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# "EFFECT OF SUBMUCOSAL AND INTRAMUSCULAR DEXAMETHASONE ON POSTOPERATIVE SEQUELAE AFTER THIRD MOLAR SURGERY - A COMPARATIVE STUDY"

**Maxillofacial Surgery**

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## ABSTRACT

**Purpose:** This prospective comparative study was undertaken to evaluate the efficacy of sub-mucosal and intramuscular administration of Dexamethasone injection immediately after the third molar surgery and compare parameters of swelling, trismus and pain between the three groups. **Materials and Methods:** 150 patients were selected and allocated into 3 groups. Group I- Submucosal Dexamethasone (8mg) injection, Group II- Intramuscular (Deltoid muscle) Dexamethasone (8mg) injection were administered immediate post-operatively and Group III- Control group were not administered any steroid. Parameters were evaluated pre-operatively and on the 2nd & 7th days. **Results:** Significant difference noted between submucosal and intramuscular group, both in postoperative swelling and pain, but there is no statistically significant difference in measurement of trismus (P value 0.036 and 0.041respectively) noted. Also number of rescue analgesic tablets taken at each interval also differed significantly. The two dexamethasone groups differed significantly from controls at all time intervals ($p < 0.05$). **Conclusion:** Submucosal Dexamethasone showed higher efficacy compared to intramuscular dexamethasone & control group in reducing the postoperative inflammatory sequelae in the surgical removal of impacted lower third molar teeth. Finding of this study has a significant clinical impact.

## KEYWORDS

impaction, dexamethasone, third molars, submucosal, intramuscular

## INTRODUCTION

The surgical extraction of lower third molars is the most frequent intervention in oral surgery and often associated with significant post-surgical sequelae that may have both a biological and social impact. Besides severe complications such as dysesthesia, severe infection, fracture and dry socket, patients frequently complain of pain, swelling and limitation in mouth opening due to the inflammatory response following the surgical injury[1,2,3].

The quality of life after lower third molar surgery is affected three times more in patients due to pain, swelling and trismus alone or in combinations compared to those who were asymptomatic[4]. Although after third molar removal, the overall complications rate is low and are minor, even those minor complications may be significant[1]. Inflammatory response as a result of surgical trauma to soft tissues and bone, induced in oral surgical procedures is a normally expected natural phenomenon and is pre requisite for the subsequent healing process[5], however more pronounced reaction causes delayed healing. The formation of postoperative oedema, its complexities and control has been the subject of interest and scientific enthusiasm to oral surgeons.

The effectiveness of glucocorticoids as anti-inflammatory agents was first reported by Hench & Kendall in 1949[7,8]. Since this initial discovery, these agents have been used in more than 50 clinical conditions with inflammatory and allergic manifestations. Dexamethasone exerts basic glucocorticoid action and is apparently 25 times more potent than hydrocortisone[10], 6 times more potent than prednisolone, 4 times more potent than triamcinolone and equipotent to betamethasone[5,11]. At equipotent and anti- inflammatory dose it essentially lacks sodium retaining properties[10]. Dexamethasone has been used extensively in oral surgery due to its high potency and half-life. Several different routes and time of administration (eg. IV, IM, pre-operative and post-operative) have been advocated. The normal hormonal effects associated with prolonged steroid therapy are essentially absent with single steroid injection.

This prospective comparative study was undertaken to evaluate the efficacy of submucosal and intramuscular dexamethasone injection on post-operative sequelae after mandibular third molar surgery.

## MATERIALS AND METHODS:

Patients reporting to the Department of Oral & Maxillofacial Surgery, Meghna Institute of Dental Sciences, Nizamabad for the removal of impacted mandibular third molars.

"This study was approved by the _Meghna Institute of Dental Sciences, Nizamabad IEC APPROVAL NUMBER 2013-2__ Hospital IRB and all participants signed an informed consent agreement"

Three groups were created with below criteria:
**Group I** - Submucosal Dexamethasone (8mg) injection administered immediate post-operatively.

**Group II**- Intramuscular (Deltoid muscle) dexamethasone (8mg) injection administered immediate post-operatively.

**Group III**- Control group were not administered any steroid.

Each group contains 50 patients and age range from 18 and above. According to Pell and Gregory classification system class II and class III & position A, B and position C impactions requiring ostectomy and odontectomy procedure were selected for this study.

Patients were subjected to a thorough evaluation of their history, clinical examination, blood investigations and radiographs. 150 patients were selected and allocated to each group equally by randomization procedure irrespective of age and sex who were free of caries, extensive periodontal disease and other inflammatory symptoms at the time of operation[33].

**Exclusion criteria[33]:**

- History of immunocompromise.
- History of allergy to the drug used.
- Recent use of any anti-inflammatory drugs or antibiotics.
- Long-term use of any drug.
- Pregnancy or lactation.
- Those who refused to take part in the study.
- Those who used other drugs during the observation period.

## METHODOLOGY:

**Pre-operative assessment:**

By evaluation of third molar position by panoramic radiograph and intra-oral periapical radiograph using Pell and Gregory classification and after patient consent, baseline data recorded at the initial visit and post-surgery days 2nd and 7th by a single clinical evaluation[4].

**Swelling:**
Facial swelling was determined by a modification of tape measuring method by Gabka & Matsumara using 4 reference points & 2measurements[4,11,42], from pogonion to lower end of auricle lobe anterioposteriorly and lateral canthus to angle of mandible superoinferiorly with reference points: S1- pogonion, S2-lower part of auricle lobe, S3- lateral canthus and S4- angle of mandible. The pre-operative measurements were considered as the baseline data of that side. Facial measurement[2] was calculated as horizontal measure plus vertical measure divided by 2. [Figure 1]

**Pain:** It was measured using a visual analogue scale (VAS).

**Trismus:** Inter-incisal distance was measured in millimetres with the help of calibrated scale between maxillary and mandibular central incisors in maximum mouth opening. In the absence of any of these two teeth, adjacent teeth were taken into consideration. [Figure 2]

These parameters were assessed at baseline and on 2nd and 7th postoperative days by the same operator.

Data were depicted as mean values and standard deviation. ANOVA was used to compare the differences among the three groups.

**Operative technique:**
All patients were comfortably seated on dental chair in semi reclined position, standard draping procedure and sterilization protocol was followed. In all the patients, anesthesia was secured with 2% lignocaine hydrochloride with 1:80000 adrenaline through inferior alveolar nerve block, lingual nerve block and long buccal nerve block. Standard Terence Wards incision was given, mucoperiosteal flap was reflected and bone removal was done using a rotary bur (round bur and straight fissure bur) under constant irrigation of normal saline to create a "gutter" along the buccal side and distal surface of the tooth. Sectioning of tooth was done and removed.

In group I patients, 8mg of dexamethasone was injected submucosal and in group II intramuscular (deltoid muscle) 8mg of dexamethasone was injected immediately post-operatively. Postoperative medication included , amoxicillin 500mg every 8h orally for 5 days and aceclofenac100mg + paracetamol 500mg + seratiopeptidase 15mg every 12 h orally. Duration of surgery was noted.

**RESULTS:**
The study included 150 patients, in which were 81 men and 69 women, mean (SD) age 26.43±6.10years, range 20–38. In Submucosal group, 23 patients are males and 27 are females. In Intramuscular group, 28 patients are males and 22 patients are females. In control group, 30 patients are males and 20 patients are females. There were no statistically significant differences in age and sex among the groups as shown in Table 1. No cases of alveolar osteitis or wound infection were reported at follow up.

**Assessment of swelling, pain and trismus:**
There was a significant increase in swelling on the 2nd post-operative day ($p < 0.05$) but not on the seventh day ($p = 0.06$) when compared preoperatively with control group. However, there was no significant difference in the magnitude of swelling in either dexamethasone group at any interval, although both showed highly significant reductions in swelling compared with the control group ($p < 0.05$) [Table 2].

Preoperative, there was no significant difference between the groups with regard to reduction in mouth opening whereas on the 2nd postoperative day the mean maximum mouth opening scores were lower in control than dexamethasone group ($p < 0.05$) [Table 3]. The mean pain score from 2nd to 7th day was significantly lower in case of dexamethasone groups than control ($p < 0.05$) [Table 4].

The two dexamethasone groups differed significantly from controls at all time intervals ($p < 0.05$), except for the intramuscular group on day 1. The accumulated number of rescue analgesic tablets taken at each interval also differed significantly between the dexamethasone and the control groups ($p < 0.05$). No patient took analgesics after day 7.

Significant difference noted between submucosal and intramuscular group, both in postoperative swelling and pain, but there is no statistically significant difference in measurement of trismus (P value 0.036 and 0.041respectively) noted. Also number of rescue analgesic tablets taken at each interval also differed significantly between the submucosal and intramuscular group [Table 5].

## DISCUSSION

**Orofacial Postsurgical Edema**
Surprisingly, some dentists consider edema a complication rather than a normal physiologic reaction to insult and injury[1]. Prostaglandins also might play a minor role in edema formation but do not appear to be the sole factor involved[44]. In most cases, greater degrees of tissue injury lead to greater amounts of edema[44]. Hupp[44] also notes that edema is variable from area to area and will accumulate more freely in areas of loose connective tissues, whereas tissues that are tightly bound down to underlying structures tend to have less swelling. Surgical experience and difficulty are recognized as significant factors in the incidence and severity of postoperative complications (including edema) after dentoalveolar surgery[43]. Laskin[45] states that edema maximizes in 24 to 48 hours, but Peterson[43] says it usually maximizes in 48 to 72 hours and is usually resolved after the first postoperative week. Any postoperative swelling that continues to expand after 3 days is thought to be additional swelling resulting from infection and is not postoperative edema[46].

**Trismus And Pain**
Trismus is defined as a limitation in maximum oral aperture, and constitutes an important postoperative complication caused by the edema and swelling associated with surgical trauma. Trismus is also partially associated to postoperative pain, and is more intense on the first day after surgery – with a mean reduction in oral aperture of 24.1%. A multicenter study found the symptoms to be more notorious during the first two days, followed by gradual improvement and resolution one week after the operation – though the condition may persist for up to 10 days after surgery.

Corticosteroids are not indicated for routine use. Rather, they should be used for more complex oral surgical procedure in which trauma is categorized as moderate to severe. Oral surgical procedures involving the removal of at least 1 partial bony or full bony impacted third molar tooth falls into this category, as do long surgical procedures which create a considerable amount of soft and hard tissue trauma. Perioperative use of corticosteroids is a pharmacological approach often used for reduction of oedema, trismus, and pain after removal of impacted mandibular third molars[1,15,33]. Corticosteroids such as dexamethasone and methylprednisolone have been used extensively in dentoalveolar surgery due to their nearly pure glucocorticoid effects, virtually no mineralcorticoid effects, and the least adverse effects on leukocyte chemotaxis[15,43]. Numerous papers have supported their systemic use in third molar surgery [2-8,14-41]. Recently, Riaz Warraich et al[40], studied on 106 patients who were randomly allocated in 2 groups with 53 patients allocated in each group for intervention, submucosal injection of dexamethasone was given in one group and the other group is control. Results showed mean facial swelling score was significantly less in those patients who were treated with dexamethasone than control, median pain score from 2nd to 10th day was significantly lower in case than control.

Few studies have objectively evaluated the effect of dexamethasone as an intramuscular injection in third molar surgery, although this route is the one most likely to be used when a steroid injection is prescribed in outpatients. Intramuscular dosing studies have suggested that this route can be effective if a single dose is given either preoperatively or postoperatively[15]. Different studies have used this route for third molar surgery and reported variable results[10]; the effect may be dose-dependent. Some authors suggested using dexamethasone 8–12 mg for the best results. In our study intramuscular dexamethasone resulted in significant reduction in swelling on postoperative 2nd day and significant reduction in pain scores, but had no significant effect on trismus compared with submucosal group and controls. The submucosal injection of dexamethasone has been reported to have a significant effect on oedema in previous studies, both of which reported a significant reduction in oedema in the immediate postoperative period compared with controls, but only a limited effect on trismus. We found that submucosal dexamethasone was associated with a significant reduction in swelling on 2nd day postoperatively compared with intramuscular group and controls, which agrees with the previous studies. These results add more strength to the concept that dexamethasone injected locally near the site of operation in a sub-therapeutic dose (4-8mg) is a valuable way to reduce edema as in our patients may have been the result of the higher concentration of

dexamethasone achieved immediately at the site of injury. Further research, however, is needed to confirm these results. Unlike previous studies, our patients reported significantly less pain at all evaluation times in the submucosal group compared with controls. Both dexamethasone groups were associated with a significant reduction in the amounts of swelling and pain, and submucosal dexamethasone had a significant effect on swelling, but the effects in the two groups were comparable for all variables. Omer Waleed Majid et al[33] conducted randomised prospective clinical trial on 30 patients, each of whom required removal of a single impacted mandibular third molar divided into 3 groups of 10 each: 2 experimental groups were given dexamethasone 4mg submucosal or intramuscularly, and the control group had no steroid. He found that submucosal dexamethasone was associated with a significant reduction in swelling on days 1 and 3 postoperatively compared with controls. These results add more strength to the concept that dexamethasone injected locally near the site of operation in a sub therapeutic dose (4 mg) is a valuable way to reduce oedema in these patients. An interesting finding was the significant reduction of trismus on day 1, which may have been the result of the higher concentration of dexamethasone achieved immediately at the site of injury. It has also been reported that steroids can be related to a reduction in the number of analgesic tablets used after extractions, which was proved in our study as well. In our study one patient had side effect of dexamethasone, transient hiccups which was subsided within 24 hours. Mark E. Peacock[47] reported a case and reviewed few reports in the literature on dexamethasone induced hiccups and none in the dental literature. Other cases of corticosteroid-induced hiccups have been reported and Dickerman et al. have described the first cases of anabolic steroid-induced hiccups. The only other adverse reaction to steroids found in the dental literature was a case of episodic psychiatric disturbance (cognitive dysfunction) in an 18-year-old female who had taken dexamethasone briefly. Souadjian and Cain[47] reviewed 220 cases of protracted hiccups and did not mention any medication in the etiology of hiccups. Garvey, who looked at postoperative cases of hiccups, came to the logical conclusion that the etiologic factor was probably drug related. Possibly associated with triggering hiccups: steroids (dexamethasone, methylprednisolone, oxandrolone, and progesterone), benzodiazepines (midazolam, lormetazepam, and lorazepam), barbiturates (methohexital), antibiotics (azithromycin), Phenothiazines (perphenazine), opioids (hydrocodone) and alcohol.

Overall, the comparable results obtained show that submucosal dexamethasone is an effective alternative to dexamethasone given systemically. The expertise of the surgeon, the discomfort caused to the patient, and the need for specific tools to give the drug are factors that may limit the use of the intramuscular route. In addition, the rate of absorption is highly dependent on the blood flow to the site. Submucosal dexamethasone, on the other hand, is quite simple, less invasive, painless, convenient for the surgeon and the patient, and offers a low-cost solution for the typical discomfort associated with the extraction of impacted lower third molars. Postoperative injection offers the advantage of concentrating the drug near the surgical area with less systemic absorption and no further manipulation of the tissues. This timing also allows the surgeon to assess the need for injected steroid accurately, according to postoperatively recorded surgical difficulty and duration of the intervention.

## CONCLUSION:

Submucosal dexamethasone is an effective alternative to dexamethasone given systemically. The expertise of the surgeon and the discomfort caused to the patient are factors that may limit the use of the intramuscular route. In addition, the rate of absorption is highly dependent on the blood flow to the site. Submucosal dexamethasone, on the other hand, is quite simple, less invasive, painless (as site is anesthetized), convenient for the surgeon and the patient, and offers a low-cost solution for the typical discomfort associated with the extraction of impacted lower third molars.

Postoperative injection offers the advantage of concentrating the drug near the surgical area with less systemic absorption and no further manipulation of the tissues. This timing also allows the surgeon to assess the need for injected steroid accurately, according to postoperatively recorded surgical difficulty and duration of the intervention.

## Conflict of Interest:

The authors declare that they had no conflict of interest.

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This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

## Results:

**Table-1: Demographic data of patients undergoing treatment in three groups.**

| Parameters | | Groups | | |
|---|---|---|---|---|
| | | Submucosal | Intramuscular | Control |
| Mean Age±SD | | 27.44±3.45 | 30.6±2.93 | 31.86±4.92 |
| Gender | Male | 23 | 28 | 30 |
| | Female | 27 | 22 | 20 |
| Position | A | 25 | 22 | 26 |
| | B | 20 | 23 | 24 |
| | C | 5 | 5 | 0 |
| Relation | II | 45 | 50 | 42 |
| | III | 5 | 0 | 8 |
| Duration of operation (min) | | 37.52±5.69 | 38.84±4.15 | 39.7±4.86 |
| Mean BMI | | 22.10±1.85 | 25.18±1.94 | 25.21±3.34 |

**Table 2: Comparison of Value of difference in swelling measurements at different time periods with pre-operative measurements in all the three groups.**

| S.no | Submucosal group | | Intramuscular group | | Control group | |
|---|---|---|---|---|---|---|
| | Mean | S D | Mean | S D | Mean | S D |
| Post op 2nd day | 3.00 | 1.548 | 4.38 | 1.416 | 5.17 | 1.615 |
| Post op 7th day | 0.82 | 0.825 | 2.25 | 1.790 | 3.04 | 1.147 |
| Overall | 1.91 | 1.046 | 3.32 | 1.553 | 4.11 | 1.187 |
| P value | 0.03 | | 0.719 | | 0.093 | |
| Level of significance | HS | | NS | | NS | |

**Table 3: Comparison of value of difference of trismus at different time periods with pre-operative measurements in all the three groups**

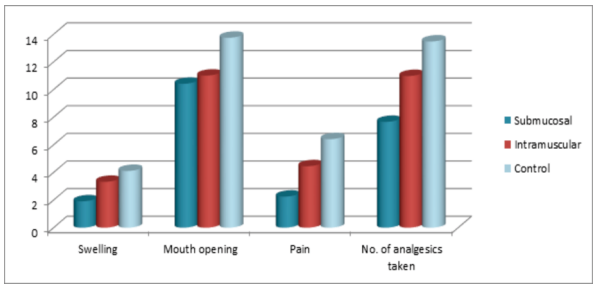
| S.no | Submucosal group | | Intramuscular group | | Control group | |
|---|---|---|---|---|---|---|
| | Mean | S D | Mean | S D | Mean | S D |
| Post op 2nd day | 16.52 | 6.686 | 17.02 | 7.328 | 17.30 | 8.958 |
| Post op 7th day | 4.32 | 4.147 | 5.80 | 5.107 | 10.20 | 10.1 |
| Overall | 10.42 | 4.281 | 11.01 | 5.085 | 13.75 | 7.570 |
| P value | 0.036 | | 0.041 | | 0.364 | |
| Level of significance | HS | | HS | | NS | |

**Table 4: Comparison of value of difference in pain measurements at different time periods with pre-operative measurements in all the three groups.**

| S.no | Submucosal group | | Intramuscular group | | Control group | |
|---|---|---|---|---|---|---|
| | Mean | S D | Mean | S D | Mean | S D |
| Post op 2nd day | 3.26 | 0.633 | 6.100 | 1.165 | 8.04 | 1.818 |
| Post op 7th day | 1.24 | 0.624 | 2.80 | 0.857 | 5.08 | 0.695 |
| Overall | 2.25 | 0.546 | 4.45 | 0.938 | 6.41 | 1.399 |
| P value | 0.024 | | 0.429 | | 0.730 | |
| Level of significance | HS | | NS | | NS | |

**Table 5: Clinical parameters based on mean difference among submucosal, intramuscular and control groups.**

| CLINICAL PARAMETERS BASED ON MEAN DIFFERENCE | | | |
|---|---|---|---|
| Parameters | GROUPS | | |
| | Submucosal | Intramuscular | Control |
| Swelling | 1.91±1.046 | 3.32±1.553 | 4.11±1.187 |
| Trismus | 10.42±4.281 | 11.01±5.085 | 13.75±7.570 |
| Pain | 2.25±0.546 | 4.45±0.938 | 6.41±1.399 |
| No. of analgesics taken | 7.66±0.99 | 10.98±0.84 | 13.48±0.89 |




**Graph 1: Clinical parameters based on mean difference among submucosal, intramuscular and control groups.**

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