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## **A comparative study of the effect of chlorhexidine gel and hyaluronic acid gel on post-operative complications following mandibular third molars surgery (Pain, Edema)**

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### **Abstract**

**Purpose:** The aim of this study was to evaluate the effect of Hyaluronic acid and Chlorhexidine 0.2% on pain and edema after impacted lower third molars surgery.

**Materials and Methods:** This clinical study was carried at oral and maxillofacial surgery department at Hama University. This study included random sample of 40 cases of impacted lower third molars. The ages of patients were between 18-25 years. The sample was divided into two groups:

First group: 20 impacted lower third molars was surgically extracted. Hyaluronic acid 0.2 % was applied in the alveolar cavity with surgical suture.

Second group: 20 impacted lower third molars was surgically extracted. Chlorhexidine 0.2% was applied in the alveolar cavity with surgical suture.

**Results:** There was significant difference between two groups in edema ( $p < 0.05$ ) on the 2<sup>nd</sup> and 3<sup>rd</sup> days for the first group (Hyaluronic acid 0.2 %) while there was no significant difference between two groups in edema on the 7<sup>th</sup> day after surgery.

There was significant difference between two groups in pain ( $p < 0.05$ ) on the 1<sup>st</sup> and 2<sup>nd</sup> days for the first group (Hyaluronic acid 0.2 %), while there was no significant difference between two groups in pain on the 3<sup>rd</sup> day after surgery.

**Conclusion:** The study showed that both of Hyaluronic acid and Chlorhexidine 0.2% have a positive effect on controlling pain and edema after surgical extraction, with preference for Hyaluronic over Chlorhexidine 0.2%.

**Keywords:** Hyaluronic acid, Chlorhexidine, Impacted molars

### **Introduction**

An unerupted tooth is one that has not emerged through the oral mucosa into the oral cavity at a developmental stage when this would usually have been expected. In most cases, such failure of eruption is the result of impaction where ectopia or an identifiable barrier (e.g. lack of space, a supernumerary tooth, odontome or cyst) prevents the normal eruption of a tooth [1].

### **Indications for Removal of the Impacted Mandibular Third Molars**

1. Pain.
2. Pericoronitis.
3. Periodontal diseases.
4. Adjacent teeth Caries.
5. Cysts.
4. Resorption of root of adjacent teeth.
5. Jaw fracture.
6. Orthodontic or Orthognathic Surgery treatment [2].

### **Classification**

**(According to Archer 1975; Kruger 1984)**

1. Mesioangular.
2. Distoangular.
3. Vertical.
4. Horizontal.
5. Buccoangular.
6. Linguoangular.
7. Inverted [3]

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## ✓ **Complications after Surgical extraction**

### **1- Pain**

The most common post-surgical morbidity expected after third molar surgery is pain. The post-surgical pain begins when the effects of the local anesthesia subsides and reaches peak levels in 6 to 12 hours postoperatively. 37.7% patients reported mild pain on the third post-operative day and 43.4% patients had no pain on the seventh post-operative day. A large variety of analgesics are available for management of post-surgical pain. The most common ones are combinations of analgetics (Metamizol), Paracetamol and nonsteroidal anti-inflammatory analgesics. Analgesics should be given before the effect of the local anesthesia subsides. Women may be more sensitive to postoperative pain than men; thus, they require more analgesics [4].

### **2- Edema**

Postsurgical edema is an expected complication after third molar surgery. It can be caused by the response of the tissues to manipulation and trauma caused during surgery. Its onset is gradual and maximum swelling is present during 48 h after surgery. Regress of the swelling is expected by the 4th day and completely resolution occurs in 7 days.

There was a statistically significant difference between edema and partial bony and complete bony impaction.

The application of ice packs to the face may make the patient feel more comfortable but has no effect on the magnitude of edema [5].

## **Study Materials**

### **Hyaluronic Acid**

Hyaluronic acid (HA) is a naturally occurring linear polysaccharide of the extracellular matrix of connective tissue, synovial fluid, and other tissues. It possesses various physiological and structural functions, which include cellular and extracellular interactions, interactions with growth factors and regulation of the osmotic pressure, and tissue lubrication. All these functions help in maintaining the structural and homeostatic integrity of the tissue. Extensive studies on the chemical and physicochemical properties of HA and its physiological role in humans have proved that it is an ideal biomaterial for cosmetic, medical, and pharmaceutical applications [6].

Hyaluronic acid (HA, also known as hyaluronan or hyaluronate) was first discovered and isolated from the vitreous body of cows' eyes by Karl Meyer and John Palmer in 1934 [7].

### **Hyaluronic Acid Applications in Dentistry**

- Treatment of temporomandibular joint disorders via injection HA [8].
- Treatment of Oral lichen planus (OLP) [8].
- HA can reduce the acute inflammatory reaction and decrease oxygen free radical damage after M3 extraction [9].
- Treatment in gingivitis and chronic periodontitis [10].
- HA can be used in implant and sinus lift procedures [10].
- HA can be used as a treatment of alveolar osteitis [11].
- HA can reduce post-operative complications following mandibular third molars surgery (Pain, Edema).

### **Chlorhexidine**

Chlorhexidine is a gold standard against which other antiplaque and antigingivitis agents are measured. Understanding the properties and limitations of the molecule

can ensure that the efficacy of the agent is maximized and the side effects are minimized allowing it to rightly remain the gold standard [12].

Chlorhexidine has been in use for almost 60 years and has been used in more than 60 pharmaceuticals and medical devices. It was marketed as a general antiseptic in the year 1950. In 1954, The Imperial Chemical industries limited developed the Chlorhexidine. In 1957, it was introduced for human use in Britain as an antiseptic for skin. Plaque inhibiting action of Chlorhexidine was first investigated by Schroeder [12].

## ✓ **Mechanism of action of chlorhexidine**

The Cell wall of bacteria is negatively charged and it also contains sulphates and phosphates. The Chlorhexidine which is cationic molecule positively charged is rapidly attracted towards negatively charged bacterial cell wall with specific and strong adsorption to phosphate containing compounds. The dicationic CHX molecule attaches to the pellicle by one cation, to the bacteria attempting to colonize the tooth surface with the other, this is called "Pin cushion effect". This interaction alters the integrity of the bacterial cell membrane and chlorhexidine is attracted towards inner membrane. Chlorhexidine binds to phospholipids in the inner membrane, which leads to increased permeability of inner membrane and leakage of low molecular weight compounds such as potassium ions. At this Bacteriostatic stage, the effects of chlorhexidine are reversible i.e. Removal of excess chlorhexidine by neutralizers allows bacterial cell wall to recover. There is a progressive damage to the membrane by increasing the concentration of chlorhexidine [13].

## **Similar studies**

- There was a statistically significant differences between Hyaluronic Acid Spray and Normal Saline Spray on the swelling values on the second postoperative day, there was no statistically significant difference in VAS scores between the two groups. So, The administration of hyaluronic acid spray was more effective than Normal saline spray in reducing swelling [14].
- There was a statistically significant differences between Hyaluronic Acid Spray and Benzylamine Hydrochloride Spray on the swelling values on the second postoperative day, there was no statistically significant difference in VAS scores between the two groups. So, The administration of hyaluronic acid spray was more effective than Benzylamine Hydrochloride spray in reducing swelling. [15].
- No difference was determined between groups (HA group and control group) in facial swelling. However, the amount of pain significantly reduced in HA groups according to visual analog scale. Therefore HA can be used to reduce usage of nonsteroidal anti-inflammatory drugs after dentoalveolar surgery [16].
- differences were found between the groups (intraalveolar application of a bioadhesive gel of 0.2% chlorhexidine group and control group) with regard to infectious complications, swelling, or wound healing. Use of analgesics and self-reported pain levels were slightly lower in the experimental group than in the control group during days 6 and 7 of the study ( $p < 0.05$ ). [17].
- There was a Statistically significant differences between groups (post operative irrigation of the surgical site with CHx and control group) on the swelling and pain values

on the 7th postoperative day, there was no statistically significant difference in VAS scores between the two groups on 2<sup>nd</sup> post operative day [18].

## Materials and methods

### 1. Study sample

This clinical study was carried at oral and maxillofacial surgery department at Hama University. This study included random sample of 40 cases of mesial impacted lower third molars. The ages of patients were between 18-25 years. The aim of this study was to compare between Hyaluronic acid and Chlorhexidine 0.2% on pain and edema after impacted lower third molars surgery.

The sample was divided into two groups:

First group: 20 impacted lower third molars was surgically extracted. Hyaluronic acid 0.2% was applied into the alveolar cavity with surgical suture.

Second group: 20 impacted lower third molars was surgically extracted. Chlorhexidine 0.2% was applied into the alveolar cavity with surgical suture.

The time between the two surgeries was 15 days.

### 2. Surgical procedures

**Anesthesia:** is achieved by: inferior alveolar nerve block, buccal nerve block, lingual nerve block, and local infiltration for hemostasis in the surgical field.

#### Removal of Impacted Mandibular Third Molar

After an envelope incision is made using a scalpel with a no. 15 blade, the mucoperiosteal flap is reflected from the distal aspect of the second molar, continuing along the incision posteriorly as far as the anterior border of the ramus. The bone covering the tooth is removed using a round bur, until the entire crown is exposed. Then, the straight elevator is placed in the mesial region and the tooth is elevated with a rotational movement distally. Then 2 cm of HA or Chx was applied into the alveolar cavity then the wound is sutured. The levels of pain were recorded on the 1<sup>st</sup>, 2<sup>nd</sup> and 3<sup>rd</sup> days using a visual analog scale (VAS) from 0 to 10, (figure 1).

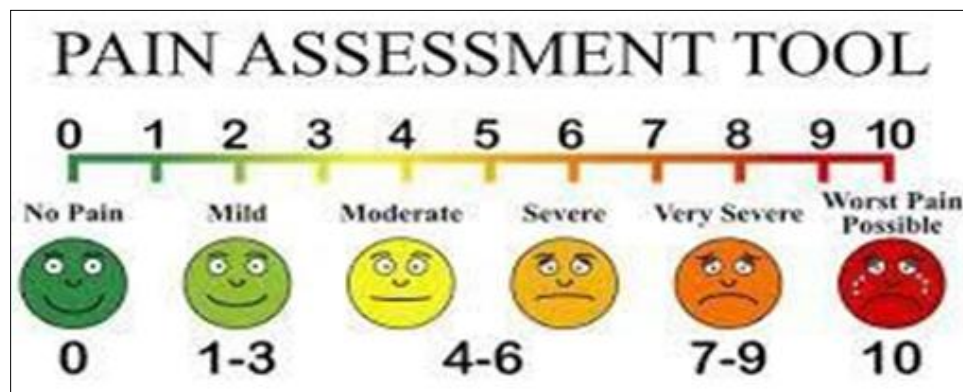


Fig 1: visual analog scale (VAS)

The edema was measured on the 2nd, 3rd and 7th days after surgery. The reference points which used to measure edema were determined by (figure 2).

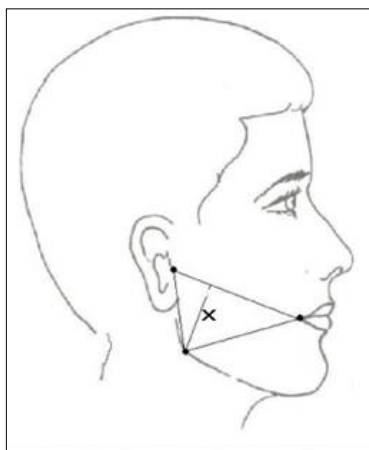


Fig 2: Reference points which used to measure edema

1. Distance from the Tragus to the Labial commissure.
2. Distance from Labial commissure to Mandible angle.
3. Distance from Mandible angle to Tragus.
4. X line.



Fig 3: Panoramic radiograph



Fig 4: Operation site before surgery



**Fig 5:** Mucoperiosteum flap



**Fig 9:** Materials application



**Fig 6:** Remove part of the bone over the crown



**Fig 10:** Operation site after suturing



**Fig 7:** Tooth extraction



**Fig 8:** The amount of used materials

## Results

A total of 20 patients requiring surgical removal of bilaterally impacted mandibular third molars were included in the present study, 12 of them were males and 8 were females with an average age of 23 years (range 18-25 years). The results of the study were evaluated statistically using SPSS Software.

There was a significant difference in the pain on the 1st and 2nd days ( $P < 0.05$ ) between the two used materials throughout all observation periods while there was no significant difference on the 3rd day ( $P < 0.05$ ) (table 1).

There was no significant difference in the (Distance from the Tragus to the Labial commissure (on the 2nd, 3rd and 7th days) ( $P > 0.05$ ) between the two used materials throughout all observation periods (table 2).

There was no significant difference in the (Distance from Labial commissure to Mandible angle) on the 2<sup>nd</sup>, 3<sup>rd</sup> and 7<sup>th</sup> days ( $P > 0.05$ ) between the two used materials throughout all observation periods (table 3).

There was a significant difference in the (Distance from Mandible angle to Tragus) on the 2nd and 3rd days ( $P < 0.05$ ) between the two used materials throughout all observation periods while there was no significant difference on the 7th day ( $P > 0.05$ ) (table 4).

There was a significant difference in the (X line) on the 2nd and 3rd days ( $P < 0.05$ ) between the two used materials throughout all observation periods while there was no significant difference on the 7th day ( $P > 0.05$ ) (table 5).

**Table 1:** Comparison of pain score (VAS) experienced by study groups Wilcoxon Signed Ranks test was carried out for evaluation of pain:

		N	The mean	w value	p value
1st day	HA	20	12.68	253.0	0.000
	CHx	20	28.33		
2nd day	HA	20	12.50	250.0	0.000
	CHx	20	28.50		
3rd day	HA	20	20.5	410	1.000
	CHx	20	20.5		

**Table 2:** Comparison of facial measurements experienced by study groups, Student test was carried out for evaluation of (Distance from the Tragus to the Labial commissure):

days	groups	The mean	Max	Min	Mean delta	T value	P value
2nd day	HA	0.78	3.50	0.00	0.025	0.125	0.900
	CHx	0.75	2.00	0.00			

**Table 3:** Comparison of facial measurements experienced by study groups, Student test was carried out for evaluation of (Distance from the Labial commissure to Mandible angle):

3rd day	HA	0.60	2.50	0.00	-0.05	-0.301	0.764
	CHx	0.65	1.50	0.00			
7th day	HA	0.00	0.00	0.00	0.00	0.001	0.999
	CHx	0.00	0.00	0.00			
days	groups	The mean	Max	Min	Mean delta	T value	P value
2nd day	HA	1.02	2.50	0.50	0.08	0.491	0.626
	CHx	0.94	2.00	0.20			
3rd day	HA	0.86	5.00	0.00	0.13	0.492	0.625
	CHx	0.73	2.00	0.00			
7th day	HA	0.00	0.00	0.00	0.00	0.001	0.999
	CHx	0.00	0.00	0.00			

**Table 4:** Comparison of facial measurements experienced by study groups, Student test was carried out for evaluation of (Distance from the Mandible angle to Tragus):

days	groups	The mean	Max	Min	Mean delta	T value	P value
2nd day	HA	-0.07	0.60	-1.00	-0.52	-3.53	0.001
	CHx	0.45	2.00	0.00			
3rd day	HA	0.07	0.50	0.00	-0.38	-2.79	0.008
	CHx	0.45	2.00	0.00			
7th day	HA	0.00	0.00	0.00	0.00	0.001	0.999
	CHx	0.00	0.00	0.00			

**Table 5:** Comparison of facial measurements experienced by study groups, Student test was carried out for evaluation of (X line):

days	groups	The mean	Max	Min	Mean delta	T value	P value
2nd day	HA	0.19	1.30	-1.10	-0.34	-1.83	0.074
	CHx	0.53	2.60	-0.30			
3rd day	HA	0.15	1.20	-0.30	-0.30	-1.95	0.058
	CHx	0.46	2.20	0.00			
7th day	HA	0.00	0.00	0.00	0.00	0.001	0.999
	CHx	0.00	0.00	0.00			

**Discussion**

The study showed that both of Hyaluronic acid and Chlorhexidine 0.2% have a positive effect on controlling pain and edema after surgical extraction, with significant difference between two groups for HA group.

We found that HA can reduce the pain on the 1st, 2nd and 3rd days after surgical extraction which corroborates the findings of N Yilmaz *et al.* 2016, our findings do not match those of Raj Merchant *et al.* 2017 who concluded that HA has no effect on reducing pain after surgical extraction.

We found that Chx can reduce the pain on the 1st, 2nd and 3rd days after mandibular third molar surgery which corroborates the findings of Ana Coello-Gómez *et al.* 2018, our findings do not match those of H.Cho *et al.* 2017 who

found that there was no significant differences in pain on the 2nd day.

Statistically significant differences were detected for the edema values between the two treatment groups on the 2nd and 3rd days after surgical procedure which corroborates the findings of Raj Merchant *et al.* 2017 and Meltem Koray *et al.* 2014, our findings do not match those of N Yilmaz *et al.* 2016, who concluded that there was No difference was determined on edema on the 1st 3rd and 7th days.

Our study showed that Chx can reduce edema after third molars surgery which do not corroborates with any previous studies, our findings do not match those of Ana Coello-Gómez *et al.* 2018 who found that there was no significant differences in edema after surgical treatment.

## Conclusions

The study showed that both of Hyaluronic acid and Chlorhexidine 0.2% have a positive effect on controlling pain and edema after mandibular third molars surgery.

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