

Efficacy of hyaluronic acid gel and spray in healing of extraction wound: a randomized controlled study

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Abstract. – OBJECTIVE: To evaluate the efficacy of 0.2% hyaluronic acid gel and 0.01% hyaluronic acid (HA) spray in the healing of extraction wounds using the ruler and digital planimetry method.

PATIENTS AND METHODS: 30 systemically healthy female participants aged between 20-60 years requiring extraction were selected. Extraction sockets receiving 0.2% HA gel Gengigel®, 0.01% HA spray Gengigel®, and where hyaluronic acid was excluded were allocated into three groups as test group A (HA gel group), test group B (HA spray group) and control group (without HA). Socket wound closure was measured post-operative on the day of extraction and 1-week post extraction using digital planimetry and ruler method. Patient satisfaction rate was evaluated for both the gel and spray.

RESULTS: The wound closure with the ruler method was 43.01% for the control group, 67.01%, and 65.82% for the gel group and spray group respectively. The wound closure with the digital planimetry method was 47.97% for the control group, 69.08% for the gel group, and 66.94% for the spray group. The gel showed better results of wound closure as compared to the spray. However, the results were not statistically significant. **CONCLUSIONS:** Hyaluronic acid offers a beneficial effect in early post-operative healing after extraction.

Key Words:

Hyaluronic acid gel, Dental extraction, Randomized control trial, Hyaluronic acid spray.

Introduction

Extraction of a tooth can have an impact on a patient's day-to-day life because it is accompanied by pain and other consequences, which may persist for a few days or more¹. Microbial adherence

and growth of both aerobic and anaerobic bacteria could function as foci of odontogenic infection². Various methods have been suggested to decrease or intercept post-operative inflammation and its other symptoms. Oral antiseptics before and after the surgical procedure have been effective in decreasing the microbial population and preventing post-surgical complications³.

Hyaluronan is often known as hyaluronic acid (HA), a biomaterial used to hasten wound healing⁴. HA gel has similar effects on healing, as well as antibacterial activity. HA is a glycosaminoglycan found in connective tissue, made up of non-sulfated disaccharide units of D-glucuronic acid and N-acetyl-D-glycosamine, which are connected by glycoside linkages, promoting a variety of healing properties during tissue formation and repair, including cell migration and differentiation^{5,6}. These substances supply the tissue with stability and flexibility. One investigation⁷ has found that hyaluronic acid plays a key role in blood vessel location, wound healing, and tissue regeneration. The hydrophilic aspect of HA promotes cellular migration while also protecting cells and extracellular matrix components through its free radical scavenging and protein exclusion properties⁸. Moreover, HA promotes various blood cell functions, particularly inflammatory responses like phagocytosis and chemotaxis⁹. Due to its anti-inflammatory properties, HA has been used in many medical fields, such as for the treatment of knee osteoarthritis¹⁰, and rheumatoid arthritis¹¹.

HA has also been employed in dentistry due to its biocompatible properties and function in biological processes associated with tissue healing¹². Clinical studies¹³ and randomized clinical trials have shown that using HA as an adjuvant treatment during periodontal surgery decreases clinical parameters and its

Table I. Comparison of the wound area measured by ruler method and digital planimetry method.

Group and Method	Day of extraction	1 week post-extraction
Control group		
Ruler method	48.60±21.25	27.70±4.35
Digital Planimetry method	29.42±12.21	15.31±1.04
Gel group		
Ruler method	45.20±21.54	14.91±3.01
Digital Planimetry method	25.68±1.60	7.94±.71
Spray group		
Ruler method	50.90±4.95	17.40±1.17
Digital Planimetry method	27.83±3.27	9.20±.53

$p < 0.05$ considered statistically significant, found between control and gel group and control and spray group by Unpaired t-test for both measurement methods.

local application in gingivitis¹⁴. HA is available in different forms such as spray and gel.

Topically applied HA-based biomaterials to inflamed areas have positive benefits in modifying and speeding up the host response¹⁵. To the best of our knowledge, no research has been done to evaluate socket wound closure after extraction comparing HA formulations. Therefore, HA application in gel and spray form was evaluated for its therapeutic efficacy in the early healing of extraction wounds.

Patients and Methods

A randomized controlled study was conducted on 30 systemically healthy female patients, aged between 20-60 years, requiring extraction in dental clinics, in the College of Dentistry, Jazan University between December 2020 to March 2021. Ethical clearance was obtained from the Scientific Research Unit of College of Dentistry, Jazan University. Patients were excluded if they used tobacco; if they were allergic or had adverse effects from local anaesthesia; if they had been on an antibiotic or anti-inflammatory medications within the last 15 days before tooth extraction or patients who required surgical extractions. Pregnant patients and patients with medical problems were also excluded.

Participants were informed of the study, including treatment and follow-up, and informed consent was obtained.

The 30 participants were divided into three groups. Sockets in test group A were treated with 0.2 percent HA gel Gengigel[®], sockets in test group B were treated with 0.01 percent HA spray Gengigel[®], and group C was a control group consisting of sockets where HA was not applied to the socket and the wound healed naturally by clotting.

Surgical Intervention

The dental surgeon with the same level of experience performed all 30 tooth extractions. Atraumatic extraction was performed using 2% Lidocaine with 1:100,000 epinephrine. After hemostasis was achieved, hyaluronic acid gel and spray were applied to the extraction wound. Hyaluronic acid gel and spray were also given to patients for home application twice daily (after breakfast and after dinner) for 1 week. Brushing was performed before application. The gel was applied using a cotton pellet, and the spray was applied in 2 puffs to the extraction socket. Patients were given instructions of not eating, drinking, or rinsing for about 30 minutes after spray/gel application.

Follow-Up Assessment

Wound surface area was measured post-operative at the day of extraction (baseline) and at 1-week post extraction using digital planimetry software (Pictzar[®] – Pro version 7.6.1. SS, NJ, USA) and ruler method. Change in the surface area between the baseline and 1-week follow-up determined the wound closure post-operatively. Patient satisfaction rate was evaluated on a scale of 10 at 1 week follow-up for both gel and spray. The wound area was evaluated using digital photographs and Pictzar software (Elmwood Park, NJ, USA). Pictzar estimated the wound surface area by overlaying the area in closed polygonal form overwound location after setting the calibration scale. Area measurements were acquired postoperatively on the day of extraction, and one-week post-extraction, thus the percentage of wound closure was obtained.

Statistical Analysis

The data were entered and analyzed using the Statistical Package for Social Sciences (SPSS) for

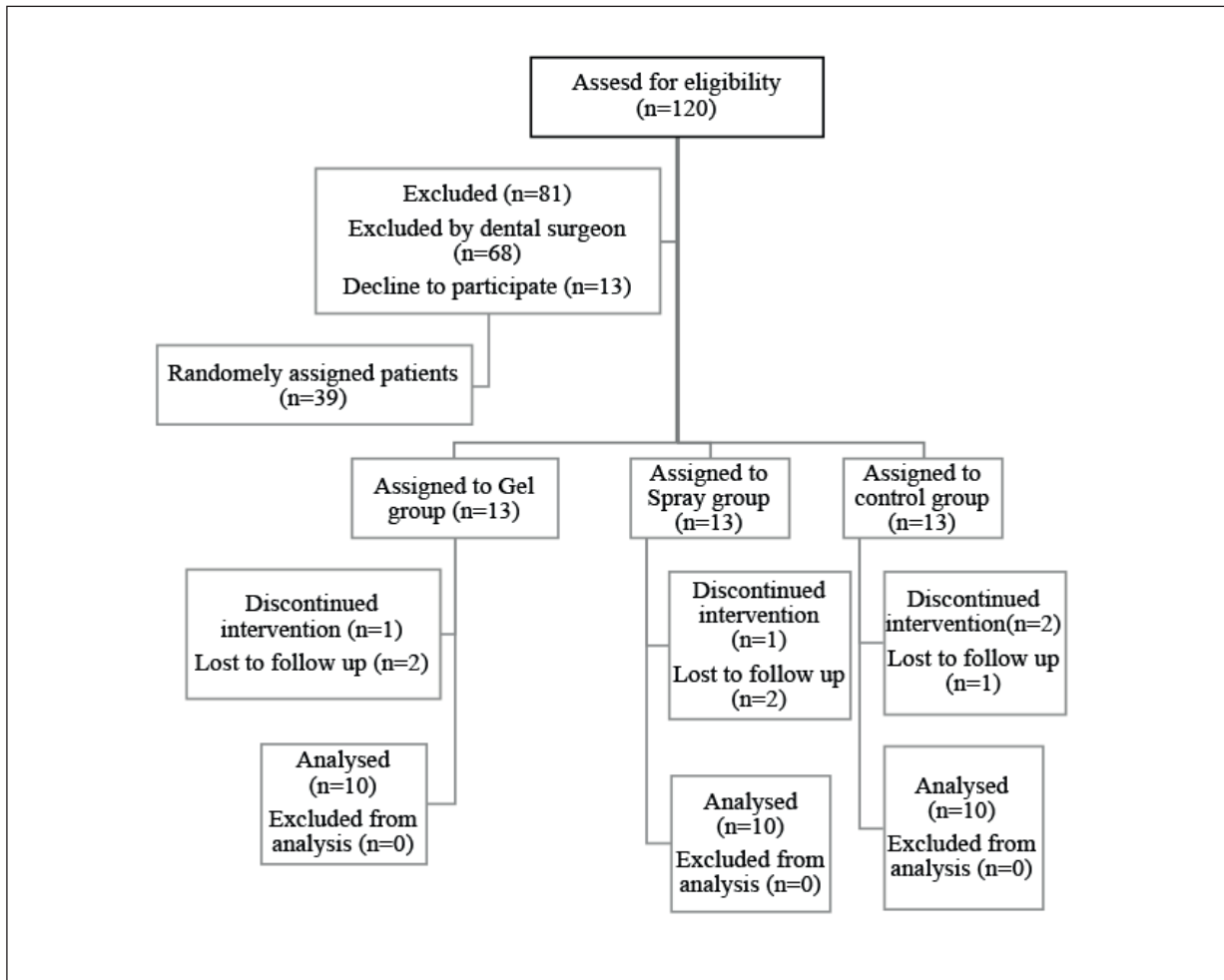


Figure 1. Flowchart of the study.

Windows 26.0 (IBM Corp., Armonk, NY, USA). Confidence intervals were set at 95%, and a p -value ≤ 0.05 was considered statistically significant. Unpaired t -test was applied to compare the area between both groups.

Results

30 female participants of the average age of 40 years were included in the study. The results showed a higher wound closure post-extraction with respect to the two test groups in comparison to the control group in both methods. Wound closure with the ruler method was 43.01% for the control group, 67.01% for the gel group, and 65.82% for the spray group. The wound closure with the digital planimetry method was 47.97%, 69.08%, and 66.94% for the control group, the HA gel group, and the HA spray group, respectively.

A statistically significant difference between the test and control groups was found. The gel group showed better results in the wound closure, as compared to the spray group, but results were not statistically significant. The spray group showed a higher patient satisfaction of 9.4, as compared to 8.2 of the gel group, but the difference was not significant. The mean wound area at baseline and 1 week after for all the groups is shown in Table I.

Discussion

The current study concentrated on HA efficacy in the forms of gel and spray in extraction sockets in systemically healthy patients. The results of the present study showed better wound closure in both HA groups compared to the control group, and the results were statistically significant. Hyaluronic acid acts as an antimicrobial barrier by retaining the wa-

ter in an aqueous solution¹⁶⁻¹⁸. This barrier reduces bacteria penetration into the tissues. HA inhibits tissue destruction and accelerates wound healing^{8,15}. Most extractions produce edema or swelling, which leads to trismus¹⁹⁻²¹. The swelling is usually at its peak at 1-2 days after surgery, beginning to decrease from the 3rd or 4th day, and is normally resolved by the end of the first week¹⁹. The current study's post-operative findings demonstrated HA to considerably reduce post-surgical edema, which results from the inflammatory process triggered by surgical trauma. This finding may relate to the high molecular weight of HA preventing excessive inflammation and consequent exacerbations²². By scavenging reactive oxygen species, including superoxide and hydroxyl radicals, and inhibiting inflammatory cell-derived serine proteinases, HA prevents tissue damage and allows faster healing^{8,15}. As HA also exhibits an osmotic buffering capacity, the anti-edematous effect may also be related^{8,23,24}. One week after the extraction, HA has an anti-inflammatory effect and enhances angiogenesis²⁵. This is consistent with our findings, which showed a substantial effect of HA on wound healing at 1 week after extraction. This is similar to the findings of Sasa et al¹⁸ and Koray et al⁴. Both approaches showed a reduction of the surface area; however, the ruler method readings were over-expressed, which agrees with Shah et al²⁶.

When compared to the gel group, the HA spray showed higher patient satisfaction, which could be attributable to the spray's ease of application. Our findings are in agreement with Koray et al⁴, who had better results of the patient's postoperative comfort with hyaluronic acid spray after surgical extraction of the lower 3rd molar. HA mitigates pain response by anti-inflammatory and anti-edematous contribution²⁷.

Several practitioners have emphasized the necessity of determining optimal therapeutic approaches to reduce and/or eliminate trismus and edema in patients undergoing the 3rd molar extraction, as well as for maximum comfort^{28,29}. In search of an agent that reduces post-extraction complications and promotes wound healing, many substances have been tested³⁰. HA is also proclaimed to be a viable candidate in periodontal tissue regeneration¹⁵.

Conclusions

Both hyaluronic acid gel and spray showed favorable effects in healing of extraction wound and patient's postoperative comfort. The limita-

tions of the study mainly concern a smaller sample size and inclusion of only female patients in the study. Further studies with a larger sample size and surgical extractions in the medically compromised individual with both the gender need to be evaluated.

Conflict of Interest

The authors declare that they have no conflicts of interest.

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