ORIGINAL ARTICLE

Clinical and radiographic outcomes of the use of Platelet-Rich Fibrin after Impacted Mandibular Third Molar Surgery: a controlled prospective study

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Abstract

Purpose
This study was aimed to assess the clinical and radiographic outcomes of the use of platelet-rich fibrin (PRF) after Impacted Mandibular Third Molar extractions.

Patients and Methods
Forty extractions of bilateral impacted mandibular third molars were performed in 20 volunteers (8 men, 12 women; 18 to 24 years old). After extraction of right and left mandibular third molars, the socket at one side received the autologous PRF (test group) and the other was filled with blood clot (control group). Digital panoramic radiographs were obtained on (7 days 3, and 6 months) postoperatively The parameters evaluated included pain, swelling, maximum mouth opening , and bone formation . Assessments for clinical parameters were made on the day of surgery and on days (2 and 7) after surgery while they were made after (7 days 3, and 6 months) for radiographic evaluation. Statistical significance was inferred at P<0.05.

Results
Statistically significant differences were detected for the swelling and trismus values between the two treatment groups on the second postoperative day (P = 0.016 and P = 0.003, respectively). Also statistically significant differences were detected for the pain values between the two treatment groups on the first and second postoperative day (P = 0.012 and P 0.050, respectively). There were no statistically significant differences in bone density between the groups at follow up periods.

Conclusions
The application of PRF reduces the severity of the immediate post-operative sequelae (swelling, trismus, pain) but has no effect on bone healing after Impacted Mandibular Third Molar extractions.

Keywords
Impacted third molar extraction; mandibular third molar socket healing; swelling; trismus; pain. Platelet- rich fibrin (PRF)

Introduction

Extraction of third molars is one of the most common procedures in oral surgery. In general terms, extraction of third molars has a negative impact in the period of four to seven days after surgery.(1)Patients refer to the postoperative swelling, pain, and trismus associated with the inflammatory response to surgical trauma as the main factors affecting their daily life(2,3)Although the incidence of healing complications is relatively low, the problems created by the disturbances in post extraction wound healing and physiologic sequelae of third molar surgery can significantly affect the patient's quality of life.(4)Socket healing is a highly coordinated sequence of biochemical, physiologic, cellular, and molecular responses involving numerous cell types, growth factors, hormones, cytokines, and other proteins, which is directed toward restoring tissue integrity and functional capacity after injury.(5-7)After dental extraction, socket healing necessarily occurs by secondary intention; 4- 6 months are required for tissue to heal to a point where it is radiologically indistinguishable from surrounding bone (8)Various methods have been suggested to enhance socket healing and to minimize the

postoperative sequelae after third molar surgery(9-12)   Platelet-rich fibrin (PRF) is the second generation of platelet concentrates after platelet-rich plasma (PRP)and it is widely used to accelerate soft and hard tissue healing(13). It consists of high concentrations of the collected platelets, which allow slow release of growth factors; These GFs include vascular endothelium growth factor (VEGF), platelet-derived growth factor (PDGF), fibroblast growth factor (FGF), epidermal growth factor (EGF), hepatocyte growth factor (HGF), insulin-like growth factor (IGF), and transforming growth factor-β (TGF-β). All of these play a role in replacing lost tissue, resurfacing of the wound, and restoring vascular integrity (14). PRF has been used in bone augmentation, angiogenesis, wound healing, and periodontal healing, with promising results (15-20). Evidence regarding the effect of PRF on immediately postoperative sequelae and on hard tissue healing following extraction of impacted third molars is sparse. Therefore this study was aimed to assess the clinical and radiographic outcomes of the use of platelet rich fibrin (PRF) on soft and hard tissue healing after Impacted Mandibular Third Molar extractions.

Materials and Methods
Patient Selection
This study was designed and performed as a prospective controlled spilt mouth study. All patients were informed of the risks and benefits of the procedure after which they signed the consent form. The study protocol was approved by an ethical committee of **Al-Andalus University for Medical Sciences**. We selected 20 patients (8 males, 12 females) between the ages of 18 and 24 years, have American Society of Anesthesiologists physical status I or II, have bilateral mesioangular or horizontally impacted mandibular third molars, have the same difficulty level of bilateral third molars based on the Pederson classification (sum score of the spatial direction of tooth value, depth of impaction, and relation with the ramus on the panoramic radiograph) (21) and all were nonsmokers. The exclusion criteria included those with signs of pericoronitis, pain before surgery, systemic diseases, possible compromised immune system, and platelet count more than 150.000/mm3, allergies or hypersensitivity to drugs, antibiotics, anti-inflammatory and cortisone medication for the 12-month period preceding surgery, and pregnant and lactating women. After extraction of right and left mandibular third molars, the socket at one side received the autologous PRF (test group) and the other was filled with blood clot (control group). The test and control sides were switched according to the order of patients. Each patient underwent two surgical operations, separated by 2 weeks.

PRF preparation
The PRF was prepared in accordance with the protocol developed by Choukroun *et al*.(13) Just prior to surgery, 8 ml intravenous blood was collected in a 10-ml sterile tube without anticoagulant and immediately centrifuged in centrifugation machine at 3000 rpm for 10 minutes (Labofuge 400R centrifuge, Heraeus, Hanau, Germany). Blood centrifugation immediately after collection allows the composition of a structured fibrin clot in the middle of the tube, just between the red corpuscles at the bottom and acellular plasma (Platelet-poor plasma) at the top. PRF results from a natural and progressive polymerization which occurs during centrifugation. PRF was easily separated from red corpuscles base [preserving a small red blood cell (RBC) layer] using a sterile tweezers and scissors just after removal from the tube and then transferred onto a sterile dampen dish and stored in refrigerator.

Surgical procedure
Pre-operative investigations included panoramic radiograph and platelet count.
Before surgery patients rinsed with 0.12% chlorhexidine for 2 minutes; they were not given pre-operative antimicrobica, or others drugs that might influence healing. All of the surgeries were performed by the same surgeon using a standard oral surgical procedure under local anaesthesia by nerve block of the inferior alveolar, lingual and buccal nerves, using 4% articaine containing 1:100,000 epinephrine (Medicaine, Septodont, France). The access was prepared with a mucoperiosteal envelope flap without releasing; bone removal, tooth sectioning, and bone contouring were performed with a low-speed handpiece under sufficient sterile normal saline irrigation; sockets were irrigated with normal saline 100 mL; After the tooth extraction the socket was thoroughly irrigated and freed from pathological tissue e.g. granulation tissue, follicular remnants and bony spicules. In the Case group, after the tooth was delivered PRF was inserted into the extraction socket and then the flap was sutured with 3-0 silk sutures .The patients were blind to the side in which PRF had been inserted. Average operative time from incision to suturing was between 30-40 minutes. Post-operatively all Patients were given antibiotics (amoxicillin and clavulanic acid 1000mg every 12 hours for 7 days), oral anti-inflammatory treatment (ibuprofen 1800 mg every day for 3 days) and 0.12% chlorhexidine gluconate rinses every 12 hours for 10 days. Oral hygiene was assessed and supportive periodontal therapy was provided for all patients at 2, 4, and 6 weeks after surgery.
All patients were given instructions on the importance of maintenance of oral hygiene. Suture

removal was done on the 7th post-operative day. Fig (1)

Study Variables

In the present study, the predictor variable was the application of PRF in the extraction socket. The variables assessed were pain, swelling, trismus and bone formation with follow-up period of 6 months. All surgeries were performed by 1 surgeon, while a second surgeon performed the measurements without being aware of what therapeutic approach was used for the different sites of treatment. Also patients did not know on which side PRF was inserted. Pain intensity was assessed using a 10-point visual analogue scale (VAS), with the patient placing a mark on the scale to indicate an intensity range from no pain '0' to severe/unbearable pain '10'(22). The severity of the pain was evaluated on the operation day and on postoperative days 2 and 7.The degree of facial swelling was determined by a modification (23) of the tape measure method described by Gabka and Matsumara (24). Three measurements were made between five reference points: the distance between the lateral corner of the eye and angle of the mandible, the distance between the tragus and soft tissue pogonion, and the distance between the tragus and outer corner of the mouth. The mean of these three measurements was calculated. Measurements were taken pre-operatively and on postoperative days 2 and 7. Trismus was evaluated by measuring the distance between the edges of the upper and lower right central incisors at maximum opening of the jaws preoperatively and on days 2 and 7 after surgery. Bone repair was assessed by digital panoramic X-rays immediately after extraction and at 3, and 6 months postoperatively (Fig. 2) . Radiographs were analyzed 3 times by the same examiner at different moments and the mean was calculated, using computerized image J program, which provides a reading of areas with a predefined size (in this case, the third molar extraction socket) for grayscale analysis, on a scale where absolute white has a value of 255 and black has a value of 0 (zero). Bone density was measured from "ROI" manager, "Measure" command was selected to give the mean gray value of the "ROI". The "ROI" was selected from the area corresponding to the extraction socket and was standardized for each patient. (Fig. 3)

Statistical analysis

The statistical analysis was performed using SPSS version 17 software (SPSS Inc., Chicago, IL, USA). The student't' test was used to determine whether there was a statistical difference between groups in the parameters measured.

Results

Forty extractions of bilateral impacted mandibular third molars were performed in 20 volunteers (8 men, 12 women; 18 to 24 years old). After extraction of right and left mandibular third molars, the socket at one side received the autologous PRF (test group) and the other was filled with blood clot (control group).

On the second postoperative day, facial swelling was significantly increased in both groups when compared to preoperative measurements; however, the facial swelling in the PRF group was lower than that in the control group and the difference between the two groups was statistically significant (P = 0.016). By the seventh postoperative day, facial swelling in both groups was minimal and there was no statistically significant difference between the two groups (Table 1).

Maximal mouth opening levels were similar preoperatively in the two groups. There was a significant decrease in mean maximal mouth opening in both groups on the second postoperative day compared to the preoperative measurement. The difference between the two groups was also statistically significant on the second postoperative day (P = 0.003). On the seventh postoperative day, almost all of the patients had regained their preoperative mouth opening and there was no statistically significant difference between the two groups (Table 2).

With regard to the mean VAS scores, pain was highest on the operation and the second days and decreased gradually in both groups on postoperative day 7. There were statistically significant differences in VAS scores between the two groups on the first and second postoperative day (P = 0.012, 0.050 respectively) (Table 3).

The mean bone density was 131.30 ± 4.067 in test group and it was 130.95 ± 4.334 in control group immediately after extraction, after three month the mean bone density was 137.10± 3.698 in test group and it was 139.15±3.937 in control group and after 6 month the mean bone density was 150.80±3.955 in test group and it was 152.30±4.846 in control group. There was no statistically significant difference in bone density between the groups at follow up periods. (Table 4).

Discussion

This study was aimed to assess the clinical and radiographic outcomes of the use of platelet rich fibrin (PRF) on soft and hard tissue healing after Impacted Mandibular Third Molar extractions. The results of the present study showed that both facial swelling and trismus to be significantly decreased in the PRF group when compared with the control group on the second postoperative day, whereas the pain was significantly decreased in PRF group on the first and the second day. The same clinical positive effect of using PRF occurred in a clinical

study by Kumar N *et al* (2015) (25) who found that the application of PRF lessens the severity of immediate postoperative sequelae**,** Pain , swelling , and interincisal distance in his study were less in the case group compared with the control group on the first postoperative day. Dohan *et al* (26) suggested that PRF addition may decrease many harmful effects at inflammatory site natural to surgical act by correcting certain destructive and noxious excesses during healing process of wound tissues and thus could be an immune regulation node with inflammation retro-control abilities and explained the reduction of postoperative infections. Ogundipe *et al* (27) studied the effect of of autologous PRP gel on postoperative pain, swelling, and trismus after surgical extraction of mandibular third molars and concluded the PRP group had decreased pain, swelling, and trismus compared with the control group, but this difference was statistically important only for postoperative pain in the present study there were no statistically significant difference in bone density between the groups at follow up periods. These results were in agreement with Gurbuzer *et al* (28) as they evaluated the osteoblastic activity in extraction sockets treated with Platelet-Rich Fibrin using bone scintigraphy based on technetium-99m methylene diphosphonate uptake and they found that PRF exhibits the potential characteristics of an autologous fibrin matrix, but might not lead to enhanced bone healing in soft tissue impacted mandibular third molar sockets after 4 weeks of surgery. Kumar N *et al* evaluated the bone density by using a scoring system in which scores were listed for the lamina dura, overall density and trabecular pattern appreciable on an IOPAR. The lamina dura, overall density, and trabecular pattern scores were higher in the case group compared with the control group, indicating a greater bone density in the case group. This difference was not statistically different between the 2 groups. However, positive effects by using platelet-rich fibrin (PRF) as sole filling material in bone formation have been showed in other studies (29-31) In a systematic review conducted by Fabbro *et al* (32) on the use of autologous platelet concentrates in post extraction socket healing, favorable soft and hard tissue healing and post-operative discomfort reduction was reported by various authors but, due to the lack of standardization of the technique for the preparation of these concentrates its true regenerative effects were unknown.

Conclusion

Within the limits of the present study we concluded that the application of PRF into the sockets after Impacted Mandibular Third Molar Surgery lessens the severity of immediate postoperative sequelae, but has no effect on bone formation.

The results of our study however, need to be confirmed in the long term and with a larger sample of patients.

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Figure 1. (A) Before extraction, (B) After extraction, (C) Application of PRF into an extraction socket, (D) After suturing.
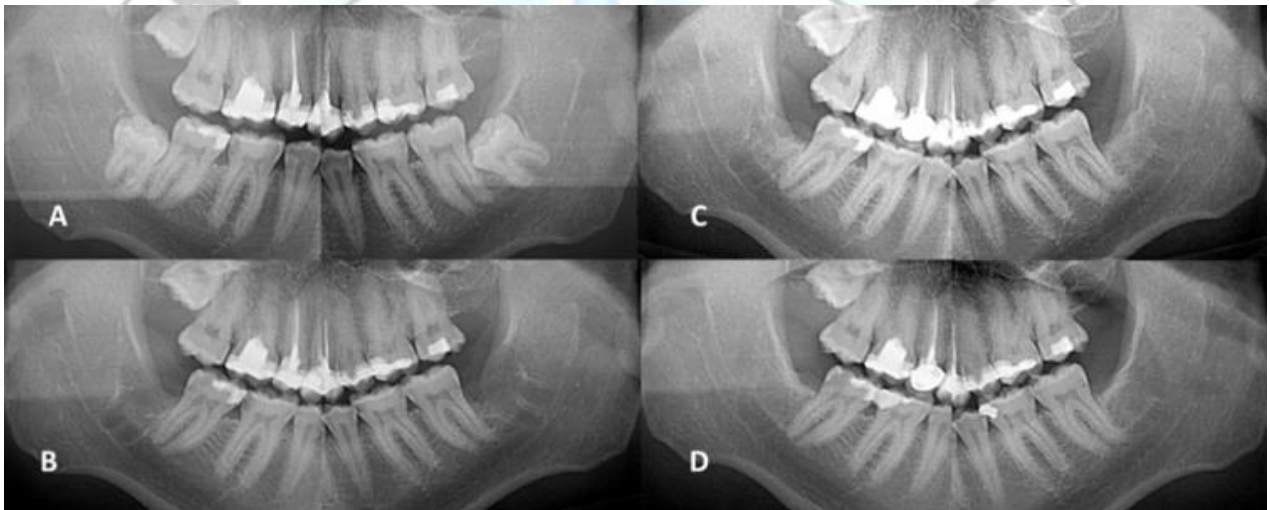

Figure 2. Panoramic radiograph of surgical site of patient with bilateral impacted mandibular third molars : (A) before extraction, (B) immediately after the extraction, (C) after 3 months , (D) after 6 months.
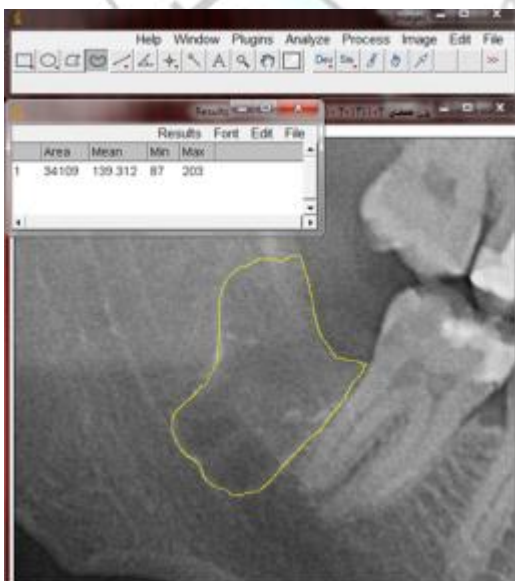

Figure 3. Measurement of bone density in the mandible, using the image analysis software image J

Table 1. Measurement of swelling (mean ± SD in mm)

Groups	Preoperative	Second day	Seventh day
Control	10.07±0.91	11.12±0.81	10.14±0.89
Test	9.91±0.55	10.75±0.51	10.10±0.48
P values	0.513	0.016	0.873

Table 2. Measurement of maximal mouth opening (mean ± SD in mm)

Groups	Preoperative	Second day	Seventh day
Control	39.54±5.02	29.75±4.31	38.72±4.95
Test	39.68±4.95	34.21±4.58	38.54±4.74
P values	0.930	0.003	0.910

Table 3. Comparison of VAS scores (mean ± SD)

Groups	Preoperative	Second day	Seventh day
Control	6.20±1.32	4.15±1.13	0.65±0.81
Test	5.15±1.18	3.45±1.05	0.60±0.82
P values	0.012	0.05	0.848

Table 4. Measurement of bone density (mean ± SD in mm).

Groups	first week	After 3 months	After 6 months
Control	130.95±4.33	139.15±3.93	152.30±1.08
Test	131.30±4.06	137.10±3.69	150.80±3.95
P values	0.794	0.98	0.290