease the bone damage, which is essential when socket preservation protocol is applied, as the cases of this study, the teeth then extracted without forcing the surrounding bone by the extraction forceps this was performed in accordance with Sadeghi., *et al* [26].

According to Holland, the PRF membrane was gently adapted to cover the socket on the study sides whereas, on the control sides the collagen membranes were adapted over the extraction socket, the edges of membranes should overlap the walls of the socket [27], this was in accordance with Mir-Mari., et al. to ensure the complete cover of the wound and to decrease the chance of displacement during suturing [28].

After adaptation of membranes on each side, the flap was closed by figure of eight sutures which are essential to secure the grafted membranes in place and aid in hemostasis [29]. This was in accordance with Raj., et al. but in contrast with Holland, where interrupted horizontal mattress was performed with resorbable suture [27], in order to adapt the membranes over the extraction socket.

According to Wood and Maely, the effect of ridge preservation technique was evaluated at three and six months, which is similar to the present study [30].

During performing this study, some limitations were encountered. The patients selection was done according to the inclusion and exclusion criteria, so all the patients were males, in order to decrease the variables that could occur if we select both genders. This patients selection was in accordance with Chang., et al. where it was described that the female gender could be an univariate risk of failure in addition to tobacco smoking [31]. The age of the patients was between 18 and 35 years, healthy and non-smoker in addition to other criteria, all of that led us to find patients hardly especially in our society. Another limitation was the explanation for the patients the importance of the PRF and the need of blood collection, which was a new treatment modality for them, and to convince them to wait 6 months before starting any treatment to replace their extracted teeth.

Despite all these limitations, the study was finished, and the results were collected, and statistics was done in order to compare the clinical and radiographic effects of PRF.

The evidence supports the use of PRF as socket preservation materials, to enhance soft tissue healing, and reduce postoperative complications [32]. However, there is no evidence to date to support the positive effect of autologous materials in bone regeneration [33] and increasing bone density in comparison with other types of membranes.

In order to evaluate, whether PRF could influence the edema and pain. The results of the present study showed that the effect of PRF on soft tissues healing was insignificant, while as comparing the face enlargement between sides with PRF and sides with collagen membrane. It was noted that side S showed less enlargement during the day1, 2 and 7, but this was not significant statistically as $p \geq 0.05$. This was in contrast to Marenzi., *et al*. and in contrast to Kumar., *et al* [34,35]. This may be related to the different healing index used for evaluation, smaller sample size, surgical extraction of teeth included in the present study, and the difficulty in distinguishing between good and very good categories of the healing index of Landry., *et al* [36].

In contrast to Al-Hamed., *et al.* the results of the present study showed insignificant effect of PRF on pain perception in comparison with the effect of collagen membrane. This may be attributed to the different extraction sites used in the two studies [32], even though the site of PRF showed less pain index in comparison with sites with collagen which was not significant statistically, this difference could be related also to the different scales used in both studies, in this study we used the four-point CRS of Bamgbose., *et al*. [14] instead of the Visual Analogue Scale used by Al-Hamed., *et al* [32].

Kumar., *et al.* reported that the usage of PRF, decreased pain and swelling values significantly on the first control day postsurgery [35].

Bilginaylar and Uyanik reported that the use of PRF decreased the pain significantly on the first, third, and seventh days post operatively, in other hand they showed no significant differences in swelling values [37]. Similar results are reported by Uyanik., *et al* [38].

According to Wang and Tsao, PRF release autologous growth factors gradually and express a strong and a durable effect on proliferation and differentiation of osteoblasts, this was shown histologically in the rats that they used in their study [39]. This was not significantly showed radiographically in our study, even though the results of this study show that the effect of the PRF enhance the bone density with time, and it is prolonged in comparison with the collagen, but as shown this effect is not statistically significant.

Faot., *et al.* found that the PRF did not enhance bone tissue repair of non-critical size defects in rabbit tibia during 4 weeks experiment [40] in contrast to Kim., *et al*. that they found that the addition of PRF, in the bone defect in the rabbit skull, increased the bone formation at the 6th week [41].

Early clinical results suggest that the use of PRF is safe and feasible, but that at present there is no clinical evidence of benefit in either acute or delayed fracture healing [42], this is similar to our findings, these findings let us to find that it could be used effectively and with comparable effects in comparison with collagen membrane as a socket preservation aid, after extraction.

On the other hand, Singh., *et al.* found that the use of PRF enhanced soft tissue healing and increased rate of bone formation [43].

Conclusion

The use of PRF is beneficial for patients as it could be used as a socket preservation aid like the collagen membrane, it could enhance the soft and hard tissue healing. It is easy to be prepared, simple and cost effective.

Bibliography

1. Olczyk, P., *et al*. "The role of the extracellular matrix components in cutaneous wound healing". *BioMed Research International* (2014): 747584.

2. Clark RA. "Biology of dermal wound repair". Dermatologic clinics 11.4 (1993): 647.

3. Walter CJ., *et al*. "Systematic review and meta-analysis of wound dressings in the prevention of surgical-site infections in surgical wounds healing by primary intention". *British Journal of Surgery* 99.9 (2012): 1185-1194.

4. Miloro M., *et al*. "Peterson's principles of oral and maxillofacial surgery (Volume 1)". PMPH-USA (2004).

5. Gaßling VL., *et al*. "Platelet-rich plasma and platelet-rich fibrin in human cell culture". *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology* 108.1 (2009): 48-55.

6. Wang RE and Lang NP. "Ridge preservation after tooth extraction". *Clinical Oral Implants Research* 23.6 (2012):147-156.

7. Bunyaratavej P and Wang HL. "Collagen membranes: a review". *Journal of periodontology* 72.2 (2001): 215-229.

8. Blumenthal NM. "The use of collagen membranes to guide regeneration of new connective tissue attachment in dogs". *Journal of periodontology* 59.12 (1988): 830-836.

9. Dohan DM., *et al*. "Platelet-rich fibrin (PRF): a second-generation platelet concentrate. Part I: technological concepts and evolution". *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology*101.3 (2006): e37-e44.

10. Naik B., *et al*. "Role of Platelet rich fibrin in wound healing: A critical review". *Journal of Conservative Dentistry* 16.4 (2013): 284-293.

11. Kökdere NN., *et al*. "The use of platelet-rich fibrin (PRF) and PRF-mixed particulated autogenous bone graft in the treatment of bone defects: An experimental and histomorphometrical study". *Dental research journal* 12.5 (2015): 418.

12. Kotsakis GA., *et al*. "Extraction Socket Management Utilizing Platelet Rich Fibrin: A Proof-of-Principle Study of the "Accelerated-Early Implant Placement" Concept". *Journal of Oral Implantology* 42.2 (2016): 164-168.

13. Hemalata M., *et al*. "Comparative Evaluation of Platelet Concentration and its Distribution in the Buffy Coat Region of Platelet Rich Fibrin in Non-diabetic and Controlled Diabetic Patients: A Light Microscopic Study". *International Journal of Advanced Health Sciences* 3.1 (2016): 6-10.

14. Dohan Ehrenfest DM., *et al*. "Three-dimensional architecture and cell composition of a Choukroun's platelet-rich fibrin clot and membrane". *Journal of periodontology* 81.4 (2010): 546-555.

15. Bamgbose BO., *et al*. "Effects of co-administered dexamethasone and diclofenac potassium on pain, swelling and trismus following third molar surgery". *Head and Face Medicine* 1.1 (2005): 11.

16. Hartshorne J and Gluckman H. "A comprehensive clinical review of Platelet Rich Fibrin (PRF) and its role in promoting tissue healing and regeneration in dentistry. Part II: preparation, optimization, handling and application, benefits and limitations of PRF". *International Dentistry* 6 (2016): 34-48.

17. Madhan G and Madhumati S. "Comparison of Ability of Platelet-rich Fibrin vs Colla Plug in maintaining the Buccal Bone Height of Sockets following Extractions in 20 Patients". *Journal of Health Sciences and Research* 8.1 (2017): 1-6.

18. Kazuo Yamamoto M., *et al*. "Evaluation of the Effect of Platelet-Rich Plasma on Alveolar Wound Healing in Rats". *International Journal of Morphology* 35.1 (2017): 251-258.

19. Avila-Ortiz G., *et al*. "Effectiveness of three different alveolar ridge preservation techniques: a pilot randomized controlled trial". *International Journal of Periodontics and Restorative Dentistry* 34.4 (2014): 509-521.

20. Bartee BK. "Extraction site reconstruction for alveolar ridge preservation. Part 2: membrane-assisted surgical technique". *Journal of Oral Implantology* 27.4 (2001): 194-197.

21. Darby I., *et al*. "Ridge preservation: what is it and when should it be considered". *Australian Dental Journal* 53.1 (2008): 11-21.

22. Kawase T. "Platelet-rich plasma and its derivatives as promising bioactive materials for regenerative medicine: basic principles and concepts underlying recent advances". *Odontology* 103.2 (2015): 126-135.

23. M Dohan Ehrenfest D., *et al*. "In search of a consensus terminology in the field of platelet concentrates for surgical use: platelet-rich plasma (PRP), platelet-rich fibrin (PRF), fibrin gel polymerization and leukocytes". *Current Pharmaceutical Biotechnology* 13.7 (2012): 1131-1137.

24. Kobayashi M., *et al*. "A proposed protocol for the standardized preparation of PRF membranes for clinical use". *Biologicals* 40.5 (2012): 323-329.

25. Desai A., *et al*. "Comparison of two incision designs for surgical removal of impacted mandibular third molar: A randomized comparative clinical study". *Contemporary Clinical Dentistry* 5.2 (2014): 170-174.

26. Sadeghi R., *et al*. "A randomized controlled evaluation of alveolar ridge preservation following tooth extraction using deproteinized bovine bone mineral and demineralized freeze-dried bone allograft". *Dental Research Journal* 13.2 (2016): 151-159.

27. Holland JW. "Influence of Platelet-Rich Fibrin on Post-extraction Alveolar Ridge Healing/Preservation: A Clinical, Radiographic and Histological Evaluation". (Doctoral dissertation, The University of Texas School of Dentistry at Houston) (2016).

28. Mir-Mari J., *et al*. "Influence of blinded wound closure on the volume stability of different GBR materials: an *in vitro* cone-beam computed tomographic examination". *Clinical Oral Implants Research* 27.2 (2016): 258-265.

29. Raj R., *et al*. "Natural Tooth Pontic: An Instant Esthetic Option for Periodontally Compromised Teeth-A Case Series". *Case Reports in Dentistry* (2016): 8502927.

30. Wood RA and Mealey BL. "Histologic comparison of healing after tooth extraction with ridge preservation using mineralized versus demineralized freeze-dried bone allograft". *Journal of Periodontology* 83.3 (2012): 329-336.

31. Chang MA., *et al*. "The outcomes and complications of 1, 2-intercompartmental supraretinacular artery pedicled vascularized bone grafting of scaphoid nonunions". *The Journal of Hand Surgery* 31.3 (2006): 387-396.

32. Al-Hamed FS., *et al*. "Clinical effects of platelet-rich fibrin (PRF) following surgical extraction of lower third molar". *The Saudi Journal for Dental Research* 8.1-2 (2017): 19-25.

33. Del Fabbro M., *et al*. "Is autologous platelet concentrate beneficial for post-extraction socket healing? A systematic review". *International Journal of Oral and Maxillofacial Surgery* 40.9 (2011): 891-900.

34. Marenzi G., *et al*. "Influence of leukocyte-and platelet-rich fibrin (L-PRF) in the healing of simple postextraction sockets: a split-mouth study". *Biomed Research International* (2015): 369273.

35. Kumar N., *et al*. "Evaluation of treatment outcome after impacted mandibular third molar surgery with the use of autologous platelet-rich fibrin: a randomized controlled clinical study". *Journal of Oral and Maxillofacial Surgery* 73.6 (2015): 1042-1049.

36. Landry RG., *et al*. "Effectiveness of benzydamyne HCl in the treatment of periodontal postsurgical patients". *Research and clinical forums* 10 (1988): 105-118.

37. Bilginaylar K and Uyanik LO. "Evaluation of the effects of platelet-rich fibrin and piezosurgery on outcomes after removal of impacted mandibular third molars". *British Journal of Oral and Maxillofacial Surgery* 54.6 (2016): 629-633.

38. Uyanık LO., *et al*. "Effects of platelet-rich fibrin and piezosurgery on impacted mandibular third molar surgery outcomes". *Head and Face Medicine* 11 (2015): 25-32.

39. Wang HL and Tsao YP. "Mineralized bone allograft-plug socket augmentation: rationale and technique". *Implant Dentistry* 16.1 (2007): 33-41.

40. Faot F., *et al*. "The effect of L-PRF membranes on bone healing in rabbit tibiae bone defects: micro-CT and biomarker results". *Scientific Reports* 7 (2017).

41. Kim TH., *et al*. "Comparison of platelet-rich plasma (PRP), platelet-rich fibrin (PRF), and concentrated growth factor (CGF) in rabbit-skull defect healing". *Archives of Oral Biology* 59.5 (2014): 550-558.

42. Griffin XL., *et al*. "The clinical use of platelet-rich plasma in the promotion of bone healing: a systematic review". *Injury* 40.2 (2009): 158-162.

43. Singh A., *et al*. "Platelet rich fibrin: a novel approach for osseous regeneration". *Journal of Maxillofacial and Oral Surgery* 11.4 (2012): 430-434.

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