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Universal Journal of Pharmaceutical Research
An International Peer Reviewed Journal
ISSN: 2831-5235 (Print); 2456-8058 (Electronic)

RESEARCH ARTICLE

CLINICAL EFFECTS OF PLATELETS RICH FIBRIN (PRF) FOLLOWING SURGICAL EXTRACTION OF IMPACTED LOWER THIRD MOLARS AMONG A SAMPLE OF YEMENI ADULTS

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Article Info:

Article History:
Received: 8 October 2022
Reviewed: 10 November 2022
Accepted: 22 December 2022
Published: 15 January 2023

Cite this article:
Makki KIF, Abbas AMA, Alhadi YAA, Al-Shamahy HA. Clinical effects of Platelets Rich Fibrin (PRF) following surgical extraction of impacted lower third molars among a sample of Yemeni adults. Universal Journal of Pharmaceutical Research 2022; 7(6):14-21.
https://doi.org/10.22270/ujpr.v7i6.864

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Abstract

Background and aims: Third molar surgery is one of the most frequent procedures in oral and maxillofacial surgery. Pain, trismus, and swelling are the majority symptoms that have an impact on patients' quality of life. Haemorrhage, alveolitis and infections are general complications. Several endeavors have been through to decrease the possibility of complications and make better patients' quality of life, such as the administration of platelet-rich plasma (PRP) or the administration of platelet-rich fibrin (PRF). The aim of this study is to determine the clinical consequences of PRF subsequent to surgical extraction of impacted lower third molars among a sample of Yemeni adults by evaluate the PRF effect on postoperative complications of pain, swelling, and mouth opening and to compare the difference in the healing process between the PRF surgery site and the control site.
Methods: The prospective study consisted of 36 patients who obtainable for subtraction of an impacted bilateral mandibular molar. Subsequent to extraction, plugs were filled up with PRF or without PRF in the study (18 patients) and comparative control (18 patients) groups, respectively. Postoperative edema was calculated using a flexible tape measure by estimating the distance between several facial features on the 2nd to the 7th postoperative days. Postoperative pain was assessed using a line-type visual analog scale (VAS) and a verbal scale (VRS); and trismus by caliper scales. Epi-Info version 7.0 was used for data analysis.
Results: There were statistical significant variations concerning the PRF group and the control group in regard to pain intensity, number of analgesics tablets used and the interincisal distance, as the *p* value were 0.001, 0.0001 and 0.001 respectively.
Conclusion: The PRF helps in reducing the post-surgical pain, edema and trismus. As well as accelerate healing process after the application to the socket of surgically extracted lower third molar.
Keywords: Edema, impacted third molar surgery, pain, Platelet Rich Fibrin (PRF), trismus.

INTRODUCTION

Wisdom teeth are most frequently impacted, which is taking into consideration as a pathological condition. The delayed formation of the third molars and the development of the size of the lower jaw meant that there was not enough space for suitable eruption. Variations in the physical activity and type of food consumed lead to jaw size reduction[1,2]. In addition, genetic factors should be taken into account[3,4]. Lack of adequate gap for the eruption of the third molar is not uncommonly discernible by periorbital inflammation, pain, formation of cyst, and root resorption of adjacent teeth[2,5]. The surgery of the third molar is one of the mainly common procedures in maxillofacial and oral surgery. Swelling, pain, and trismus are the most common signs affecting patients' quality of life. In addition, alveolitis, infections, and bleeding are common complications[6,7]. Several attempts have been done to decrease the complications risk and enhance patients' quality of life, such as platelet-rich fibrin (PRF), platelet-rich plasma (PRP) administration[8,9],

laser[10], cryotherapy, and osteotomy or flap designs, and pharmacological treatments[11-14]. Nevertheless, the precise resolution for edema and pain was not discovered. PRF thrombolysis, acquired by Chouckroun *et al.* [15], consisting of platelets, leukocytes, cytokines, and circulating dendritic cells (stem cells) secured by a fibrin matrix[15]. These elements make PRF a therapeutic biomaterial that allows for optimal healing[16]. PRF belongs to the next generation of platelet concentrates destined for simplified preparation without biochemical blood processing[17]. Extraction cavities will heal more rapidly and pain will be decreased if autologous platelet concentrate is applied to the area[15]. Several studies have shown that PRF accelerates wound healing in periodontal defects, cyst cavities, and paranasal sinuses[15,18,19]. In addition to the benefits of this method in maxillofacial surgery, its preparation and handling are simple, inexpensive and subjective in nature[20].

Although previous research has been conducted on dental caries, oral and facial abscesses of odontogenic origin, localized aggressive gingivitis (LAP), periodontitis, bacterial and fungal oral infections, interleukin-1 levels in human gingival sulcus, etc. in Sana'a Yemen[21-33], there is no information regarding the clinical effects of PRF after surgical extraction of impacted lower third molars although this is widely used in dental surgery in Yemen. Therefore, this study aimed to determine the clinical effects of PRF after surgical extraction of impacted lower third molars among a sample of Yemeni adults by evaluate the effect of PRF on postoperative complications of pain, swelling, and mouth opening and to compare the difference in the healing process between the PRF surgery site and the control site.

SUBJECTS AND METHODS

Study design: The prospective study was conducted to evaluate the effect of PRF after surgical removal of impacted mandibular third molar.

Study area: This study was carried out in the clinic of maxillofacial surgery department, Faculty of Dentistry, Sana'a University.

Study population and Sample size: The study population included patients who were referred to the Clinic of Oral and Maxillofacial Surgery, Faculty of Dentistry, Sana'a University for extraction of affected third molars in Sana'a City from December 2021 to June 2022 (time allowed for clinical work for Master's degree in Oral and Maxillofacial Surgery). Sample size was 36 impaction patients; 18 cases and 18 controls. The sample size was determined according to the availability of patients in the time period of the study.

Inclusion criteria: The inclusion criteria including patients with bilateral mandibular impaction, age over 18 years- old, nonsmoker, free from systemic diseases, with good oral hygiene, free of inflammation signs or symptoms.

Exclusion criteria: The study excluded, pregnant and/or lactating women, patients on steroidal anti-inflammatory drugs, patients with systemic diseases that reduce immunity such as diabetes, hypothyroidism, immunosuppressed patients, HIV, severe liver disease, malnutrition, adrenal insufficiency, Cushing's syndrome. The study also excluded patients taking anticoagulant medications and smokers.

Data collection: All patients underwent clinical evaluation and all data was collected in the pooled data sheet (case sheet), which was designed for a systematic recording. The intraoperative distance was measured preoperatively using calipers. Each patient was a fellow from the first to the seventh day of surgery. On these second, third, and seven days, the distance between the cuts was measured and swelling was assessed. Each patient was asked to report a pain score and the number of analgesia tablets taken from the first day of surgery to the seventh day. Each side was extracted on different dates.

Surgical procedure: Underneath all aseptic practices, 5 mL of blood was collected intravenously from the anticubital area of the patient's forearm make use of a vacutainer needle and moved into the vacuum tube without anticoagulant and centrifuged at 2,700 rpm for 12 min. The surgical site of the affected third molar was irrigated with normal saline and be prepared for the surgical practice. The inferior alveolar nerve block and the long buccal nerves were treated. A scalpel with a blade No. 15 was used to make an incision for a flap (triangular flap). A complete mucoperiosteal flap was lifted by the periosteal elevator. After that a straight hand piece of suitable speed and torque was used to eradicate the bone from the occlusal side of the tooth with normal irrigation with abundant saline. Bone gutters and minimal tooth separation were performed to allow removal of the impacted tooth with minimal trauma to the bone. After removal of the impacted tooth, an appropriate debridement was performed. A bone file was used to smooth out any sharp bone edges. The cavity was then cleaned with normal saline. The prepared 1-cm PRF was grasped by forceps and delivered into the socket (Figure 1). The prepared PRF was obtained in the middle of the tube, just between the erythrocytes at the bottom and the cellular plasma at the top. Then, the flap was closed with 3-0 black silk interrupted sutures. The suture was removed on the seventh day after surgery. The patient was only taking Paracetamol 500 mg as an analgesic, without a prescription of antibiotics.

Variables of the study

Inter-incisal distance: The inter-incisal distance was measured before the start of surgery, and on the 2nd day, 4th day and 7th day after surgery, which was reported in centimeter (cm).

Pain: It was revealed from the patient by answering the questions for the seven post-operative days, each answer had a number as following:

0=There is no pain.
1= Very mild pain.
2=Moderate pain with eating.
3=Severe pain that interferes with sleep.
4=The pain is intense and persistent in all cases.

Number of analgesic used by the patient: It was revealed from the patient by writing the number of

analgesics that was taken for the seven post-operative days in a chart given to the patient.

Swelling: It was examined in the 2nd day, 5th day and 7th day after the surgery, in which each category had a number as following:

0=No swelling.
1=Very slight swelling.
2=Slight swelling.
3=Moderate swelling.
4=Severe swelling.

Statistical method: Data presented using appropriate descriptive statistics (including frequency, mean, standard deviation and *p*-value). All data statistical analysis was performed by using the Statistical Package for Social Science (SPSS) version 24 and Excel 2010. In which, after data collection, they were recorded and entered to the SPSS for analysis.

Ethical approval: Ethical approval was obtained from the Medical Ethics Committee of the Faculty of Dentistry, Sana'a University that dated November 24-2021 with official number 2021-27. Each patient in the study signed consent. All data, including patient identification and CBCT images were kept confidential.

RESULTS

Thirty-six lower third impactions (18 patients) were evaluated post operatively for this study. Seven of the patients were males 7 (38.9%) and 11 (61.1%) were females. The mean age was 22.8±2.179 years and the age range was from 19 to 28 years old (Table 1) and (Figure 1).

Table 1: The distribution of patients according to gender and side of operations.

Parameters		With PRF N (%)	Without PRF N (%)
Gender	Male	7 (38.9%)	7 (38.9%)
	Female	11 (61.1%)	11 (61.1%)
	Total	18 (100%)	18 (100%)
Side	Right	6 (33.3%)	12 (66.7%)
	Left	12 (66.7%)	6 (33.3%)
	Total	18 (100%)	18 (100%)

Distribution of pain: There was very mild pain in 14 (77.8%) and moderate pain in 4 (22.2%) with eating in the PRF group. On the other hand, there was moderate pain in 7 (38.9%) with eating and severe pain interfering with sleep in 9 (50%) in the control group. There was a statistically significant difference between the two groups (*p*=0.001) (Table 2, Figure 2).

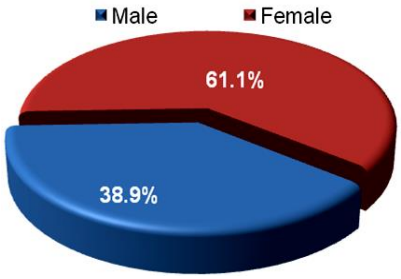

Figure 1: Distribution of data by gender.

The Linear measurements of inter-incisal distance: The mean preoperative distance in both groups was 4.32±498 mm. There was no statistically significant difference between both groups in the 2nd postoperative day. Unlike the 4th and 7th postoperative days, there was statistically significant difference between both groups (*p*=0.001). Also, there was no statistically significant difference between both groups in regard to gender (Table 3, Figure 3).

The number of analgesic used by the patient: There was statistically significant difference between both groups in the whole postoperative week in the number of analgesic used (*p*-value=0.0001). The PRF group did not use any analgesic in the postoperative 5th, 6th and 7th days. Unlike the group without PRF which used analgesics with the means of (1.72±1.487), (1.33± .029) and (1.28±0.958) respectively (Table 4, Figure 4).

Post-operative swelling in both groups: There was statistically significant difference between both groups in second, fifth and seventh postoperative day with regard to swelling (*p*-value=0.001), (*p*-value=0.034), and (*p*-value=0.001), respectively. In contrast to the fifth day, there was no statistically significant difference between both groups with regard to swelling (Table 5, Figure 5).

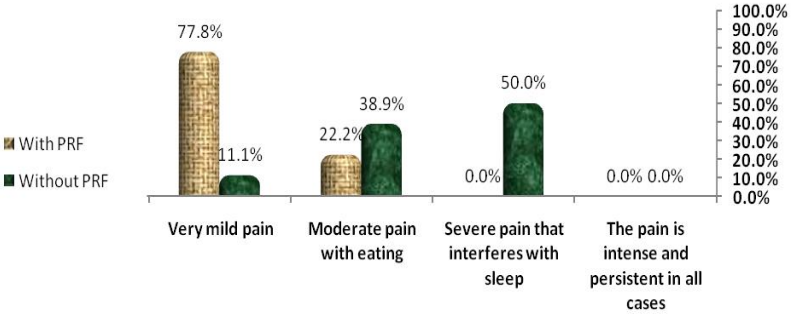

Figure 2: The level of pain in the PRF group and control group.

Table 3: The mean ±SD values of inter-incisal distance of PRF group compare with control group.

Inter-incisal distance measurement	With PRF Mean	±SD	Without PRF Mean	±SD	*p*-value
Preoperative	4.32	0.498	4.32	0.498	1.000
2nd postoperative day	3.33	0.57	2.89	0.76	0.104
4th postoperative day	3.19	0.67	2.28	0.69	0.001*
7th postoperative day	3.53	0.79	2.33	0.95	0.001*

Inter-incisal distance measurement		Preoperative		2nd postoperative day		4th postoperative day		7th postoperative day	
		Mean	*p*-value	Mean	*p*-value	Mean	*p*-value	Mean	*p*-value
With PRF	Male	4.39±0.57	0.791	3.50±0.65	0.451	3.14±0.69	0.860	3.57±0.84	1.00
	Female	4.27±0.46		3.23±0.57		3.23±0.68		3.50±0.806	
Without PRF	Male	4.39±0.575	0.79	3.29±0.76	0.104	2.57±0.84	0.246	2.29±0.95	0.930
	Female	4.27±0.46		2.64±0.67		2.09±0.54		2.36±1.00	

p-value between with PRF group and without PRF group for interincisal distance measurement (Mann-Whitney Test)

DISCUSSION

There are no published data on the effect of PRF on pain, trismus and swelling in third-molar surgery in Yemen. Also, there is a very inadequate quantity of literature on the outcome of PRF on pain and swelling in third molar surgery worldwide. The aim of this study is to investigate the effect of PRF appliance on postoperative edema and pain subsequent to surgical removal of mandibular third molars. The postoperative pain and edema with and without PRF subsequent to surgery would be equal according to the null hypothesis. The authors estimated and compared postoperative edema and pain subsequent to surgical amputation of mandibular third molars in PRF and non-PRF sockets. PRF is the second generation of platelet concentrates (PRP is the first generation). PRF contains endogenous cytokines and various immune cells; it is a fibrous membrane that adequately covers the wound and can be sutured[34].

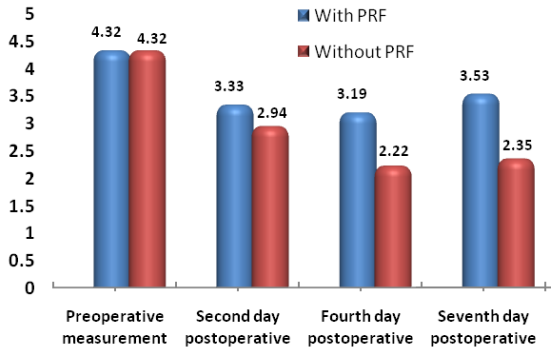

Figure 3: The mean value of inter-incisal distance in the PRF group and without PRF group.

Table 4: The mean value of number of analgesic used by the patient in the PRF group and without PRF group.

Number of analgesic used by the patient	With PRF	Without PRF	*p*-value
First day	2.5±1.000	4.13±1.628	0.0001*
Second day	2.44±0.527	4.06±1.436	0.0001*
Third day	2.33±0.516	4.08±1.084	0.0001*
Fourth day	0	3.50±1.243	0.0001*
Fifth day	0	2.73±1.104	0.0001*
Sixth day	0	2.09±0.701	0.0001*
Seventh day	0	2.10±0.738	0.0001*

P-Value between with PRF group and without PRF group for number of analgesic used by the patient (Mann-Whitney Test)

In the oral and maxillofacial region, PRF has been extensively used in sinus augmentation as the only grafting substance or in mixture with an allograft or xenograft[35]. PRF clots is also used in the treatment of acute sinus perforations without flap[36]. Preservation of extraction cavity, intrabony defects, and periodontal troubles are the other indications for the use of intraoral PRF[16]. In the current study PRF treatment reduction pain and swelling values significantly in which there was very mild pain in 14 (77.8%) and moderate pain 4 (22.2%) with eating in the PRF group while there was moderate pain in 7 (38.9%) with eating and severe pain that interferes with sleep in 9 (50 %) in the control group (Table 2). Our consequences are comparable to those reported by Kumar *et al.*,[37] where this study was conducted on 31 patients; this study reported that the use of PRF significantly reduced pain and edema values on the first control day subsequent to surgery.

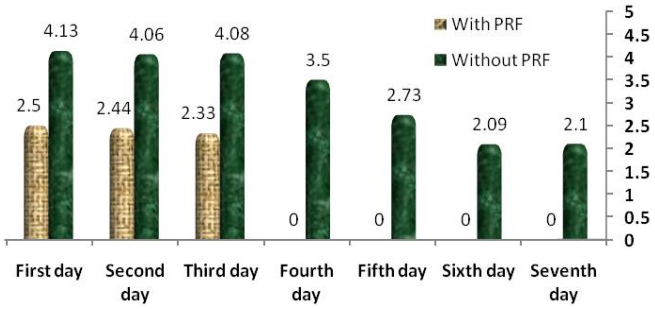

Figure 4: The number of antalgic used in the PRF group and without PRF group.

They scored these values using a Type Likert VAS as requisite by Pasqualini *et al.*,[38]. In another study of 20 bilaterally affected third molar surgeries, Singh *et al.*,[39] reported that the use of PRF after third molar surgery reduced pain in the first, third, and seventh postoperative days (measured with a Likert-type VAS); On the other hand, this result was not statistically significant once matched up to the control group. With a large sample in a multicenter study (56 patients, 102 teeth), Özgül *et al.*,[40] informed that the use of PRF subsequent to third molar extraction significantly reduced lateral edema (including tragus and commissure) on the first and third postoperative day. They reported that there were no statistically significant variations on the seventh day subsequent to surgery. They also found no significant differences in vertical swelling, which included lateral can thus measurement and gonion measurement or pain at all, intervals. In the current study, there was statistically significant variation among both groups in second and seventh postoperative day with regard to edema (*p*-value=0.012) (*p*-value=0.011) respectively, in which there was significant decrease in PRF group comparing control group (Table 5).

Table 5: The frequency of swelling in the PRF group and without PRF group.

	Swelling	With PRF N (%)	Without PRF N (%)	*p*-value
Second day	No swelling	2 (11.1%)	1 (5.6%)	0.248
	Very slight swelling	2 (11.1%)	3 (16.7%)	0.273
	Slight swelling	2 (11.1%)	7 (38.9%)	0.005*
	Moderate swelling	12 (66.7%)	7 (38.9%)	0.012*
	Severe swelling	0	0	-
	Total	**18 (100%)**	**18 (100%)**	
Fifth day	No swelling	3 (16.7%)	1 (5.6%)	0.083
	Very slight swelling	2 (11.1%)	1 (5.6%)	0.248
	Slight swelling	1 (5.5%)	3 (16.7%)	0.083
	Moderate swelling	12 (66.7%)	13 (72.2%)	0.308
	Severe swelling	0	0	-
	Total	**18 (100%)**	**18 (100%)**	
Seventh day	No swelling	3 (16.7%)	1 (5.6%)	0.083
	Very slight swelling	5 (27.8%)	3 (16.7%)	0.102
	Slight swelling	3 (16.7%)	3 (16.7%)	1.000
	Moderate swelling	6 (33.3%)	11 (61.1%)	0.011*
	Severe swelling	1 (5.5%)	0	-
	Total	**18 (100%)**	**18 (100%)**	

Current findings differ from those reported by Bilginaylar *et al.*,[41] in the 59 patients studied; the use of PRF significantly reduced pain values on the first, third, and seventh day after surgery, but had no effect on edema values. Also, current result differs from Kumar *et al.*,[37] as there were no significant variations in the edema values on the first day subsequent to surgery. They also determined that there were no statistically significant variations on the third and seventh days subsequent to surgery. They stated that a tape measure could be the reason behind the different degrees of edema. Uyanik *et al.*,[9] the impacted third molars were extracted bilaterally in 20 patients and reported that the use of PRF in surgery of the impacted third molar significantly relieved pain on days 1, 2, 3, and 7 after surgery (pain was assessed using a Likert-type VAS).

In spite of this, no significant differences were found regarding swelling, which was assessed by tape measure[9]. Also, regarding edema subsequent to surgery, according to current study, there was a statistically significant difference between the two groups on the second and seventh postoperative day regarding the absence or reduction of swelling (*p*-value=0.012) (*p*-value=0.011) respectively. Current findings are supported by Ozgul *et al.*,[42] and Dar *et al.*,[43] who found that swelling was less on the PRF sides. In contrast to the fifth day, there was no statistically significant difference between both groups in current study. This result was like that reported by He *et al.*,[44] with no statistically significant difference between both groups in the first day, but statistically significant difference between both groups in the third day.

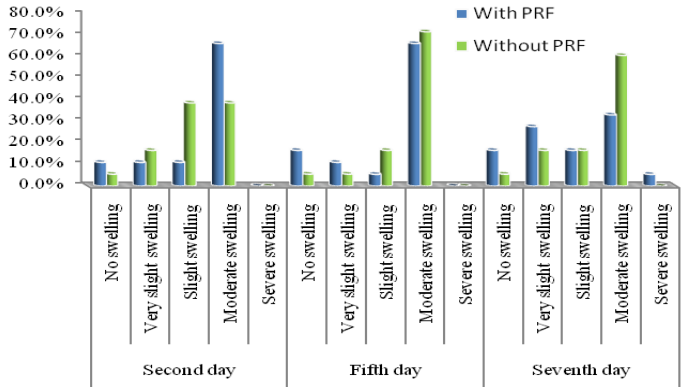

Figure 5: The frequency of swelling in the PRF group and without PRF group.

The positive effect of PRF in swelling can be explained by that, the most important specific activities of platelet-derived growth factor (PDGF) in the PRF include mitogenesis (increase in the cell population on healing cells), angiogenesis (endothelial mitosis into functioning capillaries), and macrophage activation (debridement of the wound site and a second phase source of growth factors for continued repair and bone regeneration). Therefore, a threefold or greater concentration of platelets, as was measured in PRF, can be expected to have a profound effect on swelling reduction by virtue of it swashing away the exudates due to the above-mentioned activities. However, there are some controversies in the literature regarding the effect of PRF in reduction the swelling after surgical extraction. As many authors such as Bilginaylar and Uyanik,[41,], Gülşen and Şentürk,[45] , and Trybek *et al.*,[46] who reported no significant dissimilarities among the PRF group and control group in the swelling. This dissimilarity may be related to the method of assessment. Some authors assessed by visual assessment as in current study, others by reference point in the face, flexible ruler and others used a tape measure to measure the swelling. Ozgul *et al.*,[42] used a 3-D optical scanner for the dimensions of facial swelling, which might have given more accurate recordings, however the funding of current study did not support such expenses. In addition, current findings are similar to another study of 30 patients; Asutay *et al.*,[47] reported that there were no significant variations among the PRF and control groups in all periods due to the improvement in pain and swelling values. This study used 3dMD to assess swelling, while a Likert-type VAS was used to assess pain. They reported that all operations took place in a series of two appointments[47]. On the other hand, current findings differ from Gürler *et al.*, study[48] in which they reported that application of leukocyte PRF (L-PRF) to extraction sockets of impacted third molars in 40 patients was not found to be statistically significant in terms of pain and edema after surgery. They reported that pain is assessed using a VAS-type Likert scale while edema was assessed using a flexible ruler[48].

With regard to the linear measurements of inter-incisal distance in current study, the mean preoperative distance in both groups was 4.32±0.498 mm. There was no statistically significant variation among both groups in the 2nd postoperative day. Unlike the 4th and 7th postoperative days, in which there was statistically significant variation among both groups (p=0.001). There was no statistically significant variation among both groups in regard to gender (p-value=0.001) (Table 3). These findings are similar to studies done by Trybek *et al.*,[46] and Kumar *et al.*,[49] in which the trismus was significantly higher in the control group than in the PRF study group at one, two, and seven days after surgery (p<0.05) (p=0.040) respectively. On the other hand, these results were dissimilar to other authors who have found no statistically significant variation among both groups in regard to trismus[20,41]. This dissimilarity may be related to their methods of measurements, as digital caliper reveals more accurate measurements in current study. Other possible factor that may influence this result is the measurements were revealed by non-qualified person (not the operating surgeon).

Limitation of the study

The study was extensively recent insights into the clinical effects of PRF after surgical extraction of impacted lower third molars in 18 cases of Yemeni adults, and this is a small sample size and therefore the more research needs to be conducted on a larger sample size. PRF is the second generation of platelet concentrates (PRP is the first generation). The prepared PRF consists of growth factors (VEGF), platelet-derived growth factor (PDGF)-AA, insulin-like growth factor-1, leukocytes, cytokines such as interleukin (IL)-4, IL-6, IL- 1A, circulating dendritic cells (dendritic cells) secured by a fibrin matrix. Further work on the influence of each of these factors individually is suggested.

CONCLUSION

The PRF helps in reducing the post-surgical pain, edema and trismus. As well as accelerate healing process after the application to the socket of surgically extracted lower third molar. To obtain more meaningful results, future research should use a larger sample with different evaluation methods for all variables (i.e., pain, trismus and swelling).

ACKNOWLEDGEMENT

The authors would like to acknowledge Sana'a University, Sana'a, and Yemen which supported this work.

AUTHOR'S CONTRIBUTION

Makki KIF: writing original draft, study conception and design. **Abbas AMA:** conceptualization, methodology. **Alhadi YAA:** formal analysis, research design. **Al-Shamahy HA:** data analysis, interpretation of results. All the authors reviewed the results and approved the final version of the manuscript.

DATA AVAILABILITY

The data and material are available from the corresponding author on reasonable request.

CONFLICT OF INTEREST

No conflict of interest associated with this work.

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