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EVALUATION OF THE EFFICACY OF PLATELET RICH FIBRIN ON THE FOLLOWING COMPLICATIONS AFTER SURGICAL EXTRACTION OF THE LOWER THIRD MOLAR IN SMOKER PATIENTS (RANDOMIZED CLINICAL TRIAL)

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Abstract

Much scientific evidence indicates the importance of the use of platelet-rich fibrin in the management of the healing of oral soft and bony tissues. The effectiveness of this substance is due to the growth factors and effective properties it contains in improving the healing and healing phase and relieving pain after surgery. Since the surgical extraction of the impacted third molars is one of the most common operations within the oral and maxillofacial surgeon's clinic, pain, and postoperative alveolitis are the most annoying complications for the patient.

Present study aimed to *assess the effect of platelet-rich fibrin after topical application in the cavity of the socket of the impacted lower third molar surgical extractions in smokers.*

***Material and methods**: 15 smoker patients who needed to have the lower third molars extracted under local anesthesia (n = 30) randomized with an X, O method for one of the two incisions. The two parts of the study group are one in which platelet rich fibrin is applied within the socket cavity just before suturing and another where nothing is applied.*

Postoperative pain was assessed using a visual analogue scale scale on days 1, 2, 3, 5, and 7, and by the patient's dose of analgesic. The rate of alveolitis was evaluated, and then the variables were studied by comparison between the study group and the control group.

***Results**: In the study group, the visual analogue scale values were lower with a statistically significant difference compared with them in the control group on the first, second and third days after surgery (P <0.05).*

***Conclusion**: This study indicated that the topical application of platelet-rich fibrin within the socket of the impacted lower third molar after its extraction in smokers is an effective method in relieving symptoms following surgical extractions and that it contributed positively to reducing the incidence of alveolitis.*

Keywords: *platelet rich fibrin, third molar surgery, smoking, postoperative symptoms, alveolitis.*

Introduction

There are many smoker people in the world. However, the number of smoker youth increases every year [M*aziak W, 2002*]. By the report of (WHO) world health organization Syria has most smoker youth in the Arabian world [*Mohammad Y. et al 2013*]. The extraction of the third lower molar is considered a common procedure in the clinical of dentistry [*Srivastava N et al. 2017*].The occurrence of alveolar osteitis is about 15-20% after extraction of a molar tooth [*Catellani JE et al. 1980*]. Impact tooth is a pathological situation in which a tooth cannot or will not erupt into its normal functioning position [*Fragiskos F 2007*]. The position of this tooth in the mandibular jaw may occur (Pericoronitis, absorption of root adjacent molar, cysts, tumors). The mandibular third molars are the most frequently impacted teeth that can be found in humans and impacted lower tooth may cause disorders in temporal mandibular joint (TMJ) and overjet of the tooth.

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The classification (Pell and Gregory) of impacted teeth: [*Eshghpour M et al. 2014*].

1. Impacted tooth under soft tissues.
2. Part of impacted tooth erupt through soft tissues
3. Full tooth impacted in bone

Causes of impaction: Some systematic causes such as:

1. Cleidocranial dysostosis [*Manjunath K et al.* 2008]
2. Dawn syndrome [*De Moraes et al.,* 2007]
3. Progeria [*Pekdemir et al., 2018*]

Some local causes such as: tumors, cysts and disorders in soft tissues [*Jaiswara C et al. 2016*; *Sarica I et al. 2019;*].

Risk factors: he risk factors are not following the instructions in the first place and smoking in the second place. Whereas, smoking, poor oral care, and violent extractions after surgery may have contributed to the increased incidence of dry socket in these patients [*Beit ZK 2017*].

Studies have shown that the risk factors after extraction of the lower third molar in 138 patients were observed to increase the number of patients with alveolar ostietis, much greater compared to non-smoking patients [*Balaji S, 2008]*.

Some studies have shown that younger smokers have more alveolar bone resorption and loss of periodontal attachment than non-smoking patients [*Mullally BH, 2004*].

The trismus in smokers is greater than in non-smoking patients. In addition, the incidence of pain and alveolar osteitis in smokers was higher and more common than in non-smoking patients [*Carriches CL et al. 2006*].

Smoking: The average of smoking increase in teenagers and adult male [Gardiner PS 2001; Garrett BE et al. 2016].

Smoking is believed to have effects on the cardiovascular muscle, central nervous system, and endocrine glands [*Carriches CL et al. 2006*].

It has a helpful role in weakening the immunity and reducing the blood supply to the oral tissues, especially the oral mucous membranes that are in direct contact with the cigarette, and tobacco plays a role in the rate of peripheral blood circulation as it affects the healing and health of tissues [*Balaji S, 2008*].

Some studies showed that the incidence of malignant diseases among smokers was higher than that of non-smokers, such as squamous cell carcinoma, which is the most common oral carcinoma, where it was estimated that more than 90% of malignancy cases were squamous cell carcinoma (SCC) [*Carriches CL et al. 2006*].

Nicotine causes addiction and carbon monoxide and chemical material found in tobacco have effect on blood flux [*Balaji S, 2008*].

Nicotine use increases the risk of heart disease and lung disorders and they pose great risks to pregnant women who use it, as it could harm a developing fetus [*Huang J et al. 2014*]. The tobacco plant is a nightshade, as well as nicotine, which is responsible for addiction in smokers, and is a powerful and lethal insecticide in its pure form as it leads to high blood pressure and contributes to narrowing of blood vessels [*Pauly JL et al. 2002*]. Tar is a black petroleum jelly, which is one of hundreds of additives found in tobacco that are made of organic and inorganic materials that contain carcinogens. Many of the components inside cigarettes are carcinogenic, such as hydrogen cyanide, ammonia and arsenic, as the number of carcinogens has been estimated to 43 substances [*Pauly JL et al. 2002*].

The harmful effects of smoking on public health:

- A catalyst for gum and lung cancer [*Balaji S, 2008*]
- Headache [*King JL et al. 2019*]
- Heart disease [*Qasim J et al. 2019*]
- Erectile dysfunction [*Cao, Yin et al. 2013*]

Alveolar osteitis (dry socket): According to some studies, the vitality of the mucous tissue decreases due to the weak blood supply in the area where the tooth was extracted, and this has been observed more often in smokers compared to other normal patients [*Balaji S. 2008*].

Research has shown that some patients who saw the doctor after the surgical extraction were suffering from pain, and after a clinical examination of the extraction site showed the presence of alveolar osteitis in the area, and after the interrogation, the smoking habit was found [*Beit ZK, 2017*].

According to some studies, it was found that:

- Smoking a group of cigarettes

To overcome it is possible, due to the uniting the knowledge and will of all doctors in the world

affects the blood clotting and cuts off the blood supply [*Balaji S, 2008*]

- The proportions of patients who smoke have less oral care than non-smoking patients *Carriches CL et al. 2006*].
- Smokers generally have more symptoms, complaints and complications after undergoing any general surgery [*Ra'ed M, 2013*].
- In smokers with both surgical extractions and normal extractions, there was a significant difference in alveolar osteitis compared to simple extractions in terms of pain intensity and symptoms of inflammation [*Heng CK et al. 2007*]
- After observing the patient in the first week after surgery, pain was significantly associated with smoking [*Larrazábal K. et al. 2010*]

Histological structure of platelet rich fibrin*:* The layers formed after the centrifugation process, including: platelet poor plasma at the top, where the fibrin bond is in the middle, and red blood cells at the bottom [*Gupta V et* al. 2011].

Histopathological studies of Dohan and colleagues showed that the platelet-rich fibrin clot contains approximately 97% of the platelets in the tube and more than 50% of the white blood cells [*Dohan DM et al., 2006a, 2006b; Raja V. S., Naidu E.M* , 2008] and both platelets and fibrin form large clusters of the first milliliters of the clot next to the red blood cells, and fibrin forms in them. Very mature and dense network [*Bielecki T, 2012*].

The preparation of platelet-rich fibrin is very simple and does not require special tools and does not require any anticoagulant or other substances, meaning it is nothing more than a sedimented blood without any additives [*Qiao J et al. 2017].* Platelet rich fibrin is prepared according to the technique described by Joseph Choukroun and colleagues [*Gupta V et al. 2011*]. The fibrous gelatinous mass is pulled out of the tube with forceps and separated from the associated precipitated red blood cells [*Toffler M et al.* 2009].

Clinical applications of platelet rich fibrin:

- In the field of grafting bone cavities after maxillary cyst excision, platelet-rich fibrin induces the healing of bony cavities, as these cavities normally fill with blood, because fibrin is more organized and contains many growth factors [*Vares Y, Slipyi V, 2017*].
- There are many other surgical fields such as maxillary sinus lift [*Zhao J-H Tsai et al., 2015*]
- Grafting around dental implants [*Cortese A et al. 2016*]
- Fibrin application after resection of the apical lesions of the tooth [*Singh S et al., 2013*]

MATERIAL AND METHODS

Study design: a split-mouth randomized controlled clinical trial.

The number of cases of the research sample was determined according to the G-Power program, and the research sample consisted of 15 smokers - 30 research cases. They were 5 female patients and 10 male patients. These patients are visitors of the Department of Oral and Maxillofacial Surgery at Damascus University, who meet the following conditions:

1. Patients who smoke more than 20 cigarettes a day
2. Patients with symmetrical impaction
3. Patients who are physically healthy and do not suffer from general diseases
4. Patients' ages are between 18-35 years. This age group was chosen because of the time of the emergence of the third molars and the completion of their development, whether they erupted on the dental arch or the continuation of their implantation under the bone.

Exclusion criteria:

1. The presence of general diseases or factors that prevent blood to be drawn (such as an abnormal platelet count).
2. Patients outside the previously mentioned age group.
3. Pregnancy and breast-feeding
4. Patients whose duration of surgery exceeded 30-40 minutes

After selecting the patient within the research sample and applying the inclusion criteria to him and clarifying the study procedures and objectives for him and distributing the two sites randomly to the study group and the control group (simple randomization using paper scraps written with the letter X "study" and the letter C "control").

Preparation of platelet rich fibrin:

-Tools for preparing platelet rich fibrin include:
Blood drawing tools (syringes with a 24 gauge needle - sterile glass tubes closed with a 10 ml rubber cover to collect blood - cotton - alcohol - sterile gauze)

-Centrifuge: We performed a withdrawal equiv-

alent to (30 *ml*) of the patient's autologous blood and distributed it into glass tubes of (10 *ml*) capacity without adding anticoagulant materials [*Mihaylova Z et al. 2017*]. The tubes were placed within a centrifuge controlled at 3000 *rpm* for 10 minutes [*Mihaylova Z et al. 2017*] or 2700 *rpm* for 12 minutes [*Gupta V et al. 2011*].

Surgery is divided into the following stages:

1. Anesthesia Local anesthesia was administered with a solution of lidocaine 2% with epinephrine 1/80000 in each surgery.
2. Securing the entrance to the impacted tooth
3. Bone removal
4. Extraction of the tooth
5. Application of platelet rich fibrin
6. Suturing

Postoperative care: [*Alvira-González J, Gay-Escoda C, 201*5]. The patient is prescribed a suitable drug prescription (suitable antibiotic, Augmentin 1 g - analgesic when needed, such as diclofenac potassium, not to exceed 150 *mg* per day). Results recorded after a week.

Results

The research sample consisted of 30 surgical extractions of a third lower molar that was performed on 15 patients, who were all smokers, and their ages ranged between 19 and 32 years, as each of them had two third impacted molars that needed extractions. Treating the other molar by closing the wound without applying platelet rich fibrin, so the cases of surgical extractions in the research sample were divided into two main groups, equal according to the method of treatment used (wound closure with application of platelet rich fibrin, wound closure without application of platelet rich fibrin).

Analytical statistical study: The severity of pain was measured visually and the degree of pain was determined in five different time periods (on the first day, on the second day, on the third day, on the fifth day, on the seventh day), and each degree of pain was given an incremental value according to the severity. The degree of pain is as shown in the following table (Table 1)

- To study the effect of the used treatment method on the amount of pain visually according to the time period studied:

T- student test was performed on independent samples to study the significance of differences in the mean values of visual pain between the group of wound closure with application of platelet rich fibrin and the group of wound closure without application of platelet rich fibrin in the research sample.

Table 1.

Visually study the severity of pain

The pain	The value
No pain	1
Dull pain	2
Moderate pain	3
Severe pain	4
Very severe pain	5

T- student test results for Independent Samples:

Table 2 shows the results of the T-student test for independent samples to study the significance of the differences in the average values of the amount of pain visually between the wound closure group with the application of platelet rich fibrin and the wound closure group without the application of platelet rich fibrin in the research sample, according to the time period studied.

The above table shows that the significance level value is smaller than the value 0.05 regardless of the time period studied, i.e. at the 95% confidence level there are statistically significant differences in the mean values of the amount of visual pain between the wound closure group with the application of platelet rich fibrin and the wound closure group without the application of rich fibrin. With platelets in each of the five time periods separately studied in the research sample, and since the algebraic indication of the differences between the averages is negative, we conclude that the values of visual pain between the wound closure group with application of platelet rich fibrin

Table 2.

Result of T- student test

period of time studied	difference between the two averages	computed t value	Indication level value	Indication of differences
1st	-1.60	-3.270	0.003	significant
2nd	-1.80	-3.880	0.001	significant
3rd	-1.60	-3.207	0.003	significant
5th	-1.33	-3.497	0.002	significant
7th	-1.60	-4.099	0.000	significant

and the wound closure group without the application of platelet rich fibrin in each of the time periods studied (on the first day, on the second day, on the third day, on the fifth day, on the seventh day) separately in the research sample.

Mann-Whitney U test was performed to study the significance of differences in frequency of pain score between the wound closure group with application of PRF and the wound closure group without the application of PRF in the research sample.

Mann-Whitney U test results: table shows the results of the Mann-Whitney U test to study the significance of differences in the frequency of pain score between the wound closure group with the application of platelet rich fibrin and the wound closure group without the application of platelet rich fibrin in the research sample, according to the time period studied (Table 3).

The above table shows that the significance level value is smaller than the value 0.05 regardless of the time period studied, i.e. at the 95% confidence level there are statistically significant differences in the frequency of pain score between the wound closure group with the application of platelet rich fibrin and the wound closure group without the application of platelet rich fibrin, no matter what The time period studied in the research sample was, and by studying the grade mean values, we conclude that the degree of pain in the wound closure group with the application of platelet rich fibrin was less than in the wound closure group without the application of platelet rich fibrin, and that was on each of the first, second, third, fifth and seventh days separately. In the research sample.

TABLE 3.

Mann-Whitney U test results

period of time studied	U-value for Mann-Whitney	Indication level value	Indication of differences
1st	61.5	0.013	significant
2nd	42.0	0.001	significant
3rd	48.5	0.003	significant
5th	62.0	0.012	significant
7th	26.0	0.000	significant

Study of the presence of dry socket:

Survey results of the presence of dry socket in the research sample according to the used treatment method:

Table showing the survey results about the presence of dry socket in the research sample table 4

A chi-square test was performed to study the significance of differences in the frequency of dry socket infection between the wound closure group with application of platelet rich fibrin and the wound closure group without the application of platelet rich fibrin in the research sample as follows:

The results of the chi-square test (Number of cases -30, Chi-square value - 9.6, Degrees of freedom - 1, Indication level value – 0.002) to study the significance of the differences in the frequency of dry socket inflammation between the wound closure group with the application of platelet rich fibrin and the wound closure group without the application of platelet rich fibrin in the research sample.

It is noted in the above table that the significance level value is much smaller than the value 0.05, i.e. at the 95% confidence level there are statistically significant differences in the frequency of the presence of dry socket inflammation between the wound closure group with the application of PRF and the wound closure group without the application of platelet rich fibrin in The research sample, and by studying the corresponding table of frequencies and percentages, it is observed that the percentage of dry socket inflammation in the wound closure group with the application of

TABLE 4.

Presence of dry socket

Treatment method used	percentage			number of cases		
	no dry socket	dry socket	Total	No dry socket	dry socket	Total
the wound with the application of platelet rich fibrin	9.3	6.7	100	14	1	15
Close the wound without applying platelet rich fibrin	40.0	60.0	100	6	9	15

platelet rich fibrin was smaller than in the wound closure group without the application of platelet rich fibrin in the research sample.

Discussion

Pain: The patient's discomfort is assessed on the analgesic pill indicator (the number of the analgesic tablets prescribed of diclofenac potassium) on the second day, then the third and the seventh day [*Simoneti LF et al. 2018*]

The assessment was also based on a visual analogue scale (VAS) consisting of ten ranks, which is considered 1 for absence of pain and 5 for severe crying pain [*Ogundipe OK et al., 2011*]

Alveolar osteitis: The assessment was made according to the following criteria**:** [*Blum I, 2002*]

*Pain after extraction in and around the surgical area

* Partial or complete removal of the blood clot
* Presence or absence of oral halitosis
* Presence or absence of dead tissue residues
* Exposed socket
* Presence or absence of pus in the socket

When we studied pain we found that: We disagreed with the Ra'ed study that cigarettes have nothing to do with the pain and soreness resulting from the smoking process after surgical extraction of the lower third molar in smokers [*Ra'ed M, 2013*].

The effect of platelet rich fibrin on the second day pain was variable:

- Clinically and statistically, it was found that the pain values on the second day in the majority of patients after applying fibrin were expressing (mild pain)
- Thus, we have agreed with the study (Sharma) that studied the effect of fibrin in the management of alveolar osteitis after extraction of the upper and lower molars [*Sharma A. et al. 2017*].
- We disagreed with Chen, four days after the operation, that the application of platelet-rich fibrin inside the socket cavity compared to the other fibrin-exposed side, there was no fundamental difference in both ends with fibrin applied and the non-fibrinous side in terms of pain and edema [*He Y et al., 2017*]
- Based on the results of previous research, it was found that applying fibrin-rich platelets to the socket cavity after surgical extractions of the lower third molar may reduce the development of post-extraction alveolar ostietis [*Eshghpour M. et al., 2014*].
- We agreed with Unsal that the application of fibrin to smokers after surgical extractions had positive results in relieving pain after extractions, as the number of sample cases was 50 patients (33 females, 17 males) [*Unsal H. and GN H., 2018*]

In our study:

- The amount of pain on the side applied with platelet rich fibrin was significantly lighter than on the other side without platelet rich fibrin according to the VAS scale
- Also, the size of the mouth opening (trismus) on next day after the extraction and the fourth day was better if we compared it with the trismus that occurs when performing the pattern surgical extraction.
- As for alveolar osteitis, its incidence was much lower on the side on which fibrin was applied than the side without.
- As for edema, the application of fibrin has positive results in reducing the size of the edema that occurs after the operation, if we compare it with the other empty side of the same patient.

Conclusions

The platelet rich clot (fibrin) has the ability to manage pain following surgical extraction, reduce edema and trismus, and the ability to reduce the incidence of alveolar ostietis in smoking patients.

We recommend the application of platelet rich fibrin after the surgical extraction of the lower third molar in smokers.

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