

## Review Article

### Dexamethasone After the Surgical Extraction of Impacted Third Molar: A review of literature

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#### ABSTRACT:

Third molar eruption and continuous positional changes after eruption can be related not only with race but also with nature of the diet, the intensity of the use of the masticatory apparatus and possibly due to genetic background. The surgical procedure to extract the wisdom teeth accompanies the post-operative complications like pain, swelling, trismus, bruising, and difficulty in chewing and swallowing. Corticosteroids are employed particularly after surgery to limit the accumulation of inflammatory mediators and reduce fluid transudation and edema. Dexamethasone has a wide variety of uses in the medical field. As a treatment, dexamethasone has been useful in the treatment of acute exacerbations of multiple sclerosis, allergies, cerebral edema, inflammation, and shock.

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#### INTRODUCTION

In early 1954, Mead has defined an impacted tooth as a tooth that is prevented from erupting into position because of malposition, lack of space, or other impediments. Later Peterson characterized impacted teeth as those teeth that fails to erupt into the dental arch within the expected time. Third molar eruption and continuous positional changes after eruption can be related not only with race but also with nature of the diet, the intensity of the use of the masticatory apparatus and possibly due to genetic background. The third molar impaction is occurring in about 73% of the young adults in Europe, these teeth generally erupt between the ages of 17 and 21 years.<sup>1-3</sup>

Whenever indicating extraction of third molars, dentists should have a justifiable reason, one that takes into account future treatment planning from an orthodontic, surgical, periodontal and/or prosthetic point of view. At the same time, a cost/benefit

analysis should be carried out to justify the prophylactic removal of third molars, which should only be indicated with the purpose of preventing cases that involve pathological processes, such as root resorption or caries in second molars, cysts and pericoronitis.<sup>4-6</sup>

The surgical procedure to extract the wisdom teeth accompanies the post-operative complications like pain, swelling, trismus, bruising, and difficulty in chewing and swallowing. In the past, various techniques and medications have been used to improve the quality of life of the patient in the post-operative recovery period and to minimize the adverse effects of the surgery. Corticosteroids have proven to be the most effective. Corticosteroids are natural steroid hormones that are produced in the adrenal cortex of vertebrates. They are 21 carbon compounds having a cyclopentanone perhydro phenanthrene (steroid) nucleus. The postoperative experience of

pain depends on the degree of surgical trauma suffered, requirement for bone tissue removal, and the extension of the periosteum. The role of corticosteroids in preventing postoperative pain is controversial. Corticosteroids are employed particularly after surgery to limit the accumulation of inflammatory mediators and reduce fluid transudation and edema.<sup>7-10</sup>

Dexamethasone has a wide variety of uses in the medical field. As a treatment, dexamethasone has been useful in the treatment of acute exacerbations of multiple sclerosis, allergies, cerebral edema, inflammation, and shock. Patients with conditions such as asthma, atopic and contact dermatitis, and drug hypersensitivity reactions have benefited from the use of dexamethasone. Dexamethasone is a potent glucocorticoid with very little, if any, mineralocorticoid activity. Dexamethasone's effect on the body occurs in a variety of ways. It works by suppressing the migration of neutrophils and decreasing lymphocyte colony proliferation. The capillary membrane becomes less permeable, as well. Lysosomal membranes have increased stability. There are higher concentrations of vitamin A compounds in the serum, and prostaglandin and some cytokines (interleukin-1, interleukin-12, interleukin-18, tumor necrosis factor, interferon-gamma, and granulocyte-macrophage colony-stimulating factor) become inhibited. Increased levels of surfactant and improved pulmonary circulation have also been shown with dexamethasone use.<sup>10-12</sup>

#### DEXAMETHASONE

Dexamethasone has a wide variety of uses in the medical field. As a treatment, dexamethasone has been useful in the treatment of acute exacerbations of multiple sclerosis, allergies, cerebral edema, inflammation, and shock. Patients with conditions such as asthma, atopic and contact dermatitis, and drug hypersensitivity reactions have benefited from the use of dexamethasone. Dexamethasone is a potent glucocorticoid with very little, if any, mineralocorticoid activity. Dexamethasone's effect on the body occurs in a variety of ways. It works by suppressing the migration of neutrophils and decreasing lymphocyte colony proliferation. The capillary membrane becomes less permeable, as well. Lysosomal membranes have increased stability. There are higher concentrations of vitamin A compounds in the serum, and prostaglandin and some cytokines (interleukin-1, interleukin-12, interleukin-18, tumor necrosis factor, interferon-gamma, and granulocyte-macrophage colony-stimulating factor) become inhibited. Increased levels of surfactant and improved pulmonary circulation have also been shown with dexamethasone use. Dexamethasone is metabolized by the liver and excreted in the urine mainly. Dexamethasone has a half-life of approximately 3 hours.<sup>12-14</sup>

#### LITERATURE

**Shah KL, Al Anazi YM, Khalaf YA and et al (2018)**<sup>10</sup> conducted a study to compare the therapeutic effects of 8 mg dexamethasone intramuscular administered pre-operatively vs post-operatively after the surgical extraction of impacted mandibular third molars. One hundred and fifty patients were included in the study. 150 patients constituted the study and were randomly divided into two groups. Group A received 8 mg dexamethasone (intramuscular) 1hr pre-operatively. Group B received 8 mg dexamethasone (intramuscular) immediately after the surgery. According to the gender there were 81(54%) males and 69 (46%) females, in both the groups combined. Males to females' ratio was 1.17: 1 in this study. Post-operative 1st and 3rd day follow-up showed that there was a significant difference between the two groups in terms of swelling and mouth opening (P=0.000). Overall, Group A showed much better results as far as the post-operative swelling and mouth opening was concerned. There was no statistical difference in the scores when the post-operative pain was evaluated on 1st, 3rd, and 7th day. The depth, angulation and the position of the tooth did not affect the study in terms of significance. It was concluded that preoperative administration of single dose of dexamethasone intramuscularly was more effective than the postoperative period, in reducing the swelling and trismus.

**Kindler S, Ittermann T, Bülow R (2019)**<sup>11</sup> conducted a study to evaluate the effect of craniofacial morphology on erupted or impacted third molars in a German population sample. Erupted and impacted third molars in 2,484 participants from the Study of Health in Pomerania were assessed by whole-body magnetic resonance imaging. Markers of facial morphology were determined in 619 individuals of those participants in whose 421 participants (16.7%) had at least one impacted third molar. Craniofacial morphology was estimated as linear measurements and was associated in a cross-sectional study design with impacted and erupted third molars by multinomial logistic regression models. Erupted third molars were used as reference outcome category and regression models were adjusted for age and sex. Maximum Cranial Width (Eurion-Eurion distance) was significantly associated with impacted third molars (RR: 1.079; 95% confidence interval 1.028–1.132). This association was even more pronounced in the mandible. Individuals with a lower total anterior facial height (Nasion-Menton distance) and a lower facial index also have an increased risk for impacted third molars in the mandible (RR 0.953; 95% confidence interval 0.913–0.996 and RR: 0.943; 95% confidence interval 0.894–0.995). No significant associations of third molar status with facial width (Zygion-Zygion distance), and sagittal cranial dimension (Nasion-Sella distance; Sella-Basion distance) were observed. Individuals with an increased maximal cranial width have a higher risk for

impaction of third molars in the mandible and in the maxilla. Individuals with a lower anterior total anterior facial height and lower facial index also have an increased risk for third molars impaction in the mandible.

**K.Y. Giri, A. Joshi, S. Rastogi, R. Dandriyal, N. Indra B Prasad, H.P. Singh et al (2019)**<sup>12</sup> conducted a study to evaluate the preventative therapeutic effect of pre-operative and post-operative intravenous 8 mg of dexamethasone on post-operative pain, swelling and trismus after the surgical extraction of mandibular third molars. A randomised clinical trial was conducted on 100 healthy participants (group I pre-operative and group II post-operative) with unilateral impacted lower third molars, average age  $27.7 \pm 9.7$  years with no local or systemic problems were operated under local anaesthesia. Group I received 8 mg intravenous 1 hour pre-operatively and group II received 8 mg intravenous dose of dexamethasone at the end of procedure. Post-operative pain was evaluated using a visual analogue scale (VAS) and the degree of swelling was evaluated through facial reference point variation. The presence of trismus was analysed through measurement of the inter-incisal distance (IID). These assessments were obtained before the operation and 48 hour and 7th post-operative day. No significant differences were observed in facial swelling and trismus among pre-operative and post-operative IV 8 mg doses after the surgery (student t-test;  $P > 0.05$ ). The visual analogue scale scores for pain assessment showed no clinically or statistically significant differences in both groups (student t test;  $P > 0.05$ ). Pre-operative administration of 8 mg intravenous dexamethasone is as effective as 8 mg IV post-operative dexamethasone with no clinically or statistically significant differences in the final outcomes of the third molar surgery.

**Sugravan C, Khoo LK, Kc K and et al (2020)**<sup>13</sup> conducted a study to analyse previous studies pertaining to corticosteroids and pain reduction following wisdom teeth surgery. The Science Direct, PubMed, and MEDLINE databases were searched for relevant journals according to a systematic search strategy (Patient Intervention Comparison Outcome Study). Randomized controlled trials published in English from 1998 to 2017 were extracted. Twenty-seven articles were included, with a total of 36 comparative cases. Methylprednisolone and dexamethasone were the most used corticosteroids. Intramuscular injections of corticosteroids were optimal for pain reduction, regardless of the time of administration. Corticosteroids can be used as an adjuvant for pain reduction following wisdom teeth surgery.

**Arabia S (2018)**<sup>14</sup> conducted a study to compare the therapeutic effects of 8 mg dexamethasone intramuscular administered pre-operatively vs post-operatively after the surgical extraction of impacted mandibular third molars, in Al-Qurayyat, Saudi Arabia, population. One hundred and fifty patients

who visited the Department of Oral and Maxillofacial Surgery of Gurayat specialized dental center, Al-Qurayyat, Saudi Arabia, were included in the study. The study was conducted from February 2018 to August 2018. 150 patients constituted the study and were randomly divided into two groups. Group A received 8 mg dexamethasone (intramuscular) 1hr pre-operatively. Group B received 8 mg dexamethasone (intramuscular) immediately after the surgery. According to the gender there were 81(54%) males and 69 (46%) females, in both the groups combined. Males to females' ratio was 1.17: 1 in this study. Post-operative 1st and 3rd day follow-up showed that there was a significant difference between the two groups in terms of swelling and mouth opening ( $P=0.000$ ). Overall, Group A showed much better results as far as the post-operative swelling and mouth opening was concerned. There was no statistical difference in the scores when the post-operative pain was evaluated on 1st, 3rd and 7th day ( $P=0.679$ ,  $P=0.755$ ,  $P=0.202$ ). The depth, angulation and the position of the tooth did not affect the study in terms of significance ( $P=0.626$ ,  $P=0.874$ ,  $P=1.000$ ). It was concluded that preoperative administration of single dose of dexamethasone intramuscularly was more effective than the postoperative period, in reducing the swelling and trismus.

**Sitthisongkhram K, Niyomtham N, Chaiyasamut T, Pairuchvej V, Kumar KC, Wongsirichat N (2020)**<sup>15</sup> conducted a study to evaluate the effects of preoperative and postoperative injections of 4 mg of dexamethasone into the pterygomandibular space on postoperative pain, facial swelling, and the restriction of mouth opening following lower third molar surgical removal. Twenty-seven participants with bilateral symmetrical lower impacted third molars were included in this study. Each participant was randomly allocated to one of two groups. Group A received injections of 1 ml dexamethasone (4 mg/mL) and 1 mL placebo into the pterygomandibular space before and after surgery, respectively. Group B received the same doses of placebo before surgery and dexamethasone after surgery. A significant restriction of mouth opening on the second postoperative day was observed in both groups. Nonetheless, the postoperative restriction of mouth opening, facial swelling, postoperative pain, and analgesic consumption after lower third molar surgical removal were not significantly different in the two groups. Regardless of the time of administration, dexamethasone injections into the pterygomandibular space resulted in satisfactory control of the postoperative sequelae of the mandibular third molar surgical removal.

**Gaspar BDS, de Castro JKS, Ferraro-Bezerra M, Amora-Silva BF, de Barros Silva PG, de Vasconcelos V, Avelar RL, Alencar PNB (2020)**<sup>16</sup> conducted a study to evaluate the effects of pre- and postoperative administration of dexamethasone for

upper and lower third molar surgery. A randomized, triple-blind clinical trial with a split-mouth design was conducted with a sample composed of 30 patients. Participants were divided in two groups: Group A (one dose of dexamethasone 12 hours after surgery) and Group B (one dose of placebo 12 hours after surgery). All patients received single dose of dexamethasone (8mg) and nimesulide (100mg) per oral route, one hour before surgery. The outcome variables were: pain, total number of analgesics taken, interval between analgesics, swelling and trismus. Those parameters were evaluated in different timepoints. Quantitative data were subjected to the Kolmogorov-Smirnov normality test and compared by means of the paired t-test and ANOVA. Group A showed less swelling and trismus 48h after surgery ( $p=0.167$ ), but no statistical significant difference were found. On assessment of postoperative pain 16 hours after surgery, the scores were higher in Group B (placebo) ( $p=0.031$ ).

**Hiriyanna NM, Degala S (2021)**<sup>17</sup> conducted a study to investigate objective facial measurements, mouth opening and compared them with subjective scores on a visual analogue scale and quality of life (QOL) recovery questionnaire. Patients were randomly divided into two groups and received 8 mg DX as either submucosal or intravenous injection 5 min after administration of local anaesthesia. Data was collected at 2nd and 7th post-op intervals. Thirty patients were evaluated in the study. SM route behaved similarly to IV route in producing changes in facial measurements [ $P = 0.533$ ], mouth opening [ $P = 0.533$ ] and pain [VAS] scores [ $P = 0.533$ ] at early and late intervals. Questionnaire subscale scores were not significantly different between groups, but total mean score was significant [ $P = 0.050$ ] with a measure of variance 17.54 in group IV compared with 39.54 of group SM showing that subjectively, IV route brought better recovery. Submucosal route can be an effective less invasive, painless, straightforward alternative to systemic administration of corticosteroid for improving QOL recovery in mandibular third molar surgery.

## DISCUSSION

Third molars are the most frequently impacted teeth because of their particular topography, phylogeny and ontogeny. They are directly or indirectly associated with numerous disorders in the mouth, jaw and facial regions. Therefore, the extraction of third molars is one of the most common surgical procedure for Oral and Maxillofacial surgeons. Development of mandibular third molars starts in the ramus of the mandible at about the age of seven years. The third molars are the last teeth to erupt in all races despite racial variations in the eruption sequence. Racial variation in facial growth, jaw and teeth size, nature of diet, extent of generalized tooth attrition, degree of use of masticatory apparatus and genetic inheritance are the crucial factors which determines the eruption

pattern, impaction status and the incidence of agenesis of third molars.<sup>16-18</sup>

Impacted teeth were seldom a problem for Neolithic man. Their highly abrasive diet caused attrition of teeth resulting in a reduction of mesiodistal distance of the dentition. This allows the mesial migration of teeth and adequate space was available for the eruption of the third molars. But with the arrival of refined food and consequential reduction in the masticatory functional load, today, the rate of impaction of third molars shows a significant increase (John Hunter theory of nature and nurture). Mead believed that delay in eruption causes impaction of teeth. Various causes have been suggested in the literature for the impaction of the third molar. It has been suggested that the gradual evolutionary reduction in the size of the human mandible/maxilla has resulted in too small mandible/maxilla that may accommodate the corresponding molars. It has also been found that the modern diet does not offer a decided effort in mastication, resulting in loss of growth stimulation of jaws, and thus the modern man has impacted and unerupted teeth.<sup>12-16</sup>

The current general approach in dealing with impacted third molars is on the basis of clinical judgment; periodic evaluation by some clinicians and early extraction by others. Most expected complications following third molar surgery include sensory nerve damage, dry socket, pain, swelling, trismus, infection and hemorrhage. These complications are disturbing for young patients, especially if they become permanent in cases of inferior alveolar or lingual nerve injuries. In addition to factors related to surgery, the position and angulations of third molars are strongly associated with the number and degree of postoperative morbidities.<sup>10</sup>

The procedure of impacted third molar removal can cause trauma to the highly vascularized loose connective tissue area, and may cause acute inflammation with intense discomfort, as well as pain during the immediate post-operative phase. Postoperative pain is a subjective sensation, and depends on various factors such as patient age, sex, anxiety, and surgical difficulty. The pterygomandibular space is highly vascular with loose areolar tissue, and is one of the spaces related to the lower third molar region. Trismus is one of the clinical symptoms of pterygomandibular space infection. With good surgical technique, gentle manipulation of the tissue and analgesic administration after surgery can reduce postoperative side effects, although pain is not controlled completely in most cases.<sup>8-10</sup>

Corticosteroids have potent anti-inflammatory activity, and have been used at different dosages and through various routes of administration to lessen the inflammatory effects of third molar surgical removal. Glucocorticoids act at every step in the inflammatory process to decrease circulating lymphocytes, inhibit

capillary dilatation and fibroblast proliferation, and alter prostaglandins and leukotrienes synthesis. As the suppression of these factors exerts a profound effect on tissue inflammation, corticosteroids are used in surgical procedures to reduce the acute inflammatory conditions that occur postoperatively. Acute inflammation induced by tissue damage plays a major role in development of postoperative pain. Moreover, locally applied glucocorticoids have a direct inhibitory effect on signal transmission in nociceptive C-fibers and ectopic neuroma discharge in injured nerves. By virtue of its potential anti-inflammatory effects, dexamethasone is useful in lowering pain, and is currently the most powerful anti-inflammatory drug, with a long half-life. Dexamethasone is considered safe for periods shorter than two weeks even in amounts above physiological doses. Dexamethasone is an effective way of minimising swelling, trismus, and pain after removal of impacted lower third molars. It offers a simple, safe, and cost-effective treatment in moderate and severe cases.<sup>11-16</sup>

The post-operative tissue response in 3rd molar extractions is highly unpredictable. Gender, weight, duration of surgery, degree and depth of impacted tooth, surgical methods used, density of bone, skill of the operator, angulation and size of the tooth, a proximity of the tooth to the vital structures, amount of the tooth developed and association with a pathological lesion affect the post-operative swelling, pain, trismus, compromised oral intake of fluids and diet, aesthetic deformity, fracture of the angle of the mandible and infection. Acute postoperative pain following third molar surgery is predominantly a consequence of inflammation caused by tissue injury. Its course depends on the degree of surgical trauma suffered, the need for bone tissue removal, and the extension of periosteum displacement. Inflammatory complications after third molar surgery still remain an important factor in quality of life of patients at the early postoperative periods. Oral surgeons should be aware of the different modalities of alleviation of these complications to make postoperative recovery more comfortable for patient.<sup>12</sup>

Corticosteroids have been used since long by many surgeons to decrease the post-operative sequelae in 3rd molar surgeries. According to the literature review conducted by Francesco and co-authors analysis of the scientific publications in the last 20 years revealed that there were no definite protocols relative to different molecules or regimens, time and route of administration of corticosteroids in preventing the post-operative adverse effects in 3rd molar surgeries. Dexamethasone, dexamethasone sodium phosphate, dexamethasone acetate, methylprednisolone, methylprednisolone acetate and methylprednisolone sodium succinate have been extensively studied in the last 5 to 6 decades and their therapeutic effects, in the 3rd molar surgery, have been documented. It is a proven fact that Long-acting steroids give better results than short-acting ones and intramuscular and

intravenous routes of administration have almost same effects.<sup>13,14</sup>

## CONCLUSION

Superior post-operative therapeutic effects are achieved by pre-operative administration of 8 mg intramuscular injection of dexamethasone. Post-operative swelling and trismus are significantly reduced in the early post-surgical period.

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