



## THE EFFICACY OF HYALURONIC ACID GEL ON POSTOPERATIVE SEQUELAE FOLLOWING EXTRACTION OF IMPACTED LOWER THIRD MOLARS

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### ABSTRACT

**Objectives:** The aim of the study was to assess the efficacy of hyaluronic acid gel on postoperative, dry socket, pain, trismus and edema after extraction of impacted lower third molars. **Subjects and methods:** Twenty impacted lower third molar teeth were extracted in ten patients under local anesthesia and under aseptic precautions. Split mouth design was followed. According to random allocation, 0.8% HA gel placed into the extraction socket in one side (group 1), while in the other side (group 2), only a gauze pack was placed. Dry socket, pain, trismus and edema were recorded after 24 hours, 72 h, one week and two weeks postsurgery. **Results:** There was no statistically significant difference in the incidence of dry socket between both groups. The pain score of patients in group 1 was significantly lower than patients in group 2 in all follow up intervals. Trismus was significantly higher in group 1 than group 2 in all intervals. The patients in group 1 have significantly less edema than patients in group 2 in all follow up intervals. **Conclusion:** Hyaluronic acid 0.8% gel application after extraction of impacted mandibular third molars has no significant effect on the incidence of dry socket, but it has a positive effect on postoperative pain, trismus and swelling.

**KEY WORDS:** Hyaluronic acid, third molar teeth, dry socket, pain, swelling.

### INTRODUCTION

Extraction of impacted molars is the most commonly performed procedures in oral surgery which making complications like sensory nerve damage, dry socket, pain, swelling, trismus, infection<sup>(1,2)</sup>.

Several treatment modalities have been advocated to prevent or reduce the incidence of dry socket. They include the use of antiseptic mouth washes as chlorhexidine, antifibrinolytic agents, antibiotics,

steroids, clot supporting agents and intra-alveolar dressings. These measures are oscillating between failure and success to reduce the occurrence of dry socket after extraction<sup>(3-18)</sup>.

Dry socket is associated with 0.5% to 5% of routine dental extractions and in about 25–30% of extractions of impacted mandibular third molars. It occurs due to degradation of the blood clot making a denuded socket with severe pain. The pain

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starts from the first to the third postsurgical days and accompanied with foul taste, or halitosis. It results in loss of a patient's production, and health, Thus, it is helpful to find an easy way to prevent incidence of dry socket<sup>(19,20)</sup>.

Recently Hyaluronic acid was introduced as a technique in prevention of post-operative sequelae due to its numerous advantages, such as enhancing the wound healing and anti-inflammatory effect. Hyaluronic acid HA is one of the major linear polysaccharides of the extracellular matrix which can be found in various body tissues especially in connective tissue and synovial fluid<sup>(21,22)</sup>.

The efficacy of hyaluronic acid on post extraction sequelae of impacted third molars was evaluated with a controversy results. Koray et al<sup>(23)</sup> concluded that no evidence of a reduction in pain levels was detected and that 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. On the other hand, Yilmaz et al<sup>(24)</sup> found that it has no effect on facial swelling and maximum mouth opening. However, the amount of pain significantly was reduced.

As dry socket occurs more often after extraction of impacted mandibular third molars, it is postulated to use HA gel as a socket dressing after surgery in an attempt to reduce the incidence of dry socket. The null hypothesis is that hyaluronic acid gel has no effect on the incidence of dry socket. So, the objective of this study is to evaluate the efficacy of 0.8% HA gel formulation on the incidence of dry socket<sup>(25,26)</sup>.

## SUBJECTS AND METHODS

This randomized controlled study was performed on ten patients with bilateral mesioangular impacted mandibular third molars indicated for surgical removals. The patient's age ranged between 18 to 30 years. They were selected from the out-patient's clinic, Faculty of Dental Medicine, Al -Azhar University, Boys, Cairo. The patients were treated

at the Oral and Maxillofacial Surgery Department. These patients were randomly assigned to one of two groups (group 1 or group 2); patients in group 1 (study group) received 0.8% HA gel placed into the extraction socket while patients assigned in group 2 received no gel.

The inclusion criteria were; healthy patients with bilateral mesioangular impacted mandibular third molars, healthy gingival and periodontal tissues and good oral hygiene. Patients with history of radiotherapy or chemotherapy to the head and neck were excluded. Immunocompromised patients, smokers, pregnant or lactating mother were also excluded from the study. Patients were fully informed about the treatment procedures and follow up examination. Appropriate institutional ethical clearance and written informed consent were obtained.

A complete medical history was taken at the first visit including chief complaint, patient age and sex, and the presence of associated symptoms and/or diseases. Panoramic x-ray view was utilized for evaluation of the location and configuration of impacted lower third molar, surrounding bone, mandibular canal and adjacent tooth.

### Preoperative assessment:

The maximal mouth opening was assessed and measured with a digital vernier scale. The patients were asked to open their mouth maximally to measure the distance (in millimeters) between the cutting edge of the right maxillary and right mandibular central incisors<sup>(27)</sup> (Fig. 1A).

Edema was assessed by measuring cheek dimensions in millimeters with a flexible measuring tape. Standard point marks were initiated with a marker prior to surgery on the following facial regions: angle of the mandible, tragus, labial commissure, nasal border, soft tissue pogonion and laterally to the outer corner of the eye<sup>(28)</sup>. Three reference lines were created from the aforementioned points; 1- AC: the most posterior point on the tragus to the lateral point on the corner of mouth (Fig. 1B), 2- AD: the most posterior point on the tragus to the soft tis-



FIG (1) (A) Measuring maximum mouth opening using digital vernier scale, (B) Measuring AC reference plane with a flexible measuring tape, (C) Measuring AD reference plane with a flexible measuring tape, (D) Measuring BE reference plane with a flexible measuring tape.

sue pogonion (Fig. 1C), 3 – BE: the lateral canthus of the eye to the most inferior point on the angle of the mandible (Fig. 1D). The sum of AC+AD+BE was considered as the preoperative base line facial dimension value.

#### **Surgical procedure:**

Under complete aseptic technique, the patients were operated under local anesthesia. artpharmadent 1:100,000® 4% was used for inferior alveolar, lingual and buccal nerves block. In both groups a three sided mucoperiosteal flap was utilized for exposure of the impacted lower third molars Figure (2A). The bone covering the tooth was removed, using rose head bur on a low speed hand piece under abundant

irrigation of normal saline, until the entire crown was exposed Figure (2B). Using a fissure bur sufficient amount of bone was removed using the guttering technique on the buccal and the distal aspect of the tooth Figure (2C). The tooth was sectioned using a high-speed hand piece with fissure bur and removed with the suitable instrument. Figure (2D).

Following removal of the third molar, patients assigned in group 1 received 0.8% HA gel in the form of pre-filled syringes 1ml from RICERFARMA EU Company placed into the extraction socket while patients assigned in group 2 received no gel Figure (2E, 2F). The flap was then repositioned back to its original position and sutured using 3-0 black silk.

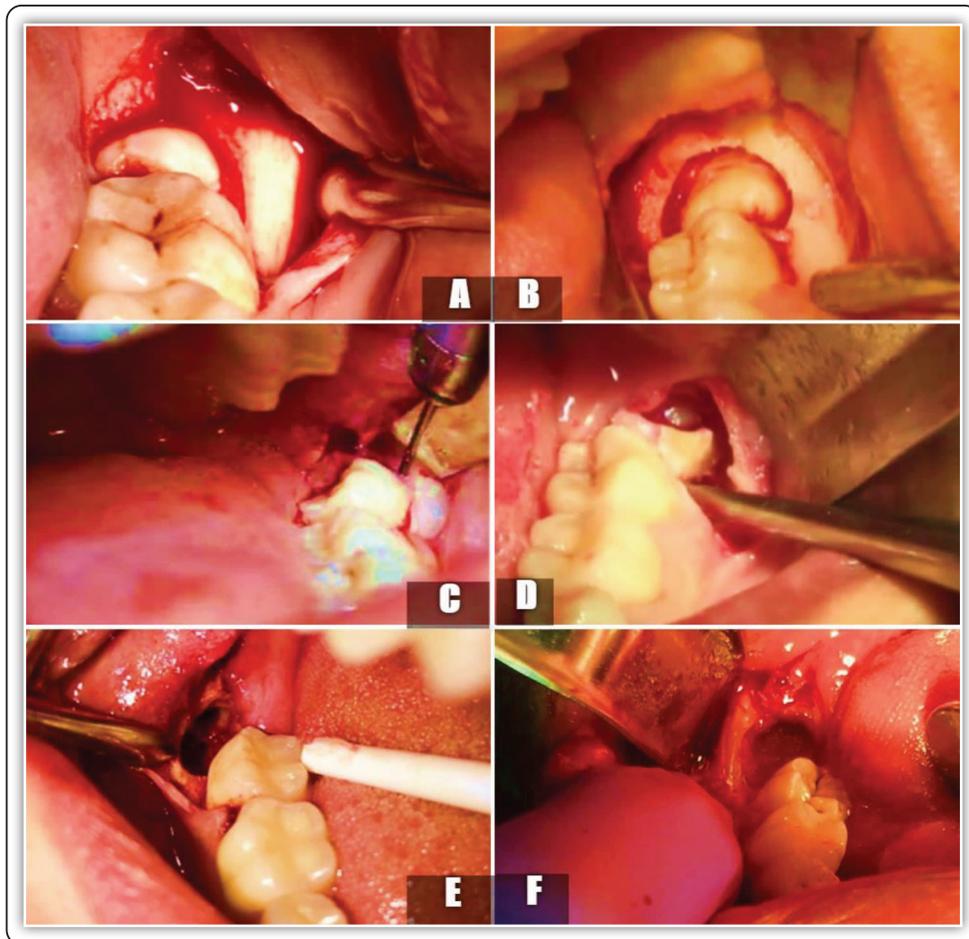


FIG (2) (A) Incision and mucoperiosteal flap reflection , (B) The bone covering the tooth was removed, (C) Tooth sectioning using a high-speed hand piece with fissure bur , (D) Final delivery of the root was performed with straight elevator ,(E) Debrided socket , (F) HA gel 0.8% applied to the extraction socket before suturing.

### Post-operative care:

Patients were dismissed with written and verbally informed post-operative instructions. They were instructed to bite down on the gauze pack that has been placed over the surgical area, making sure it remains in place almost for an hour and then discarded. Patients were asked to apply ice pack on the side of the face where the surgery was performed to help reduce swelling. Rinsing was avoided for 24 hours after extraction. Smoking was not allowed for 24 hours following surgery. They were allowed to take soft diet for the first two days. Ibuprofen 600mg was prescribed to be taken

whenever needed. Sutures were removed on the 7<sup>th</sup> postoperative day.

### Post-operative assessment:

For all patients, the follow-up was done after 24 hours, 72 h, one week and two weeks. During their appointments at the clinic, the extraction site was thoroughly inspected for bleeding, signs of infection, food impaction, dehiscence, pain, and / or dry socket formation. A positive diagnosis of dry socket was made on the basis of clinical and subjective findings. The clinical findings included evidence of one or more of the following; socket may be filled with food debris with or without

halitosis, absence of clot, necrosis of blood clot, and exposed bone<sup>(29)</sup>. Pain was assessed using a numeric pain rating scale modified visual analog scale<sup>(30)</sup>. On the VAS, the leftmost end represented the absence of pain (score 0) and the rightmost end indicated the most severe pain (score 10). The maximal mouth opening: was measured in millimeters using Vernier scale as done before surgical intervention<sup>(27)</sup>. Cheek dimension: was measured in millimeters with a flexible measuring tape as done before surgical intervention<sup>(28)</sup>.

**Statistical analysis**

Microstat7 for windows statistical package (Microstat Co) was used for statistical analysis in this study. Dry socket data was analyzed using descriptive statistical analysis (Fisher’s exact test). One-Way ANOVA was used to compare between time intervals in each group followed by calculating Least Significant Difference (LSD) for paired comparisons between each interval in the same group. Independent Student “t” test was used to compare both groups in each interval. The value of the K-S (Kolmogorov-Smirnov) test statistic (D) is 0.20127; the *p*-value is 0.7422. Difference was considered statistically significant when  $p \leq 0.05$ .

**RESULTS**

Twenty impacted lower third molar tooth extractions were performed for 10 patients (6 male and 4 female). All patients have completed the whole period of the study. Postoperative healing was uneventful. Parasthesia, bleeding, or altered nerve sensation were not observed in any patient postoperatively. Neither infection nor dehiscence was recorded

Dry socket occurred in only one patient (10%) in group 2. No dry socket (0%) was recorded in patients treated with the Hyaluronic acid (group1). There was no statistically significant difference between both groups (table 1).

**TABLE (1)** Comparison between group 1 and group2 regarding incidence of dry socket

	Dry socket	No dry socket	Total	Test	P
Group 1	0	10	10		
Group 2	1	9	10	FE	1.0000
Total	1	19	20		

Data expressed as frequency (Number-percent)

P: Probability \*:significance <0.05

Test used: fisher exact for data expressed as frequency

Descriptive statistics including mean values and standard deviations SD of the pain score recorded for both groups as function of evaluation time are summarized in table (2). In both groups there was statistically significant decrease of pain score after 24 hours until the end of the follow up period. The pain score of patients in group 1 was significantly lower than patients in group 2 in all follow up intervals.

**TABLE (2)** Comparison of mean pain scores within groups and between groups along observation periods

Pain	Group 1		Group 2		“t”	Probability
	Mean	St Dev	Mean	St Dev		
24 Hours	6.80	0.42	8.30	0.48	7.398	0.0000
72 Hours	3.60	0.70	6.10	1.29	5.399	0.0000
1 Week	1.50	0.85	3.90	1.10	5.458	0.0000
2 Weeks	0.30	0.48	1.50	0.53	5.308	0.0000
F ratio	199.973		100.855			
Probability	0.0000		0.0000			
LSD	0.576		0.831			

Descriptive statistics including mean values and standard deviations SD of the maximal mouth opening recorded for all groups as function of evaluation time are summarized in tables (3). In both groups there was statistically significant decrease of interincisal distance after 24 hours followed by significant increase until the end of the follow up period. The interincisal distance in group 1 was

significantly higher than group 2 in all intervals. At the end of the follow up period after 2 weeks, the interincisal distance in group 1 returned to normal while in group 2 it was significantly lower than preoperative record.

Descriptive statistics including mean values and standard deviations SD of the cheek dimension recorded for all groups as function of evaluation time are summarized in tables (4). In both groups

there was statistically significant increase of facial swelling after 24 and 72 hours followed by significant decrease until the end of the follow up period. The facial swelling of patients in group 1 was significantly lower than patients in group 2 in all follow up intervals. At the end of the follow up period after 2 weeks, the facial swelling in group 1 returned to normal while in group 2 it was significantly higher than preoperative record.

**TABLE (3)** Comparison of mean interincisal distance within groups and between groups along observation periods

Interincisal Distance	Group 1		Group 2		“t”	Probability
	Mean	St Dev	Mean	St Dev		
Preoperative	42.85	1.42	42.85	1.42		
24 Hours	29.25	3.70	25.90	2.13	2.481	0.0116
72 Hours	36.31	1.41	31.70	3.27	4.093	0.0003
1 Week	40.71	1.26	36.70	3.09	3.793	0.0007
2 Weeks	42.73	1.38	40.15	3.11	2.399	0.0137
F ratio	77.804		62.975			
Probability	0.0000		0.0000			
LSD	1.861		2.441			

**TABLE (4)** Comparison of mean cheek dimension within groups and between groups along observation periods

Cheek Dimension	Group 1		Group 2		“t”	Probability
	Mean	St Dev	Mean	St Dev		
Preoperative	282.50	10.43	282.50	10.43		
24 Hours	293.10	11.96	307.00	17.67	2.060	0.027
72 Hours	305.40	18.26	327.20	23.25	2.332	0.016
1 Week	289.80	12.21	304.00	13.29	2.488	0.011
2 Weeks	283.30	10.64	289.00	10.75	1.192	0.124
F ratio	5.082		12.096			
Probability	0.0020		0.0000			
LSD	11.767		14.312			

## DISCUSSION

Surgical extraction of lower third molar has been described as the most common procedure in oral surgery. The postoperative phase is commonly identified unpleasant by patients. During the healing period, pain experience, swelling, trismus and dry socket are the most common symptoms of patients<sup>(31,32)</sup>. This study was designed to evaluate the effect of hyaluronic acid gel as a topical therapy which guarantee a better delivery of high concentrations of pharmacologic agent on the incidence of dry socket and local signs of inflammation, including trismus, facial swelling, and pain after impacted lower third molar surgery<sup>(33)</sup>.

The incidence of dry socket following routine extraction of erupted teeth has been reported as 1% to 3%. The reported incidence following the extraction of impacted mandibular third molars ranges from 1% to 65%. This great variability is most likely due to differences in diagnostic criteria and uncontrolled variation within the population evaluated. In well controlled prospective studies with carefully defined diagnostic criteria, the incidence of dry socket falls to 20 %<sup>(34)</sup>. In the present study, the incidence of dry socket was 10 % in group 2 and 0 % in group 1. The 0% indicated that HA is able to reduce the incidence of dry socket but this was statistically nonsignificant. This is in accordance with Koray et al<sup>(23)</sup> who found that HA treated patients showed no case of dry socket.

The severity of pain, degree of trismus, and amount of swelling are the primary indicators of patients' discomfort following surgical extraction of an impacted mandibular third molar tooth. These complications are due to the difficulty encountered with surgical extraction of impacted mandibular third molar<sup>(35,36)</sup>. Pain associated with dry socket is highly intense and continuous, which can be assessed by VAS scoring system<sup>(30)</sup>. In the present study, significant decrease of pain score occurred after 24 hours and continuously decreased until the end of the follow up period in

both groups. The pain score of patients in group 1 was significantly lower than patients in group 2 in all follow up intervals. This may be attributed to the anti-inflammatory contribution of HA. This is in accordance with Gocemen et al<sup>(37)</sup> who found that HA applied after lower third molar surgery could decrease postoperative pain by reducing leucocyte infiltration and increasing angiogenesis. Results of pain is also in agreement with Riccardo et al<sup>(38)</sup> who reported that pain perception was always lower in the HA containing group during the first 7 days after surgery. A result of current study is in disagreement with that of Koray et al<sup>(23)</sup>. They've evaluated the efficacy of HA spray after lower third molar surgery and detected no evidence of a reduction in pain levels.

Trismus constitutes a distressing immediate postoperative complication following surgical removal of impacted mandibular third molar tooth, which is caused by the swelling associated with surgical trauma. Patients of both groups exhibited postoperative trismus as evidenced by reduction of the interincisal distance. The postoperative interincisal distance was decreased significantly in both groups after 24 hours of surgery and followed by progressive increase to almost the preoperative values at the end of the follow up period. The HA treated sockets group showed higher interincisal distance values than the untreated sockets group at all follow up intervals. By the end of follow up period, the interincisal distance in HA treated sockets group returned to normal while in the other group it was significantly lower than preoperative value. This is agreed to the results of Koray et al<sup>(23)</sup>. They stated that hyaluronic acid appears to offer a beneficial effect in the management of trismus during the immediate postoperative period following impacted third molar surgery.

Postoperative swelling is a common event after surgical removal of impacted third molar and may affect, only for few days, the social life of the patient. It occurs due to inflammatory processes triggered

by manipulation of the soft tissues or bone removal. In both groups there was statistically significant increase of facial swelling after 24 and 72 hours followed by significant decrease until the end of the follow up period. The facial swelling of patients in group 1 was significantly lower than patients in group 2 in all follow up intervals. These findings suggest that HA is effective in controlling the postsurgical swelling originating from the inflammatory process initiated by the surgical trauma. This result may be attributed to the prevention of excessive inflammation and subsequent exacerbations by the HA. This is in agreement with the results of Koray et al<sup>(23)</sup>. They concluded that hyaluronic acid appears to offer a beneficial effect in the management of swelling during the immediate postoperative period following impacted third molar surgery.

## CONCLUSION

Based on the results of the current study, HA 0.8% gel application after extraction of impacted mandibular third molars has no effect on the incidence of dry socket but it has a positive effect on postoperative pain, trismus and swelling.

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