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RESEARCH ARTICLE

EVALUATION OF ROLE OF HYALURONIC ACID IN MANAGEMENT OF POST OPERATIVE SEQUALE OF MANDIBULAR THIRD MOLAR DISIMPACTION - A SPLIT-MOUTH COMPARATIVE STUDY

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Abstract

Aim of the study: To determine the efficacy of Hyaluronic acid gel in management of postoperative complications after impacted mandibular third molar surgery.

Materials and Method : This prospective, single-centeredstudy follow a split mouth-design, where the patients were act as their own control. A total of 40 patients were included in study.The study subjects were assigned into two groups: Control Group and Study Group (0.8 % Hyaluronic acid gel). Once selected, each patient will be assigned a serial number. According to their respective serial numbers, patients with odd serial number will be administered 2ml 0.8% hyaluronic acid gel (Gengigel) in the postextraction socket of impacted mandibular third molar of the left side, and the right side will act as control, an interval of 4 weeks is kept between the 2 surgeries. In even numbered patients, the right side extraction socket will be administered 2 ml 0.8 % hyaluronic acid gel (Gengigel)and the left side acted as the control. . Post-operative pain, trismus, swelling & soft tissue healing were evaluated on 1st, 3rd and 7th postoperative days .

Results:0.8 % Hyaluronic acid gel has shown a beneficial results in the reduction of postoperative pain on 7th day and soft tissue healing on 3rd and 7th days , the results were statistically significant, although the results for trismus and swellingwas not statistically significant.

Conclusion : The efficacy of Hyaluronic acid gel has proven to be an important therapeutic adjuvant for reducing postoperative pain & improve soft tissue healing following mandibular third molar surgery and thus improving patients quality of life.

Introduction:-

Impaction of the third molar is occurs in up to 73% of young adults in Europe. Mandibular third molar are the most prevalent impacted teeth with no differences reported between genders. One of the most common procedures in oral and maxillofacial surgery is the surgical extraction of wisdom teeth. However, several complications can develop

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during surgical extraction of wisdom tooth, such as nerve injury, bone fractures, escape of the tooth or the root of the tooth to anatomical site, adjacent tooth damage, delayed healing, inflammation, pain, swelling, and trismus. Pain, swelling, and trismus are the most common complications that occur after impacted lower third molar surgery.[1]

All these complications have undesirable effects on quality of life for patients. Many previous studies were based on decreasing the complications after impacted tooth surgery by use of local or systemic steroid, non-steroidal anti-inflammatory drugs consumption and antibiotic prophylaxis are common medication methods. However, these medications may result in significant systemic side effects and are contraindicated in a subset of patients. These issues encouraged researchers to investigate the topical application of agents without systemic side effects, such as Hyaluronic acid (HA) applied directly to extraction site. [1,2]

Hyaluronic acid (HA) is a naturally occurring non-sulfated glycosaminoglycan (GAG) non-protein compound with distinct physico-chemical properties of repeating β-1,4-D-glucuronic acid and β-1,3-N-acetylglucosamine units. The structural formula of HA is shown in. HA has excellent viscoelasticity, high moisture retention capacity, high biocompatibility, and hygroscopic properties. At a concentration as low as 0.1%, HA chains can provide high viscosity. By having these properties, HA acts as a lubricant, shock absorber, joint structure stabilizer, and water balance- and flow resistance-regulator .[3]

Lee et al. investigated the efficacy of the topical application of 0.2% HA gel for oral ulcers in patients with RAU and the oral ulcers of Behçet's disease (BD). In this study, HA gel application improved subjective parameters (number of ulcers, healing period, visual analogue scale [VAS] for pain, and objective parameters (number of ulcers, maximal area of ulcer, and inflammatory signs such as swelling and local heat). [4]

Aim & Objectives:-

Aim:-

To determine the efficacy of Hyaluronic acid gel in management of postoperative complications after impacted mandibular third molar surgery.

Objectives:-

1. To evaluate the post-operative pain, swelling, trismus& soft tissue healing following third molar surgery.
2. Evaluate the effect of hyaluronic acid in managing post-operative sequale after disimpaction of impacted mandibular third molar and compare it with standard healing.

Materials & Methods:-

This prospective, single-centered study follow a split mouth-design, where the patients were act as their own control. The study subjects were assigned into two groups: Control Group and Study Group (0.8 % Hyaluronic acid gel). 40 patients satisfying the selection criteria were included for the study.Allprocedures was performed under local anesthesia. Once selected, each patient will be assigned a serial number. According to their respective serial numbers, patients with odd serial number will be administered 2ml 0.8% hyaluronic acid gel (Gengigel) in the postextraction socket of impacted mandibular third molar of the left side, and the right side will act as control, an interval of 4 weeks (washout period) is kept between the 2 surgeries. In even numbered patients, the right side extraction socket will be administered 2 ml 0.8 % hyaluronic acid gel (Gengigel)and the left side acted as thecontrol. This was done to eliminate psychological bias. Post-operative pain, trismus, swelling & soft tissue healing were evaluated on 1st, 3rd and 7th postoperative days.

Inclusion Criteria:

1) Patients in the age group of 18 to 40 years
2) Have bilaterally impacted lower third molar impaction with equal surgical difficulty.
3) Have no systemic disease.
4) Patients with no unexpected oral habits, no smokers and with no intraoral pathology.

Exclusion Criteria:

1) Patients having a history of allergy or adverse effect to antibiotics, analgesic, local anesthetics, pregnancy, or bleeding disorders.

2) Patients using contraception or corticosteroids which can affect the postsurgical healing phase and amount of swelling on face.
3) Patients have difficulty in cooperation.

Surgical Phase:
• Sterilization for asepsis was maintained for all patients.
• The operation procedure was performed according to conventional surgical impacted third molar extraction. Routine regional anaesthesia was applied including Inferior alveolar nerve block, lingual nerve block and long buccal along with buccal infiltration using lignocaine 2% with epinephrine 1:2,00,0000.
• Wards incision was given and mucoperiosteal flap was elevated.
• Bone guttering was done on the buccal and distal aspect done.
• After removal of impacted mandibular molars, patient with odd number study group was taken and 2 ml 0.8 % hyaluronic acid gel (Gengigel) applied on postextraction socket of left side and on the right side of control group flaps were sutured after a blood clot formed at the extraction site, In even numbered patients, the right side extraction socket were administered 2 ml 0.8 % hyaluronic acid gel (Gengigel)and the left side acted as the control. Both the surgical removal of impacted mandibular molar done with 4 weeks of gap.
• Wound closure achieved by simple interrupted suture using 3-0 black braided silk.
• The patients were instructed not to eat or drink for 1 hour after the use of the gel.
• All patients were administered I.M Diclofenac sodium injection postoperatively. Postoperatively, patients underwent antibiotic treatment (oral amoxicillin 500 mg with 125 mg clavulanic acid, thrice a day for 5 days) with analgesic medication, additionally oral hygiene (warm saline rinses) instructions were given.

Postoperative Clinical Assessment
Visual analog scale (VAS) which has a 10 units number line marked by degrees was used for detecting the degree of postoperative pain. According to this scale, score of 0 indicated“absence of pain” and score of 10 indicated “excessive pain.” The intermediate scores have been indicated “moderate pain.” The exact question was “On the scale, how much pain are you having for today?” In addition, it contains facial expression illustrations to direct the patients. Brokelman et al. reported that VAS scale is a simple instrument to evaluate the postsurgical pain and satisfaction of a patient with the intraclass coefficient of 0.95.[2]

Trismus was evaluated by measuring the distance between the edges of the upper and lower right central incisors (Interincisal) at maximum opening of the jaws on the 1st day,3rd day and 7th day after surgery.

In this study, assessment of facial swelling was determined by using modification ofGabka and Matsumara method. The measurement points included :

Three measurements were made between five reference points:
1. The distance between the lateral corner of the eye and angle of the mandible,
2. The distance between the tragus and soft tissue pogonion,
3. The distance between the tragus and outer corner of the mouth.[5]

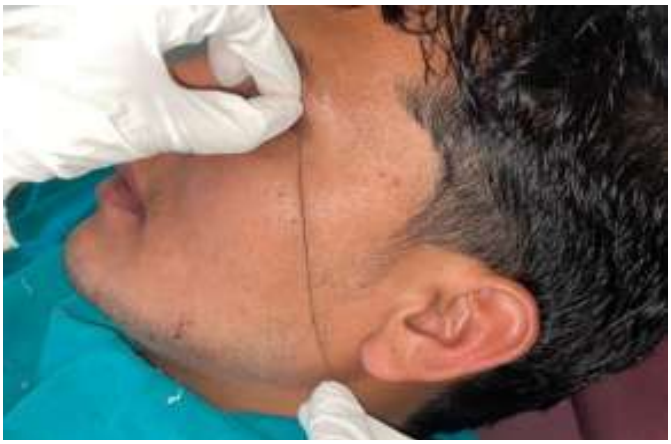

Fig. 1:- (A) Linear distances between the angle of the mandible to eye side transcutaneous.

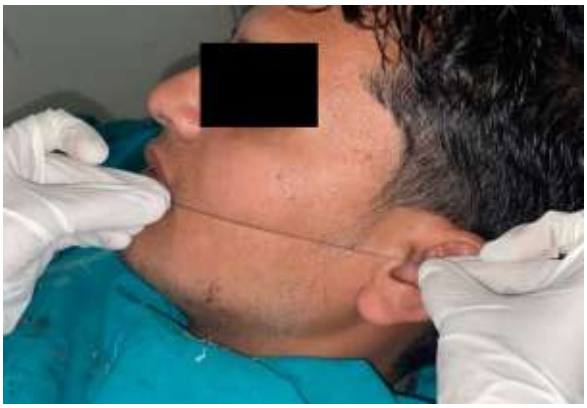

Fig. 1:- (B) Linear distances from the tragus to the corners of the mouth.

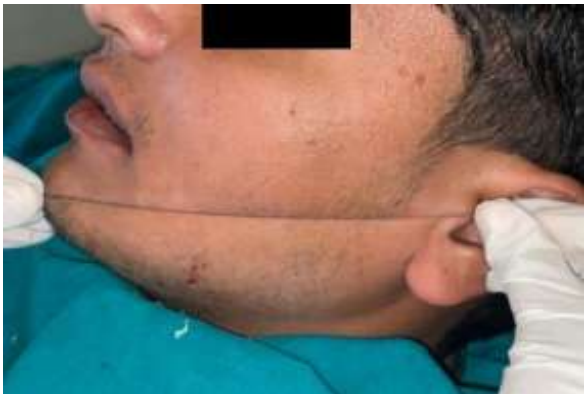

Fig. 1:- (C) Linear distances from the tragus to pogonium.

The soft tissue healing would be evaluated and graded according to Landry R, Turnbull R and Howley T soft tissue healing index as on 1st, 3rd and 7th days postoperatively. Numerous methods have been described for theassessment of wound healing in oral soft tissues. The first published index, the Healing Index (HI), was introduced by Landry et al. in 1988 and evaluated the parameters of tissue colour, bleeding response to palpation, presence of granulation tissue, characteristics of the incision margins, and the presence of suppuration. This index assesses wound healing using scores from 1 to 5: a wound with very poor healing receives a score of 1, whereas excellent healing receives a score of 5.[6]

Results:-

A total of 40 patients were included in the study, wherein the mean age was 25.70±5.67 and the male: female ratio was 21:19

Table 1:-Distribution of study subjects based on gender.

Gender	No. of patients	Percentage
Male	21	52.5 %
Female	19	47.5 %
Total	40	100 %

Table 2:-Age distribution of study subjects.

Age in Years	No. of patients	Percentage
16-20 Years	8	20.0%
21-25 Years	15	37.5%
26-30 Years	9	22.5%
31-35 Years	7	17.5%
36-40 Years	1	2.50%
Mean age 25.70±5.67		

Table 3:- Intergroup Comparison of mean pain scores between the groups.

	Group	Mean	Std. Deviation	Std. Error Mean	P value	Significance
Day 1	Control Group	4.850	0.975	0.154	0.374	Non Significant
	Study Group	4.650	1.026	0.162		
Day 3	Control Group	3.850	1.166	0.184	0.362	Non Significant
	Study Group	3.650	0.735	0.116		
Day 7	Control Group	2.250	0.630	0.099	0.015	Significant
	Study Group	1.900	0.632	0.100		

On the day 1 the mean pains scores in the control group was 4.850 and 4.650 in the study Group. The difference between the groups was statistically nonsignificant when analyzed using independent t test. On the Day 3 the mean pain score was 3.850 in the control group and 3.650 in the study group. The difference between the groups was statistically non-significant when analyzed using independent t test On the Day 7 the mean pain score was 2.250 in the control group and 1.900 in the study group, The difference between the groups was statistically significant when analyzed using independent t test with p value of 0.015.

Table 4:-Intergroup comparison of mean swelling scores between the groups.

	Group	Mean	Std. Deviation	Std. Error Mean	P value	Significance
Day 1	Control Group	12.845	0.849	0.134	0.853	Non-Significant
	Study Group	12.810	0.837	0.132		
Day 3	Control Group	12.870	0.830	0.131	0.608	Non-Significant
	Study Group	12.775	0.804	0.127		
Day 7	Control Group	12.340	0.848	0.134	0.615	Non-Significant
	Study Group	12.375	0.894	0.141		

On the day 1 the mean swellings scores in the control group was 12.845 and 12.810 in the study Group. The difference between the groups was statistically nonsignificant when analyzed using independent t test. On the Day 3 the mean swelling score was 12.870 in the control group and 12.775 in the study group. The difference between the groups was statistically non-significant when analyzed using independent t test On the Day 7 the mean swelling score was 12.340 in the control group and 12.375 in the study group, The difference between the groups was statistically nonsignificant when analyzed using independent t test.

Table 5:- Intergroup comparison of mean trismus scores between the groups.

	Group	Mean	Std. Deviation	Std. Error Mean	P value	Significance
Day 1	Control Group	37.800	5.552	0.877	0.872	Non-Significant
	Study Group	38.000	5.556	0.878		
Day 3	Control Group	40.950	5.098	0.806	0.681	Non-Significant
	Study Group	41.350	3.393	0.536		
Day 7	Control Group	43.650	4.215	0.666	0.614	Non-Significant
	Study Group	44.150	4.599	0.727		

On the day 1 the mean mouth opening (trismus scores) in the control group was 37.800 and 38.000 in the study Group. The difference between the groups was statistically non-significant when analyzed using independent t test. On the Day 3 the mean mouth opening (trismus scores) was 40.950 in the control group and 41.350 in the study group. The difference between the groups was statistically non-significant when analyzed using independent t-test. On the Day 7 the mean mouth opening (trismus scores) was 43.650 in the control group and 44.150 in the study group. The difference between the groups was statistically non-significant when analyzed using independent t test.

Table 6:- Intergroup comprison of mean healing scores between the groups.

	Group	Mean	Std. Deviation	Std. Error Mean	P value	Significance
Day 1	Control Group	2.850	0.662	0.104	0.480	Non-Significant
	Study Group	2.950	0.597	0.094		
Day 3	Control Group	3.650	0.863	0.136	0.040	Significant
	Study Group	4.200	0.632	0.100		
Day 7	Control Group	4.250	0.776	0.122	0.049	Significant
	Study Group	4.700	0.432	0.107		

On day 1 the mean healing scores in the control group was 2.850 and 2.950 in the study Group. The difference between the groups was statistically non-significant when analyzed using independent t test. On the Day 3 the mean healing score was 3.650 in the control group and 4.200 in the study group. The difference between the groups was statistically significant when analyzed using independent t test On the Day 7 the mean healing score was 4.250 in the control group and 4.700 in the study group, The difference between the groups was statistically significant when analyzed using independent t test.

Discussion:-

The present study was designed to evaluate the efficacy of hyaluronic acid on the control of pain, swelling, soft tissue healing &trismus following impacted mandibular third molar surgery. The results of the present study showed that both pain and soft tissue healing to be significantly improved in the hyaluronic acid group.

In our study, On the day 1 the mean value for pain scores in the control group was 4.850 and 4.650 in the study group. The difference between the groups was statistically non-significant when analyzed using independent t test. On the Day 3 the mean pain score was 3.850 in the control group and 3.650 in the study group. The difference between the groups was statistically non-significant when analyzed using independent t test, On the Day 7 the mean pain score was 2.250 in the control group and 1.900 in the study group, The difference between the groups was statistically significant when analyzed using independent t test with p value of 0.015. In our study there is a significant decrease in the VAS score in the HA group compared to the control group & the difference was significant on the 7th day.Wang F et al.[7] also conducted a meta-analysis to compare the efficacy and safety of intraarticular HA and CS in the treatment of knee OA. They found that intraarticular HA and intraarticular CS have equal efficacy for decreasing pain in short term (1 month) and intraarticular HA is more effective than CS after 3 months; besides, no difference was observed between HA and CS for adverse effects. Nevertheless, the number and quality of the included studies in their meta-analysis are restricted, and they mistook the data of the maximum knee flexion during gait analysis for active range of knee flexion. [7]

In our study, on the day 1 the mean swellings scores in the control group was 12.845 and 12.810 in the study Group. The difference between the groups was statistically non-significant when analyzed using independent t test. On the Day 3 the mean swelling score was 12.870 in the control group and 12.775 in the study group. The difference between the groups was statistically non-significant when analyzed using independent t test On the Day 7 the mean swelling score was 12.340 in the control group and 12.375 in the study group, The difference between the groups was statistically non-significant when analyzed using independent t test. In our study, efficacy of hyaluronic acid to decrease swelling is not statistically significant when compared between study & control group.

Swelling following the surgical removal of teeth is an expected finding during the postoperative course. In the past, many different approaches, including drains, laser therapy and medications with enzymes, muscle relaxants or corticosteroids were clinically evaluated in an effort to minimize these post-operative sequelae.[8]

In our study, on day1 the mean mouth opening (trismus scores) in the control group was 37.800 and 38.000 in the study Group. On the Day 3 the mean mouth opening (trismus scores) was 40.950 in the control group and 41.350 in the study group. On the Day 7 the mean mouth opening (trismus scores) was 43.650 in the control group and 44.150in the study group. The intragroup comparison of mean mouth opening scores was not statistically significant in both the groups when analyzed using One Way ANOVA. In our study, efficacy of Hyaluronic acid in subsiding trismus after third molar disimpaction is not statistically significant when compared between control and study group on 1st, 3rd & 7th day.

In Guazzoet al.[9] study, patients mouth opening measurements had returned to presurgery level by the 14th day with no significant differences between the two groups (control, amino acid and sodium hyaluronate). Gocmenet al[10]. reported that there was no statistically significant between local injection of HA at 0.8% after third molar extraction on mouth opening limited when compared to pre-op, 1 hour, the third day and seventh day. Their results are similar to Afat et al[11]., who evaluated the effects of leukocyte- and platelet-rich fibrin (L-PRF) alone and combined with a hyaluronic acid (HA) sponge; there was no significant difference among groups in trismus.[9,10,11]

In our study, on day 1 the mean healing scores in the control group was 2.850 and 2.950 in the study Group. The difference between the groups was statistically non-significant when analyzed using independent t-test. On the Day 3 the mean healing score was 3.650 in the control group and 4.200 in the study group. The difference between the groups was statistically significant when analyzed using independent t-test, On the Day 7 the mean healing score was 4.250 in the control group and 4.700 in the study group. The difference between the groups was statistically significant when analyzed using independent t-test. In our study 0.8% Hyaluronic acid gel used to appreciate the extent of soft tissue healing after third molar disimpaction.

There are a few studies in the literature that investigated the effect of HA on wound closure. They concluded that HA accelerates wound closure rate and re- epithelization. Juhaszet al[12]stated a reduction in the wound size .[12]

Nowadays, HA is one of the most widely used active ingredients in cosmetic formulations. General perception about skin regeneration is of constant interest for both industry professionals and consumers. It is evident that the skin is an indicator of individual's health and HA is one of the main factors for healthy skin. As shown above, hyaluronic acid is a biopolymer considered of primary interest from a scientific point of view, due to its multitude of applications in cosmetic and biomedical fields. Such being the case, exploration on this ingredient is increasing in many interdisciplinary domains targeting, on the one hand, the improvement of production processes in terms of biotechnology and on the other hand the development of new formulations incorporatinghyaluronan or HA-based innovative ingredients. Scientific efforts are moving nowadays towards the production of appropriate molecular weight biopolymers. This specific aspect relies precisely to the biological function, as indicated by bibliographic studies. Although HA was synthesized a very long time ago, it is still needed to investigate this active ingredient in terms of physico-chemical and biological properties.[13]

Conclusion:-

In our study we use hyaluronic acid gel & evaluate its efficacy in subsiding the post-operative complications such as pain, swelling, trismus& compromised soft tissue healing which we encounter after removal of impacted mandibular third molar. The study we conducted was a comparative split mouth study, and it was found that hyaluronic acid gel is statistically significant in decreasing pain as well as improving soft tissue healing. No significant results were obtained for hyaluronic acid gel in decreasing the post-opererative edema. The mouth opening assessed on post-

operative days 1,3 and 7 indicated that the mean mouth opening was better with the hyaluronic acid study group compared to the control group, although the results were not statistically significant. Hyaluronic acid is thus found to be a beneficial adjuvant therapeutic agent and is functional for improving patient's postoperative quality of life following mandibular third molar surgery.

Our study group consisted of a limited number of patients with a limited follow up period. Hence a more extensive study on number of patients with a longer of follow up period is required to appraise the use of Hyaluronic acid in subsiding the post-operative sequalae following removal of impacted mandibular third molar.

Declaration:
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Nil.

Conflict of interest:
There are no conflict of interest

Ethical Approval :
Approved

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