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Efficacy of hyaluronic acid spray on swelling, pain, and trismus after surgical extraction of impacted mandibular third molars

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Abstract. The aim of this study was compare the efficacies of two oral sprays in reducing swelling, pain, and trismus after the extraction of impacted mandibular third molars. This prospective double-blind, randomized, crossover clinical trial included 34 patients with bilateral symmetrically impacted mandibular third molars of similar surgical difficulty. Hyaluronic acid or benzydamine hydrochloride spray was applied (two pumps) to the extraction area, three times daily for 7 days. Swelling was evaluated using a tape measure method, pain with a visual analogue scale (VAS), and trismus by measuring the maximum inter-incisal opening. Assessments were made on the day of surgery and on days 2 and 7 after surgery. Statistically significant differences were detected for the swelling and trismus values between the two treatment groups on the second postoperative day ($P = 0.002$ and $P = 0.03$, respectively). However, there was no statistically significant difference in VAS scores between the two groups. The administration of hyaluronic acid spray was more effective than benzydamine hydrochloride spray in reducing swelling and trismus. Although no evidence of a reduction in pain levels was detected, hyaluronic acid appears to offer a beneficial effect in the management of swelling and trismus during the immediate postoperative period following impacted third molar surgery.

Keywords: impacted third molar; hyaluronic acid; benzydamine hydrochloride; swelling; trismus; pain.

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The surgical extraction of impacted third molars is one of the most common procedures in oral and maxillofacial surgery. Patients refer to the postoperative swelling, pain, and trismus associated with the inflammatory response to surgical trauma as the main factors affecting their daily life.[1–3] There are several other complications associated with the extraction of impacted third molars, the most common being alveolar osteitis and postoperative infection,[4,5] which can be a

burden for both the patient and the surgeon.

To prevent or reduce postoperative inflammation and associated symptoms, adequate anti-inflammatory therapy is needed.[6] Corticosteroids and anti-inflammatory drugs are the options most often used to ameliorate these postoperative symptoms. Corticosteroids are used widely to decrease the oedema and trismus related to third molar surgery.[7] The potential side-effects of perioperative corticosteroid use are adrenal suppression, delayed wound healing, and increased susceptibility to infection.[1,3]

Hyaluronan or hyaluronic acid (HA) is a biomaterial that has been introduced as an alternative approach to enhance wound healing.[8] HA is a major carbohydrate component of the extracellular matrix and can be found in many tissues.[9] It has multifaceted roles in biology, utilizing both its physicochemical and biological properties, and also has many properties that make it a potentially ideal molecule for assisting wound healing: inducing beneficial early granulation tissue formation, inhibiting destructive inflammation during the healing phase, and promoting re-epithelialization and also angiogenesis.[9–11] By virtue of its non-immunogenicity and non-toxicity,[9,10] its use has been established in many medical disciplines, such as ophthalmology, dermatology, and rheumatology.[10,12] The synthetic form of HA for topical oral use is available in a gel or liquid preparation.

Benzydamine hydrochloride (BnzHCl) is a non-steroidal drug with analgesic, anti-inflammatory, and antimicrobial properties.[13,14] Its mechanism of action is not entirely known, but the drug may affect the formation of thromboxanes and alter the rate of prostaglandin production, thereby inhibiting platelet aggregation and stabilizing cell membranes.[13,15] It is often recommended for the relief of inflammatory conditions of the oral cavity[14,15] and is commonly used as a mouth rinse or mouth spray at a concentration of 0.15%.

The aim of this study was to compare the efficacies of HA and BnzHCl sprays in reducing swelling, pain, and trismus after the surgical extraction of impacted mandibular third molars.

Materials and methods

Patient selection

This study was a prospective double-blind, randomized, crossover clinical trial. The study received approval from the institutional ethics committee. Forty patients were enrolled in the study and provided a signed statement of informed consent. All patients had bilateral symmetrically impacted mandibular third molars. Thirty-four patients (15 male, 19 female; mean age 23.35 ± 3.89 years) completed the study.

Patients with no systemic disease, history of allergy, or bleeding problems, those who co-operated with the study and with postoperative follow-up, and those who had bilateral symmetrically impacted mandibular third molars with total or partial bone cover and of comparable surgical difficulty were included in the study.

The following patients were excluded from the study: those with signs of pericoronitis and/or pain before surgery, those who were pregnant or nursing a baby, those in whom the extraction of the retained third molar lasted for more than 30 min or the operation time differed by more than 5 min between the two sides, those who had undergone antibiotic or other medication therapies during the preceding 2 weeks, those who had active carious lesions and/or periodontal diseases, and those who had contraindications to the drugs or anaesthetics used in the surgical protocol.

Study design

All of the patients were operated on by the same experienced oral and maxillofacial surgeon and assistant in order to minimize differences due to operator variability. Each patient underwent two surgical operations, separated by 4 weeks. In the first operation, the right third molar was extracted. The patients were divided randomly into two groups: after the operation the patient was given either BnzHCl spray (Tanflex oral spray, 30 ml, 0.15% BnzHCl; Abdi Ibrahim Pharmaceutical Company, Istanbul, Turkey) or HA spray (Gengigel spray 50 ml, 0.2% HA; Farmalink Saglik Urunleri San. ve Tic. Ltd. Sti., Istanbul, Turkey) and instructed to apply the spray, two pumps to the extraction area three times a day, for 7 days. In the second operation, the left third molar was extracted and the other spray was given to the patient. Both the surgeon and the patient were blinded to the spray given. The patients were instructed not to eat or drink for 1 h after the use of both sprays.

Surgical protocol

All patients underwent the procedure under inferior alveolar and buccal nerve blocks using articaine with 1:200,000 epinephrine. A three-cornered flap was raised to gain access to the third molar, and buccal osteotomy and sectioning were carried out when necessary. Once the tooth had been extracted, the alveolus was irrigated with sterile saline solution at room temperature to eliminate debris and the bone edges were smoothed; the flap was then repositioned and the closure was performed with 3–0 silk. All patients received prophylactic antimicrobial and non-steroidal anti-inflammatory/analgesic drugs, and written postoperative instructions. The postoperative medication for both groups was 1 g amoxicillin two times a day and 550 mg naproxen sodium every 8 h for 4 days.

Table 1. Criteria and scores of the Pederson scale.[22]

Criteria	Score
1. Spatial relationship	
Mesioangular	1
Horizontal/transverse	2
Vertical	3
Distoangular	4
2. Ramus relationship	
Class 1: sufficient space	1
Class 2: reduced space	2
Class 3: no space	3
3. Depth	
Level A: high occlusal level	1
Level B: medium occlusal level	2
Level C: low occlusal level	3
Difficulty score	
Difficult	7–10
Moderate	5–6
Easy	3–4

The degree of surgical difficulty was rated before the extractions by a single investigator, who performed the preoperative patient selection. The Pederson scale was used for this purpose[16]; the extractions were classified as easy, moderate, or difficult (Table 1).

The degree of facial swelling was determined by a modification[17] of the tape measure method described by Gabka and Matsumara.[18] Three measurements were made between five reference points: the distance between the lateral corner of the eye and angle of the mandible, the distance between the tragus and soft tissue pogonion, and the distance between the tragus and outer corner of the mouth. The mean of these three measurements was calculated. Measurements were taken preoperatively and on postoperative days 2 and 7.

Pain intensity was assessed using a 10-point visual analogue scale (VAS), with the patient placing a mark on the scale to indicate an intensity range from no pain '0' to severe/unbearable pain '10'.