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A REVIEW ON SUBMUCOSAL ADMINISTRATION OF CORTICOSTEROIDS IN THIRD MOLAR SURGERY

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ABSTRACT

The classic signs of inflammation, which includes edema, erythema, pain and loss of function, commonly occurs after a routine or difficult third molar surgical procedure. The inflammatory process is necessary for the healing to occur, but often excessive inflammation which causes the patient unnecessary pain, trismus and edema. Corticosteroids reduce inflammation via the inhibition of phospholipase A2, which is the first enzyme involved in the conversion of phospholipids into arachidonic acid, therefore blocking the synthesis of other products such as prostaglandins, leukotrienes and substances related to thromboxane A2. In essence, corticosteroids prevents the formation of these end products which is a broth of potent inflammatory mediators causing the signs and symptoms. This articles has focussed to review on submucosal administration of corticosteroids in third molar surgery.

Key words: corticosteroid–submucosal–pain–swelling–trismus

1 INTRODUCTION

Corticosteroids (CS) are an important class of naturally occurring and synthetic steroid hormones that affect virtually every aspect of human physiology. The most important glucocorticoid derived from the adrenal gland is cortisol (sometimes called hydroxycortisone). The adrenal cortex consists of three zones. The zona glomerulosa, located immediately beneath the capsule, synthesizes aldosterone, the most potent mineralocorticoid (MC) in humans. The zona fasciculata (middle zone) produces cortisol (hydrocortisone), the principle circulating glucocorticoid (GC). Adrenal-androgens are secreted by both zona fasciculata and zona reticularis (innermost zone). GC secretion is regulated by adrenocorticotropic hormone (ACTH), produced in the anterior pituitary and released in secretory bursts throughout the day and night. ACTH production is in turn driven by corticotrophin releasing hormone (CRH) from the hypothalamus. Pulses of ACTH occur every 30-120 minutes. Varying amplitude of ACTH pulses leads to the normal diurnal rhythm of cortisol production.[1–3]

The surgical extraction of impacted mandibular third molars is one of the most commonly performed procedures in oral surgery. Patients experience a range of uncomfortable signs and symptoms after extraction including pain, trismus, facial oedema, and functional discomfort of the oral cavity, because of muscular oedema and spasm.[2,4] Corticosteroids exert an important anti-inflammatory action, reducing liquid transudation and oedema formation, decreasing cell exudates, inhibiting vascular dilatation and reducing fibrin deposit around the inflamed area. The mechanisms responsible for these effects include inhibiting the leukocyte chemotaxis to the inflammatory focus, inhibition of fibroblast function and endothelial cells, and suppression of the production of numerous chemical inflammation mediators.[5,6] Although corticosteroids are most effective during the first 24 hours post-surgery, their effect can also be noticed for 3 days. This articles has focussed to review on submucosal administration of corticosteroids in third molar surgery.

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2 REVIEW OF LITERATURE

The most researched outcome on the use of corticosteroids in oral surgery revolves around their effect in reducing post-operative pain, swelling and trismus in third molar surgery, orthognathic surgery and mandibular fracture. Over the last six decades, the use of corticosteroids for third molar surgery had been studied extensively in different formulations, dosings, routes and sites of administration (7)(8)(9). These corticosteroids include dexamethasone (per-oral/p.o.), dexamethasone acetate (intramuscular), dexamethasone sodium phosphate (intravenous and intramuscular), methylprednisolone , methylprednisolone acetate and methylprednisolone sodium succinate (both intravenous and intramuscular)[10-13].

Graziani et al in 2008, studied the effect of endo-alveolar and sub-mucosal administration of dexamethasone sodium phosphate to prevent inflammatory sequelae after surgical removal of lower third molars was studied. He included forty-three patients who underwent bilateral extractions of lower third molars and were randomly assigned to receive either dexamethasone 4 mg (group A) or 10 mg (group B) as endo-alveolar powder or 10 mg as sub-mucosal injection (group C) unilaterally. The controlateral site served as control and did not receive any steroid administration. Facial edema, trismus and pain perception were evaluated at the 2nd and 7th postoperative day. A multivariate analysis revealed that treatment and ostectomy time were both significantly positively associated with the degree of postoperative trismus and edema and found that both sub-mucosal and endo-alveolar administration of dexamethasone are effective in reducing postoperative sequelae of surgical removal of lower wisdom teeth.[14]

In a study by Majid et al in 2011, included thirty patients, each of whom required removal of a single impacted mandibular third molar under local anaesthesia, were randomly allocated to one of 3 groups of 10 each. The 2 experimental groups were given dexamethasone 4 mg submucosally or intramuscularly, and the control group had no steroid. Both dexamethasone groups showed significant reduction in swelling and pain compared with the control group at all intervals. Submucosal dexamethasone resulted in significantly less trismus than controls on day 1 postoperatively, but there were no significant differences among the groups at the other times.[10]

Majid et al in 2011 evaluated the effect of a submucosal 4-mg dexamethasone injection on postoperative sequelae and QOL was measured after third molar surgery compared with an intramuscular 4-mg dexamethasone injection and a control group and stated that submucosal injection of dexamethasone 4 mg is an effective therapeutic strategy for improving the quality of life after surgical removal of impacted lower third molars with a comparable effect on postoperative sequelae to intramuscular injection.[15]

Antunes et al in 2011 conducted a prospective, controlled, randomized trial involving 60 lower third molar surgeries in 67 patients. The sample was randomly divided into three groups: group A (local injection), group B (tablets), and group C (control). Both the oral administration and local injection of dexamethasone proved effective in reducing pain, edema, and trismus compared to control group following lower third molar surgeries, achieving similar results.[11]

Nair et al in 2013, included a total of 100 patients requiring surgical removal of a single mandibular third molar .The experimental group (50) received dexamethasone 4 mg as submucosal injection and control group (50) received no drugs. None of the patients developed wound infection or any serious postoperative complications. Postoperative edema tended to be less severe on the second postoperative day in the experimental group and the result was statistically significant. There were no significant differences in the reduction of pain and trismus between the two groups studied.[11]

In 2013, Warraich et al, included 100 patients in their study, requiring surgical removal of third molar under local anesthesia, were randomly divided into 2 groups, group I receiving 4mg dexamethasone as submucosal injection and the control group II received no steroid administration. Facial swelling was quantified by anatomical facial landmarks. Furthermore, pain and patient satisfaction, as well as neurological score and the degree of mouth opening were observed from each patient and found that patients receiving dexamethasone showed significant reduction in pain, swelling, trismus, a tendency to less neurological complaints and improved quality of life compared with the control group.[16]

Majid & Mahmood in 2013, in their study he included a total of 72 patients (32 males and 40 females) were included in the study and were randomly divided into six equal study groups: five treatment groups received dexamethasone 4 mg as intramuscular injection, intravenous injection, oral tablets, submucosal injection and endoalveolar powder; and control group which received no dexamethasone. Swelling, trismus and pain were evaluated at the first, third and seventh day post-operatively. A modified questionnaire was used to measure different aspects of QOL. All dexamethasone groups showed statistically significant improvement in swelling and pain at all intervals and in trismus at day 1 and day 3 intervals as compared to control. QOL measures also showed significant improvement.[17]

A randomised double-blind clinical trial was conducted by Bhargava et al in 2014, on 60 patients with class II position B impaction of mandibular third molars. Sixty transalveolar extractions were performed prospectively with ten patients randomly allocated to each of the six study groups (group T: intra-space injection of Twin mix; group S: submucosal dexamethasone; group M: intramuscular dexamethasone; group V: intravenous dexamethasone; group O: per-oral dexamethasone; group C: control group, no dexamethasone). Mean operative visual analogue scale scores did not show statistical variation, and post-operative visual scores indicated better patient comfort in the steroid groups with statistically significant difference between group T and the control group on the first, third and the seventh postoperative day. Mean increase in distances between tragus and soft tissue menton to assess facial swelling showed strong statistically significant difference between the first

and the third post-operative day between the control group and group T (p value <0.0001). Association of trismus was found less with the steroid treatment groups when compared to the control group.[18]

Zerener et al in 2015 in their study, included a total of 78 patients (aged 18 to 35) were divided into three groups randomly (control, dexamethasone, and triamcinolone acetonide). In the experimental groups, dexamethasone and triamcinolone acetonide were injected into submucosa at about 1 cm above the surgical area submucosally. The control group of patients did not take any drug submucosally but the same surgical procedure was applied. There were statistically significant differences between the control and experimental groups on the different days of the postoperative period. The effect of triamcinolone acetonide on pain started on the first day postoperatively and the effect of triamcinolone acetonide on trismus and pain was better than other groups at the third and seventh days. However, there was no statistically significant difference between the effects of dexamethasone and triamcinolone acetonide regarding postoperative complications.[16]

Ibikunle AA et al in 2016, conducted a randomised controlled trial in which subjects were randomly distributed into three groups of 62 subjects each, Group A consisted of subjects who received 40 mg oral prednisolone; Group B consisted of subjects who received 40 mg submucosal injection of prednisolone while Group C consisted of subjects who did not receive prednisolone. Measurements for facial width/facial swelling, pain, and mouth opening were recorded preoperatively and postoperatively. The postoperative evaluation points were postoperative days 1, 3, and 7. These measurements were compared with the preoperative values both within and among the groups. A considerable increase in the mean postoperative values for pain, facial width and trismus was observed. Notably, subjects who did not receive prednisolone showed comparatively higher values for the measured parameters throughout the postoperative evaluation period. Subjects who received submucosal injection of prednisolone showed overall lower values compared to those who received oral prednisolone.[19]

Deo et al in 2016, in their study, included forty healthy adult subjects of either gender, underwent surgical removal of the lower impacted third molar under local anaesthesia and after being randomly assigned to receive either 8 mg dexamethasone submucosal injection or normal saline injection in proximity to surgical site. Facial swelling, trismus showed significant reduction immediate postoperative day in dexamethasone groups. Patient perception postoperative pain on VAS score was not significant but overall improvement in QOL was observed.[8]

Saravanan et al in 2016, in their study, included 2 groups in which the group 2 (20 patients) is the study group in which all the patients had single dose of pre-operative sub mucosal dexamethasone of 4 mg/2 ml. The group 1 patients (20 patients) received single dose of pre-operative intra muscular dexamethasone of 4 mg/2 ml. The control group (20 patients) did not receive steroid in any form. The postoperative pain, swelling and trismus were assessed for all the groups. The submucosal dexamethasone group showed marked improvement in the mouth opening in the follow ups than the intra muscular dexamethasone group. In those five cases of bilateral impaction, in study groups 1 and 2, the mouth opening was very much significant when sub mucosal dexamethasone was given. [12]

Navneet Singh et al in 2017, in their prospective study he included a total of 44 patients undergoing third molar surgery, who were divided in two groups – Group A who received 4mg of submucosal dexamethasone and Group B who received 4 mg of intramuscular dexamethasone during the extraction of third molars. Swelling, trismus and VAS scores were measured in both the groups on 3rd and 7th postoperative days and found that there was no significant difference in swelling, pain and trismus index between both the groups. [20]

Daniel lim et al in 2017, in their prospective, randomized, double-blind study, included 65 patients who required surgical removal of impacted mandibular third molars with Class II or position B impaction (Pell and Gregory classification). Patients were randomly assigned to 1 of 3 groups: dexamethasone, methylprednisolone, or placebo (control) and found that both methylprednisolone and dexamethasone significantly reduced swelling and trismus whereas the methylprednisolone group had significantly less pain and consumed a lower amount of analgesics during the early postoperative days.[21]

Mojsa et al in 2017, in their study, ninety patients were included and split randomly into three equal study groups (30 patients in each): the 'before' group received dexamethasone 15 min before surgery and placebo 15 min after surgery; the 'after' group received placebo 15 min before surgery and dexamethasone 15 min after surgery; the 'placebo' group received placebo 15 min before surgery and placebo 15 min after surgery. Postoperative pain was recorded by the patients using a visual analogue scale, numerical rating scale, and the McGill Pain Questionnaire at 1, 2, 4, 6, 8, 12, and 24 h after surgery. The patients also recorded the total number of analgesic doses consumed during the 24 h after the procedure. Swelling (determined using linear measurements of the face) and trismus (determined through measurement of maximum mouth opening) were assessed at 48 h, 72 h, and 7 days following surgery. Better control of pain, swelling, and trismus was demonstrated for dexamethasone in comparison to placebo. Postoperative dexamethasone provided better pain control than preoperative dexamethasone. There was no difference in total rescue analgesic intake between the preoperative and postoperative dexamethasone groups.[22]

Khalida et al in 2017, in their randomised control study, included 50 patients requiring surgical removal of an impacted third molar and divided in to two group I patients received one regimen single dose of 4 mg dexamethasone sub mucosally, group II received no drug. The postoperative sequelae were assessed and statistically significant reduction in pain and swelling was noted in dexamethasone group.[23]

Chug et al in 2018, in their study, allocated the participants randomly to three groups: the placebo group received

normal saline injection (control), while the 8 mg dexamethasone group and 40 mg methylprednisolone group received submucosal injections of these steroids preoperatively. Each participant was assessed for postoperative pain, swelling, and trismus, along with a subjective assessment of QOL through a structured questionnaire. The participants administered dexamethasone showed significant reductions in pain and trismus compared to the control group ($P < 0.05$). Submucosal injection of dexamethasone was found to be superior to methylprednisolone only in terms of the reduction in swelling. QOL was minimally affected in patients administered dexamethasone as compared to methylprednisolone and control subjects[24].

Daniel lim et al in 2017, in their study, included 60 patients and were randomly assigned to three different groups, namely the saline control group, the (4 mg) dexamethasone group and the (40 mg) methylprednisolone group where the agents were administered as a preemptive submucosal injection. Postoperatively, patients were prescribed with standard analgesic and antibiotic. Pain was assessed on postoperative day one, two, five and seven based on visual analogue scale and the amount of analgesic consumed. The methylprednisolone group experienced significantly less pain and consumed less analgesic on postoperative day one and two when compared to control group.[25]

Arora et al in 2018, in their prospective randomized study, included 45 patients requiring surgical removal of an impacted third molar. Selected patients were divided randomly into three groups of 15 patients each: group I patients received one regimen single dose of 4 mg dexamethasone sub mucosally, group II received one regimen single dose of 8 mg dexamethasone sub mucosally, and group III (control group), no dexamethasone was given but only received injection of normal saline sub mucosally after establishing local anaesthesia. The postoperative sequelae were assessed on the second and seventh postoperative day. As compared to group III, groups I and II showed statistically significant reduction in pain and swelling whereas no statistically significant difference was found between the test groups.[9]

3 CONCLUSION :

The submucosal route of corticosteroid administration is a viable alternative to the other routes. Indeed, it exhibited significant comparative advantages over other route of administration. In addition, it offers a safe, simple, cost-effective method, which produces a high concentration of the drug at the operative site, thereby lessening the systemic effects.

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