Original Article

An Evaluation of Effects Of Platelet-rich-fibrin on Postoperative Morbidities after Lower Third Molar Surgery

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ABSTRACT

Objectives: The aim of the present study was to assess whether the use of platelet-rich fibrin (PRF) decreased the pain, swelling, and trismus levels of postoperative third molar surgery. **Materials and Methods:** In a double-blinded, split-mouth randomized study, thirty patients (6 male/24 female, mean age 20.32 years) with bilateral symmetric impacted third molars were enrolled in this study to receive surgery. The PRF mass was randomly placed in one of the extraction sockets, whereas the other socket was left without treatment. The outcome variables were pain, maximum mouth opening (trismus), swelling (edema), and the presence of dry socket which were measured using a 10-point visual analog scale, manual calipers, and 3dMD facial imaging system which was used for the 1st time in the third molar surgery. **Results:** Statistical analyses revealed that there were no significant differences between the control and study groups regarding postoperative pain, swelling, and trismus ($P > 0.05$). **Conclusion:** The results of this study suggest that PRF was not observed to have a positive effect on postoperative discomfort, so even though, PRF is presumed to have positive effects on healing and recovery processes.

KEYWORDS: *3dMD, pain, platelet-rich fibrin, swelling, third molar surgery, trismus*

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INTRODUCTION

The surgical extraction of an impacted third molar is a routine but traumatic procedure which is performed by oral and maxillofacial surgeons. Third molar surgery involves a few postoperative complications such as pain, swelling, and trismus, which are affected by many factors and variables.[1] Certain challenges cause esthetic and functional problems for surgeons and patients.[2] The outcome of various clinical and surgical procedures in the third molar surgery is affected by several factors such as patient, defect, and surgical variables.[2,3] An awareness of systemic conditions and drugs that could affect bone and adjacent soft tissues may be important to identify patients at increased risk of poor clinical and postoperative results.[3] To prevent or reduce these complications, many studies have investigated the use of various drugs, biological factors, and surgical techniques.[4]

Platelet-rich fibrin (PRF) is a second generation platelet concentrate which was first introduced by Dohan *et al*.[5] Platelet complexes have been reported to have effects on hemostasis, osteogenesis, angiogenesis, bone growth, and microbial growth.[6] The production of PRF is easier than that of platelet-rich plasma (PRP) and does not require any additional factor or procedure. PRF basically consists of a fibrin matrix, leukocyte cytokines, and growth factors (platelet-derived growth factor [PDGF], transforming growth factor beta [TGF-β], epidermal growth factor [EGF], fibroblast growth factor, keratinocyte growth factor, insulin-like growth factor, platelet-derived EGF, interleukin-8, tumor necrosis factor alpha, connective tissue growth factor, and granulocyte

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macrophage colony stimulating factor).[7] Platelet concentrates have been used to stimulate both soft and hard tissue healing.[3,6]

Many authors have mentioned platelet concentrates is an effective supply that means improving the healing of both hard and soft tissues, resulting in reductions in pain, swelling, and trismus.[8-16] However, there are some controversial results in the literature,[17] and there have been low numbers of systematic studies carried out to date.

As a consequence of improvement in three-dimensional (3D) devices, maxillofacial imaging plays an important role in clinical examinations. Thus, external soft tissues of the craniomaxillofacial region can be recorded appropriately, faster and in a more noninvasive way than by traditional methods.[18] Traditional methods have limitations for investigating craniomaxillofacial changes but the 3dMD imaging system provides more accurate data and is stored in digital format.[19,20] To the best of our knowledge, up-to-date the effect of PRF on swelling has not been assessed with 3dMD imaging system.

Primarily, the purpose of this study was to assess the effects of PRF on the postoperative period of the third molar surgery by evaluating pain, trismus, and swelling (edema). Second, we aimed to evaluate swelling with the 3dMD imaging system which was used for the 1st time in the lower third molar surgery. The investigators hypothesize that PRF could be beneficial to reduce postoperative morbidities of the lower third molar surgery.

Materials and Methods

Study design/sample

The present study was a randomized, double-blinded, split-mouth, single-center clinical trial conducted in the Department Oral and Maxillofacial Surgery, Faculty of Dentistry, İnönü University, between April 2014 and November 2014. Approval for the study was granted by the Human Ethics Committee of İnönü University. All procedures followed were in accordance with the ethical standards of the committee responsible for human experimentation (Institutional and National) and with the Helsinki Declaration of 1975, as revised in 2008. All patients gave written informed consent for the surgical procedures and to participate in the clinical trial.

The study comprised thirty voluntary healthy patients (6 male/24 female) with asymptomatic, symmetric bilateral mesioangular impacted lower third molars. Inclusion criteria were that the patients were over 18-year-old, asymptomatic, and completely bone impacted symmetric bilateral mesioangular lower third molars. Exclusion criteria were any systemic disease, local infection, cigarette or tobacco usage, oral contraceptive usage, pregnancy, lactation, penicillin/paracetamol/chlorhexidine allergy, and asymmetric or semi-impacted third molars.

Surgical procedure

All the operations were carried out by the same maxillofacial surgeons (FA and OG) using a standardized procedure: Local and regional anesthesia was administered with 40 mg/mL of articaine (Ultracain; Sanofi Aventis, PharmaVision San.Tic., A.Ş., Topkapı, İstanbul) with epinephrine 0.012 mg/mL. A full thickness three-cornered mucoperiosteal flap was raised over the surgical site. Lower third molars were extracted using round and fissure burrs under saline irrigation. All the necrotic tissue was removed and the socket was irrigated twice with 20 mL 0.9% saline. After extraction, PRF mass was placed into the socket on one side as the study site and the other as the control site was left empty. Sample allocation was done by simple randomization. The mucoperiosteal flap was repositioned and sutured with 4/0 silk.

Postoperatively, all patients were prescribed 1000 mg amoxicillin-clavulanic acid two times daily, 500 mg paracetamol orally two times daily, and 0.2% chlorhexidine mouth rinse three times daily for 1 week.

The second operation was carried out 4 weeks after the first operation.

Platelet-rich fibrin preparation

Immediately before the surgical procedure, 10 mL of blood was drawn into test tubes without an anticoagulant from all the patients in all operations (both study and control sites). Because the patients were blinded to which side was experimental and which was the control. The blood sample was centrifuged for 12 min at 2700 rpm. After centrifugation, the PRF clot was obtained, separated from the RBC base using scissors, and placed in the curetted rinsed empty socket in the study group.

Postoperative evaluations

A visual analog scale (VAS) was used to evaluate postoperative pain. A 10-point VAS with a score of 0 equals "no pain" and 10 equals "very severe pain" was used to assess pain. The patient marked the scale at 6 h, 12 h, then 1, 2, 3, 4, 5, 6, and 7 days after surgery.

For the evaluation of the degree of trismus, mouth opening distance was recorded preoperatively and on postoperative days 2 and 7 by measurement of the maximal distance of the inter-incisor opening with manual calipers.

In follow-up appointments, if patients experienced any persistent and progressive pain, it considered to dry socket.

3dMD evaluations

3D photographic images were taken by the 3dMD face (3dMD, Atlanta, GA)® photogrammetric system. The 3dMD system uses a synchronized digital multicamera configuration, with three cameras on each side (1 color, 2 infrared) that capture a photo in lifelike quality pictures [Figure 1]. The distance (patient to camera) was standardized during the study. The system can capture 180° facial images from ear to ear. 3D images were loaded in the 3dMD software 3dMD Vultus (3dMD, Atlanta, GA). T_0 and T_1 image files were opened with 3dMD vultus (3dMD, Atlanta, GA) and images superimposed on forehead and bridge of the nose as suggested by the manufacturer. The forehead and the bridge of the nose were not affected by swelling. After superimposition, the swelling was calculated by selecting the area of the swelling and volume of differences between two images was obtained [Figure 2]. A preoperative 3dMD image was taken immediately before surgery for comparison with the postoperative appearance. Postoperative 3dMD images were taken on the 2nd and 7th days by the same researcher.

Statistical analysis

Recorded data were analyzed using the IBM-SPSS 20.0 software (Statistical Package for the Social Science, SPSS Inc., Chicago, IL, USA). The Shapiro–Wilk test was used to test for normal distribution of data of individual parameters. Differences in individual parameters among the groups were tested using the independent sample *t*-test for normally distributed variables (trismus) and the Mann–Whitney U-test for abnormally distributed variables (swelling and pain). Pearson's correlation test was used to assess if a statistically significant relationship existed between two categorical variables. A $P < 0.05$ was accepted as statistically significant ($\alpha = 5\%$, power >80%).

Results

The study included a total of thirty patients, comprising 6 males and 24 females with a mean age of 20.32 years (range: 18–29 years). Tooth sectioning was done in 16 sites (eight controls, eight studies). The postoperative complication of the dry socket was observed in three patients in the control group and in 1 in the study group. Statistical analyses showed no significance in the differences between both groups for the all variables (pain, edema, trismus, and presence of dry socket) ($P > 0.05$) [Table 1]. The mean operation time (starting from the first incision to the last suture) was 12.44 ± 3.55 min for the control group, 14.63 ± 7.95 min for the study group ($P > 0.05$) [Table 1].

Table 1: The average values of pain, swelling, maximum mouth opening, and number of dry socket in platelet-rich fibrin treated and nonplatelet-rich fibrin treated groups

	Control group	Study group	*P*
Pain			
6th h	43.47±32.16	49.65±31.45	0.53
12th h	31.00±28.83	31.24±30.58	1.00
1st day	22.20±21.70	27.35±31.70	0.94
2nd day	18.67±22.39	18.59±19.48	0.94
3rd day	17.73±24.90	22.00±23.77	0.60
4th day	15.80±22.85	14.76±19.00	0.85
5th day	13.40±22.96	11.47±16.62	0.71
6th day	8.27±15.59	10.47±18.21	0.55
7th day	4.87±11.42	8.18±15.52	0.46
Swelling			
2nd day	20.47±10.63	19.85±9.45	0.94
7th day	5.79±5.01	7.25±5.73	0.27
Trismus (maximum mouth opening) (mm)			
Preoperative	45.06±5.96	45.70±5.62	0.74
2nd day	32.72±7.19	31.04±8.29	0.58
7th day	37.54±5.62	36.76±8.98	0.77
Duration of surgery (min)	12.44±3.55	14.63±7.95	0.20

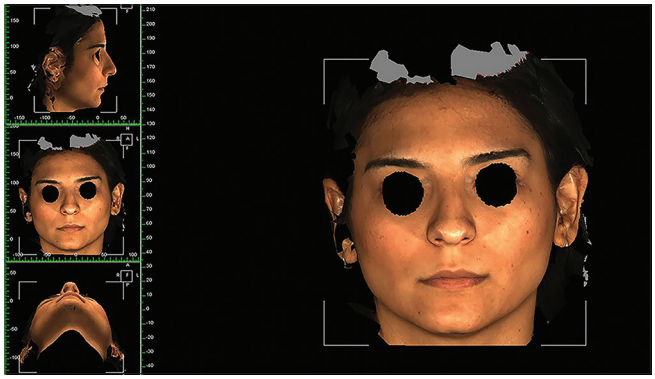

Figure 1: Patient's head as captured by the system

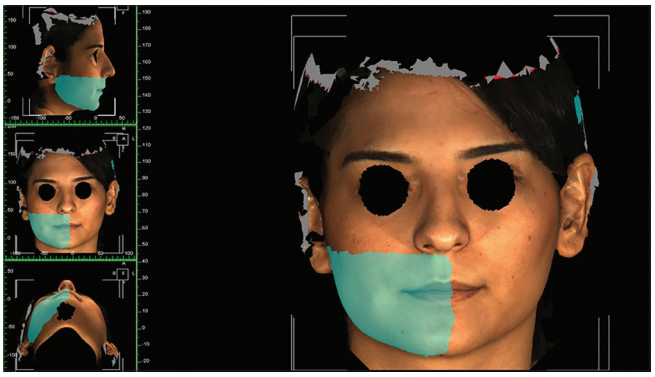

Figure 2: The region of the swelling is selected (blue)

Discussion

This study aimed at assessing the possible effects of PRF on postoperative morbidities (pain, edema, and trismus) in the third molar surgery. The effects of PRF were evaluated by VAS (for assessing pain), 3dMD imaging system (for assessing edema), and manual caliper (for assessing trismus).

Pain, trismus, and swelling are almost universal complications. The removal of impacted third molars can negatively impact the quality of life of patients. Gender, type and depth of impaction, level of difficulty, experience of the surgeon, patient medical condition, as well as smoking and use of oral contraceptive pills may affect postoperative complications.[21,22] Moreover, in surgical extraction of the third molars, dry socket has been found to develop in up to 30% of cases.[23] In the present study, only four sites developed dry socket (4 of 60 teeth, 6.7%), and there was no statistically significant difference between the groups. Relatively low frequency of dry socket may be due to good oral hygiene motivation. Third molar extraction presents a challenge to surgeons and so to solve or reduce these problems, many drugs, biofactors, and methods have been studied.

PRP and PRF are among the most advantageous tools in widespread use in surgery clinics. PRF second generation platelet concentrate has been less studied and compared to PRP, has the advantages of being cost-effective, easy to manipulate, lack of biochemical handling, and does not dissolve quickly.[24] Therefore, PRF can function as an autologous natural 3D scaffold which can carry fibrin, platelets, leukocytes, growth factors, and cytokines.

Growth factors contained within PRF are gradually released owing to the fibrin structure.[25] TGFβ-1, PDGF, and VEGF are the main growth factors effective in wound healing, and the sustained release of these growth factors is important for angiogenesis and tissue regeneration.[26] In an experimental study on mice, Bir *et al*.[27] suggested that platelet concentrates showed earlier recovery of blood flow within 2 weeks in the ischemic hind limb. Enhanced wound healing may be attributed to stimulated neovascularization in the damaged area in the short-term.

PRF, also known as a healing biomaterial, has been studied in both soft and hard tissues.[8-15,28] Kulkarni *et al*.[11] reported that a PRF dressing on a palatal wound from the harvesting of a free gingival graft improved the healing process in ten patients. Acar *et al*.[8] showed that PRF can enhance bone regeneration in calvarial defects in rabbits. Hoaglin and Lines[29] reported PRF to be a preventive biofactor in the development of dry socket. A 90% decrease in the incidence of the dry socket was determined in patients where PRF was used in the lower third molar surgery.[29] Joseph *et al*.[9] performed open flap debridement in the management of horizontal periodontal defects together with the use of PRF gel and membrane and achieved positive results in horizontal alveolar bony defects. PRF can be used in various disciplines of medicine and dentistry and may be considered a therapeutic biomaterial. However, despite the evident regenerative benefits, clinical application is still ambiguous.

The effect of platelet concentrates on postoperative morbidities of the third molar surgery is controversial. Rosamma Joseph *et al*.[14] reported that PRF can reduce postoperative pain after periodontal surgery. It has been suggested that PRF is a healing biomaterial that decreases pain and discomfort, owing to fibrin bandage and growth factor release.[7] However, according to clinical studies by Arenaz-Búa *et al*.[17] and Ozgul *et al*.,[20] there was no positive effect on pain with PRP/PRF, which is consistent with the findings of the current study. Ogundipe *et al*.[13] suggested that PRP gel has a beneficial effect on pain after the third molar surgery. In the present study, there was no statistically significant difference between the pain scores of the study and control groups. The difference in the pain scores between the current and the study of Ogundipe *et al*.[13] may be due to the sample of the studies, different flap technique or difficulty levels of surgeries.

Oral and maxillofacial surgeries may cause the spasm of some muscles, especially masseter (trismus). To evaluate trismus, the maximum mouth opening was measured with manual callipers. According to the findings of the current study, there was no statistically significant difference between the trismus scores of the two groups, which is similar to the findings of Arenaz-Búa *et al*.[17] However, Ogundipe *et al*.[13] and Simon *et al*.[15] reported that PRP had positive effects on trismus. These different findings are probably due to distinctions between PRP and PRF, but there is no evidence for this theory.

3D imaging of the facial region is a promising and effective tool in orthognathic, maxillofacial, facial, and reconstructive plastic surgery. Clinically, the 3dMD system can be used to measure edema and volumetric changes in the maxillofacial region. It can be considered a valid and reliable method to evaluate the effects of clinical interventions.[30] To the best of our knowledge, this is the first study to demonstrate the effects of PRF on facial swelling (edema) in the third molar surgery with the 3dMD system.

Kaur and Maria,[10] Kumar *et al*.,[12] and Ozgul *et al*.[20] reported that facial swelling can be reduced with platelet concentrates. However, the results of the current study are

not consistent with that conclusion. The current findings are supported by those of Arenaz-Búa *et al*.[17] who reported no statistically significant difference in swelling between study and control groups.

Limitations of the present study include the small sample size and that there was no information about analysis between genders.

Conclusion

There are very limited data in the literature about the effect of PRF on pain, trismus, and swelling in the third molar surgery. The results of this clinical study showed that PRF has no significant positive effect on postoperative pain, swelling, and trismus after the surgical removal of impacted lower third molars.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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This study design was approved by the Ethical Committee for Human Experiments of İnönü University and informed consent was obtained from all patients. The authors declare no potential conflicts of interest with respect to the authorship and/or publication of this article. Special thanks to Prof. İsmet Doğan for statistical analysis.

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Conflicts of interest

There are no conflicts of interest.

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