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RESEARCH ARTICLE

EFFECT OF SUBMUCOSAL DEXAMETHASONE INJECTION AFTER THIRD MOLAR SURGERY – A RANDOMIZED CONTROLLED TRIAL

***,[1]Dr. Rohit Chawla, [1]Dr. Ajay Bibra, [2]Dr. Mohan Alexander, [3]Dr. Rajat Bhandari and [4]Dr. Sonam Mahajan**

[1]Department of Oral and Maxillofacial Surgery, Genesis Institute of Dental Sciences and Research, Ferozepur, Punjab
[2]Department of Oral and Maxillofacial Surgery, D.J. College of Dental Sciences and Research, Modinagar, U.P.
[3]Department of Oral and Maxillofacial Pathology, Genesis Institute of Dental Sciences and Research, Ferozepur, Punjab
[4]Department of Conservative Dentistry and Endodontics, Genesis Institute of Dental Sciences and Research, Ferozepur, Punjab

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ABSTRACT

Background: The post surgical sequeale following surgical removal of impacted third molars such as pain, swelling and trismus can cause distress to the patients and affect the quality of life. Many clinicians have attempted to reduce these sequelae by using NSAIDs and Corticosteroids like dexamethasone and methylprednisolone. Recently studies have been conducted to test the efficacy of local submucosal injection of corticosteroids.

Aim: To evaluate the effects of submucosal injection of dexamethasone on postoperative discomfort after third molar surgery. Methods and Material: 60 patients requiring surgical removal of impacted mandibular third molar were randomly divided into two groups of 30 each - 1ml placebo for control group and 4 mg of dexamethasone sodium phosphate 1 ml for test group injected submucosally followed by oral administration of ibuprofen 400 mg postoperatively for each group. Each subject was evaluated on 2nd and 7th postoperative days. Trismus and facial edema was recorded as the difference between preoperative and postoperative values. Postoperative pain was evaluated by the number of analgesic tablets consumed and using a 8-point visual analog scale (VAS).

Statistical Analysis: Data was analyzed by Student t- test / Mann Whitney test, Chi-square test and Friedmann test.

Results: Increase in mouth opening was seen in group B on 2nd and 7th day respectively ($p<0.00$) as compared to group B. Swelling had decreased in both groups on 7th day ($p <0.000$) as compared to day 2. Similarly, pain also reduced in both groups on 7th post-operative day ($p< 0.034$).

Conclusion: Submucosal injection of dexamethasone locally reduces swelling, trismus and also pain and can be used routinely in 3rd molar surgeries without any adverse effects.

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INTRODUCTION

The surgical removal of impacted third molars is one of the most frequent interventions in oral and maxillofacial surgery (Geoffrey L Howe, 1988). Besides infrequent but serious complications such as fracture, infection, dysaesthesia, etc, patients often complain of pain, swelling and trismus.

****Corresponding author: Dr. Rohit Chawla,***
Department of Oral and Maxillofacial Surgery, Genesis Institute of Dental Sciences and Research, Ferozepur, Punjab

These post surgical sequeale can cause distress to them and affect the quality of life after the surgery. Many clinicians have attempted to reduce these post surgical sequelae by using non steroidal anti- inflammatory drugs. Corticosteroids like dexamethasone and methylprednisolone have also been extensively used due to their purely glucocorticoid effects and long half life (Elhag *et al*., 1985). Recently studies have been conducted to test the efficacy of local submucosal injection of corticosteroids. Since there are not many reports about their efficacy, complications, etc, we decided to conduct a randomized control trial to investigate the effect of such

injections on the sequelae of surgical removal of impacted mandibular 3rd molars.

Aim & Objectives

To evaluate the effects of submucosal injection of dexamethasone on postoperative discomfort after third molar surgery. To determine whether glucocorticosteroids (dexamethasone) can control the post surgical sequeale of third molar surgery.

MATERIALS AND METHODS

A randomized double blind study was conducted among patients who reported to the Department of Oral and Maxillofacial Surgery requiring surgical removal of impacted mandibular third molars. The exclusion criteria included pregnant and lactating women, medically compromised patients, any pathology/infection at site of surgery, chronic use of medication (antihistaminic, antidepressant) that obscure the assessment of inflammation, use of any antibiotic/anti inflammatory drugs within two weeks of study. 60 patients who met the inclusion criteria were randomly divided into two groups of 30 each - Group A placebo & Group B dexamethasone. The subjects were randomly allotted to two groups by random number generated from computer. Third molar positions were evaluated using intraoral periapical radiographs by Winter's classification. The following baseline data were recorded :-

- Mouth opening was taken as maximum distance between upper & lower central incisors as measured by ruler (to the nearest mm).
- Facial swelling was evaluated by two measurements made between 3 reference points: mid tragus to pogonion and mid tragus to corner of mouth taking mid tragus as a base point.
- Preoperative pain was recorded using an 8 points visual analog scale ranging from no pain (0) to very severe pain (8).

Medications

Subjects were randomly allotted to two groups-4 mg of dexamethasone sodium phosphate one ml for test group and 1ml of normal saline (placebo) for control group were injected submucosally buccal to 3rd molar in these patients. They were prescribed ibuprofen 400 mg postoperatively and instructed to take one each when they experienced moderate pain.

The patients were instructed to avoid all drugs other than those prescribed and not to seek medical help elsewhere for postoperative problems and contact the investigator immediately in case of any complaints.

Postoperative assessment

Each subject returned for evaluation on 2nd and 7th postoperative days. Trismus and facial edema was recorded as the difference between preoperative (baseline) and postoperative values by the same investigator. Postoperative pain was evaluated by having the patients report the number of analgesics tablet consumed. Pain was rated preoperatively as well as on the 2nd and 7th postoperative day of surgery using a 8-point visual analog scale (VAS) ranging from "no pain(0) to very severe pain (8)". The details that were recorded included the tooth to be removed, the type of impaction, duration of surgery (incision to suturing), mouth opening, trismus, swelling and category of operator according to experience.

Surgical Procedure

Local anaesthesia was obtained by inferior alveolar nerve block, lingual nerve block and long buccal nerve block. A standard Ward's incision was placed. Mucoperiosteal flap was reflected and the bone exposed. Bone removal was carried out by guttering technique on the buccal and distal side. After adequate amount of bone removal the tooth was delivered out of socket by using an elevator, socket was irrigated with normal saline and complete hemostasis was achieved before wound closure using one or two sutures.

Statistical Analysis

Data was evaluated and statistically analyzed by Student T- Test / Mann Whitney Test, Chi-Square Test, Friedmann Test and Kruskal Wallis Test.

RESULTS

Table I shows the mean difference in the mouth opening in both dexamethasone and placebo groups on the preoperative day, postoperative day 2 and day7. The mean value in group A on preoperative day was 49.20 mm whereas in group B it was 47.03. There was a marked decrease in the mouth opening on the 2nd postoperative day with a mean value of 22.47mm in group A, and 36.77mm in group B. On the 7th postoperative day group A showed a mean value of 37.00 mm whereas group

Table 1. Mouth opening in both groups

Mouth Opening	Group-a (n-30)		Group-b (n-30)		*p*- value
	Mean ± SD	Median	Mean ± SD	Median	
Pre- Operative (Baseline)	49.20 ± 3.93	50	47.03 ± 3.67	47	0.77
Post-Operative Day Two	22.47 ± 6.44	22	36.77 ± 5.56	37	0.00
Post-Operative Day Seven	37.00 ± 3.69	37.50	44.70 ± 3.91	45	0.00

Table 2. Facial Oedema (Mid tragus – pogonion)

Oedema	GROUP -A (n-30)		GROUP-B (n-30)		*p*- value
	Mean ± SD	Median	Mean ± SD	Median	
Pre- Operative (Baseline)	149.53 ± 5.09	150	147.73± 4.68	149	0.160
Post-Operative Day Two	161.23 ± 5.96	161.23	152.60 ±4.90	153	0.000
Post-Operative Day Seven	156.83 ± 5.44	156.83	149.30 ± 4.71	150	0.000

B showed 44.70 mm with significant p- value on 2nd and 7th day (<0.00 on both days). Table II shows measurement of swelling mid tragus to pogonion. There was no swelling in both the groups on preoperative day. On 2nd postoperative day, all the patients had swelling with a mean of 161.23 mm in group A whereas 152.60 mm mean was found in group B with p < 0.000.On the 7th postoperative day, swelling had decreased in both groups with mean value of 156.83 mm in group A and 149.30 mm in group B with statistical significance (p <0.000).

Table 3. Facial Oedema (MID Tragus – Corner of Mouth)

OEDEMA	GROUP-A (n-30)		GROUP-B (n-30)		P – value
	Mean ± SD	Median	Mean ± SD	Median	
Pre- Operative (Baseline)	118.60 ± 4.67	120.00	118.93 ± 5.62	120.00	0.08
Post-Operative Day Two	131.33 ± 6.21	131.50	123.67 ± 5.51	124.00	0.000
Post-Operative Day Seven	126.17 ± 5.25	127.00	121.20 ± 5.20	122.00	0.000

Table 4. Pain score by vas

PAIN	GROUP-A (n-30)		GROUP-B (n-30)		p- value
	Mean ± SD	Median	Mean ± SD	Median	
Pre- Operative (Baseline)	1.63 ± .490	2.00	1.60 ± .498	2.00	0.160
Post-operative Day Two	6.17 ± 1.02	6.00	4.47 ± 1.63	4.00	0.000
Post-operative Day Seven	5.03 ± 1.03	5.00	4.40 ± 1.22	4.00	0.034

Table 3 shows the presence of swelling from mid tragus to corner of mouth. On the 2nd postoperative day, all the patients had swelling with mean 131.33 mm in group A whereas it was 123.67 mm mean in group B (p<0.000).On the 7th postoperative day, swelling had decreased in both groups with mean value of 126.17 mm in group A and 121.20 mm in group B which is statistically significant(p<0.000). Table 4 shows the pain score by VAS in both groups. Preoperatively no patient had pain in both groups. On the postoperative day2, patients experienced pain with mean value of 6.17 in group A and 4.47 in group B according to VAS score (p<0.000).On day 7, patients experienced pain with mean value of 5.03 in group A and 4.40 in group B p< 0.034.

DISCUSSION

The effect of steroids on post-surgical sequeale of third molar removal has been evaluated in many clinical trials. Most studies have reported that steroids significantly reduce the swelling, pain, and trismus whereas a few have not shown any benefit from the administration of steroids. We agree with Neupert *et al*. (1992), that these studies are difficult to compare because a variety of steroids were evaluated using dissimilar study designs and methods for evaluating swelling and pain. We used the method described by Schultze-Mosgau *et al*. (1995), to measure facial edema by measuring the distance from mid tragus to corner of mouth and mid tragus to pogonion. Obviously this method is not as accurate as computed tomography or magnetic resonance imaging for making precise measurements of facial soft tissue volume. However, it is a non invasive, simple, cost effective and time saving method, which provides numeric data for determination of soft tissue contour changes. For edema, Esen *et al*. (1999), did a randomized controlled trial in 20 healthy patients who were to undergo surgical removal of bilateral, symmetrically placed, mandibular third molars. Facial edema was evaluated by ultrasound and computed tomography. They concluded that subjects receiving corticosteroids showed 42% less swelling on second postoperative day than control group. In contrast to our study they used more sensitive methods of measuring edema with (CT scan and ultrasonography), and for trismus they used Boley's (vernier) gauge. Moreover this is level one study as trial was designed on a double blind, cross over, placebo controlled basis and supports our data. Graziani *et al*. (2006), did a randomized controlled trial in 43 patients who were selected for bilateral removal of lower wisdom teeth in two sessions spread over 4 week interval. They reported that use of dexamethasone 4mg as a topical injection reduced neither trismus nor pain. Our data showed that sub mucosal administration of 4mg dexamethasone resulted in highly significant decrease not only in edema but also trismus and pain. Also, direct application of steroid in traumatized tissue as done by F.Graziani *et al* in their study may reduce the inflammation related events (Anne Pedersen, 1985). This is in agreement with the study done by Eugene J. Messer and John J.Keller, (1975), where they gave 1c.c injection of dexamethasone into masseter muscle and concluded that direct application of steroid in traumatized tissue reduces inflammation process. E .Vegas Bustamante *et al*. (2008) did a randomized cross over double blind study in 40 patients (between March 2003 and September 2004) who required extraction of both lower third molars. They concluded that when 40 mg methylprednisolone was injected into masseter muscle, it significantly reduces swelling, trismus and postoperative pain. Results of this level 1 study coincides with the present observations, although involving a different dose and a route of administration but class of drug, glucocorticosteroid is same, but a drug's effects are determined in large part by the way it's administered. A simple rule of thumb is that the quicker a chemical enters the bloodstream, the more intense its effects. Steroids can be injected under the skin ("skin-popping") or shot into deep muscles (intramuscular injection). Since drugs must move through more layers of body tissue with these methods, onset of effects is delayed by about 15-30 minutes. The intramuscular route affords good plasma drug concentrations and prolonged anti inflammatory action with a single pre- or postoperative dose (Michael, 1990). Moreover this technique is convenient for surgeon since injection is carried out in proximity to surgical area, and also for the patient, since injection is performed in a region that is anaesthetized. In the present study administration of

dexamethasone resulted in significantly less degree of swelling on second post-operative day ($p<0.000$) in thirty patients (test group). The facial measurements reached the baseline by seventh day ($p<0.000$) compared with placebo. This was in agreement with various studies by Anne Pedersen (1985), Graziani F, D'Aiuto F, Arduino PG, Tonelli M, and Gabriele M (2006). Moreover our data is based on a randomized double blind placebo controlled trial that showed significant reduction in facial edema on 2nd postoperative day when maximum facial swelling is expected[11] and on 7th day. However Milles and Desjardins have reported that swelling may increase on third day after surgery in patients treated with corticosteroids (Maano Milles and Paul, 1993). The authors state that there is need to continue corticosteroid therapy for a minimum of three days to maintain blood level of drug. Their result suggested that less than 40 mg of methylprednisolone is capable of decreasing swelling by 34%to 42%. This single dose failed to sustain the effect on edema formation, however which led them to recommend that sustained release formulation or a multiday course may be preferable. Alternatively, a higher single dose, as suggested by Beirne and Hollander, also may exert a more sustained effect. But our findings suggest that single dose 4 mg dexamethasone reduces the post surgical sequeale till 7th day postoperatively except pain which was reduced till 2nd day postoperatively.

Contrary to the above studies and the present study, Neupert III EA, Lee JW, Philput GB and Gordon JR showed that there was no significant decrease in swelling between dexamethasone and control groups (Neupert, 1992). In contrast to these studies our data suggests that steroids significantly reduce pain. On second postoperative day, the mean rating for patient pain in test group was 4.47 and 6.17 in placebo group. The difference of 1.70 on VAS was significant ($p <0.000$). Pain decreased on 7th day but it was not statistically significant, but the number of analgesics consumed by patient in test group were less. The discordance might be due to 2-3 times higher steroid doses in previous studies (Vegas-Bustamante, 2008). Studies assessing pain were limited. Many studies have assessed pain by number of analgesics taken after the surgery (Holland, 1987). But we measured both ways objectively by measuring the number of ibuprofen consumed by patient postoperatively and on VAS scale. A study by Dionne *et al* was designed to evaluate the relationship between locally released prostanoids and anti-inflammatory effects of corticosteroids. They suggested that TXB_2 is basically an indicator of COX 1 production and is significantly suppressed by dexamethasone pretreatment in the immediate postoperative period and after pain onset, indicative of an effect on cox-1.The small, non significant effect of dexamethasone on PGE_2 levels at same point (0 to 80 minutes post surgery) is not consistent, however, with a cox1 mediated effect, because PGE_2 is a product of both cox1 and cox2 and should be suppressed by cox1 inhibition as well (Raymond, 2003). Dionne *et al* concluded that dexamethasone in humans may suppress Cox I associated with TXB_2 production in one cell type while having little effect on Cox 1 mediated production of PGE_2 in other cell types. They further added that corticosteroid's primary mechanism is thought to involve effects on leukocyte and macrophage accumulation at inflammatory site (Metz, 1981) and prevention of prostaglandin synthesis by inhibiting arachidonic acid cascade[16] thereby reducing transudation of fluids and lessening edema. As compared to placebo, administration of ketoprofen and dexamethasone reduces tissue levels of bradykinin and prostaglandin E_2 (Raymond, 2003). In addition, a single preoperative injection of methylprednisolone produces a substantial and prolonged reduction in mediator release and post surgical pain. According to Marc Leone *et al* (level1study) 1mg/kg of methylprednisolone is effective for relieving pain after surgical removal of third molars (Marc Leone, 2007). A single preoperative injection of methylprednisolone produces a substantial and prolonged reduction in mediator release and post surgical pain. They used micro dialysis probes to check antibradykinin effect and they found subjectively there is reduction of pain after the administration of steroid. Hyrkas *et al* found that the administration of methyl prednisolone with diclofenac resulted in greater pain relief than diclofenac alone (Hyrkas, 1993). Our results indicated that use of dexamethasone as sub mucosal injection not only reduces postoperative pain but trismus and edema also. Anne Pedersen (1985), who did a double blind placebo controlled study in 30 patients, who needed prophylactic removal of bilateral, symmetrical impacted wisdom teeth in mandible. She concluded that prophylactic steroid treatment is effective in reducing postoperative complaints. She further added that steroid administration had significantly reduced swelling on 2nd postoperative day (49%) and (35%) on 7th post operative day. According to her pain after 48 hours is less in test group (steroid) than the control group and they consumed 37% less pain killers, and had 40% less pain on 7th postoperative day. All these findings coincide with our study. The study by C. S. Holland[13] is also in agreement with our study, he compared the influence of methylprednisolone with that of a placebo on postoperative pain and swelling, and on healing. The results showed that the mean post-operative swelling at 24 hours was reduced by 56% ($p= .0003$) when methylprednisolone was used compared with the opposite side of the same patient when the placebo was used. The severity of pain was also reduced on first postoperative day. Moreover the face bow method used in this clinical trial has also been shown to have an adequate level of accuracy and consistency (Holland, 1979) compared with other methods like clinical observation or method described by Schultze-Mosgau[4], as this method does not only measure linear measurements but also horizontal. The results of this study provide a basis for the sub mucosal administration of corticosteroids such as dexamethasone sodium phosphate to control post-operative pain, swelling and trismus following third molar surgery.

Conclusion

The study showed that submucosal injection of dexamethasone locally reduces swelling, trismus and also pain. We are of the opinion that since this injection seems to be beneficial without any adverse effects, it may be used routinely in 3rd molar surgeries.

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