

Effect of platelet rich-fibrin on alveolar osteitis incidence following surgical removal of impacted mandibular third molars: A comparative study

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ABSTRACT

Background: Postoperative morbidity after extraction of the impacted mandibular third molar (IMTM) is inevitable. One of the most common postoperative complication is alveolar osteitis (AO) which is a painful non healed socket. Many researches were attempted to prevent the occurrence of AO by introducing and applying a new materials inside the extraction socket. Platelet rich fibrin (PRF) is a biological complex fibrin matrix where autologous platelets and leucocytes are present, used to enhance tissue healing process and reduce the early adverse effects of the inflammation.

Aims: To evaluate the effect of PRF on the incidence of AO. Also to assess PRF effect on pain, swelling, and trismus following the surgical removal of IMTM and compare it with the control group.

Materials and methods: This clinical prospective study was conducted from October 2016 to October 2017 at the Department of Oral & Maxillofacial Surgery, College of dentistry/University of Baghdad; and Al-Sadr Specialized Health Center. A total number of 50 IMTMs were surgically removed from 45 patients who met the inclusion criteria (21 males and 24 females) with age ranged from 16-41 years. The cases were divided into two groups: a study group (25 cases) where PRF were placed inside the extraction socket and control group (25 cases) where traditional surgery were performed. AO, trismus and swelling were assessed at the 2nd and 7th postoperative day. Pain scored by numeric rating scale daily by the patients.

Results: The study showed that age, gender, side of impaction, oral hygiene condition, impacted tooth classification, surgical difficulty, and the time of procedure in both control and study groups had nearly similar distribution with non-significant difference. At the 1st follow up period: Trismus (P-value = 0.834) and Swelling (P-value = 0.592) were non-significant between the two groups. AO had overall incidence of 4% occurred only in the control group, while the PRF group had no occurrence (0%), but the difference was statistically non significant. Postoperative pain had no significance difference in both groups. At the 2nd follow up period there was no significant difference regarding trismus, swelling, and incidence of AO between both groups.

Conclusion: Local application of PRF can reduce the incidence of AO but not to a significant level. PRF had no effect concerning postoperative pain, swelling, and trismus.

Keywords: Platelet rich fibrin, alveolar osteitis, impacted mandibular third molar. (Received: 15/1/2018; Accepted: 30/2/2018)

INTRODUCTION

Impacted teeth are most frequently found among mandibular third molars and may lead to pericoronitis, periodontitis, damage to neighboring teeth, crowding of the anterior teeth, and temporomandibular symptoms. Furthermore, the impacted teeth is a potential origin of odontogenic cysts and tumors. Therefore, impacted mandibular third molars (IMTMs) are usually extracted^[1].

New statistics submits that 72.2% of the world population has at least one impacted tooth (often lower third molar). Pain, edema, trismus, bleeding and alveolar osteitis (AO) are the most common complications following the surgical extraction of impacted teeth. Pain reaches peak levels of 6 to 12 hours and swelling 2 to 3 days postoperatively. Trismus is a temporary muscle spasm and subside gradually after the surgery^[2].

Dry socket or AO is a common postoperative complication usually associated with the extraction of IMTMs and defines as an intense pain within and around socket of the extracted tooth, had an onset between the 1st and 3rd day after the extraction with a complete or partial blood clot disintegration^[3]. It is interruption in healing process that disturb the conversion of the mature blood clot into granulation tissue^[3]. Several methods were used to control the immediate inflammatory response including secondary closure technique, window excision of the mucosa, use of drains, suture-less or single suture technique, administration of antibiotics, analgesic, corticosteroid, and by the application of low level laser therapy^[4].

Many researchers attempt to find a successful method for prevention of alveolar osteitis including local and systemic antibiotic,

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chlorhexidine rinse or gel, steroid, eugenol containing dressing, antifibrinolytic agent, low level laser therapy, biodegradable polymers, topical hemostatics, oxidized regenerated cellulose, and dextranomer granules [5].

Platelet rich fibrin (PRF) is a biological autologous material obtained simply by centrifugation of the patient's own blood without anticoagulants. Its fibrin matrix encompasses platelets and leukocytes as well as a variety of cytokines and growth factors, and it was presented to accelerate soft tissue healing [6].

The effect of PRF on the postoperative inflammatory response (pain, swelling, and trismus) and on the AO incidence after its placement in the socket of surgically extracted IMTMs were evaluated in this research.

MATERIALS AND METHODS

This clinical prospective study was conducted from October 2016 to October 2017 at the Department of Oral & Maxillofacial Surgery, College of dentistry/University of Baghdad; and Al-Sadr Specialized Health Center.

A total number of IMTMs 50 teeth were allocated in two groups, Study group (25 tooth) in which the impacted tooth was extracted and PRF was immediately applied in the socket and Control group (25 tooth) in which the impacted tooth was removed without application of PRF. Any patient age ≥ 15 who had unilateral or bilateral unerupted, partially, or fully IMTMs which indicated for surgical extraction were included in this study. The exclusion criteria was:

1. Acute pericoronitis or IMTM associated with pathologies.
2. Smoker and pregnant patients.
3. Medically compromised patients and patients who take chemotherapy or radiotherapy in the last year.

Preoperative assessment

Medical and dental history were documented and clinical examination (extraoral & intraoral) were performed for each patient. Oral hygiene condition was assessed by the Greene and Vermillion method as mentioned by Alkhadra [7], were scored as follow:

- Good oral hygiene = 1
- Fair oral hygiene = 2
- Bad oral hygiene = 3

Preoperative orthopantomography (OPG) was taken for the patient to assess the location and configuration of impacted third molar, adjacent tooth, mandibular canal, and surrounding bone. The class and depth of the impacted tooth were documented according to Pell and Gregory's classification. While angulation were classified according to Quek, et al. (2003) method [8] by drawing lines to represent the intersected longitudinal axes of the second and third molars then measuring the angle formed between them:

- Vertical impaction: 10° to -10° .
- Mesioangular impaction: 11° to 79° .
- Horizontal impaction: 80° to 100° .
- Distoangular impaction: -11° to -79° .
- Others: 101° to -80° .

Scoring the surgical difficulty

The difficulty of extraction were divided into 3 categories: slightly difficult, moderately difficult, and very difficult according to Pederson index [9] (Table 1).

Table 1 Pederson's difficulty index.

Criteria	Value
Angulation	
Mesioangular	1
Horizontal	2
Vertical	3
Distoangular	4
Depth of IMTM	
Position A	1
Position B	2
Position C	3
Class of IMTM	
Class I	1
Class II	2
Class III	3
Index = sum of angulation, depth, and class	
	Total
Slightly difficult	3 - 4
Moderately difficult	5 - 6
Very difficult	7 - 10

Surgical procedure

The patients was received information about the proposed surgical procedure and its risk, so they signed in an informed consent to proceed with the recommended treatment. The surgeries were performed under local anesthesia (3

cartridges of 2% Lidocaine with 1:80,000 adrenaline) by the same operator.

Incision for horizontal mucoperiosteal flap was started just distolateral to the impacted tooth and continue buccally around the gingival margins till it reach the mesial side of the 2nd molar where a vertical buccal releasing incision were performed (Bayonet flap).

The mucoperiosteal flap was reflected and the bone was removed to expose the cervical line of the tooth using round or fissure burs and a low speed/ high torque surgical straight handpiece. If required, the tooth was sectioned into pieces to facilitate delivery from the socket. After tooth removal, the socket was irrigated with 10 mL of normal saline then suturing with 3/0 black silk suture in control group.

PRF preparation and application

In the study group, after intentionally making the tooth subluxated and before elevate it completely from the socket, blood aspiration to prepare the PRF began. Ten mL of autogenous venous blood was collected from an appropriate vein in the antecubital fossa.

The obtained blood was immediately transferred to a plain 10 mL blood collecting tube and centrifuged at 3000 rounds per minute for 10 minutes. At the end of this process, the yellow shiny gelatinous part in the middle of the tube was the PRF (Fig.1).

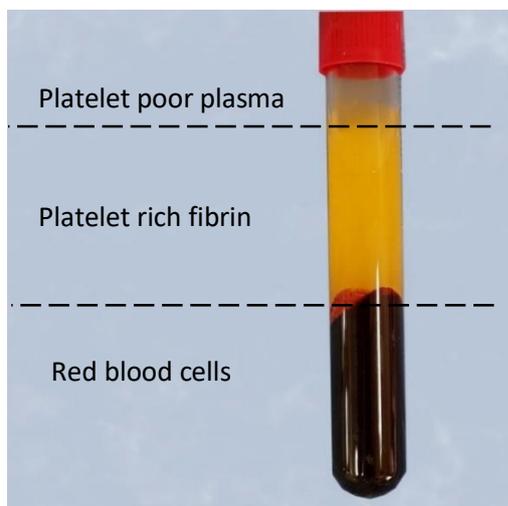


Figure 1: layers after blood centrifugation

Using tweezers gently the PRF were pulled out and placed in a sterile wet gauze mesh, scraping the bulk of RBC layer carefully by surgical scalpel leaving the buffy coat intact (Fig. 2)



Figure 2: Platelet-rich fibrin

When the centrifuge rotation nearly reach its ending, the tooth or the root (if the crown was sectioned previously) was removed, the bone was smoothed /and the socket was irrigated with normal saline, place the PRF gently inside the socket, then suturing the flap (Fig. 3). The time of the operation was recorded from the incision to the end of suturing for each surgery.



Figure 3: platelet-rich fibrin inside the socket

Evaluation procedure

Four variables were evaluated in this study: mouth opening, swelling, pain, and the incidence of AO. The follow up took place in the 3rd and 8th days. The surgical operation day was considered as the 1st day.

The following terms were used:

T₀ = the day of operation (preoperative).

T₁ = the second postoperative day.

T₂ = the seventh postoperative day.

The degree of maximum mouth opening were recorded using a sliding caliber by measuring the distance from the incisal edges of the upper

left to the lower left central incisor as the mouth opened to its limit.

The extent of the swelling was measured by swelling measurement device (SMD). The idea was to measure the distance of the skin that will protrude postoperatively in 16 different points around the angle of the mandible in mm.

SMD consist of a modified disposable impression tray which could be detached and fixed easily to the device by a nuts and built-in bolts and a two perforated rectangular plates facing the angles of the mandible extraorally. Each plate contain a 20 parallel holes (5 columns and 4 rows). These holes has a diameter that fit a calibrated straight cylinder bar (Fig. 4).

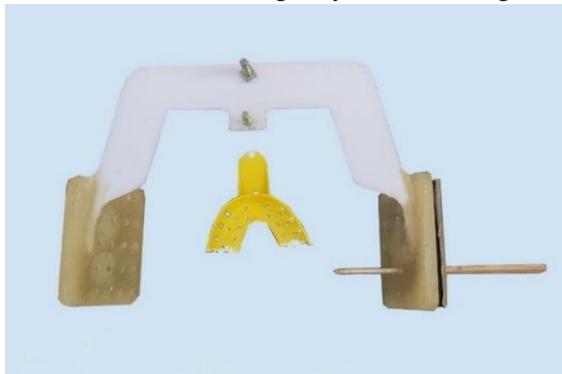


Figure 4: Swelling measurement device

The technique of measurement was: Making an impression for the upper teeth by modified disposable tray after checking its fitness in the patient mouth, removal of the tray from the patient's mouth when the impression material was sat, fixing the tray to the SMD. Now, reinserting the SMD with its fixed tray again in the patient's mouth while the lower jaw in rest position for making the measurement. The upper impression work as a reference point for the SMD and exactly take the same position any time it inserted inside the patient's mouth.

The distance between the inner surface of the perforated plate and the skin was recorded, this done by a calibrated straight cylinder bar which enter to the holes of the plate and move medially till it touch the skin, this process was repeated in a selected 16 holes in the plate.

The mean measurement was calculated before the surgery at T0 as a baseline and similar measurements were carried out at T1 and T2 (Fig. 5).



Figure 5: Using the swelling measurement device at 1st follow up period.

The pain was scored by the patient using numeric rating scale (NRS), where the number 0 represent no pain while number 10 represent the worst imaginable pain. The time to utilize the pain chart was determined by the operator at 10 pm and the patients were informed to restrict at that time daily for 7 days.

The diagnosis of AO was done by an expert surgeon other than the operator to reduce the bias. The socket should had partial or complete blood clot loss and a pain score in NRS (≥ 6) in the extraction site at the time of checking to consider it as AO with or without foul odor.

The patients were instructed to return if they experienced any persistent and progressive pain between follow-up visits. The cases of AO were treated by normal saline irrigation of the socket and packing it with Alvogel® (India). Antibiotic and analgesic were also prescribed.

Statistical analysis

SPSS version 14.0 were used in order to analyze and assess the results of this study utilizing the following inferential data analysis: Two independent-samples t-test, homogeneity-of-variance, matched paired-samples t-test, and repeated measures analyzes groups of related dependent variables.

RESULTS

Study sample comprised 45 patients (21 males & 24 females) aged 16-41 years with 50 IMTMs. 25 IMTMs regarded as control group and the remaining 25 IMTMs as study group.

The results show that distribution of age, gender, side of impaction, oral hygiene condition, and the IMTMs classification (angulations, depths, and classes) between both groups were nearly similar and had non statistical significant difference. Furthermore, the age group (20-24 years) and

females accounted with the vast majority of attendance (40%) and (56%) respectively. Also, mesioangular (52%) and position A (58%) had the higher prevalence in IMTMs classification while class I and class II had equal distribution (48%). The results displayed that vast majority of the studied sample had a moderately difficult surgical extraction according to Pederson index (Fig. 6).

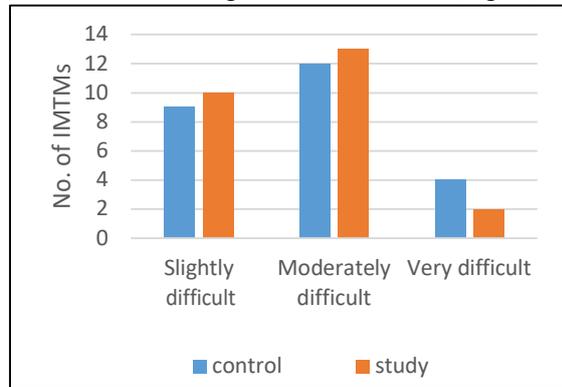


Figure 6: Distribution of impacted teeth according to Pederson difficulty index

Adding to that no significant difference were found which indicate similar distribution of the surgical difficulties between the control and study groups.

The mean time spent for surgical operation were listed in Table (2) which had a non-significant difference between both groups.

Table 2: Mean of surgical operation time.

Group	Mean (Min.)	SD	SE	t-test	
				t	Sig.
Control	36.52	13.47	2.69	-1.643	0.107
Study	44.76	21.14	4.23		NS

SD: standard deviation. SE: standard error. NS: non significant

Trimus and swelling

The degree of mouth opening and the extent of swelling were measured at T₀, T₁, and T₂; however, there were no statistically significant differences between the groups (Table 3). The amount of swelling were recorded by SMD.

Pain

The results display that studied samples had mostly a parallel behavior concerning pain parameter throughout 7 postoperative days as it scored by the patient daily using NRS, which reduced on passing of times. Besides that, no significant differences were obtained between the study and control group at each days (Table 4).

Table 3: The mouth opening and swelling between both groups.

Parameter		Study Mean (SD)	Control Mean (SD)	P value
Mouth opening (mm)	T ₀	49.9 (6.9)	50.7 (7.4)	0.697 NS
	T ₁	39.5 (10.2)	39 (8.4)	0.834 NS
	T ₂	46.5 (7.6)	47.4 (8.1)	0.710 NS
Swelling (mm)	T ₀	34.8 (7.6)	34.7 (5.8)	0.972 NS
	T ₁	32.9 (8.4)	31.6 (5.3)	0.592 NS
	T ₂	34.7 (7.9)	34.3 (5.7)	0.839 NS

SD: standard deviation. NS: non significant

Table 4: Pain score between both groups using numeric rating scale.

Days	Study Mean	Control Mean	P value
Day 1	5.88	5.16	0.380 NS
Day 2	3.92	4.08	0.843 NS
Day 3	3.12	2.56	0.445 NS
Day 4	1.76	1.96	0.676 NS
Day 5	1.68	1.32	0.476 NS
Day 6	1.40	1.08	0.584 NS
Day 7	0.64	0.72	0.809 NS

NS: non significant

Alveolar osteitis

The overall incidence of AO in this study was (4%) as shown by the results and were recognized

PRF group, while no occurrence of AO were detected at T₂ in both groups, in addition to that no significant difference at each period were detected between the study and control groups (Table 5).

Table 5: Incidence of alveolar osteitis.

T	AO	Study	Control	Total	P value
T ₁	+	0 0%	2 8%	2 4%	0.245 NS
	-	25 100%	23 92%	48 96%	
T ₂	+	0 0%	0 0%	0 0%	1.000 NS
	-	25 100%	25 100%	50 100%	

T: times. AO: alveolar osteitis. (+) presence. (-) absence. NS: non significant

DISCUSSION

Surgical removal of impacted mandibular third molars (IMTMs) are always associated with soft

and hard tissue trauma, so postoperative morbidity can't be eliminated completely. Surgeons in oral and maxillofacial continuously pursue a new materials or a modified surgical technique to improve outcomes. Platelet-rich fibrin (PRF) was utilized in various surgeries as a bioactive material which is obtained from the patient's own blood to enhance soft and hard tissues healing.

In the present study, the mean preoperative (T_0) mouth opening in the control group was 50.72 ± 7.48 mm and in the PRF group was 49.92 ± 6.96 mm (Table 3). The P-value was 0.834 in T_1 and 0.71 in T_2 between both groups, and this showed that PRF application had no effect regarding postoperative trismus. These finding is supported by other studies^[11, 12] who concluded a non-significant difference regarding mouth opening postsurgically. Other study in contrast had stated a significant difference on the 1st postoperative day^[13].

The surgical extraction of IMTMs may cause limitation in mouth opening as a result of either inflammation involving the muscles of mastication or direct trauma to the TMJ^[14]. The etiology of trismus may be sited away from the local effect of the PRF, so the muscles of mastication and the TMJ located far from the local benefit of PRF and its releasing factors. The maximum extent of swelling in the current study were observed at T_1 , and in comparison between both groups at T_1 and T_2 the result showed less amount of swelling in the study group at each periods but it doesn't reach to a statistical significant level. In support to this result other clinical studies concluded a statistically no significant difference between study and control group^[12, 15, 16, 17]. On the other hand, other clinical studies were reported a significant difference regarding swelling reduction in the PRF group^[13, 18].

Three cytokines TNF- α , IL-1, and IL-6 play a major role in acute inflammation as they increase blood vessels permeability and this in turn increase the osmotic pressure of the interstitial fluid, the result is exudate edema^[19].

PRF had a high concentrations of anti-inflammatory cytokines IL-4, but also showed identical high serological concentrations of proinflammatory mediators, such as IL-1 β , IL-6 and TNF- α ^[20]. This balance may explain the

non-effectiveness of PRF to reduce postoperative swelling into a significant level. In the present study, the pain was gradually reduced in a significant difference till 6th day in the control group, and to 5th day in the study group. In the remaining days the pain was decreased in a non-significant rate.

In comparison of pain between the study samples, this study found no significant difference at 10 pm for each day. In accordance to this, studies^[17, 21, 22] which evaluate the pain by visual analogue scale and showed a statistically non-significant differences between PRF and non PRF groups. However, in a bilaterally IMTMs study by Kumar et al. (2016) recorded a significantly pain reduction in experimental group compare to the control^[23].

This controversies in pain assessment may be belong to the patients' pain tolerance Kemp et al. (2012) concluded that visual analogue scale appears to be unreliable for obtaining objective information about the experiential dimensions of pain^[24]. Inflammatory mediators (e.g. bradykinin, histamine, 5-hydroxytryptamine) which are released after tissue injury have known as endogenous pain-inducing substances, which are able to sensitise or excite the peripheral terminals of nociceptive neurons and caused an inflammatory pain^[25]. In our knowledge, no clinical study was reported that PRF application prevent the releasing of pain inducing mediator after the surgery, and this may be the reason behind the uneffectiveness of PRF on the postoperative inflammatory pain.

As shown by the result of this study, the total incidence of AO was 2 cases (4%) among 50 cases only occur at T_1 in control group. The low incidence of AO may be attributed to the limited sample size and to the avoidance of some of AO risk factors such as, the operator performed the surgery with minimum trauma as possible, aseptic surgical field, exclusion of medically compromised and smoker patients, and no attendance of patients used oral contraceptives drug. Supporting that, there is a relationship between elevated surgical difficulty and AO, since trauma causes delayed healing through compression of the thin compact alveolar bone of the socket, thrombosis in underlying vessels, reduced

tissue resistance that predisposes the wound to infection [26].

In the study group where the PRF applied, there was no occurrence (0%) of AO compared to two cases in the control group, but it doesn't reached to a statistical significant level between groups. This result come in agreement with Asutay et al. (2016) who found in a clinical study a non-significant result between of PRF and control groups [12]. In contrast, other clinical studies achieved a significant reduction of AO following the application PRF with a ranges of incidence 0-2.6% in study group and 9.5-16% in control group [1, 27, 28].

The absence of the development of AO in the socket which were filled with PRF may be accounted to the PRF properties as reported by Choukroun et al. (2006) who concluded that fibrin matrix of the PRF guides the epithelial cells and fibroblasts migration and increase their metabolism when cover the injured tissues, also PRF consider as biomaterial encouraging neovascularization, and it is a natural support to immunity [29].

This study concluded that local application of PRF can reduce the incidence of AO but not to a significant level. PRF had no effect concerning postoperative pain, swelling, and trismus. The limitation of this study were: small sample size and non-randomized method.

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الخلاصة

الخلفية: إعتلال المريض بعد العملية الجراحية لقطع سن العقل المظفور حالة حتمية. التهاب مغرز السن هو حالة مؤلمة بسبب عدم شفاء مغرز السن وعادة تصاحب القلع الجراحي لسن العقل المظفور. العديد من البحوث العلمية تحاول منع حدوث التهاب مغرز السن بعد العملية الجراحية باستخدام مواد جديدة داخل مغرز السن المقطوع. الليفيين الغني بالصفائح الدموية هو مصفوفة ليفين حيوية معقدة تحتوي على صفائح دموية وكريات دم بيضاء ذاتية المنشأ، يستخدم لتعزيز عملية شفاء الأنسجة ولتقليل الاعراض الجانبية المبكرة للتهاب.

الأهداف: تقييم فعالية الليفيين الغني بالصفائح الدموية على حدوث التهاب مغرز السن وعلى استجابة الأنسجة الملتهبة متضمنة: الألم، الانتفاخ، والضرر بعد العملية الجراحية لإزالة سن العقل المظفور في الفك السفلي.

المواد وطرق البحث: المجموع الكامل لخمسين سن عقل مظفور في الفك الأسفل تمت إزالتها جراحيا من 45 مريض تالقت فيهم شروط الإدخال لهذه الدراسة السريرية (21 ذكر و 24 أنثى) بأعمار تتراوح بين 16-41 سنة. تم تقسيم الأسنان المظفورة الى مجموعتين. في المجموعة الضابطة (25 حالة) تم اجراء العملية الجراحية التقليدية، بينما في مجموعة الدراسة (25 حالة) وضع الليفيين الغني بالصفائح الدموية داخل مغرز السن المقطوع حديثا. عمر المريض، جنسه، جانب السن المظفور، حالة صحة ونظافة الفم، استخدام عقارات منع الحمل الفموية، تصنيف السن المظفور، الوقت المنقضي لاجراء العملية، وصعوبة العملية (Pederson index) تم تدوينها. قيم الضرر والانتفاخ سجلت قبل العملية كقاعدة بيانات اساسية وفي اليوم الثالث والثامن بعد العملية. سجل الألم يوميا من قبل المريض خلال سبعة ايام باستخدام (Numeric rating scale). قيم حدوث التهاب مغرز السن في اليوم الثالث والثامن بعد العملية. تمت عملية قياس الانتفاخ بجهاز قياس الانتفاخ. التحليل الاحصائي تم باستخدام معامل التوافق، (t-test) المستقل، (t-test) الثنائي، و (Levene's test).

النتائج: أظهرت الدراسة بان العمر، الجنس، جانب السن المظفور، حالة صحة ونظافة الفم، صعوبة الجراحة، ووقت انجاز العملية في المجموعة الضابطة ومجموعة الدراسة كانت متساوية تقريبا في الانتفاخ في كلا المجموعتين بدون اهمية احصائية، مما يشير الى ان عينة البحث كانت قابلة للمقارنة. لم تسجل حالة لمريض يأخذ عقار منع الحمل الفموي في فترة الفحص الأولي: الضرر (قيمة P=0.834) والانتفاخ (قيمة P=0.592) لم يحسب لهما اختلاف ذو اهمية معنوية بين المجموعتين. نسبة حدوث التهاب مغرز السن في هذه الدراسة كان 4% و حددت فقط في المجموعة الضابطة. الألم من اليوم الاول ولغاية اليوم السابع لم يتغير تغير فعال احصائيا بين المجموعتين. في فترة الفحص الثانية لم يوجد اختلاف يعتد به احصائيا بخصوص الضرر، الانتفاخ، والالتهاب مغرز السن. تقييم موقع القلع كشف عن افضلية بمنع تحلل خثرة الدم في مجموعة الدراسة عند مقارنتها مع المجموعة الضابطة.

الاستنتاج: استعمال الليفيين الغني بالصفائح الدموية موضعيا يقلل حدوث التهاب مغرز السن ولكن بمستوى غير مهم احصائيا. تحلل خثرة الدم تقل في موقع القلع بعد وضع الليفيين الغني بالصفائح الدموية في مغرز السن. الليفيين الغني بالصفائح الدموية لم يكن فعال حيال الألم، الانتفاخ و الضرر بعد العملية.