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EFFICACY OF HYALURONIC ACID INJECTION LOCALLY ON POSTOPERATIVE COMPLICATIONS AFTER SURGICAL REMOVAL OF IMPACTED MANDIBULAR THIRD MOLARS

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KEYWORDS

Impacted Third Molars ;
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ABSTRACT

Introduction: Odontectomy is a popular dental surgery treatment. However, nerve injury, bone fractures, delayed healing, inflammation, soreness, edema, and trismus might result. These conditions lower patient quality of life. Many research reduced post impacted tooth surgical problems. Hyaluronan (HA) is a biomaterial that accelerates wound healing. **Aim:** to evaluate efficacy of Hyaluronic acid injection locally on control of swelling, pain and trismus in surgical removal of impacted mandibular third molars. **Patients and methods:** This study was a randomized clinical control trial and was conducted on 20 adult healthy patients who required surgical extraction of impacted lower third molar with bilateral, symmetrical lower impacted third molars that need surgical extraction. Each patient has two sides (right and left side) one of them was treated by experimental materials (Group B) and the other side was left without treatment as a control group. **Results:** The overall difference in VAS was significant according to groups, Time points, and interaction between groups and time). Truisms mouth opening (TMO) in the control group showed an average (±SD) of 40.87±7.97, 29.11±9.88, 34.50±8.55, 40.97±8.18; respectively. However, The TMO in the treated group showed an average (±SD) of 40.87±7.97, 34.50±8.07, 37.80±6.46, and 41.38±7.81; respectively. The linear relationship in TMO with time showed a direct (positive) relationship as revealed by simple linear regression. The mean swelling parameters in the control group showed an average (±SD) of 10.51±0.85, 12.12±0.89, 11.34±0.54, and 10.76±0.58; respectively. However, the mean swelling parameters in the treated group and showed an average (±SD) of 10.51±0.85, 11.24±0.78, 10.64±0.85, and 10.17±0.45; respectively. Regression trendline showing the linear correlation between time and mean swelling parameters. **Conclusion:** HA injection after extraction of impacted mandibular third molars has a positive effect on postoperative pain, trismus and swelling.

INTRODUCTION

The surgical extraction of wisdom teeth is one of the most common procedures in oral surgery. However, numerous complications can develop, such as nerve injury, bone fractures, delayed healing, inflammation, pain, swelling, and trismus [(1)]. All these conditions have negative effects on quality of life for patients. Many studies were based on reducing the complications after impacted tooth surgery [(2)].

For instance, local or systemic steroid, non-steroidal anti-inflammatory drugs consumption, and antibiotic prophylaxis are

common medication methods. Pharmacological therapy, especially corticosteroids, seems an effective method to increase postoperative oral quality of life for surgically extracted impacted third molars[3].

Hyaluronan or hyaluronic acid (HA) is a biomaterial that has proven valuable as an excellent alternative approach to accelerate wound healing [4]. HA is found in all living organisms in locations that include synovial fluid, embryonic mesenchyme, vitreous humor, skin and other many organ and tissues of the body [5]. HA interacts with growth factors and is involved in the regulation of osmotic pressure and tissue lubrication. It also interacts with many receptors that mediate cell detachment in mitosis, cell migration, tumor metastasis, and inflammation [6].

In periodontology, the hydrating property of HA is frequently used in aesthetic treatments [7]. Hyaluronic acid has been employed in the treatment of gingivitis, recessions, and periodontal pockets, and as grafts and implants generally [8]. Therefore, the purpose of this clinical trial was to investigate whether there is any beneficial value of local administration of Hyaluronic acid on the postoperative pain, trismus, and swelling.

PATIENTS AND METHODS

The a randomized clinical control trial was conducted on 20 patients in department of Oral and Maxillofacial Surgery, Faculty of Dentistry, Suez Canal University, after being waived from the approval of the research ethics committee (Approval no. 280/2020). Patients required surgical extraction of impacted lower third molar twenty patients with bilateral, symmetrical lower impacted third molars that need surgical extraction.

Patients were selected and divided randomly into two equal groups; 20 teeth for each group. The same patient is considered as control and study group at the same time as follow:

- **Group A:** Underwent surgical extraction of impacted lower third molar without injection of hyaluronic acid locally. (Control group).
- **Group B:** Underwent surgical extraction of impacted lower third molar with Injection of hyaluronic acid locally. (Study group)

Inclusion criteria:

Individuals have no systemic disease, age >18, with bilaterally impacted lower third molars. Both genders were included.

Exclusion criteria

History of allergies to antibiotics, analgesics, or local anesthetics. Female patient either pregnant or using contraceptives. Patient using corticosteroids and analgesics for 15 days before surgery which can affect the postsurgical healing phase and amount of swelling on the face. Patient with acute infection such as pericoronitis and/or pain on the tooth at site of extraction.

All patients were informed about all details of the surgical procedures, the Expected complications, the whole study schedules, and the taken photos to be shared in that scientific research. Then they signed an informed consent Appendix (D).

I. Preoperative preparation:

Medical and dental examination sheets were performed for all Patients of the study. The sheet included full personal data, chief Complain, history of chief complains, medical history, and dental History Digital panoramic radiograph was done before surgical extraction of the lower impacted

third molar to evaluate depth and angulation of Impaction. The anticipated degree of difficulty of the impacted molars that evaluated by the radiographic findings were at the same degree for all patients.

II-Preoperative measurements:

1. **Facial contour:** Preoperative assessment of facial contour was measured by the tape measure method described by **Gabka and Matsumara** [8]. 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 average of the sum of three distances was considered as the baseline measurement.
2. **Mouth opening:** The amount of mouth opening was recorded by measuring the maximum interincisal distance between the maxillary and mandibular central incisors in (mm) by using a digital caliper before surgery.
3. **Pain record:** The level of pain was recorded by using visual analog scale (VAS) in which the patients were asked to mark the degree of perceived pain on a 10-cm Horizontal line, with 0 (left side) indicating no pain and 10 (right side) Indicating the most terrible pain [9].

Surgical protocol:

A) Anesthetic technique:

All patients were anesthetized by using 2% Mepivacaine hydrochloride with levonordefrin 1:20,000 presented in carpule 1.8 ml. The amount was two carpules for every case. All the patients were anesthetized by inferior alveolar, lingual & long buccal nerve block Techniques.

B) Operative Procedure:

All of the patients included in the study were operated on by the same oral and maxillofacial surgeon and assistant in order to minimize differences due to operator variability. Two surgical operations were done for each patient:

Group A (control group): surgical removal of impacted third molar was done without injection of hyaluronic acid. All patients were undergone the procedure under inferior alveolar, lingual and buccal nerve blocks.

An incision was made a full mucoperiosteal triangular flaps were raised starting from the anterior ramus and extending with a sulcular incision and a vertical releasing incision from the mesial aspect of the second molar. The osteotomy was performed around the impacted tooth under constant irrigation with saline solution. The irrigation was done during the surgical procedures by using 0.9% saline to hydrate the dehydrated cell. Curettage of the socket was done by using bone curette for removal of granulation tissue or debris in the socket after the tooth delivery. The flap was sutured using black silk suture (3-0 Silk). The sutures were removed at the seventh day follow up. The patient was informed to come for follow-ups at 2, 5, 7 days after operation.

Group B (study group): the hyaluronic acid was injected before and immediately after surgery. All patients were undergone the procedure under inferior alveolar, lingual and buccal nerve blocks then the injection of hyaluronic acid was done 10 minutes before surgery in study group only. An incision was made a full mucoperiosteal triangular flaps were raised starting from the anterior ramus and extending with a sulcular incision and a vertical releasing incision from the mesial aspect of the second molar. Once the tooth extracted, the alveolus was irrigated with sterile saline solution at room temperature to eliminate debris and the bone edges

were smoothened. The flap was repositioned and the closure was done with 3–0 black silk. After that another amount of hyaluronic acid 1 ml was injected submucosally at site of surgery. The patient was informed to come for follow-ups at 2, 5, 7 days after operation.

Drug prescription protocol:

All patients in both groups were subjected to the following drugs after the surgery. A- Amoxicillin 500mg (flumox*) available as 500mg Capsules every 8 h for 7 days. B-paracetamol 500 mg every 12 h for 7 days.

Postoperative instructions:

All patients were informed of the expected occurance of facial swelling, pain, and trismus. Sterile gauze pack was kept on the wound and the patients were advised to bite for one hour. Avoid rinsing or spitting for 24 hours after surgery. Avoid smoking for 24 hours after the surgery. Avoid of hot drinks, hot foods, hard foods, and eating on the operating side.

Post-operative evaluation:

The degree of facial swelling was determined by the tape measure method described by **Gabka and Matsumara** [8].

Trismus was evaluated by measuring the distance between the edges of the Upper and lower right central incisors at maximum opening of the jaws using Vernier caliper, on 2nd, 5th and 7th day after surgery .

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". The severity of the pain was evaluated on the operation day and on postoperative days 2nd, 5th and 7th.

Statistical analysis

The data were collected, checked, revised, and organized in tables and figures using Microsoft Excel 2016. Data were subjected to outliers' detections and normality statistical tests to detect whether the data were parametric or nonparametric. Data were analyzed for both graphical and numerical descriptive statistics; parametric data were presented as mean and standard deviation, and nonparametric data as Frequency (n, %). Inferential statistics for evaluating and comparing treatments and tie of investigations were performed by repeated measures analysis of variance (ANOVA) or corresponding nonparametric analyses at significance levels of 0.05. Differences between control and treated groups were performed using independent samples test for parametric and Mann-Whitney for nonparametric data at 0.05 level.

RESULTS

The current study showed the distribution of study patients according to gender males was presented by 9 (45%) and females 11 (55 %), the difference between genders was significant as revealed by chi-square test **(Table 1)**.

The VAS in the control group showed an average (±SD) of 10.00±0.00, 7.67±0.52, 5.00±0.63, and 1.33±0.52; respectively. The difference between time points pre-operative, 2, 5 and 7 days after treatments was significant (p<0.001) as revealed by repeated measure ANOVA. However, The VAS in the treated group and showed an average (±SD) of 10.00+0.00, 5.67±0.52, 3.17±0.41, 0.67±0.52; respectively. The difference between time points pre-operative, 2, 5 and 7 days after treatments was significant (P<0.001). The difference between the control and treated group at preoperative was non significant. However, after 2 and 5 days was highly

significant (P<0.001) as revealed by independent t-test. The overall difference in VAS was significant according to groups (P<0.001), Time points (P<0.001), and interaction between groups and time (P<0.001). The linear relationship in VAS with time showed an inverse (negative) relationship as revealed by simple linear regression **(Table 2, Figure 1)**.

The TMO in the control group showed an average (±SD) of 40.87±7.97, 29.11±9.88, 34.50±8.55, 40.97±8.18; respectively. The difference in between TMO time points pre-operative, 2, 5 and 7 days was significant (P>0.05) as revealed by repeated measure ANOVA. However, The TMO in the treated group showed an average (±SD) of 40.87±7.97, 34.50±8.07, 37.80±6.46, and 41.38±7.81; respectively. The difference in TMO between time points pre-operative, 2, 5 and 7 days after treatments was non-significant (P>0.05) as revealed by repeated measure ANOVA. The difference between the control and treated group at preoperative, 2, 5, and 7 days postoperative was non significant (P>0.05) as revealed by independent t-test. The difference in TMO between time points (P=0.023), the overall difference in TMO was non-significant according to groups (P>0.05), and interaction between groups and time (P>0.05). The linear relationship in TMO with time showed a direct (positive) relationship as revealed by simple linear regression **(Table 3, Figure 2,3)**.

Table 1. *Sociodemographic parameters of study patients including gender*

		Frequency		Chi-square test	
		n	**%**	**Chi-**	**sign**
Gender	**Male**	9	45.0	0.2	0.655 ns
	Female	11	55.0		
	Total	20	1.0		

Table 2. *Descriptive statistics of VAS in terms of mean, and standard deviation.*

Time	**VAS Pain**				***p*-value**
	Control		**Treated**		
	Mean	**SD**	**Mean**	**SD**	
0	10.0 a	0.00	10.0 a	0.00	>0.999 ns
2	7.7 b	0.52	5.7 c	0.52	<0.001***
5	5.0 d	0.63	3.2 e	0.41	<0.001***
7	1.3 f	0.52	0.7 g	0.52	0.049*
ANOVA RM	<0.001***		<0.001***		
Repeated measures ANOVA					
Group	<0.001***				
Time	<0.001***				
Group x Time	<0.001***				

, **, * significant at p<0.05, <0.01, <0.001; NS, non-significant at p>0.05*

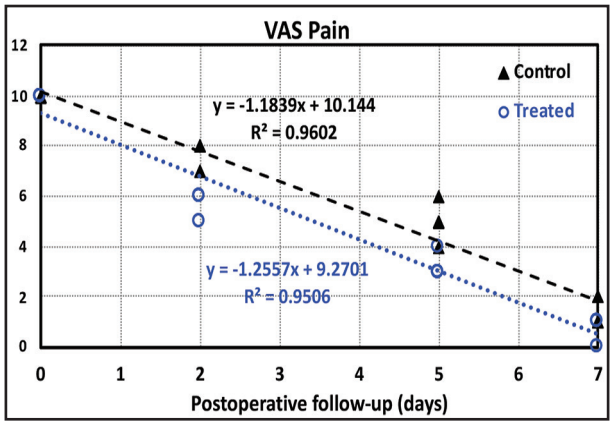

Fig. (1) Regression trendline showing the linear correlation between time and VAS pain.

Table 3. *Descriptive statistics of TMO in terms of mean, and standard deviation.*

Time	Trismus (mouth opening)				*p*-value
	Control		Treated		
	Mean	SD	Mean	SD	
0	40.9 a	7.97	40.9 a	7.97	>0.999 ns
2	29.1 b	9.88	34.5 ab	8.07	0.325 ns
5	34.5 ab	8.55	37.8 ab	6.46	0.468 ns
7	41.0 a	8.18	41.4 a	7.81	0.930 ns
ANOVA RM	0.081 ns		0.393 ns		
	Repeated measures ANOVA				
Group	0.340 ns				
Time	0.023 *				
Group x Time	0.832 ns				

, **, * significant at p<0.05, <0.01, <0.001; NS, non-*

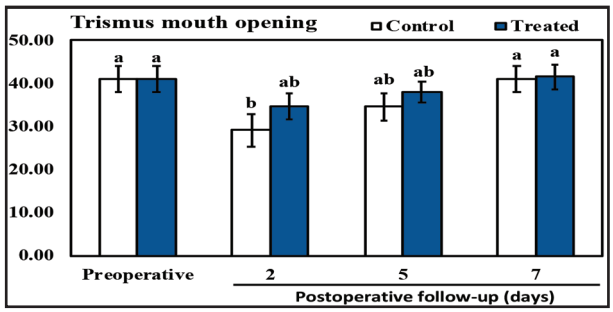

Fig. (2) Bar chart presenting the TMO of in terms of mean and error bars represent the standard error. Bars with different letters are significantly different according to Dun's Bonferroni posthoc test.

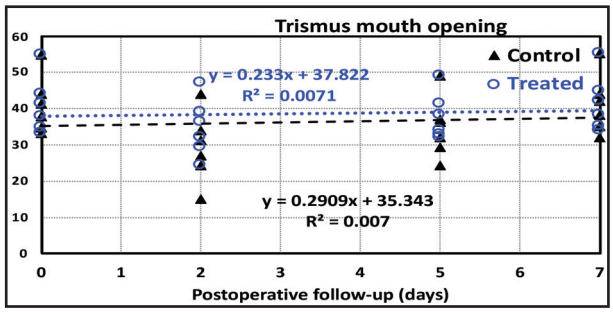

Fig. (3) Regression trendline showing the linear correlation between time and TMO.

The mean swelling parameters in the control group showed an average (±SD) of 10.51±0.85, 12.12±0.89, 11.34±0.54, and 10.76±0.58; respectively. The difference between time points pre-operative, 2, 5 and 7 days after treatments was significant (P=0.005). However, the mean swelling parameters in the treated group and showed an average (±SD) of 10.51±0.85, 11.24±0.78, 10.64±0.85, and 10.17±0.45; respectively. The difference between time points pre-operative, 2, 5 and 7 days after treatments was non significant (P>0.05) as revealed by repeated measure ANOVA. The difference between the control and treated group at 0 and 5 days was non-significant (*P*>0.05), however, it was significant at 2 and 7 days as revealed by independent t-test. The treated group showed significantly lower mean swelling at 2 and 7 days. Regression trendline showing the linear correlation between time and mean swelling parameters **(Table 4, Figure 4)**.

Correlation matrix presenting the interrelationships between variables. Upper right triangle present the two tailed significance test, lower left triangle present the correlation coefficient +, positive correlation; -ve, negative correlation, Weak (r= 0.1-0.3), moderate (r=0.4-0.59), strong correlation (r>0.60) **(Table 5)**.

Table 4. *Descriptive statistics of mean swelling parameters in terms of mean, and standard deviation.*

Time	Mean swelling				*p*-value
	Control		Treated		
	Mean	SD	Mean	SD	
0	10.5 bc	0.85	10.5 bc	0.85	>0.999 ns
2	12.1 a	0.89	11.2 ab	0.78	0.049*
5	11.3 ab	0.54	10.6 bc	0.85	0.121 ns
7	10.8 bc	0.58	10.2 c	0.45	0.039*
ANOVA RM	0.005**		0.525 ns		
	Repeated measures ANOVA				
Group	0.015*				
Time	<0.001***				
Group x Time	0.508 ns				

, **, * significant at p<0.05, <0.01, <0.001; NS, non-significant at p>0.05*

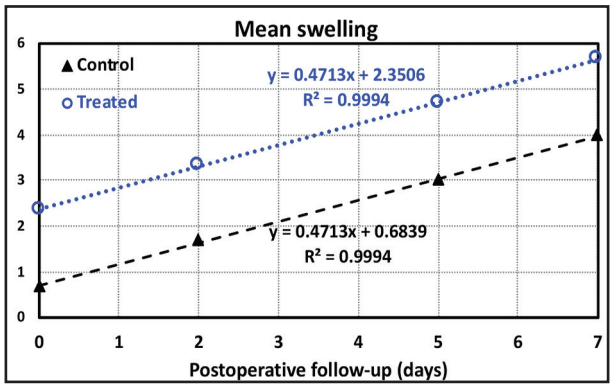

Fig. (4) Regression trendline showing the linear correlation between time and mean swelling parameters.

Table 5. *Correlation matrix presenting the interrelationships between variables.*

	Group	Time	All	VAS	TMO	TMO_Sw	Tpg	CA	Mean
Group		1.000	***<0.001*** **	0.262	0.366	0.366	**0.024 ***	0.259	0.568
Time	0.00		***<0.001*** **	***<0.001*** **	0.576	0.177	**0.043***	0.735	0.263
All	0.87	0.49		***<0.001*** **	0.308	0.139	**0.003****	0.281	0.280
VAS Pain	-0.17	-0.96	-0.617		0.509	0.098	**0.036***	0.578	0.164
Mouth opening	0.13	0.08	0.15	-0.10		0.581	***0.008****	***<0.001*** **	0.248
TMO_Swelling	0.13	0.20	0.22	-0.24	-0.08		0.778	0.444	***<0.001*** **
Tpg_Swelling	-0.33	-0.29	-0.42	0.30	-0.38	-0.04		0.389	0.634
CA_Swelling	-0.17	-0.05	-0.16	0.08	-0.49	-0.11	0.13		0.988
Mean_swelling	0.08	0.16	0.16	-0.20	-0.17	0.99	0.07	0.002	

, **, *, significant at p<0.05, <0.01, <0.001; ns, nonsignificant at p>0.05*

DISCUSSION

Odontectomy of mandibular third molar tooth is a popular oral surgical technique. However, nerve injury, bone fractures, delayed healing, inflammation, soreness, edema, and trismus are common complications that in turns lower the patient's quality of life [10,11]. Hyaluronan (HA) is a biomaterial that accelerates wound healing. All creatures have hyaluronic acid in synovial fluid, embryonic mesenchyme, vitreous humor, skin, and other organs and tissues [7].

Our results of current study was in accordance with **Shuborna *et al.*** [12] who aimed to investigate the effectiveness of intra-socket HA solution to reduce these uncomfortable post-operative pain. In regard to the mean VAS scores, there was a significant difference between the HA and control group for pain on the first, second, and third days after LTMI, according to the 100 mm VAS with P value is 0.001, 0.002, 0.002 on Day 1, 2 and 3 respectively. Total analgesic consumption also noted for the first 7 days post LTMI. They prescribed standing doses of paracetamol 500 mg for reducing pain and tramadol 50 mg prescribed only for rescue purpose, in this study they found only 2 patients that took tramadol 50 mg on the control side of the split-mouth study, they calculated overall analgesic consumption only for Paracetamol but not for tramadol. The results show that the HA group took significantly lesser analgesics compared to the control group with P value is 0.001.

Zaki *et al.* [13] aimed to assess the efficacy of hyaluronic acid gel on postoperative, dry socket, pain, trismus and edema after extraction of impacted lower third molars. 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 HA-group was significantly lower than patients in control group at all follow up intervals.

Al-Saadi *et al.* [14] compared the outcomes of 1% hyaluronic acid oral gel and advanced platelet-rich fibrin on the expected postoperative sequels (pain, swelling, and trismus) following the surgical extraction of the impacted mandibular third molar. The statistical analyses showed a significant difference among all groups on all postoperative days except between the HA and A-PRF groups on the first and seventh postoperative days. The decrease in pain during the postoperative days was more in the A-PRF group, followed by the HA group, and the slightest decrease was in the control group.

Our results agreed with several previous studies as by **Starzyńska *et al.*** [15] and **Muñoz *et al.*** [16] demonstrating the effectiveness of HA gel or APRF in reducing post-operative pain.

Results of pain was also in agreement with **Guazzo *et al.*** [17] who reported that pain perception was always lower in the HA containing group during the first 7 days after surgery. On the other side, results of current study were in disagreement with that of **Koray *et al.*** [18] who evaluated the efficacy of HA spray after odontectomy of mandibular 3rd. molar teeth and detected no evidence of a reduction in pain levels. However, it may be due to the improper time of application when using HA spray.

In 2014 the previous study in 2016 the article of **Merchant *et al.*** [19] showed that HA spray can significantly reduce swelling and trismus compared to control group, but no role in controlling pain. This could be because the 'spray' form could only act on the superficial surface of the mucosa which does not offer enough contact with an extraction socket.

In 2016 another study of **Yilmaz *et al.*** [20] regarding HA on 3rd molar extraction sites showed beneficial effect in terms of reducing pain but not on swelling and trismus. In their study all post-op parameters showed significantly less swelling, pain

and trismus in the experiment group compared to the control group. This could be attributed to the higher concentration of HA in their study (0.7 ml) as opposed to the (0.5 ml).

Our results suggest that HA did not improve pain on the first postoperative day when compared with patients who received placebo or no treatment. This result is similar to that presented in the literature in which the effectiveness of HA in pain control after tooth extractions in general was evaluated. The results can be difficult to explain because pain is a subjective sensation and can be influenced by the threshold of each individual and previous experience. On the third and seventh days, it was observed that HA provided a lower average of pain when compared with the control group.

Concerning trismus after odontectomy of mandibular 3rd.molar in the current study, mouth opening in the control group showed a significant difference in MO between pre-operative, two, five and seven days after surgery was significant (P>0.05). However, The MO in the treated group and showed an average (±SD) of 40.87±7.97, 34.50±8.07, 37.80±6.46, and 41.38±7.81; respectively. The difference in MO between time points pre-operative, 2, 5 and 7 days after treatments was non significant (P>0.05). The difference between the control and treated group at preoperative, 2, 5, and 7 days postoperative was non significant (P>0.05).

In a study performed by **Zaki *et al.*** [13], 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 pre-operative record.

In comparison to our results, **Shuborna *et al.*** [12] revealed that Maximal inter-incisal distance levels were found almost similar preoperatively for both two groups. Immediate pre-operative measurement of trismus value is (37.55 ± 4.98 mm) and (37.77 ± 5.67 mm) for study and control group respectively with P-value 0.798 which is not statistically significant. Although both groups developed trismus within the 2nd post-operative day, their results found statistically significant higher mouth opening in the study group (26.07 ± 4.42) compared to the control group (21.62 ± 5.50) with P-value 0.001. However, the mouth opening increases within the end of the week for both groups, but here also significant difference was found between HA and control group. On the seventh postoperative day, the mouth opening in HA Group was (34.24 ± 5.14 mm) and control group was (29.10 ± 5.92 mm) with P-value 0.001 which showed statistical significance.

Zaki *et al.* [13] reported that 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.*** [18] who made their study on 34 patients 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

Al-Saadi *et al.* [14] showed that regarding the trismus, Multiple pairwise comparisons (Tukey's HSD method) showed highly significant differences

among all groups on all postoperative days except between the HA and A-PRF groups.

The mean swelling parameters in the control group showed an average (±SD) of 10.51±0.85, 12.12±0.89, 11.34±0.54, and 10.76±0.58; respectively. The difference between time points pre-operative, 2, 5 and 7 days after treatments was significant. However, the mean swelling parameters in the treated group and showed an average (±SD) of 10.51±0.85, 11.24±0.78, 10.64±0.85, and 10.17±0.45; respectively.

In a study performed by **Zaki *et al.*** [13], 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 their results. 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 1returned to normal while in group 2 it was significantly higher than preoperative record.

Zaki *et al.* [13] 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.*** [18] concluded that hyaluronic acid appears to offer a beneficial effect in the management of swelling during the immediate post-operative period following impacted third molar surgery.

Al-Saadi *et al.* [14] concluded that regarding the swelling, statistical analyses showed significant differences among groups on all postoperative days except between HA and A-PRF groups. The grade of swelling was higher in the control group on all postoperative days than in the HA and A-PRF groups.

Afat *et al.* [21] evaluated the effectiveness of leukocyte platelet rich fibrin (L-PRF) versus (L-PRF) combined with a HA sponge on sequalae after LTMI. The results showed that L-PRF in combination with HA, has the potential to reduce swelling after LTMI.

In 2018, **Bayoum *et al.*** [22] documented that HA provides a positive impact on postoperative swelling and trismus after LTMI. For all these beneficial reason the use of HA has been recognized in various sites and conditions in the oral cavity.

Incontrast to our result **Yilmaz *et al.*** [20] who made their study on 25 patients founded that there was no statistically significant difference between facial swelling in HA and control groups.

CONCLUSION

Based on the results of the current study, HA injection after extraction of impacted mandibular third molars has a positive effect on postoperative pain, trismus and swelling.

Further evaluation of effect of hyaluronic acid injection injection on postoperative pain, trismus and swelling after extraction of impacted mandibular third molars.

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