Effects of Leukocyte- and Platelet-Rich Fibrin Alone and Combined With Hyaluronic Acid on Pain, Edema, and Trismus After Surgical Extraction of Impacted Mandibular Third Molars

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Purpose: In this prospective, randomized, double-blind controlled study, we evaluated the effects of leukocyte- and platelet-rich fibrin (L-PRF) alone and combined with a hyaluronic acid (HA) sponge on pain, edema, and trismus after mandibular third molar surgery.

Patients and Methods: In total, 60 patients were included in this study. The patients were randomly divided into 3 groups: L-PRF group (L-PRF was applied to the socket), L-PRF–plus–HA group (L-PRF combined with HA was applied to the socket), and control group (nothing was applied). The primary outcome variables were edema (tragus to pogonion, tragus to labial commissure, and angulus mandibulae to lateral canthus), trismus on postoperative days 2 and 7, and postoperative pain scores on a visual analog scale from hour 6 to day 7.

Results: After extraction, the tragus-to-pogonion values were significantly higher in the control group both on day 2 (higher than L-PRF–plus–HA group) and on day 7 (higher than both groups). The mean increase in tragus–to–labial commissure values on day 2 was significantly higher in the control group than in the L-PRF–plus–HA group. The mean increase in angulus mandibulae–to–lateral canthus values on days 2 and 7 was significantly higher in the control group than in the L-PRF and L-PRF–plus–HA groups. There was no significant difference among groups in trismus and visual analog scale pain scores. Analgesic intake on the day of surgery in the L-PRF–plus–HA group was significantly lower.

Conclusions: Our results imply that L-PRF, particularly when combined with HA, can be used to minimize postoperative edema after mandibular third molar surgery. However, further studies with larger samples are required.

J Oral Maxillofac Surg ■*:1-7, 2017*

Surgical extraction of an impacted mandibular third molar (M3) is one of the most common dental surgical procedures.[1] In the days after M3 surgery, pain, facial swelling, and restriction of mouth opening decrease the patient's quality of life.[2]

Various surgical techniques and materials have been described to decrease postoperative complications and accelerate the healing process after M3 surgery.[1,3-14] Leukocyte- and platelet-rich fibrin (L-PRF) is a platelet concentrate obtained from the patient's own blood that contains all of the components of blood that are involved in wound healing and immunity.[15] It contains abundant growth factors and other cytokines, including platelet-derived growth factor,

Received from Department of Oral and Maxillofacial Surgery, Faculty of Dentistry, Marmara University, Istanbul, Turkey.

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Conflict of Interest Disclosures: None of the authors have any relevant financial relationship(s) with a commercial interest.

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Received July 28 2017

Accepted December 1 2017

0278-2391/17/31468-4

https://doi.org/10.1016/j.joms.2017.12.005

transforming growth factor β1, and insulin-like growth factor.[15,16] Several animal and human studies have shown that platelet concentrates applied to a tooth-extraction socket can decrease postoperative complications and improve healing.[3,4,9,10,12,13,17-20]

Hyaluronic acid (HA), a high-molecular-weight glycosaminoglycan and one of the major components of extracellular matrix, can be found in numerous tissues including joint synovial fluid and vitreous humor of the eye.[6,21] HA has many properties that make it an ideal molecule to facilitate wound healing, including inducing beneficial early granulation tissue formation, inhibiting destructive inflammation during the healing phase, and promoting re-epithelialization and angiogenesis.[11,21] In addition, it has been shown to decrease the levels of inflammatory mediators, and it can be safely used as an anti-inflammatory agent.[6,11,22] HA in the solid form is commonly used as a biocompatible, biodegradable, and nonimmunogenic wound dressing.[21,23-26]

Various platelet concentrations in combination with different HA forms are applied in many medical fields to accelerate wound healing, reduce scar tissue, protect the wound site from external factors, decrease the number of dressings, and increase postoperative patient comfort.[23-25,27] This study explored the clinical effect of L-PRF alone and L-PRF combined with an HA sponge (Hyaloss Matrix; Anika Therapeutics, Bedford, MA) compared with a control group after M3 surgery.

Patients and Methods

This prospective, randomized, double-blind controlled study enrolled 60 patients from the Department of Oral and Maxillofacial Surgery, Faculty of Dentistry, Marmara University, Istanbul, Turkey. This study followed the Declaration of Helsinki in terms of medical protocol and ethics. Ethics committee approval for this clinical investigation was obtained from the appropriate institution (Marmara University Faculty of Dentistry Ethics Committee, protocol code 2016-50), and all participants signed an informed consent agreement.

To standardize the study, all 3 groups comprised patients with a unilateral partially erupted M3 who underwent extraction surgery on an elective basis. The M3 positions were evaluated on preoperative radiographs based on the Pell and Gregory classification. The inclusion criteria were M3s with class 2 position B vertical impaction. All patients were aged between 18 and 30 years, nonsmokers, and classified as physical status I using the guidelines of the American Society of Anesthesiologists. The exclusion criteria included procedures taking more than 30 minutes, patients who did not follow postoperative instructions, and patients who showed signs of alveolar osteitis and infection. A custom random-number generator was used by the third investigator (O.G.) to randomly assign patients to 3 groups. Patients did not know their group assignments until the study was completed.

To obtain L-PRF, immediately before surgery, 2 blood samples were collected in 10-mL tubes without anticoagulant by a surgical nurse, and the samples were immediately centrifuged at 3,000 rpm for 10 minutes. L-PRF in 1 of the tubes was pressed into a membrane between 2 sterile metal surfaces by the third investigator (O.G.), as described by Dohan et al.[15] In the L-PRF–plus–HA group, the serum exudate released during pressing was adsorbed to the HA sponge, allowing for the application of HA with its cytokine-binding and carrier molecule properties.

The surgeon who performed the surgical procedures was blinded to a patient's group until the tooth extraction was completed. All tooth extractions in all groups were performed by the same investigator (İ.M.A.) using the same procedure and following the same surgical steps. After surgical extraction of the impacted M3, the third investigator (O.G.) informed the surgeon of the patient's group assignment.

In the L-PRF group (n = 20), L-PRF from 1 of the tubes was applied to the socket, and a L-PRF membrane obtained from the other tube was applied under the flap covering the socket. In the L-PRF–plus–HA group (n = 20), the HA sponge was placed between the 2 layers of L-PRF. Nothing was applied to the socket in the control group (n = 20).

In all groups, flap closure was performed with No. 3-0 silk sutures, leaving the gingiva over the socket for secondary healing, as described by Pasqualini et al.[14] Standard postoperative medication was prescribed in all groups, and sutures were removed on day 7.

The primary outcome variables were edema and trismus on postoperative days 2 and 7 and visual analog scale (VAS) pain scores from postoperative hour 6 to day 7. All preoperative and postoperative measurements were performed by the second investigator (E.T.A.), who was blinded to the patients' group assignments until the study was completed. This investigator did not participate in randomization or operations.

EVALUATION OF POSTOPERATIVE EDEMA

The distances from the tragus to pogonion (TPO), tragus to labial commissure (TCO), and angulus mandibulae to lateral canthus (ACA) were measured with a flexible ruler and recorded preoperatively. These 3 measurements were repeated on postoperative days 2 and 7, and the differences between these values and the preoperative measurements were calculated.