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## **Comparative analysis of effect of submucosal dexamethasone and methylprednisolone injection on post-operative sequelae after third molar surgery in a randomized double blind manner**

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**Abstract**---Background: Postoperative oedema is a consequence of tissue injury during surgery and the raising of muscular attachments, and appears as a result of direct trauma to blood and lymph vessels. Postoperative pain is a common phenomenon after surgery, due to surgical trauma and the release of pain mediators. After surgical extraction of impacted lower third molars, the pain is most intense 3-5 hours following extraction, just after the cessation of local anesthesia. Several methods of controlling the immediate inflammatory response associated with the third molar surgery abound in the literature. Aim of the study: To compare the effect of submucosal dexamethasone and methylprednisolone injection on post-operative sequelae after third molar surgery in a randomized double blind manner. Materials and methods: 45 Subjects for the present study were selected and divided into 3 groups of 15 patients each (group I- submucosal dexamethasone, group II sub-mucosal methylprednisolone, group III – submucosal placebo, normal saline) from amongst the patients who reported to OPD, at random basis irrespective of side, age, caste, creed, gender and socioeconomic status. Study was carried out in those patients who required surgical removal of impacted mandibular 3rd molars. Results: It was observed that 53 patients belonged to age group of 18-28 years, 32 patients belonged to 29-38 years, and 5 patients belonged to 29-48 years. Group 1 and group 2 shows

significant reduction in pain score throughout the follow up period as compared to group 3. Whereas, there is no statistically significant difference between group 1 and group 2. Conclusion: Within the limitations of the present study, it can be concluded that pain control was better in patients who received either dexamethasone or methylprednisolone, and also the consumption of analgesics and/or rescue tablets was significantly reduced.

**Keywords**---pain control, third molar, dexamethasone, methylprednisolone.

## **Introduction**

The surgical extraction of lower third molars is the most frequent intervention in oral surgery. It is an invasive procedure that involves extensive tissue trauma and a considerable postoperative inflammatory response. Although the inflammatory process is necessary for healing, when exacerbated, patients frequently complain of pain, swelling and limitation in mouth opening following the surgical injury<sup>1, 2</sup>. Reduction of postsurgical complications from exodontia is an area of concern to all practicing oral and maxillofacial surgeons, as well as their patients.

Postoperative oedema is a consequence of tissue injury during surgery and the raising of muscular attachments, and appears as a result of direct trauma to blood and lymph vessels. This condition represents fluid accumulation in the interstitial area due to transudation from injured blood vessels and fibrin obstruction of lymph drainage. The size of the oedema depends on the extent of tissue injury and looseness of the connective tissue. Oedema is usually maximal 12–48 h after surgery, but may completely resolve in 5–7 day.<sup>3</sup> Postoperative pain is a common phenomenon after surgery, due to surgical trauma and the release of pain mediators. After surgical extraction of impacted lower third molars, the pain is most intense 3–5 hours following extraction, just after the cessation of local anesthesia.<sup>4</sup> Trismus is defined as a limitation in maximum oral aperture, and constitutes an important postoperative complication caused by the edema and swelling associated to surgical trauma. Trismus is also partially associated to postoperative pain, and is more intense on the first day after surgery<sup>5</sup>. All three phenomena (pain, swelling, and trismus) may reflect the formation of prostaglandins and other mediators of pain and swelling from membrane phospholipids released as a result of surgery.<sup>6</sup>

Several methods of controlling the immediate inflammatory response associated with the third molar surgery abound in the literature. These include different surgical closure techniques (with or without incorporation of drains, primary closure), various flap designs, various pharmacological agents (NSAIDs, Steroids, enzymes) other modalities (cold applications, ozone therapy).<sup>7</sup> With regard to the pharmacological approach, there are various strategies for minimizing the clinical manifestations after surgery by inhibiting the synthesis and/or release of the inflammatory mediators of acute inflammation. A reduced level of mediators at the site of tissue injury will lessen the increase in vascular permeability. As a result, interstitial fluid accumulation and tissue pressure will be decreased.

For 60 years non-steroidal anti-inflammatory drugs (NSAIDs), various steroids, enzymes, and antihistamines have been used to reduce postoperative complications.<sup>8</sup> Non-steroidal anti-inflammatory drugs are often recommended after surgical extraction of impacted lower third molars to abolish postoperative pain, but some of them may manifest side effects such as gastrointestinal irritation, systemic bleeding tendency, and allergic reactions. Enzyme therapy found to be effective but patient compliance with lengthy drug regimen can be an issue. Corticosteroids have an inhibitory action on the enzyme phospholipase A2, which reduces the release of arachidonic acid at the site of inflammation. These anti-inflammatory effects of steroids are the basis for their clinical utility.<sup>9</sup> Various corticosteroids such as betamethasone, triamcinolone, prednisolone, hydrocortisone, dexamethasone, methylprednisolone, etc., are prescribed to control post-operative sequelae. In choosing an agent best suited for mandibular third molar surgery, one would desire a steroid with minimal mineralocorticoid activity that maintains a therapeutic plasma level throughout the immediate postoperative period (when the acute inflammatory reaction is most intense. Methylprednisolone and dexamethasone fulfill both the criteria.<sup>10</sup> Hence, the present study was conducted to compare the effect of submucosal dexamethasone and methylprednisolone injection on post-operative sequelae after third molar surgery in a randomized double blind manner.

### **Materials and Methods**

Approval of ethical committee was taken prior to the study. 45 Subjects for the present study were selected and divided into 3 groups of 15 patients each (group I- submucosal dexamethasone, group II sub-mucosal methylprednisolone, group III – submucosal placebo, normal saline) from amongst the patients who reported to OPD, at random basis irrespective of side, age, caste, creed, gender and socioeconomic status. Study was carried out in those patients who required surgical removal of impacted mandibular 3rd molars. Necessary laboratory investigations, radiographic investigation and assessment (IOPA and /or OPG) and clinical assessment in terms of pain, swelling and mouth opening were carried out pre-operatively. Post-operatively clinical evaluation was done at 1st, 3rd and 7th day post operatively.<sup>11</sup>

### **Inclusion Criteria**

- Patients belonging to ASA class I and II.
- Patients who agreed to be a part of study protocol.

### **Exclusion Criteria**

- ASA class III and IV.
- Presence of oral sepsis, Pregnancy threatened cases.
- Irradiated mandible/jaw.
- Patients with known allergy to drugs to be used in the study (e.g. inj. Xylocain, inj. Augmentin and tab Crocin )

Written informed consent was taken from all the patients prior to inclusion in the study. In all patients IOPA or OPG were taken. Note was made regarding difficulty

index using Pederson's difficulty index. To ensure that the patient and the surgeon were unaware of the drug to be administered, the corticosteroid and saline injection were covered and coded as "patient no." by the nurse/ auxiliary, which was revealed at the end of the study. Patients were divided randomly into Group I, Group II, and Group III in a double blind manner.

- Group I – 1 ml Sub-mucosal injection of 4mg Dexamethasone solution in vicinity of tooth to be removed 10 minutes prior to surgery.
- Group II – 0.5 ml Sub-mucosal injection of 20 mg Methylprednisolone solution in vicinity of tooth to be removed 10 minutes prior to surgery.
- Group III – 1 ml of normal saline as placebo in vicinity of tooth to be removed 10 minutes prior to surgery.

Both the operating surgeon and the patient were blind to the group to which patient belongs. Post-operative observations were done by an unbiased observer.

### **Post-operative Assessment**

Assessment included clinical evaluation of the following parameters:

- Pain
- Facial swelling
- Trismus

Normality of the data was tested using Kolmogorov-Smirnov and Shapiro-Wilk test and data was found to be normally distributed, so parametric tests like repeated measure ANOVA, post-hoc tests were applied to compare all the parameters. Proportions were compared using chi-square test, evaluation and results of which are as follows the data was interpreted at confidence interval of 95% and the levels of significance were as follows

- $p > 0.01$ ; not significant
- $*p < 0.05$ ; significant
- $**p < 0.001$ ; highly significant

### **Results**

Table 1 shows the age wise distribution of patients. It was observed that 53 patients belonged to age group of 18-28 years, 32 patients belonged to 29-38 years, and 5 patients belonged to 29-48 years. Table 2 shows the results of mean and standard deviation of the change in VAS- Score from the pre-operative day to the subsequent 1st, 3rd and 7th post-operative day and the p- value of significance between each group. Group 1 and group 2 shows significant reduction in pain score throughout the follow up period as compared to group 3. Whereas, there is no statistically significant difference between group 1 and group 2. Table 3 represents the mean and standard deviation of number of analgesic tablets taken by the patient post- operatively to post-operative day 1, from post-operative day 1 to post-operative day 3, from post-operative day 3 to post-operative day 7. Patients falling within Group 1 and group 2 demonstrated lesser

need for analgesics as compared to group 3. Table 4 represents analysis and comparison of mean and standard deviation number of rescue tablets taken by the patient post-operatively when not relieved of pain from analgesic tablet in each group and the p- value of significance between each group. Similar to trends of analgesic tablet consumption rescue tablets were consumed in more quantity by group 3.

Table 1: Age Wise Distribution of Patients

Age –group (in years)	No. of Patients (n)
18-28	53 (59%)
29-38	32 (36%)
29-48	5 (5%)
Total	90

Table 2: Analysis and comparison of Pain (VAS- Score)

VAS- Score	Group 1	Group 2	Group 3	p value		
				1 v/s 2	1 v/s 3	2 v/s 3
Pre- Op	3.2 ± 2.1	3.97 ± 2.9	3.23 ± 2.6	0.24	0.74	0.35
Post-op Day 1	2 ± 1.7	1.87 ± 1.9	4.67 ± 1.7	0.53	0.00	0.00
Post-op Day 3	0.83 ± 1.44	0.57 ± 1.16	3.37 ± 1.56	0.40	0.00	0.00
Post-op Day 7	0.1 ± 0.31	0.13 ± 0.571	1.77 ± 1.04	0.67	0.00	0.00

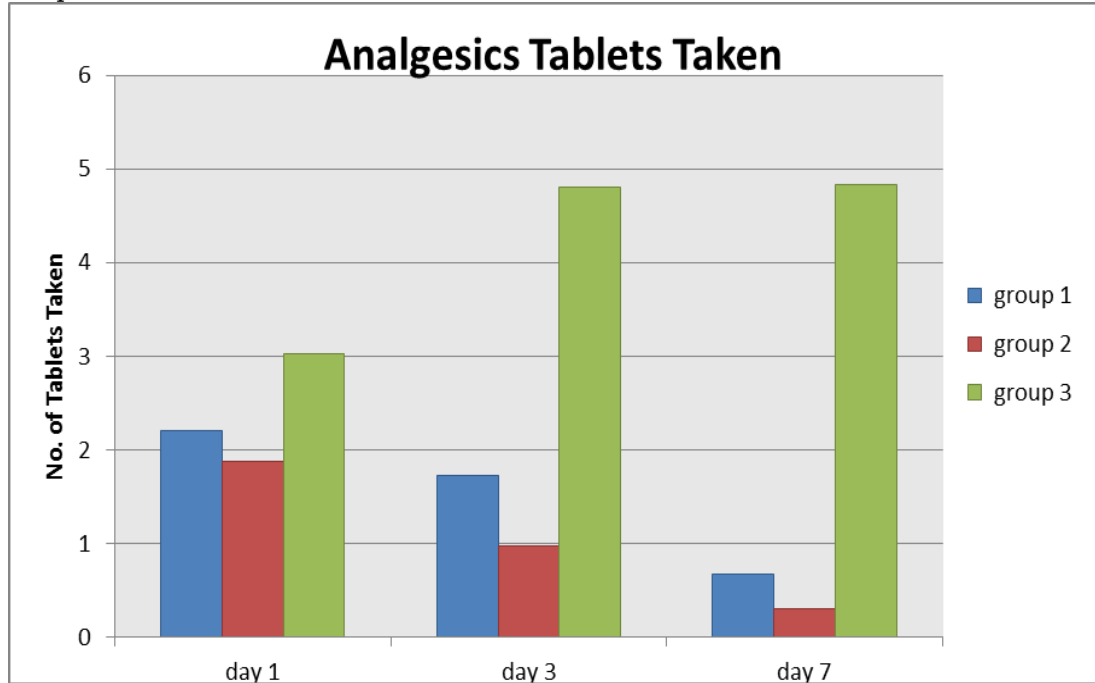
Chi- square test \*\*p<0.001; highly significant

Table 3: Analysis of Analgesics Consumed

Tablets taken	Group 1	Group 2	Group 3	P value		
				1 v/s 2	1 v/s 3	2 v/s 3
Till post-op day 1	2.2 ± 0.84	1.87 ± 0.77	3.03 ± 0.55	0.17	0	0
From post-op day 1 to day 3	1.73 ± 1.36	0.97 ± 0.85	4.8 ± 1.4	0.018	0	0
From post-op day 3 to day 7	0.67 ± 1.2	0.3 ± 0.6	4.83 ± 2.66	0.322	0	0

Chi- square test \*\*p<0.001; highly significant

Graph 1



The graph represents comparison between group 1, 2 & 3 in terms of analgesic tablets taken throughout post-op period

Table 4: Analysis of Rescue Tablets Consumed

	Group 1	Group 2	Group 3	P value		
				1 v/s 2	1 v/s 3	2 v/s 3
Mean no. of RESCUE TABLETS	0.43 ± 0.81	0.23 ± 0.50	2.97 ± 1.4	0.441	0	0

Chi- square test \*\*p<0.001; highly significant

### Discussion

The lower third molar is the most common impacted tooth in oral cavity since it accounts for 40% of the total impacted tooth reported<sup>5</sup>. Its surgical removal is one of the most frequent interventions done in dental clinic. When body tissue is injured regardless of the cause, the normal physiologic response is inflammation as a part of healing process. Since the region of surgery is mostly composed of loose connective tissue that contains blood and lymph vessels, a series of functional and structural alterations is expected after extraction, mostly expressed as pain, swelling and trismus. These expected sequelae influence the patient's Quality of Life in the immediate postoperative<sup>5, 11</sup>. There is also considerable variation from patient to patient in occurrence and relative severity of the inflammatory response<sup>12</sup>. The purpose of this study was to clinically evaluate and compare the effect of single sub-mucosal injection of

Dexamethasone (4mg/ml) and Methylprednisolone (20mg/0.5ml) in mandibular third molar surgery in terms of effect on pain in a clinically controlled, randomized and double blind manner. Pain is a symptom commonly expected after surgery and may vary considerably, according to surgical difficulty and individual pain thresholds. Following third molar extraction, the pain intensity peaks after 3–5 h and the pain continues for 2–3 days postoperatively, gradually diminishing by the seventh postoperative day<sup>13</sup>. Similar trends of pain intensity was observed in control group (Group-3) but patients in study groups i.e. dexamethasone (group 1) and methylprednisolone (group 2) showed significantly lower pain intensity throughout the post-operative days as compared to control. Although there was no statistically significant difference in between both the study groups. Omer Waleed Majid (2011)<sup>11</sup> compared the effect of postoperative intra-muscular dose for 4mg of dexamethasone, post-operative sub-mucosal dose for 4mg of dexamethasone and control (no steroids). They evaluated effects on patient's quality of life and pain swelling and trismus following lower third molar surgery Both dexamethasone groups showed a significant reduction in swelling and pain compared with the control group at all intervals. On comparison the effect of the 2 routes of dexamethasone was statistically non-significant for all parameters. Similarly in present study post-operative pain values were evaluated by VAS-Score and the results showed significant lower score in dexamethasone and methylprednisolone group as compared to control group. F. Graziani, F. D'Aiuto et al (2005)<sup>14</sup> studied the effect of endo-alveolar powder (10mg) and sub-mucosal injection (4mg) of dexamethasone sodium phosphate to prevent inflammatory sequelae after surgical removal of lower third molars. They stated that acute postoperative pain following third molar extraction is predominantly a consequence of inflammation caused by tissue injury. They suggested that although corticosteroids alone do not seem to have a clinically significant analgesic effect but steroids can be related to a reduction in the number of analgesic tablets consumed after surgical extractions. Similar findings were observed in present study, as in control group (group 3) number of analgesics and rescue tablets taken were higher when compared to dexamethasone (group 1) and methylprednisolone group (group 3).

Majid OW et al<sup>15</sup> compared the effects of post-operative dexamethasone sub-mucosal injection of 4mg, dexamethasone intramuscular injection of 4mg and control (no steroid). They reported significantly less pain at all evaluation times in both the intramuscular and sub-mucosal group compared with controls. They suggested that if we increase the dose of dexamethasone we can achieve clinically effective analgesia. However, Grossi GB et al<sup>2</sup> conducted a study to compare the effect of two different dosages (4mg and 8mg) of dexamethasone given submucosally after onset of anesthesia. They suggested that increasing the dose of dexamethasone to 8mg provided no further benefit than 4mg dose in pain control, evaluated in terms of number of analgesic tablets taken. In present study dose of dexamethasone was given sub-mucosally 4mg after onset of local anesthesia which provided significant lower VAS scores and lesser number of analgesic and rescue tablets taken as compared to control group.

Ustun et al<sup>16</sup> compared the effects of preoperative intravenous administration of 1.5 mg/kg and 3 mg/kg of methylprednisolone sodium succinate (MP) on post-operative inflammatory sequelae of third molar surgery. They concluded that

there was no clinical benefit of higher dosage of methylprednisolone in terms of pain control, swelling and trismus. In my study a dosage of 20mg of methylprednisolone was used and similarly significant reduction in terms of pain was observed in study group (group 1 and group 2) as compared to control (group 3). Ibrahim S. Gataa <sup>12</sup> compared the efficacy of preoperative oral administration of 10 mg methylprednisolone tablet, local administration of MP (10 mg) and control group, receiving no drug. They observed no significant effect of methylprednisolone preoperative given by any route on pain control. They stated that low dose of 10 mg is the reason of less effect on pain. In my study we used 20 mg of MP and got significant reduction in pain score as compared to control which is in concurrence with other studies which used higher dosages (40mg, 80mg and 125mg)<sup>19, 63, 68</sup> and showed similar results. Emin Esen et al <sup>17</sup> compared the effects of single pre-operative dose of 125 mg (intravenous) with control on post-operative sequelae of third molar surgery. They observed significant lower mean of number of analgesic tablets taken by the patient ( $1.70 \pm 0.21$ ) as compared to the control group on first postoperative day. Results of this study are similar to the present study as up to first post – operative day patients in methylprednisolone group (group 2 ) mean number of analgesics (paracetamol 750mg) taken ( $1.87 \pm 0.77$  ) were also significantly less than control group (group 3) ( $3.03 \pm 0.55$ ). Also mean number of rescue tablets (Diclofenac 50mg) taken by methylprednisolone group (group 2) were ( $0.23 \pm 0.50$ ) significantly less than control group (group 3) ( $2.97 \pm 1.4$ ).

## Conclusion

Within the limitations of the present study, it can be concluded that pain control was better in patients who received either dexamethasone or methylprednisolone, and also the consumption of analgesics and/or rescue tablets was significantly reduced.

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