

## Original Article

# Efficacy of Use of Single Dose Submucosal Injection of Dexamethasone in Impacted Mandibular Third Molar Surgery

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### ABSTRACT:

**Purpose:** The purpose of this preliminary randomized prospective clinical trial was to evaluate and compare the effect of single dose perioperative administration of dexamethasone sodium phosphate by submucosal and intramuscular route on postoperative discomfort after mandibular third molar surgery. **Materials and Methods:** This is a prospective randomized clinical trial. We prospectively evaluated 40 patients requiring surgical removal of single mandibular impacted third molar under local anesthesia by randomly allocating them to three groups: submucosal dexamethasone group, intramuscular dexamethasone group and no dexamethasone (control) after onset of local anesthesia. Maximum inter-incisal distance and facial contours were measured at baseline and at post surgery days 2, 5 and 7. Subjects completed a questionnaire assessing postoperative pain intensity using Visual Analogue Scale. **Results:** On 2<sup>nd</sup> postoperative day facial edema showed a significant reduction in submucosal group as compared with the intramuscular and control group. On 5<sup>th</sup> postoperative day, there was no significant change between the submucosal and intramuscular group, but both groups showed significant difference in comparison to control group. There was no significant difference in edema on the 7<sup>th</sup> postoperative day between all the three groups. The submucosal group had a limited and nonsignificant affect on pain when compared with intramuscular group on 2<sup>nd</sup> postoperative day but showed a marked reduction in pain on 5<sup>th</sup> postoperative day when compared with intramuscular group and control group. On 7<sup>th</sup> postoperative day there was non-significant affect on pain between submucosal and intramuscular groups. The comparison of mean value of trismus on 2<sup>nd</sup> and 5<sup>th</sup> postoperative days between submucosal and intramuscular groups is significant, showing less decrease in interincisal opening in submucosal group. On the 7<sup>th</sup> postoperative day the mean value of trismus in all the three groups is non-significant. **Conclusions:** Parenteral use of dexamethasone 8mg as a single submucosal injection at site of surgery peri-operatively is effective in the reduction of postoperative sequelae in terms of pain, swelling and edema after mandibular impacted third molar surgery.

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**This article may be cited as:** Sahore M, Parmar M. Efficacy of Use of Single Dose Submucosal Injection of Dexamethasone in Impacted Mandibular Third Molar Surgery. J Adv Med Dent Scie Res 2018;6(1):65-72.

## INTRODUCTION

Impaction is the cessation of eruption of a tooth caused by a physical barrier or ectopic positioning of a tooth. Impaction of the third molar teeth is a common disorder which often necessitates their removal. The condition frequently affects young adults who are invariably healthy and free from systemic disease.<sup>1</sup> Management of impacted teeth includes surgical removal, surgical and orthodontically assisted eruption, transplantation and observations that includes documented clinical and imagery inspections.<sup>2</sup> In majority of cases, impacted third molars are removed under local anesthesia, however combination of local anesthesia and sedation or endotracheal anesthesia can also be used.<sup>1</sup> The surgical removal of impacted third molars can result in considerable pain, swelling and dysfunction.<sup>3,4</sup> The acute

inflammatory responses to tissue injury are modulated by locally released mediators of inflammation acting synergistically to produce plasma extravasations & edema & to sensitize peripheral nociceptors, resulting in hyperalgesia.<sup>5</sup> Proposed biochemical mediators of inflammation includes kinins, prostaglandins, histamine, & serotonin. Bradykinin & kallidin are two kinins that act independently as well as synergistically with products of the arachidonic acid cascade to produce both hyperalgesia as well as increased vascular permeability.<sup>6</sup> Prostaglandins are derived from the precursor arachidonic acid, whose metabolism can proceed along one of two major pathways: cyclooxygenase or lipooxygenase. The cyclooxygenase pathway produces PGE<sub>2</sub>, PGD<sub>2</sub>, PGF<sub>2</sub>, PGI<sub>2</sub>, and thromboxane(A)<sub>2</sub>, whereas lipooxygenase pathway leads to

formation of leukotriens. These end products have a central role in the inflammatory processes in injured tissues.<sup>7,8</sup>

The use of third molar extraction patients in pharmacologic studies on evaluating inflammatory parameters has many strengths. The patients entering in these studies comprise a homogenous population of young, healthy subjects who ensure a high degree of compliance. The surgery is localized, performed with a standardized technique. These attributes minimize the effects of concomitant systemic disease and medications that may modify or confound the study results.<sup>9</sup> To control postoperative inflammation and symptoms associated with surgical removal of third molars, it is necessary to provide an adequate anti-inflammatory therapy.<sup>10-20</sup> Owing to their ability to block the arachidonic acid cascade, thereby inhibiting the activity of cyclooxygenase pathway, which in turn, reduces the biosynthesis of prostaglandins (that play a major role in causing pain & inflammation). Nonsteroidal anti-inflammatory drugs have been significantly used in the management of postoperative pain in dentistry and medicine.<sup>21</sup> The side effects associated with the use of NSAIDs are numerous, but primarily they are related to gastrointestinal disturbance, hematologic, and renal disorders, as well as their propensity to cause skin and mucosal reactions.<sup>7</sup> The anti-inflammatory and immunomodulating effects of glucocorticoids have been known for decades and have found extensive therapeutic use in a wide range of diseases of which inflammatory responses are a main feature.<sup>22</sup> Suppression of each stage of inflammatory response appears to be the major action of glucocorticoids. Their major role in reducing the inflammatory response is to inhibit the production of vasoactive substances such as prostaglandins and leukotriens, as well as decreasing the number of chemical attractants such as cytokines.<sup>7</sup>

Various steroids preparations and routes of administration have been evaluated to lessen the inflammatory sequelae following third molar surgery.<sup>23</sup> Findings from the studies which have evaluated the efficacy of orally administered corticosteroids suggest that their efficacy is not convincing, because this route gives a delayed onset of action, can create an erratic response due to pharmacokinetics of the drugs and relies on patient compliance. The studies which have evaluated corticosteroid efficacy after a single intravenous administration have shown an immediate but short lived pharmacologic response. Thus further administration (oral or intramuscular) may be required to supplement the intravenous dosing. The intramuscular route of administration has slower onset of action than the intravenous route, and the rate of absorption is highly dependent on the rate of blood flow to the site of administration. The onset of action is still faster than the oral route, and long acting depot preparations can be injected. Single dose intramuscular dosing studies suggest that this route of administration can be effective when given either preoperatively or postoperatively.<sup>7</sup>

Corticosteroids such as dexamethasone has been used extensively in dentoalveolar surgery due to their purely glucocorticoid effects, virtually no mineralocorticoid effects and the least adverse effects on leukocyte chemotaxis. Dexamethasone has a longer duration of action and is considered more potent than other glucocorticoids. Presumably injection of low dose dexamethasone in the surgical site achieves a higher effective drug concentration at the site of injury without loss due to distribution to other compartments or the onset of elimination.<sup>23,25</sup> However the clinical use of glucocorticoids should be moderate and rational, for limited time and dose because, according to endocrinology analyses, after 5<sup>th</sup> day of use the therapy starts to produce immunosuppression by alteration of hypothalamic-pituitary axis.<sup>24</sup> The potential for side effects depends on the intensity and duration of therapy. A single large dose or a short duration of therapy with corticosteroids causes few adverse effects.<sup>7</sup>

Many studies have determined the effectiveness of steroids after oral surgical procedures, but currently there is no standard dosing regimen for oral and maxillofacial surgeons to follow. The pattern of administration generally used is characterized as short term, high dose or pulse therapy<sup>25</sup>. The null hypothesis was that the perioperative use of submucosal dexamethasone in impacted third molar surgery would suppress postoperative acute inflammation. Most practitioners follow an empiric dosing strategy that is often inadequate and provide a subtherapeutic effect. This ambiguity in dosage variations and an effective route of administration has made us to conduct a research with a specific aim to evaluate the relative efficacy of perioperative effect of single dose of 8mg dexamethasone administered by submucosal route with intramuscular route on postoperative sequelae after mandibular third molar surgery. Dexamethasone was selected in this study as it is potent, causes minimal sodium retention, and has a long biologic half life.<sup>19</sup>

#### MATERIALS AND METHODS:

**Study Design:** To address the research purpose, we designed and implemented a prospective randomized controlled study to evaluate the relative efficacy of perioperative single dose of 8mg of dexamethasone with intramuscular route on postoperative sequelae after mandibular third molar surgery. The study protocol was duly approved by the ethical committee of H.P. Government Dental College and Hospital Shimla. 30 out patients of both genders between 20 to 35 years requiring surgical removal of single mandibular impacted third molar under local anesthesia, who reported to department of Maxillofacial and Oral Surgery, were selected in this study. Informed consent was obtained from all patients, following which by block random method they were allocated into three groups: Group A-submucosal dexamethasone, Group B-intramuscular dexamethasone, Group C: no dexamethasone. Inclusion criteria were asymptomatic impacted mandibular

third molars with moderate difficulty index. Criteria for exclusion of patients included uncontrolled hypertension, uncontrolled hyperglycemia, significant impairment of pulmonary, cardiovascular, hepatic, renal function, blood dyscrasias, previous or existing history of gastric ulcers, thyroid disease, adrenal insufficiency, steroid induced psychosis, pregnancy, known hypersensitivity, idiosyncratic reactions to any of the study medications. All selected candidates were free of pain and other inflammatory symptoms that included swelling, hyperemia and decreased mouth opening at time of surgery. In addition, surgery lasting more than 60 minutes, surgical complications making procedure noncomparable during observation period was also causes of exclusion. For standardization of the sample, the degree of surgical difficulty of impacted tooth was assessed on the presurgical panoramic radiograph using Pell and Gregory, and Winter's criteria. Cases of equivalent degree of surgical difficulty categorized by Pedersen's Difficulty Index were included in the study design.

**Data Collection:** After the patients consented to participate in the study, baseline data was recorded. Medical and dental history, demographic information, blood investigations, radiographic findings were recorded in a case sheet. At initial visit and postsurgery days 2, 5, and 7 the information data variables were recorded by a single examiner.

The level of facial swelling was measured by a modification of tape measuring method described by Gabka and Matsumura.<sup>25</sup> The measurements were made preoperatively and on 2<sup>nd</sup>, 5<sup>th</sup>, and 7<sup>th</sup> postoperative days. Two measurements were made between 3 reference points: tragus, pogonion and outer corner of mouth. The preoperative measurements were considered as baseline for that side. The difference between each postoperative measurement and baseline indicated (facial swelling) edema for that day. The maximum distance between the mesio-incisal corners of the maxillary and mandibular right central incisors was taken as the maximum interincisal mouth opening measured by a ruler to the nearest millimeter. The measurements were carried out just before surgery and on postoperative days 2, 5 and 7. The difference between each postoperative and preoperative measurement indicated trismus for that day.

Following each operation a questionnaire composed of VAS of 6 units concerning postoperative pain, and the number of analgesic tablets consumed was given to the patients. Accordingly, pain was recorded as: "0- no pain"(patient feels well), "1- slight pain" (if patient is distracted he /she does feel pain ), "2-mild pain"(patient feels pain even if concentrating on some activity ), " 3-severe pain"(patient is disturbed but can continue with normal activities), "4- very severe pain "(patient is forced to abandon normal activities), "5-extremely severe pain"(patient must abandon every type of activity & feels the need to lie down). For each patient,

the appropriate score was recorded in the questionnaire for 7days.

**Statistical Analysis:** The value of continuous variables was expressed as mean  $\pm$  SD. The distribution of discrete variables in patients and control group was expressed as percentages. The significance of difference in mean values of continuous variables between study groups and control group was estimated by student's t test. The significance of difference in distribution of discrete variables between the groups was estimated with chi square test. Two tailed p value of <0.05 was taken statistically significant.

**Surgical Procedure:** On the day of surgery following completion of preoperative case sheet and consent documentation, surgery was carried out. All the surgeries were performed by the surgeons of Oral and Maxillofacial Department under similar conditions. An oral rinse of 15 ml of 2% chlorhexidine solution was performed prior to giving classical inferior nerve and long buccal nerve block, using 2% lignocaine with 1:100,000 epinephrine as local anesthesia. At the report of subjective symptoms of anesthesia dexamethasone 8 milligram was injected into the buccal vestibular tissues or in the deltoid region of the test groups. The subjects no other concomitant medication. The surgical procedure was standardized by reflection of three cornered buccal mucoperiosteal flap by buccal guttering technique under copious irrigation with sterile physiologic saline solution. Tooth delivery was followed by wound toileting, including removal of granulation tissue and remnants of tooth follicle if any. The flap was repositioned and primary closure achieved by 3-0 black silk interrupted sutures. Duration of surgery was noted as the period between the incision and last suture. After surgery the patient were given usual postoperative instructions and were prescribed an antibiotic coverage of oral amoxicillin 500mg +clavulanic acid 125mg thrice daily for three days. Analgesic preparation of diclofenac sodium was also prescribed to be taken as required for pain relief. External cold application was also advised during 1st postoperative 24 hours. The day after surgery, the patients were instructed to start home use of chlorhexidine 0.2% twice daily for 1 week. Before discharge it was ensured that all patients were instructed to complete the pain self assessment questionnaire.

## RESULTS:

This randomized controlled trial enrolled 30 subjects undergoing surgical removal of mandibular impacted third molars. There was no significant age or gender differences between the treatment and the control groups (  $p > 0.05$ ). Classification of impacted mandibular third molars in each group was done according to Pell and Gregory classification and Winter's classification. 33 % of teeth were mesioangular, 23% vertical and 44% horizontal. Position A was found to be associated with 53% of teeth as against 47% of teeth in position B. 90% of teeth were in Class II

10% of teeth were in Class III. 43% of teeth were unerupted, 57% partially erupted. All impactions were of moderate difficulty index. There were no statistically significant differences between the study groups with regard to the duration of surgery. (table 1)

**Table 1. DEMOGRAPHIC DATA**

|                                 |                   | Group A   |   | Group B   |   | Group C   |   | Significance |
|---------------------------------|-------------------|-----------|---|-----------|---|-----------|---|--------------|
| <b>Mean Age</b>                 |                   | 28.5±5.70 |   | 28.2±5.15 |   | 26.3±5.57 |   | NS           |
| <b>Sex Ratio (Male: Female)</b> |                   | 8         | 2 | 8         | 2 | 6         | 4 | NS           |
| <b>Angulation</b>               | Mesioangular      | 3         |   | 5         |   | 2         |   | NS           |
|                                 | Vertical          | 1         |   | 1         |   | 5         |   | NS           |
|                                 | Horizontal        | 6         |   | 4         |   | 3         |   | NS           |
|                                 | Distoangular      | 0         |   | 0         |   | 0         |   | NS           |
| <b>Class</b>                    | I                 | 0         |   | 0         |   | 0         |   | NS           |
|                                 | II                | 10        |   | 8         |   | 9         |   | NS           |
|                                 | III               | 0         |   | 2         |   | 1         |   | NS           |
| <b>Position</b>                 | A                 | 6         |   | 4         |   | 6         |   | NS           |
|                                 | B                 | 4         |   | 6         |   | 4         |   | NS           |
|                                 | C                 | 0         |   | 0         |   | 0         |   | NS           |
| <b>Eruption Status</b>          | Partially erupted | 8         |   | 5         |   | 4         |   | NS           |
|                                 | Unerupted         | 2         |   | 5         |   | 6         |   | NS           |
|                                 | Erupted           | 0         |   | 0         |   | 0         |   | NS           |

**Table 2. COMPARISON OF POSTOPERATIVE EDEMA (Tragus to Corner of Mouth) BETWEEN GROUP A, B & C**

| Time interval                           | Group | Mean change ± SD from preoperative period | Comparison | t value | P value | Statistical inference |
|---|-------|---|------------|---------|---------|-----------------------|
| <b>2<sup>nd</sup> postoperative day</b> | A     | 2.2±3.01                                  | A & B      | 2.48    | <0.05   | S                     |
|   | B     | 5.1±2.13                                  | A & C      | 3.98    | <0.001  | S                     |
|   | C     | 9.4±4.85                                  | B & C      | 2.56    | <0.05   | S                     |
| <b>5<sup>th</sup> postoperative day</b> | A     | 0.6±0.966                                 | A & B      | 0.21    | >0.05   | NS                    |
|   | B     | 0.5±1.08                                  | A & C      | 2.83    | <0.05   | S                     |
|   | C     | 2.9±2.378                                 | B & C      | 2.90    | <0.01   | S                     |
| <b>7<sup>th</sup> postoperative day</b> | A     | 0.4±0.843                                 | A & B      | 0.24    | >0.05   | NS                    |
|   | B     | 0.3±0.948                                 | A & C      | 0.77    | >0.05   | NS                    |
|   | C     | 1±2.30                                    | B & C      | 0.88    | >0.05   | NS                    |

**Table 3. COMPARISON OF POSTOPERATIVE EDEMA (Tragus to Pogonion) BETWEEN GROUP A, B & C**

| Time interval                           | Group | Mean change ± SD from preoperative period | Comparison | t value | P value | Statistical inference |
|---|-------|---|------------|---------|---------|-----------------------|
| <b>2<sup>nd</sup> postoperative day</b> | A     | 3.1±3.34                                  | A & B      | 2.16    | <0.05   | S                     |
|   | B     | 6.2±3.04                                  | A & C      | 2.78    | <0.05   | S                     |
|   | C     | 8.5±5.14                                  | B & C      | 1.21    | >0.05   | NS                    |
| <b>5<sup>th</sup> postoperative day</b> | A     | 0.3±0.94                                  | A & B      | 0.99    | >0.05   | NS                    |
|   | B     | 0.9±1.66                                  | A & C      | 1.96    | >0.05   | NS                    |
|   | C     | 2.9±4.09                                  | B & C      | 1.43    | >0.05   | NS                    |
| <b>7<sup>th</sup> postoperative day</b> | A     | 0±0                                       | A & B      | 0       |         |                       |
|   | B     | 0±0                                       | A & C      | 1.27    | >0.05   | NS                    |
|   | C     | 2±0.9                                     | B & C      | 1.27    | >0.05   | NS                    |

**Table 4. COMPARISON OF POSTOPERATIVE TRISMUS BETWEEN GROUP A, B & C**

| Time interval                           | Group | Mean change ± SD from preoperative period | Comparison | t value | P value | Statistical inference |
|---|-------|---|------------|---------|---------|-----------------------|
| <b>2<sup>nd</sup> postoperative day</b> | A     | 5.8±5.4                                   | A & B      | 3.48    | <0.01   | S                     |
|   | B     | 12.8±7.6                                  | A & C      | 2.96    | <0.01   | S                     |
|   | C     | 13.8±5.0                                  | B & C      | 1.16    | >0.05   | NS                    |
| <b>5<sup>th</sup> postoperative day</b> | A     | 2.5±3.4                                   | A & B      | 2.15    | <0.05   | S                     |
|   | B     | 9.3±9.48                                  | A & C      | 2.61    | <0.05   | S                     |
|   | C     | 9.7±7.3                                   | B & C      | 0.052   | >0.05   | NS                    |
| <b>7<sup>th</sup> postoperative day</b> | A     | 2.1±3.31                                  | A & B      | 1.35    | >0.05   | NS                    |
|   | B     | 5.8±10                                    | A & C      | 1.52    | >0.05   | NS                    |
|   | C     | 6.1±9.63                                  | B & C      | 0.09    | >0.05   | NS                    |

**Table 5.** COMPARISON OF POSTOPERATIVE PAIN BETWEEN GROUP A, B & C

| Time interval                     | Group | Mean change $\pm$ SD from preoperative period | Comparison | t value | P value | Statistical inference |
|-----------------------------------|-------|---|------------|---------|---------|-----------------------|
| 2 <sup>nd</sup> postoperative day | A     | 1.7 $\pm$ 0.483                               | A & B      | 1.09    | >0.05   | NS                    |
|                                   | B     | 1.9 $\pm$ 0.316                               | A & C      | 4.62    | <0.001  | S                     |
|                                   | C     | 2.7 $\pm$ 0.483                               | B & C      | 4.38    | <0.001  | S                     |
| 5 <sup>th</sup> postoperative day | A     | 0.3 $\pm$ 0.483                               | A & B      | 4.58    | <0.001  | S                     |
|                                   | B     | 1 $\pm$ 0                                     | A & C      | 5.33    | <0.001  | S                     |
|                                   | C     | 1.7 $\pm$ 0.674                               | B & C      | 3.27    | <0.01   | S                     |
| 7 <sup>th</sup> postoperative day | A     | 0.1 $\pm$ 0.316                               | A & B      | 1.56    | >0.05   | NS                    |
|                                   | B     | 0.4 $\pm$ 0.516                               | A & C      | 1       | >0.05   | NS                    |
|                                   | C     | 0.4 $\pm$ 0.516                               | B & C      | 2.44    | <0.05   | S                     |

**EDEMA:** Edema was measured from base of tragus to outer corner of mouth and from base of tragus to soft tissue pogonion. The difference preoperative and postoperative measurement was recorded in millimeters. It was found that on 2<sup>nd</sup> postoperative day, the difference in mean postoperative edema was statistically significant in submucosal dexamethasone group SD 3.1 $\pm$  3.34 and intramuscular dexamethasone group SD 6.2 $\pm$ 3.04. The findings were also statistically significant between the submucosal dexamethasone group and no dexamethasone group SD 8.5 $\pm$ 5.14. On the 5<sup>th</sup> postoperative day, the mean postoperative edema was significant between submucosal dexamethasone group SD0.6 $\pm$ 0.096 and no dexamethasone group SD 8.5 $\pm$ 5.14. By the 7<sup>th</sup> postoperative day the facial swelling restored to the normal facial contour in all the three groups. (table 2,3).

**TRISMUS:** The mean value of trismus for the submucosal dexamethasone group on the 2<sup>nd</sup> and 5<sup>th</sup> postoperative days was SD 5.8 $\pm$ 5.4 and SD 2.5 $\pm$ 3.4 respectively. The mean value of trismus for intramuscular dexamethasone group was SD 12.8 $\pm$ 7.6 and SD 9.3 $\pm$ 9.4 on 2<sup>nd</sup> and 5<sup>th</sup> day respectively. The comparison of mean value of trismus showed statistically significant findings between these two groups. On the 7<sup>th</sup> postoperative day the mean value of trismus in all the three groups was nonsignificant ( $p>0.05$ ). It was conferred that the greatest decrease in interincisal opening was for the no dexamethasone group on the 2<sup>nd</sup> and 5<sup>th</sup> postoperative days. Subjects receiving dexamethasone by intramuscular route had minimal decrease in interincisal mouth opening during the postoperative period. In all the three groups trismus was most severe on the 2<sup>nd</sup> and 5<sup>th</sup> postoperative days following surgery and began to return to normal interincisal opening by 7<sup>th</sup> postoperative day. (table 4).

**PAIN:** Postoperative pain level was evaluated by VAS (0-5) during the 7 days postoperative period. Postoperative pain levels tended to be less severe in the groups receiving dexamethasone in comparison to the control group. On 2<sup>nd</sup> postoperative day the pain difference between submucosal dexamethasone group SD1.7 $\pm$ 0.48 and the intramuscular dexamethasone group SD 1.9 $\pm$ 0.31 was nonsignificant. On the 5<sup>th</sup> postoperative day pain was statistically significant

between all three groups with the submucosal dexamethasone group showing less severity of pain in comparison to other two groups, as intramuscular dexamethasone group SD 1 $\pm$ 0 and no dexamethasone group sd1.7 $\pm$ 0.67. Comparison of mean value of pain on the 7<sup>th</sup> postoperative day was nonsignificant between submucosal dexamethasone group SD 0.1 $\pm$ 0.31 and intramuscular dexamethasone group SD 0.4 $\pm$ .51, whereas there was significant difference between pain levels in intramuscular dexamethasone group and no dexamethasone group SD 0.4  $\pm$ .41. Categorical pain responses demonstrated that use of dexamethasone by submucosal route offered added advantage of pain control over intramuscular route in impacted third molar surgery. (table 5).

#### DISCUSSION:

By pharmacologically controlling the extent of the inflammatory process, the intensity or severity of postoperative sequel of third molar surgery may be reduced.<sup>21</sup> The preemptive strategies using analgesics and corticosteroids, which focus on modulating and preventing the production of inflammatory mediators of inflammation, have been advocated. Efficacy in control of postoperative sequel has been demonstrated in trials assessing betamethasone, methylprednisolone and dexamethasone.<sup>16, 19, 26- 28</sup>

**EDEMA:** Edema results due to rise in osmotic pressure and increased capillary permeability leading to transudation of fluid from blood vessels into tissues and occlusion of lymphatic system by fibrin clots derived from plasma. Laskin states that postoperative edema peaks in 24 to 48 hours, but Peterson says that it usually maximizes in 48 to 72 hours and is resolved after the first postoperative week.<sup>29</sup> Most glucocorticoids do not exert their effect beyond 24 hours if given as a single dose, therefore to maintain their efficacy doses should be maintained for 3 to 5 days which in turn may cause hypothalamic pituitary axis suppression.<sup>7</sup> This study shows significant reduction in postoperative edema using dexamethasone by submucosal route as compared with intramuscular route as well as control group for first two postoperative days when inflammation is at peak. Neupert et al conducted a study to quantify the effects

of 4mg of dexamethasone on reducing postsurgical sequelae after third molar surgery. They noted no statistically significant differences in facial swelling during postoperative period.<sup>30</sup> Giovanni Battista Grossi et al in their study to evaluate the effect of submucosal administration on discomfort after third molar surgery found significant reduction in edema on 2<sup>nd</sup> postoperative day, which confounded the results of our study.<sup>23</sup> Messer and Keller on their work on the use of intraoral dexamethasone after extraction of mandibular 3rd molars noted a predictable decrease in post-operative discomfort by using intramuscular dexamethasone immediately after surgery.<sup>15</sup> In a well conducted trial with patients serving as their own control, Graziani et al investigated the effect of endoalveolar application of 4mg and 10 mg of dexamethasone powder and submucosal injection of dexamethasone in 43 subjects undergoing bilateral surgical extraction of mandibular 3rd molar, with regard to edema analysis, each treatment subgroup showed a reduced postoperative degree of edema compared with control group, as highly significant on 2nd postoperative day as after one week.<sup>23,31</sup> In agreement with Graziani et al, our data shows that the submucosal administration of dexamethasone 8mg resulted in a highly significant decrease in edema on 2nd postoperative day as compared with other groups.<sup>23,29</sup> In contrast with Graziani et al but in agreement with previous reports of Schmelzeisen and Frolich, our results showed no statistically significant difference between all three groups when postoperative swelling was evaluated on 7th postoperative day, but the effect of dexamethasone was most pronounced on 2nd post operative day, when most of the swelling occurred.<sup>23,27</sup> Michael. R, Mark F. et al conducted a systematic search of the literature to apply metaanalytical methods to measure the effects of corticosteroids on edema and pain at early and late postoperative periods after third molar removal. The findings of the study of meta-analysis collaborated with our study that perioperative administration of corticosteroids produced a reduction in edema and improvement in the range of motion after 3rd molar removal.<sup>32</sup>

**PAIN and TRISMUS:** Glucocorticoid administration has been found to suppress tissue levels of bradykinin and in release of neuropeptides from nerve endings, both of which enhance nociception in inflamed tissues. The established reduction in prostaglandin synthesis mediated by glucocorticoids might further contribute to analgesia. A direct inhibitory effect of locally applied glucocorticoids on signal transmission in nociceptive C- fibers and ectopic neuroma discharge have been demonstrated.<sup>22</sup> Trismus is muscle stiffness that limits mouth opening and is caused by fluid accumulation within muscles adjoining the operative site.<sup>26</sup> Trismus measured in this study as a decrease in maximal interincisal opening, is a significant postoperative sequale caused by edema and may also be associated due

to postsurgical pain. Although reduction of postoperative pain, generally accompanies a reduction of edema, steroids alone do not have a clinically significant analgesic effect.<sup>10</sup> On 2<sup>nd</sup> postoperative day the nonsignificant values in mean pain levels between submucosal dexamethasone group and intramuscular dexamethasone group may be explained on the basis of study of Troullos ES et al<sup>6</sup>, which stated that the inhibition of the endogenous analgesic beta endorphin from the posterior pituitary may account for lesser analgesia in initial postoperative period.<sup>6</sup> Dionne et al conducted a study in which dexamethasone 4 milligrams was given orally at 12 hours and 4 milligrams intravenously one hour before surgery. As marker of inflammation samples of PGE2 and TXB2 were collected. It was found that dexamethasone decreased levels of PGE2 and TXA2 but had minimal effect on pain on the day of surgery.<sup>5</sup> We agree with these results only during immediate postsurgery period, as there was no account of pain levels after 180 hours of surgery in Dionne et al study. Results in our study showed less severity of pain during the 7 postoperative follow up period. A direct inhibitory action of glucocorticoids on signal transmission in nociceptive C-fibers account for the decreased pain levels in submucosal dexamethasone group and intramuscular dexamethasone group as compared with the control group after 2<sup>nd</sup> postoperative day.

Neupert et al made an interesting finding that even if there were no differences in daily pain, global pain experience was significantly affected by the corticosteroids. They also noted that trismus was significantly reduced, and with larger incisal opening, the patients tended to experience less pain.<sup>30</sup> Like earlier reports of Skjelbred, Sisk, Beirne, Holland, Troullos, Campbell, Baxendal this study is in accordance with the fact that the glucocorticoid administration substantially reduces pain in minor dental surgical procedures.<sup>3,6,17,19,33</sup> Our data is also in accordance with the previous reports of Jose Rodrigus and meta-analytical analysis of Markiewicz et al which showed that the administration of a steroid showed a significant difference in the measurement of the degree of swelling and marked improvement in the range of motion in the treated group.<sup>10,34</sup> Moreover, the perioperative treatment with a corticosteroid had a limited but significant effect on trismus when compared with control groups.

In the present study it was observed that perioperative submucosal administration of dexamethasone reduces the incidence of postoperative inflammatory complications such as pain, edema and trismus. Single perioperative dose of 8mg dexamethasone via submucosal route at the site of surgery is more efficacious in reducing the postoperative sequel of third molar surgery than 8mg of dexamethasone via intramuscular route in the same surgical procedure. Patients who were not subjected to dexamethasone had higher incidence of postoperative complications to the patients who were subjected to intraoperative dexamethasone.

**CONCLUSIONS:**

Third molar surgery is a traumatic procedure and the most common in Oral and Maxillofacial Surgery field. Being a highly vascularized area, predominantly constituted by loose connective tissue, a series of functional and structural alterations is expected among them of which, swelling, pain and trismus is most common.<sup>10</sup> To control postoperative inflammation and symptoms associated, it is necessary to adopt a careful surgical technique and to provide an adequate anti-inflammatory therapy<sup>10</sup>.

Many different regimens of glucocorticoids administration have been recommended to decrease the postoperative sequel of pain, trismus and edema following removal of impacted third molars. In choosing a therapeutic regimen for glucocorticoid administration, a number of decisions must be made, including the type of steroid, the dosage and the route of administration, single versus multiple dosing, and finally, the timing of the administration relative to surgical procedure.

Selecting a route of administration can be influenced by operator / patient convenience and operator experience. In most instances parenteral dosing must be restricted to the pre and post-operative periods. The intravenous route offers instantaneous blood levels, but requires provider expertise and additional armamentarium. The intramuscular route offers the advantage of negating the need for repetitive postoperative dosing by permitting the use of repository drug forms; however, operator experience, patient discomfort, and added armamentarium may be a hinderance. The convenience of oral dosing has a general appeal; however patient compliance must be relied upon for it to be effective.<sup>13</sup>

Following conclusions were made on the basis of comparison of results in between the three groups:-

The results of this study provided a basis for the submucosal administration of dexamethasone sodium phosphate to achieve reduction of postoperative pain, edema and trismus comparable with other routes of administration. Most glucocorticoids used in oral surgery do not exert their effect beyond 24 hours if given as a single dose. To maintain their anti-inflammatory efficacy, steroid doses should be maintained for a minimum of 3 days to maximize their benefit and minimize their risk of hypothalamic pituitary axis suppression.<sup>7</sup>

In previous studies it has been presumed that, injection of 8mg dexamethasone in the surgical site via submucosal route achieves a higher effective drug concentration at the site of surgery without loss due to distribution to other compartments or the onset of elimination. This drug dosage achieves therapeutic blood levels with no adverse effects.

Moreover, when surgical removal of 3rd molar is performed under local anesthesia, there is a convenience for both the surgeon and the patient to use the submucosal route.<sup>23</sup> On other hand intramuscular route of administration has a slower onset of action, and the rate of absorption is highly dependent on the rate of blood flow to the site of

administration.<sup>7</sup> This study has lead to the conclusion that the submucosal use of steroids such as dexamethasone can be a valuable tool to control postoperative inflammatory complications of third molar surgery.

**REFERENCES:**

1. Meechan JG, Seymour RA. The use of third molar surgery in clinical pharmacology. *Br Dent J* 1993; 31: 360-365.
2. Alling CC, Catone GA: Management of impacted teeth. *J Oral Maxillofac Surg* 1993; 51(suppl): 3-6.
3. Sisk AL, Hammer WB, Shelton DW, Joy ED. Complications following removal of impacted third molars: the role of the experience of the surgeon. *J Oral Maxillofac Surg* 1986; 44: 855-859.
4. Sisk AL, Bonnington GJ: Evaluation of methylprednisolone and flurbiprofen for inhibition of the postoperative inflammatory response. *Oral Surg* 60:137, 1985.
5. Dionne RA, Gordon SM, Rowan J, Kent A, Brahmin JS. Dexamethasone suppresses peripheral prostanoid levels without analgesia in a clinical model of acute inflammation. *J Oral Maxillofac Surg* 2003; 61:997-1003.
6. Troulous ES, Hargreaves KM, Butler DP, Dionne RA: Comparison of nonsteroidal anti-inflammatory drugs, ibuprofen and flurbiprofen, with methylprednisolone and placebo for acute pain, swelling, and trismus. *J Oral Maxillofac Surg* 1990; 48: 945-95.
7. Kim K, Brar P, Jakubowski J, Kaltman S, Lopez E, Lauderdale F. The use of corticosteroids and nonsteroidal antiinflammatory medication for the management of pain and inflammation after third molar surgery: a review of literature. *J Oral Surg Oral Med Pathol Oral Radiol Endod* 2009; 107:630-640.
8. Gersema L, Baker K. Use of Corticosteroids in Oral Surgery. *Journal of Oral Maxillofacial Surgery* 1992; 50 (3): 270-7.
9. Jackson DL. Determination of the antiinflammatory effects of methylprednisolone on the sequelae of third molar surgery. *J Oral Maxillofac Surg* 1999; 57:1206-1208.
10. Filho JRL, Maurette PE, Allias M, Cotinho M, Fernandes C. Clinical comparative study of the effectiveness of two doses of dexamethasone to control postoperative swelling, trismus and pain after the surgical extraction of mandibular impacted third molars. *Med Oral Patol Oral Cir Bucal* 2008; 13(2): E129-32.
11. Beeman CS. Third molar management: A case for routine removal in adolescent and young orthodontic patients. *J Oral Maxillofac Surg*. 1999 Jul; 57(7):824-30.
12. Berge TI, Boe OE. Predictor evaluation of postoperative morbidity after surgical removal of mandibular third molars. *Acta Odontol Scand*. 1994 Jun; 52(3):162-9.
13. Conard SM, Blakey GH, Shugars DA, Marciani RD, Phillips C, et al. Patients' perception of recovery after third molar surgery. *J Oral Maxillofac Surg*. 1999 Nov; 57(11):1288-94.
14. Savin J, Ogden JR. Third molar surgery- a preliminary report on aspects affecting quality of life in the early postoperative period. *Br J Oral Maxillofac Surg*. 1997 Aug; 35(4):246-53.
15. Messer EJ, Keller JJ. The use of intraoral dexamethasone after extraction of mandibular third molars. *Oral Surg* 1975; 40: 594-598.
16. Huffman CG. Use of methylprednisolone sodium succinate to reduce post-operative edema after removal of impacted molars: *J Oral Surg* .1977; 35 (3): 198.

17. Skjelbred P, Lokken P. Post-operative pain and inflammatory reaction reduced by injection of a corticosteroid . A controlled trial in bilateral oral surgery. *European Journal of Clinical Pharmacology* 1982; 21:391-6.
18. Bystedt H, Nordenram A. Effect of methylprednisolone on complications after removal of impacted mandibular third molars. *Swedish Dental Journal* 1985; 9 (2): 65- 69.
19. Beirne OR, Hollander B. The effect of methylprednisolone on pain, trismus and swelling after removal of third molars. *Oral Surgery, Oral Med, Oral Pathol* 1986; 61(2):134.
20. Holland C.S. Influence of methylprednisolone on post-operative swelling following oral surgery. *British journal of oral and maxillofacial surgery* 1987; 25: 293-299.
21. Bamgbose BA, Akinwande JE, Adeyemo WL, Ladeinde AL, Arotiba GT, Ogunlewe MO. Effects of co-administered dexamethasone and diclofenac potassium on pain, swelling and trismus following third molar surgery. *Head and Face Medicine* 2005; 1:11.
22. Holte K, Kehlet H. Perioperative single-dose glucocorticoid administration: pathophysiologic effects and clinical implications. *J Am Coll Surg* 2002; 195(5): 694-711.
23. Grossi GB, Maiorana C, Garramone RA, Borgonovo A, Farronato D. Effect of submucosal injection of dexamethasone on postoperative discomfort after third molar surgery: a prospective study. *J Oral Maxillofac Surg* 2007; 65: 2218-2226.
24. Williamson LW, Lorson EL, Osborn DB: Hypothalamus pituitary- adrenal suppression after short term dexamethasone therapy for oral surgical procedures. *J Oral Surgery* 38: 20, 1980.
25. Montgomery MT, Hogg JP, Roberts DL, Redding S. The use of glucocorticosteroids to lessen the inflammatory sequelae following third molar surgery. *J Oral Maxillofac Surg* 1990; 48: 179-187.
26. Morre PA, Brar P, Smiga ER, et al. Preemptive rofecoxib and dexamethasone for prevention of pain and trismus following third molar surgery. *Oral Surg Oral Med Oral Pathol* 2005; 99:E1.
27. Schmelzeisen R, Frolich JC. Prevention of postoperative swelling and pain by dexamethasone after operative removal of impacted third molar teeth. *Eur J Clin Pharmacol* 1993; 44: 275.
28. Ustun Y, Erdogan O, Esen E. Comparison of the effects of 2 doses of methylprednisolone on pain, swelling, and trismus after third molar surgery. *Oral Surg Oral Med Oral Pathol* 2003; 96: 535-539.
29. Alexander RE, Thronson RR. A review of perioperative corticosteroid use in dentoalveolar surgery. *Oral Surg Oral Med Pathol Oral Radiol Endod* 2000; 90(4): 406-415.
30. Neupert EA, Lee JW, Philput CB, Gordon JR. Evaluation of dexamethasone for reduction of postsurgical sequelae of third molar removal. *J Oral Maxillofac Surg* 1992; 50:1177-82.
31. Graziani F, Arduino PG , Tonelli M, Gabriele M . Perioperative dexamethasone reduces post-surgical sequelae of wisdom tooth removal . *Int Journal of Oral and Maxillofacial Surgery*. 2006; 35: 241-246.
32. Michael R, Mark F, Eric L, Thomas B. Corticosteroids reduce postoperative morbidity after third molar surgery: A systemic review and meta- analysis. *J Oral Maxillofac Surg* 2008; 66:1881-1894.
33. Baxendale BR, Vater M , Lavery KM . Dexamethasone reduces pain and swelling following extraction of third molar teeth. *Anaesthesia* 1993; 48 (II): 961-4.
34. Markiewicz MR, Brady MF, Ding EL, Dodson TB. Corticosteroids reduce postoperative morbidity after third molar surgery: A systemic review and meta- analysis. *J Oral Maxillofac Surg* 2008; 66:1881-1894.

**Source of support:** Nil

**Conflict of interest:** None declared

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