Effect of Platelet-Rich Fibrin on Frequency of Alveolar Osteitis Following Mandibular Third Molar Surgery: A Double-Blinded Randomized Clinical Trial

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Purpose: To evaluate the effectiveness of platelet-rich fibrin (PRF) in preventing the development of alveolar osteitis (AO).

Materials and Methods: In a double-blinded study, patients with bilateral impacted mandibular third molars underwent surgical extractions, with one socket receiving PRF and the other one serving as a control. The surgeon and patient were unaware of the study or control side. The predictor variable was the PRF application and was categorized as PRF and non-PRF. The outcome variable was the development of AO during the first postoperative week. Other study variables included age, gender, smoking status, irrigation volume, extraction difficulty, surgeon experience, and number of anesthetic cartridges. Data were analyzed using χ^2 and *t* tests, with the significance level set at a *P* value less than .05.

Results: Seventy-eight patients (mean age, 25 yr) underwent 156 impacted third molar surgeries. The overall frequency of AO was 14.74% for all surgeries. The frequency of AO in the PRF group was significantly lower than in the non-PRF group (odds ratio = 0.44; $P < .05$).

Conclusion: Based on the results of the present study, PRF application may decrease the risk of AO development after mandibular third molar surgery.

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Alveolar osteitis (AO) is the most common complication after permanent tooth extraction.[1] The frequency of AO after mandibular third molar surgery varies from 5% to 30%.[2] Although AO is self-limited and resolves after 5 to 10 days, the patient will experience progressive pain starting 1 to 3 days after surgery, a foul taste, regional lymphadenitis, and halitosis, which requires up to 4 follow-up visits in 45% of cases.[1,3]

In the development of AO, various risk factors have been identified, including the difficulty of surgery,[4] amount of trauma,[5] experience of the surgeon,[5] age,[6] smoking habits,[7,8] amount of socket irrigation,[9] preoperative infection,[10,11] gender,[12] use of oral contraceptives,[12,13] and menstrual cycle in women.[14] In addition, to prevent the occurrence of AO, various protocols have been proposed by researchers, including steroidal anti-inflammatory drugs, systemic antibiotic prescription, chlorhexidine mouthwash, local antibiotics, chlorhexidine gel, antifibrinolytic agents, and clot support agent application.[15,16]

Platelet-rich fibrin (PRF) is the second generation of platelet concentrates after platelet-rich plasma (PRP). In addition to the fact that PRF contains various autologous cytokines and immune cells, it is a fibrin membrane that covers the wound appropriately and can be sutured. Hence, PRF possesses cicatricial capacity

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and its specific structure makes it an appropriate membrane to improve the healing process.[17] PRF has been used in bone augmentation, angiogenesis, wound healing, and periodontal healing, with promising results.[18]

The aim of the present study was to investigate whether the frequency of AO after surgical removal of mandibular third molars differs when PRF is applied in the alveolar socket. The null hypothesis was that the frequency of AO with application of PRF after surgery would equal that without PRF. The specific aims of the research were *1)* to determine the frequency of AO after surgical removal of impacted mandibular third molars with and without PRF application and *2)* to compare the frequency of AO in the PRF sockets with the non-PRF controls.

Materials and Methods

The present study was conducted at the Mashhad Dental Clinic of Oral and Maxillofacial Surgery (Mashhad, Iran). The ethical board of the Mashhad University of Medical Sciences approved the study protocol and all patients provided a signed, detailed informed consent.

STUDY DESIGN

To address the study purpose, the authors designed and implemented a split-mouth, double-blinded clinical trial based on the consent statement and the published guidelines.[19]

STUDY SAMPLE

The study population consisted of patients presenting for the evaluation and management of bilateral impacted lower third molars from January 2009 to January 2010.

To be included in this study, the patients had to be 18 to 35 years of age, have American Society of Anesthesiologists physical status I or II, have bilateral mandibular third molars, have the same difficulty level of bilateral third molars based on the Pederson classification (sum score of the spatial direction of tooth value, depth of impaction, and relation with the ramus on the panoramic radiograph).[20,21]

Patients were excluded as study subjects if they had pericoronitis of the mandibular third molar(s), received antibiotic regimen during the previous 2 weeks, had a smoking habit, were lactating or pregnant, were using oral contraceptives, had any lesions found on the panoramic radiograph, had any complications during extractions, or had received more than 2 anesthetic cartridges during surgery.

STUDY VARIABLES

In the present study, the predictor variable was the application of PRF in the extraction socket. For each patient, PRF was placed in one of the sockets and the other socket received no treatment.

The outcome variable was the frequency of AO. The criteria for diagnosing dry socket were progressive and severe pain during the first postoperative week, foul taste, halitosis, regional lymphadenitis, or loss of clot in the extraction socket.

Moreover, data regarding demographic variables (age, gender), preoperative variables (radiographic extraction difficulty, surgeon experience), and perioperative variables (volume of irrigation, number of local anesthetics) were collected.

DATA COLLECTION

Before surgery, 10 mL of venous blood from each patient was obtained from the cephalic or basilica vein with a 19-gauge needle. The blood sample was immediately centrifuged at 3,000 rpm (Labofuge 400R centrifuge, Heraeus, Hanau, Germany) for 10 minutes. At the end of the process, the fibrin clot in the middle of the tube was PRF.

An experienced surgeon performed all surgeries using the same protocol: povidone iodine was applied around the mouth; anesthesia was obtained using 2% lidocaine with 1:80,000 epinephrine cartridges; the access was prepared with a mucoperiosteal envelope flap without releasing; bone removal, tooth sectioning, and bone contouring were performed with a low-speed handpiece under sufficient sterile normal saline irrigation; sockets were irrigated with normal saline 100 mL; and the flap was sutured with 3-0 silk sutures. Postoperative prescriptions were amoxicillin (500 mg 3 times daily, n = 21) and acetaminophen (500 mg 3 times daily, for a maximum of 3 days).

The 2 impacted mandibular third molars of each patient were removed in 1 appointment. After the removal and before suturing, PRF was randomly inserted into one of the sockets (PRF group, n = 85). The contralateral socket was considered a control (non-PRF group, n = 85). An operator blinded to the surgery performed the PRF insertion and suturing. Hence, the patients and the surgeon were blind to the side in which PRF had been inserted. The randomization data were kept unknown by another investigator until the end of the study. Randomization of the socket side was performed using a coin flip.

Two follow-up appointments were held at days 2 and 7 postoperatively. Furthermore, patients were asked to return if they experienced any persistent and progressive pain between follow-up visits. If so, a calibrated examiner, who was unaware of the grouping, examined patients for clinical signs of AO.

Cases of AO were treated with socket irrigation using normal saline and an intra-alveolar dressing with Alvogyl iodoform (Septodont, Cambridge, ON,