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ORIGINAL ARTICLE

Clinical effects of platelet-rich fibrin (PRF) following surgical extraction of lower third molar

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KEYWORDS

PRF;
Third molar;
Pain;
Analgesic consumption;
Socket complications;
Soft tissue healing

Abstract *Objective:* The purpose of this study was to assess the effect of platelet-rich fibrin (PRF) on postoperative pain, analgesic consumption, soft tissue healing and socket complications following the extraction of mandibular third molars.
Methods: A total number of 50 impacted third molars were surgically removed from 47 patients (13 males and 34 females; with a mean age of 25.24 ± 7.04 years). PRF clots were placed in the extraction sockets of patients included in the study group, while the sockets remained empty in the control group. The variables assessed were pain, analgesic consumption, soft tissue healing and socket complications encountered during the first postoperative week.
Results: In the study group, a significantly less pain was recorded in the fifth, sixth and seventh postoperative days ($P = 0.041$, 0.031 and 0.005 respectively). Patients included in the study group also significantly consumed less analgesics for the second, third, sixth and seventh postoperative days ($P = 0.019$, 0.039, 0.045 and 0.020 respectively). PRF significantly reduced the incidence of alveolar osteitis ($P = 0.037$) but not the infected or inflamed sockets ($P = 1.00$ and 0.312 respectively). No significant difference was observed between PRF and control groups regarding soft tissue healing ($P = 0.187$).
Conclusion: PRF could reduce alveolar osteitis, pain, and analgesic consumption following removal of impacted mandibular third molars.

1. Introduction

Extraction of impacted mandibular third molars is the most frequent procedure performed by oral surgeons. This procedure may be associated with considerable postoperative complications including pain, trismus, edema, surgical site infection as well as alveolar osteitis (AO).[1,2]

AO is one of the most common painful postoperative complications following surgical extraction, with an incidence ranging from 7% to 32.6%.[3,4] Different modalities have been investigated in an attempt to prevent AO. However a great

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controversy still exists regarding the most appropriate and effective method.[5,6]

Platelet rich plasma (PRP) is reported to reduce pain and inflammation as well as to improve soft tissue healing following tooth extraction.[7] Despite the benefits of PRP in maxillofacial surgery, its cost and preparation method are considered limiting factors for its routine use.[8]

PRF is the second generation of platelet concentrate. It is prepared with a simple and inexpensive processing without biochemical blood handling.[9] PRF has multiple applications in oral surgery, including socket preservation, endodontic surgery, and implant surgery.[10–12]

The role of PRF on potential postoperative complications following mandibular third molar surgery is unclear. This study was designed to evaluate the role of PRF on soft tissue healing, socket complications, pain and analgesic consumption following extraction of impacted lower third molars (ILTMs).

2. Methods

A prospective, randomized, controlled clinical trial was conducted from January 2014 to January 2015 at Oral and Maxillofacial Surgery department, Faculty of Dentistry, Mansoura University (Mansoura, Egypt). The ethical board of Faculty of Dentistry approved the study protocol and all patients provided signed informed consents.

A total of 50 ILTMs were removed from 47 patients. The inclusion criteria were presence of at least one impacted lower third molar (ILTM) requiring extraction, absence of systemic diseases, age $\geqslant$18 years and the ability to cooperate with the requirements of the study protocol. Pregnant female patients, patients on oral contraceptive drugs and smokers were excluded from the study. Patients were randomized by the closed-envelop method and divided into two groups. A PRF clot was inserted in each of the extraction sockets of patients included in the study group (24 patients; 25 ILTMs), while no material was placed in the sockets of patients included in the control group (23 patients; 25 ILTMs).

Preoperative investigations included medical and dental history, chief complaint, oral hygiene evaluation, a periapical and panoramic radiograph. In addition, the indication of tooth removal and the difficulty level of ILTMs based on Pederson classification[13] were recorded.

2.1. Operative procedure

A standardized surgical procedure was performed by the same operator for all patients. Under strict aseptic conditions, an inferior alveolar nerve block with buccal infiltration, were given using 2% mepivacaine hydrochloride with 1:20,000 levonordephrine*. A mucoperiosteal envelope flap was utilized for all surgeries. Bone removal and tooth sectioning were performed as deemed necessary using a low-speed handpiece under copious saline irrigation. After tooth removal, PRF clot was prepared and placed in the extraction sockets of patients included in the study group, while no material was placed in the control sockets. Subsequently, flap closure was achieved using 3–0 silk sutures.

Postoperatively, identical postoperative instructions were given to all patients. Postoperative medications consisted of Amoxicillin 500 mg† 4 times/day for five days, Ibuprofen 400 mg 3 times a day as an analgesic for the day of surgery and chlorhexidine mouthwash 2 times/day for 7 days. Patients were instructed to continue on the analgesics in case of persistent pain and to record the dose. Sutures were removed on the seventh postoperative day.

2.2. Steps of PRF preparation

Preparation of PRF required a table centrifuge (Fig. 1), and blood collection kit including a 24-gage needle and 5 ml blood collection tube. PRF was prepared as following:

1. 5 ml of venous blood was drawn into the tube without anticoagulant and was immediately centrifuged at 3000 rpm for 10 min.
2. After which it was separated into the following three layers: upper straw-colored acellular plasma, the middle layer containing the PRF, and the red-colored lower fraction containing red blood cells (RBCs) (Fig. 2).
3. The upper straw-colored layer was removed and the PRF was collected 2 mm below to the lower dividing line (Fig. 3).

2.3. Assessment

Patients were followed up to one week postoperatively unless the patient condition necessitated longer follow up period. Pain, analgesic consumption, soft tissue healing and socket complications were evaluated. The patients were given a questionnaire and were instructed to record their pain level using visual analogue scale (VAS)[14] and the number of analgesic tablets used from the second to the seventh postoperative days.

Soft tissue healing was assessed on the seventh postoperative day using the healing index reported by Landry et al.[15], which depends on tissue color, presence of bleeding on palpation, epithelialization of wound margins, granulation tissue, and suppuration.

Socket complications were evaluated following the criteria described by Cheung et al.[16] as follows:

- Acutely infected socket was diagnosed by a painful socket with pus swelling, and erythema in combination with an elevated body temperature.
- AO was diagnosed by the presence of a continuous throbbing postoperative pain in and around the extraction socket that was not adequately relieved by analgesics. The pain was associated with partially or completely disintegrated blood clot or an empty socket with or without halitosis.
- Acutely inflamed socket was diagnosed by a painful socket with profoundly inflamed tissue but without pus or systemic fever.

Cases of AO were treated with socket irrigation using normal saline and the sockets were dressed with Alvogyl iodoform and systemic analgesics were prescribed (Fig. 4a–4f).

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† Emox; Egyptian International Pharmaceutical Industries Company, EIPCO, Alexandria, Egypt.

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Fig. 1 Centrifuge machine.

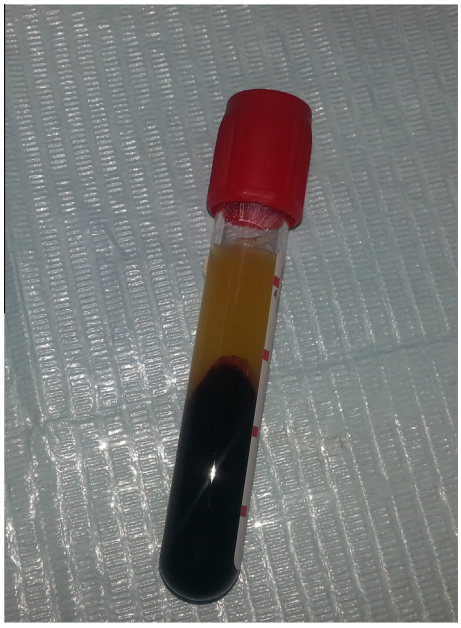

Fig. 2 Layers of centrifuged blood.

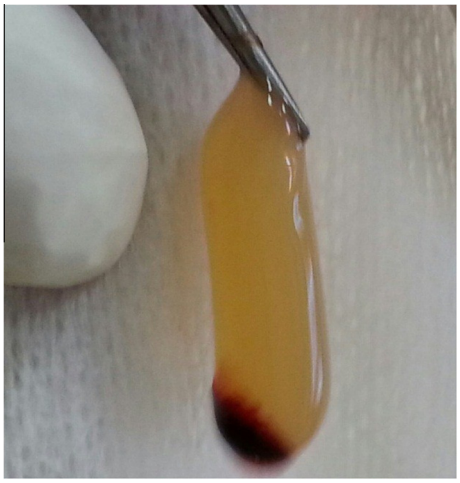

Fig. 3 PRF clot.

2.4. Statistical analysis

Data were analyzed using SPSS version 16.0 (SPSS, Inc, Chicago, IL). Mann–Whitney and *t*-tests were used for quantitative data and chi-square test was used for qualitative data. All comparisons were conducted at a 5% level of significance.

3. Results

Age, sex, tooth angulation, anesthetic cartridges used, and the difficulty level of mandibular third molar were comparable and no statistically significant difference was observed between PRF and control groups (Table 1).

In this study, PRF patients significantly recorded less pain for the fifth, sixth and seventh postoperative days ($P = 0.041$, 0.032 and 0.005 respectively), whereas no differences were observed for the second, third, and fourth postoperative days ($P = 0.152$, 0.078 and 0.057 respectively). In addition, less analgesic consumption was recorded in the PRF group for the second, third, sixth and seventh postoperative days ($P = 0.019$, 0.039, 0.045 and 0.020 respectively). No significant difference was found for the fourth and fifth postoperative days ($P = 0.054$ and 0.070 respectively) (Table 2).

Regarding soft tissue healing, insignificant difference was observed between the two groups ($P = 0.187$) and the mean values of the study and the control groups were 4.52 (0.71) and 4.20 (0.95) respectively. The healing scores in the PRF group were 3 cases with good, 6 cases with very good and 16 cases with excellent healing scores whereas 2 cases with poor, 3 cases with good, 8 cases with very good and 12 cases with excellent healing scores in the control group. (Table 3).

Considering the socket complications, PRF significantly reduced the incidence of AO compared with the control group ($P = 0.037$). However, there were no significant differences between the two groups regarding the incidence of infected or inflamed sockets ($P = 1.00$ and 0.312 respectively) (Table 4).

4. Discussion

Platelet-rich fibrin is characterized by the slow polymerization during its preparation that generates a fibrin network very similar to the natural one that enhances cell migration and proliferation. Being a reservoir of platelets, leukocytes, cytokines and immune cells, PRF is reported to allow slow release of cytokines; TGF, PDGF, VEGF, and EGF which play a critical role on angiogenesis and tissue healing and cicatrization.[9,17,18] PRF also reported to enhance angiogenesis, support immunity, and to enhance the coverage of injured tissues through its positive effect on epithelial cells and fibroblasts.[18]

Although, PRF preparation is simple, inexpensive process, and requires no additives, rapid blood handling is an important factor in success of its preparation. Failure in quick handling of the blood sample results in a diffuse polymerized fibrin within the glass tube and only a small blood clot without consistency will be obtained.[17]

The evidence supports the use of PRF and PRP as socket preservation materials to enhance soft tissue healing and reduce postoperative complications. However, there is no evidence to date to support the positive effect of autologous materials in hard tissue regeneration.[7,19]

Fig. 4a Preoperative panoramic radiograph showing bilateral mesioangular angulated mandibular third molars.

Fig. 4b A photograph showing left mandibular third molar.

Fig. 4c A photograph showing elevated envelope flap.

Complications following third molar surgery are not uncommon. Pain and delayed healing are perhaps the most frequently encountered complications. AO is a painful and relatively common complication that necessitates intervention for treatment. The incidence of AO following removal of ILTMs varies from 7% to 32.6%.[3,4] In accordance with the previous studies, an incidence of 8% was recorded in the present study.

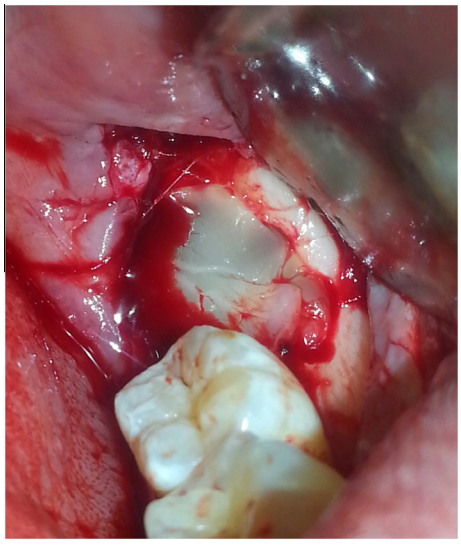

Fig. 4d A photograph showing the PRF clot placed inside the socket.

Fig. 4e A photograph showing closure of the wound.

Fig. 4f A photograph showing soft tissue healing after one week.

AO is a multi-factorial condition. However, all involved factors eventually result in failure of maturation of the initially formed blood clot.[6,20] Consequently, whatever the modality utilized to prevent or treat AO, promoting the normal healing is always the target. Different materials have been extensively researched in an attempt to prevent AO.[6] Autogenous materials prepared from the patient's blood are always more promising, as they contain a concentrate of a considerable number of the factors required for normal wound healing.[7,21,22]

PRF is a healing biomaterial, perhaps this could explain the significant difference in the incidence of AO encountered in the PRF group compared with the control group. The positive role of PRF in the prevention of AO was also reported by Hoaglin and lines[23] and Eshghpour et al.[24]

Infected sockets following tooth extraction could develop as a result of poor oral hygiene, compromised immunity, or a pre-existing infection.[25] Only two infected sockets (4%) were encountered in the present study, which was in agreement with the results of other studies.[26,27] The immunological properties of PRF resulting from its content of leukocytes, could be useful in the prevention of surgical site infection.[28] Nevertheless, insignificant role of PRF in the prevention of infected sockets was found. This, however, could be related to the small sample size, good health of the patients, and the strict oral hygiene instructions followed by patients including in this study.

In order to evaluate whether PRF could influence the healing of soft tissue overlying the extraction sockets, the Landry et al. index[15] was used in the present study. We found the effect of PRF on soft tissues healing to be insignificant, which was in contrast to Marenzi et al.[29] 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.[15]

Relief of postoperative pain is an essential criterion in the overall success of tooth extraction. In addition, most of the potential postoperative complications are in fact manifested as pain. In the present study, the degree of pain was measured using the VAS and the number of analgesic tablets taken for

Table 1 Sex, age, tooth angulation, difficulty level, and anesthetic cartridges used for patients included in this study.

Items	PRF group (n = 25)		Control group (n = 25)		P-value
	No	%	No	%	
Sex					
Male	6	24.0	7	28.0	0.747*
Female	19	76.0	18	72.0	
Age					
Mean ± SD (Range)	25.80 ± 6.72 (18–46)		24.68 ± 7.443 (18–48)		0.579†
Tooth angulation					
Mesioangular	5	20.0	5	20.0	0.783*
Horizontal	8	32.0	5	20.0	
Vertical	10	40.0	12	48.0	
Distoangular	2	8.0	3	12.0	
Difficulty level‡					
Slightly difficult	4	16.0	4	16.0	0.918*
Moderately difficult	18	72.0	17	68.0	
Very difficult	3	12.0	4	16.0	
Anesthetic cartridges used					
Mean (SD)	3.16 (.86)		3.50 (.73)		0.140

Data presented as numbers with the percentages within each group, or mean ± standard deviation. PRF, platelet-rich fibrin; SD, standard deviation.

* Using chi-square test.

† Using t-test.

‡ Based on the Pederson scale regarding the sum score of spatial direction mandibular third molar, depth of impaction and its relationship with the ramus on panoramic radiograph.

Table 2 VAS scores and analgesic consumption among PRF and control groups.

Items	PRF group (n = 25)		Control group (n = 25)		P-value
	Mean (SD)	Median	Mean (SD)	Median	
Visual analogue scale*					
POD2	3.08 (2.75)	3	4.24 (2.86)	3	0.152
POD3	1.92 (2.27)	1	2.88 (2.36)	3	0.078
POD4	1.20 (1.73)	0	2.16 (2.37)	1	0.057
POD5	0.80 (1.55)	0	1.28 (1.54)	1	0.041
POD6	0.48 (1.50)	0	0.72 (1.40)	0	0.031
POD7	0 (0)	0	0.52 (1.41)	0	0.005
Analgesic consumption*					
POD2	1.32 (1.11)	1	2.12 (1.20)	2	0.019
POD3	0.88 (.88)	1	1.40 (.86)	1	0.039
POD4	0.64 (.75)	0	1.08 (.81)	1	0.054
POD5	0.44 (.58)	0	0.84 (.80)	1	0.070
POD6	0.16 (.37)	0	0.52 (.71)	0	0.045
POD7	0 (0)	0	0.24 (.52)	0	0.020

Data presented as mean ± standard deviation and median.
POD, postoperative day; PRF, platelet-rich fibrin; SD, standard deviation.
* Using Mann Whitney test.

Table 3 Soft tissue healing scores between PRF and control groups.

Items	PRF group (n = 25) Mean (SD)	Control group (n = 25) Mean (SD)	P-value
Soft tissue healing score	4.52 (0.71)	4.20 (0.95)	0.187*

Data presented as mean ± standard deviation.
PRF, platelet-rich fibrin; SD, standard deviation.
* Using t-test.

Table 4 Socket complications encountered in PRF and control groups.

Items	PRF group (n = 25)		Control group (n = 25)		P-value
	No	%	No	%	
Acutely inflamed socket	1	4.0	0	0	0.312*
Alveolar osteitis	0	0	4	16.0	0.037
Acutely infected socket	1	4.0	1	4.0	1.00

Data presented as numbers with the percentages within each group.
PRF, platelet-rich fibrin.
* Using chi-square test.

pain relief. This study revealed that PRF significantly reduced postoperative pain and analgesic consumption following surgical removal of impacted third molars. This, although could not be detected clinically, could reflect a better and faster healing of the extraction sockets. This is in agreement with other studies.[29,30]

The decrease in pain or analgesic consumption, although statistically significant for few postoperative days, should be considered with caution because it is based on the subjective visual analogue scale, pain sensation, and response to analgesics, which differ from patient to another.

The main limitations of the present study were the small sample size, short follow-up and non-blinded study. Larger sample size, longer follow-up and double blinded split-mouth study; with a similar degree of difficulty of ILTMs for each patient are recommended for further evaluation.

5. Conclusion

Within the limitations of the present study, platelet-rich fibrin (PRF) application after mandibular third molar surgery is a good biologic material that reduces postoperative pain, analgesic consumption and alveolar osteitis. However, it has insignificant effect on soft tissue healing following removal of impacted mandibular third molars.

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Conflict of interests

The authors declare no conflict of interest.

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