Betamethasone and methylprednisolone usage in lower third molar surgery : Review literature

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Abstract

The surgical extraction of lower third molar is the most frequent intervention in oral surgery. This procedure is often associated with significant postoperative sequalae that may have both a biological and social impact. Beside severe complications such as dysaesthesia, severe infection, fracture and dry socket, patients frequently complain of pain, swelling and limitation in mouth opening due to inflammatory response following the surgical injury. Many previous studies of lower third molar surgery have focused on reducing pain, facial swelling and trismus. Although inflammatory response is good for healing but an exacerbated response can cause all of the complications. Nowaday, clinicians mostly prescribe betamethasone and methylprednisolone to overcome these complications. This review is to conclude ideas of betamethasone and methylprednisolone use in lower third molar surgery.

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Introduction

Pain, trismus, and swelling are the common results of removal of lower third molar surgery. Many surgeons routinely use betamethasone and methylprednisolone for patients after lower third molar surgery based on generalized and rarely mentioned regarding type, dosage, and duration of administration.

Our objective is to review some available literature and use the information to give suggestions to surgeons for the rational use of betamethasone and methylprednisolone preoperative and postoperative until further studies can clarify these issues and provide additional evidence based guidelines on dose form, dosage, and duration of administration

Postsurgical Sequalae after Lower Third Molar Surgery

Surgical removal of the lower third molars is the most common surgical procedure in oral and maxillofacial surgery. Due to the anatomical position of impacted third molars, both soft and hard tissue trauma occur during surgery, resulting in postoperative swelling and trismus. Most oral and maxillofacial surgeons consider swelling rather than a normal physiologic reaction to insult and injury. When hard and soft tissue are injured, the normal physiologic response is inflammation and leading to swelling. Swelling will occur after every surgical intervention and should be expected.

The physiological response of the body tissues to injury of any cause is inflammation and pain, which vary for each patient. After every surgical intervention, inflammatory mediators (prostaglandins, leukotrienes, bradykinin, platelet activating factor, etc.) are released into the tissues in response to this irritation, with a subsequent increase in vascular dilatation and permeability, causing facial swelling and enhancing the interstitial tissue response.[1,2]

Swelling occurs as osmotic pressures rise, capillary permeability is altered, transudation of fluid occurs through vessels into area of damage, and local lymphatic system becomes obstructed by fibrin and fibrinogen clots derived from plasma and adjacent injured tissues. Fluid then accumulates in the interstitial spaces. Oftenly, greater degrees of tissue injury lead to greater amounts of swelling.[4,5] Swelling is variable from site to site 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.[6]

Postoperative facial swelling is difficult to assessed because it involves 3 dimensions of measurement with an irregular, convex surface and can manifest itselff internally as well as externally. Patients who have a chubby cheek appear to have less swelling than lean patients.[7] Many researchers have tried various swelling measurement techniques and make comparisons between patient populations. Visual analog scales, standardized stereo radiographic, computerized tomography, modified face bow devices, ultrasonography, facial plethysmographs, or various other ways of taking direct facial measurements.[8-15] These methodologies have been validated for accuracy, reproducibility, or statical reliability.

Experience of surgeons and difficulty are recognized as significant factors in the incidence and severity of postoperative swelling and trismus after lower third molar surgery.[16-19] Inexperience doctors will generally encounter more postoperative swelling than highly experienced surgeons, all other variables being equal with short duration and tissue are handled gently.

Duration of facial swelling after lower third molar surgery has not well documented

and is probably variable to each patient and procedure. Peterson[20] states that swelling maximized in 2-3 days after lower third molar surgery, but Laskin states that usually facial swelling maximizes in 1-2 days. Excessive patient's activity might increase the amount of facial swelling, no study compare the facial swelling responses of resting versus execessive physically patients after lower third molar surgery.

Steroid use to control facial swelling and trismus

Steroid are well known adjuncts to surgery for suppresing tissue mediators of inflammation, thereby reducing transudation of fluids and lessening swelling.[16] Some reduction of postoperative pain generally accompanies a reduction of facial swelling, and steroids have some inhibitory effects on prostaglandins. But steroids alone do not have a clinically significant analgesic effect.[7,11] In fact, the use of steroids might increase the patient's reaction to pain by suppressing β -endorphin levels.[21] Many patients also experience a mild euphoric, or mood altering, effect from steroids that theoretically might help them cope with postoperative sequelae,[22,23] but this effect is poorly studied in patient underwent lower third molar surgery and might be highly variable. Long-term use of steroids can delay healing and increase susceptibility to infection, but these effects are not clinically significant with the typical short-term usage protocols in lower third molar surgery.[24]

To gain the significant outcome, steroids need to administered in exceed doses than the normal physiologic amounts of released by the body.[23] Steroids commonly eliminated from the blood less than 24 hours, but some forms delay the anti inflammatory effects up to 3 days.[24] Steroids are involved in the synthesis of immunoreactive and regulatory proteins, including vasocortin, angiotensinconverting enzyme (which degrades bradykinin) and lipocortin.[26,27] Some authors state that steroids stabilize cellular membranes and have a suppressive effect on lymphocytes, monocytes, and eosinophils.[4,23,25]

The body's natural glucocorticosteroid is hydrocortisone or cortisol. The normal daily output by the adrenal glands is reported to be between 15 mg and 30 mg, but up to 300 mg can be supplied in times of crisis.[23,25,28] Steroids also have numerous other desirable effects and side effects with which clinicians should be familiar before using the drugs.

Betamethasone and Methylprednisolone forms

Methylprednisolone used more commonly than betamethasone, but betamethasone has a longer duration of action. Methyprednisolone oral, methylprednisolone acetate, and methylprednisolone sodium succinate is the most common that used in lower third molar surgery.[16,28] Betamethasone sodium phosphate has recommended by some authors because it is more potent compare to methylprednisolone. Betamethasone has two forms, betamethasone sodium phospate (short acting) and betamethasone acetate (long acting).[14,29]

All the forms are nearly pure glucocorticosteroid effects and virtually no mineralocorticosteroid effects.[22] Methylprednisolone has been told have the least side effects on leukocyte chemotaxis compare to betamethasone. The longer acting forms will generally have more depressing effect to adrenal glands.[30] Longer acting steroids suit to major surgery cases.

Contraindication

Steroids are said to be absolutely contraindicated for use in patients with active or incompletely treated tuberculosis, active viral or fungal infections (especially ocular herpes),

active acne vulgaris, primary glaucoma, or patients with a history of acute psychoses or psychotic tendencies.[4,28,31] However, the recommendations are primarily based on longterm chronic steroid use rather than single-dose or short-term use.[24,25] Nevertheless, it is prudent to minimize use in these patients until more data emerge on the risks of short-term usage. Because some formulations of steroids contain methylparaben or sulfites, allergic reactions are possible in susceptible patients.[25] There have been at least 30 documented allergic reactions and numerous side effects reported in the literature.[28] Preoperative medical consultation might be prudent for patients with diverticulitis, peptic ulcers, Cushing's syndrome, renal insufficiency, uncontrolled hypertension, uncontrolled diabetes mellitus, pregnancy, lactation, acute or chronic infections, or myasthenia gravis.[4,23,28,31] The adverse effects on hypertension and glaucoma are related to mineralocorticoid activity and are not a problem with the newer derivatives, such as methylprednisolone.[22]

Adverse Effects

Casually use of steroids is not recommended. As in any other aspect of the healing arts, the risks need to be weighed against the anticipated benefits of use. Some authors have suggested that the side effects should contraindicate the use of steroids after minor procedures, but these views are not well supported in the literature.[19,24,32] The data have disproved any significant risks when steroids are used as a single dose or are confined to protocols of less than 3 to 5 days.[23,24,28] Most systemic effects, such as changes in levels of sodium, potassium, or plasma cortisol, are minor, transient, and do not exceed the normal ranges of variation.[33] Sisk and Bonnington[34] noted that single-dose therapy does not really increase susceptibility to infection but can delay the diagnosis of infection by masking some signs and symptoms. All hormone levels return to normal by the seventh postoperative day in the typical protocols.[11,31] The use of oral forms might cause gastrointestinal upset, and steroids are best taken with food.[28] Steroids can cause depression or psychoses in certain patients, but this effect is fairly unpredictable.

The various steroid preparations are not equal in potency or duration of effect. A hundred milligrams of cortisone is equivalent to 80 mg of hydrocortisone (cortisol, the body's natural product), 16 mg of methylprednisolone, and 3 mg of betamethasone.[24] Hydrocortisone use is limited by its short biologic half-life of 8 to 12 hours. Methylprednisolone has an intermediate half-life of 18 to 36 hours, whereas betamethasone have longer half-lives of 36 to 54 hours.[22] The acetate forms have low solubility that acts as a sustained-release depot for 1 to 2 weeks (peak effect, 4-8 days), giving these forms some clinical advantage when a longer effect is needed.

Steroids	Equivalent dose	Biologic half life	Available forms
Hydrocortisone	25 mg	8-12 hours	V, M, O
Methylprednisolone	4 mg	18-36 hours	V, M, O
Betamethasone	0.6-0.75 mg	36-54 hours	V, M, O

V, Intravenous; M, Intramuscular; O, Oral

Dose of administration in lower third molar surgery

The dosage and duration of action of the steroids have clinically significant effects on the overall amount of swelling after surgery. As with any other medications, steroids must be used properly to derive the maximum anticipated benefit. These critically important effects are rarely addressed in references advocating postoperative steroid use and include the following:

1. All steroids must be administered before the infliction of tissue damage (several hours before, in oral usage), not during or after surgery.[6,24,26] Oral forms must be given at least 2 to 4 hours in advance of the procedure to allow for adequate tissue levels.[24,26,27] Peak levels for bradykinin release occur within 3 hours after tissue trauma. Few data exist on the subject of optimal lead times for preoperative intramuscular administration.

2. A higher steroid dose will yield more satisfactory results.[13,22,23] Gersema and Baker state the steroid dosage should exceed the maximum daily output, equivalent to 300 mg of cortisol, for maximum effect. Gersema and Baker and Beirn and Hollander[11] recommend the administration of a high-loading dose of 125 mg of methylprednisolone parenterally (a dosage that is equivalent to 23 mg of betamethasone). This dose has yielded the best results and has not created any clinically significant problems for patients without contraindications. Messer and Keller[7] recorded no side effects when up to 12 mg of betamethasone or equivalent were administered.

3. Rebound swelling can occur if the duration of use is inadequate; therefore, it is important to maintain levels of short-duration steroid formulations for more than 1 day.[12,13,16] Peterson[16] and Milles and Desjardins[13] state there is a need to continue corticosteroid therapy for a minimum of 3 days because swelling in patients treated with steroids does not appear to peak until the third day after surgery. This has not been well studied, however. With most forms, single-use steroid effects wear off after the first day, and rebound swelling occurs. Milles and Desjardins[13] recommend a sustained release form of steroid, such as Depo-Medrol (methylprednisolone acetate) in a higher single dose of 40 mg. A study by Huffman[35] did not show any statistically significant clinical differences between the use of 40 mg and 125 mg doses of methylprednisolone. The alternative is to place the patient on a multiple-day dosage regimen of an oral steroid after surgery. Tapering of doses is not mandatory in shortterm dosing.[24,37] Follow-up dosage requirements have not been adequately studied.

4. Use of usual dosages of steroids over 3 to 4 days has no significant adverse effects on healing and they do not suppress adrenal function to a significant degree.[23,24,28] Cortisol levels return to normal value in 5 to 7 days.[11,32] Many authors refer to administering a high dose, followed by an abrupt discontinuance or rapidly tapering doses as "pulsed therapy."[22,31] However, this is generally associated with therapeutic, not prophylactic, use.

Discussion

Most surgeons utilize corticosteroids based on the recognized efficacy to control surgery outcomes and to yield a comfortable post-surgery period.[32] However, there are no definite protocols relative to different molecules or regimens, time and route of administration. Many investigations have been performed on the control of postoperative swelling in oral surgery. Post-surgical facial swelling affects the daily life of the patient. Many authors have advocated the use of steroids to limit postoperative swelling due to their suppressive

action on trasudation, but few have made definitive recommendations supported by randomized clinical trials.[24,34]

In most of the studies, the use of steroid drugs has been analyzed. Specifically, steroids include compounds with short and long duration of action. In the last years, compounds that are more frequently used in oral surgery are methylprednisolone that are 4–5 times more efficacious than the natural compound cortisol[34,35] and can be administered orally or IM or IV. Betamethasone has a longer duration of action and is more efficacious.

All the studies reported in literature have utilized different molecules, dosages, routes and time of administration. While using corticosteroids in the postoperative period, it is preferable to administer drugs 1 h before surgery, if they are administered parenterally, or 2–4 h in advance, if taken orally.[24] It is also important to continue therapy for more than 24 h in order to obtain a long lasting postoperative effect.[10,36,37] In the studies examined, betamethasone has been administered in the submucosa[38] orally,[39,40] IM[41] and IV,[36,42] whereas methylprednisolone has been administered orally,[10] IM in the masseteric muscle and IV.10,42 However, results obtained cannot be compared as, although studies often had an internal control, as they analyzed in the same patient, in independent excisions, treatment versus no pharmacological intervention, the timing, dosage and route of administration differed in independent studies.

In some cases, a single pre-operative administration has been adopted,[10,36,42] whereas in others, the treatment has been administered before and after surgery[39,] In all these studies, positive results were obtained, confirming the general antiinflammatory properties of steroids irrespective of specific compound, dosage and timing. The immediate postoperative endoalveolar or submucosal administration of betamethasone produces a beneficial effect in preventing inflammatory sequelae of lower third molar surgery.

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