



## APPLICATION OF CORTICOSTEROIDS IN ORAL AND MAXILLOFACIAL SURGERY – A REVIEW

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### ABSTRACT

Corticosteroids are potent anti-inflammatory drugs that resemble cortisol, a naturally produced hormone by the body. Their main use is to reduce inflammation, especially when the body mistakenly triggers inflammation where it shouldn't exist. Corticosteroids are widely used in the treatment of diseases, disorders and conditions affecting the oral and maxillofacial area and the adjacent associated structures. The diseases of the oral and maxillofacial region may be either local or the manifestation of systemic problem. Corticosteroids have their widest application in the management of acute and chronic conditions which have an allergic, immunologic, or inflammatory basis. Most of the oral and maxillofacial surgeons utilize corticosteroids based on their efficacy to control outcomes of surgery and to yield a comfortable post-surgery period. This paper reviews the uses of corticosteroids in oral and maxillofacial surgery.

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## INTRODUCTION

Corticosteroids are anti-inflammatory drugs which resemble cortisol, hormone which is naturally produced by the body. The most important usage of corticosteroids is to reduce inflammation, especially when the body triggers inflammation mistakenly where it shouldn't have existed. Corticosteroids are commonly used in the treatment of disorders, diseases, and conditions which affects the oral and maxillofacial area. The diseases of the oral and maxillofacial region may be two types either local or the manifestation of systemic problem (Krishnan, 2018). Corticosteroids (CS) are well known for their properties to reduce inflammation, fluid transudation and edema. Corticosteroids is very efficacious anti-inflammatory agents and for that reason they are very routinely used in several various conditions (Zandi, 2012).

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This paper reviews the uses of corticosteroids in oral and maxillofacial surgery.

**PHYSIOLOGY:** There are commonly three groups of steroids hormones which are produced in the adrenal cortex: the glucocorticoids, androgens and mineralcorticoids. Adrenal cortex secretes glucocorticoids which is effective on the metabolism of protein and carbohydrates. The zona fasciculata is responsible for the secretion of glucocorticoids, cortisol and corticosterone and small amount of adrenal androgen and estrogens. The secretion of these cells are well controlled by the hypothalamic pituitary axis (HPA) via adrenocorticotrophic hormone (ACTH) (Moss, 1989). Corticosteroids are chemically very alike to endogenous cortisol which is vital in protein, carbohydrate, and fat metabolism, in maintenance of vascular reactivity, and body adaption to stress.<sup>1</sup>The adrenal gland usually produces about 24-30 mg of cortisol every day, but may increase in production up to 300 mg of cortisol in times of stress. The cortisol secretion is mainly regulated by circadian rhythm, which is a stress-related response, and a

great negative feedback mechanism between the adrenals, hypothalamus, and pituitary. The hypothalamic-pituitary-adrenal axis becomes suppressed and may even take up to 12 months to recover when supraphysiologic doses of corticosteroids (>30 mg cortisol equivalent) are given for 14 days or more. A ability to react to stress, has been shown to return within 2 weeks to 1 month (Sanghavi, 2015).

#### The normal secretion rate of the two principal corticoids is

- ) Hydrocortisone: 10-20 mg daily
- ) Aldosterone: 0.125 mg daily.

#### CLASSIFICATION OF CORTICOSTEROIDS:

Corticosteroids are steroid hormones and are of two types which is produced in the adrenal cortex, they are glucocorticoids and mineralocorticoids. Glucocorticoids, corticosterone and cortisol, have countless effects and can react on almost all cells in the body. For example, glucocorticoids regulates the metabolic activity, immune function, and behaviour. Circulation glucocorticoid levels is increased in response to a variety of stressors under control of the hypothalamic-pituitary-adrenal (HPA) axis. Hypothalamic releases corticotropin-releasing hormone (CRH) which triggers pituitary release adrenocorticotrophic hormone (ACTH), henceforth which stimulates glucocorticoid production by the zona fasciculata of the adrenals. The adrenals secretes cortisol, corticosterone, or combination both, which depends on the species (Taves, 2011). Glucocorticoids (GCs) are frequently the first-line therapy for autoimmune diseases which also includes various neurological conditions which is commonly associated with complications and comorbidities. These comprises of both short term and long-term complications that are frequently related to the dose and cumulative dose of GCs. In General, low dose is up to 7.5 mg/d, medium dose is >7.5 mg and <30 mg/d, high dose is >30 mg but <100mg/d, and very high dose is greater than 100mg/d of prednisolone (Gensler, 2012).

Mineralocorticoids, like aldosterone, which promote sodium reabsorption in transporting epithelia of the kidneys, salivary glands, and large intestine. Circulation of aldosterone concentrations rises in response to low blood volume or sodium depletion under control of the renin-angiotensin system (RAS). The kidney releases renin, which therefore converts angiotensinogen to angiotensin I. Angiotensin I is further cleaved by angiotensin-converting enzyme (ACE) into active angiotensin II. Angiotensin II is responsible for mineralocorticoid production by the zona glomerulosa of the adrenals (Taves, 2011).

**MECHANISM OF ACTION:** The main classic signs of inflammation, which incorporates edema, erythema, pain and loss of function, commonly happens after a normal or difficult surgical procedure. The inflammatory process is most important necessity for the healing process to occur, but excessive inflammation causes unnecessary pain, trismus and edema to the patient. Corticosteroids reduces inflammation by inhibiting the phospholipase A2, which is the foremost enzyme that is involved in the conversion of phospholipids into arachidonic acid, but blocking the synthesis of various other products such as prostaglandins, leukotrienes and substances are related to thromboxane A2. In essence, corticosteroids is responsible in preventing the formation of these end products which is potent inflammatory mediators which cause the signs

and symptoms that are described above.<sup>4</sup> They do have the ability to standardise lysozyme membranes, reduction in the release of inflammation which causes lysozymes, and decreasing the permeability of capillary that prevents diapedesis (Krishnan, 2018).

#### Actions of corticosteroids are broadly divided into

- ) Glucocorticoids: Affects carbohydrate, protein, and fat metabolism.
- ) Mineralocorticoids: Affects Na+, K+, and fluid balance (Tripathi, 2003).

#### CORTICOSTEROIDS IN THIRD MOLAR SURGERY:

Postoperative pain followed by extraction of the impacted third molars may cause severe distress to the patient. Analgesics and anti-inflammatory drugs which are prescribed postoperatively will relieve pain, reduce swelling, and trismus to the maximum and are responsible for the healing without side effects. Therefore, drugs, like corticosteroids, which exert both analgesic and anti-inflammatory effects should be recommended for the management of postoperative pain and discomfort (Seymour, 1984). Corticosteroids can have analgesic properties which are indirect analgesic effects, but are not analgesic drugs. They can be recommended in combination with analgesics for the reduction of inflammatory symptoms, also including pain. Methylprednisolone and dexamethasone are the commonly suggested drugs that can be effective in decreasing the pain after the impacted mandibular third molar surgery. The most effective for pain reduction routes are intramuscular and intravenous routes. Preoperative period is the perfect timing for injecting corticosteroids to obtain maximum benefit for pain reduction (Sugravan, 2020).

**CORTICOSTEROIDS IN TRAUMA:** Steroids are widely recommended after oral surgical procedures which limit postoperative inflammation. Hooley and Hohl in 1974 explained the proper use of steroid in the prevention of postoperative edema. He further concluded by saying that topical use of steroid can prevent ulceration and excoriation which are resulted during the retraction during surgery of the lips and mouth (Bhanot, 2016).

#### CORTICOSTEROIDS IN ORTHOGNATHIC SURGERY:

Orthognathic surgery is a very unique attempt in the field of facial surgery. Patient appearance and occlusal function are significantly improved, without affecting the patient's well-being. The aim of orthognathic surgery is to recreate the normal and proper relationship between the maxilla and the mandible which helps to improve mastication, speech and esthetics. To minimize the risk of wound healing surgeons commonly prescribe antibiotics before or after orthognathic surgery. Although there is a harmony on the increased risk of infection following surgery, but the degree to which antibiotics prevents infections and what type and dose of antibiotics must be used is still controversial. Steroids are widely administered in post-operative pain, trismus, swelling, nausea and vomiting and helps in reducing inflammatory reactions following orthognathic surgery. The Short term systemic corticosteroid therapy has been more frequently used after oral and maxillofacial surgery, especially orthognathic surgery. Corticosteroids are well known for the reduction of inflammation, fluid transudation, and edema. Preoperative prescription of systemic corticosteroids are widely prescribed

in orthognathic surgery to prevent postoperative complications (Jamali, 2019).

**CORTICOSTEROIDS IN TMJ SURGERIES:** Horten in the year 1953 reported the usage of intraarticular injection of steroids into the temporomandibular joint (TMJ) space. He was first person to perform this procedure in the TMJ. He was then inspired by Hollander and colleagues' work in which they injected hydrocortisone into other arthritic joints. Kopp et al. in the year 1985 injected betamethasone into the TMJ space in a small group of patients with TMJ pain and dysfunction and the results showed that betamethasone was effective in reducing joint pain up to 4 weeks. About 6 years later, Kopp and colleagues again performed intraarticular injection using methylprednisolone which also showed similar promising results up to 4 weeks. Bjørnland et al. injected betamethasone into the TMJ space in osteoarthritis patients with myofascial pain. He concluded that Betamethasone managed to reduce joint pain, whereas sodium hyaluronate which was administered to other study group was concluded to be more effective. Another very promising use of corticosteroids is for the management of disc displacement without reduction. Samiee et al. concluded that combined intraarticular injection with local anaesthetic and corticosteroids had improved results in mouth opening.

**ADRENAL INSUFFICIENCY AND ORAL AND MAXILLOFACIAL SURGERY:** Adrenal insufficiency (AI) is commonly known as an endocrine disorder which is characterized by inadequate production of adrenal androgens, mineralocorticoids and glucocorticoids by the adrenal cortex (Khalaf, 2013).

**Adrenal crisis prophylaxis:** Acute adrenal crisis, along with the lack of mineralocorticoids and glucocorticoids, is a important medical emergency. The symptoms are abdominal pain, weakness, hypotension, dehydration, nausea, and vomiting. The laboratory findings are hyperkalemia, hyponatremia, hypoglycemia, uremia, and acidosis. This is responsible for decreased glucocorticoid response towards stress, and to precipitate an adrenal crisis.

## MANAGEMENT

- ) Intravenous fluids (in the form of 5% dextrose in normal saline).
- ) Primary adrenal insufficiency: Start on 20-25 mg hydrocortisone per 24 h.
- ) Secondary adrenal insufficiency: 15-20 mg hydrocortisone per 24 h; if borderline fails in cosyntropin test considers 10 mg or stress dose cover only.
- ) Hydrocortisone should primarily administered intravenously. If any improvement is noticed within 24 h, the hydrocortisone dose may be reduced. It should changed to an oral formulation when the patient becomes stable. In the morning the dose can be declined by one-third to one-half the doses daily until a maintenance dose of 20 mg and 10 mg in the afternoon or at night. Few patients may only need a dose of 20 mg/day on total (i.e., 20 mg every morning, or 15 mg in the morning and 5 mg in the afternoon or at night).
- ) The condition that is responsible for the crisis, like infection, should be found out and the underlying cause must be treated (Arlt, 2009).

## MANAGEMENT OF PRE AND POST-OPERATIVE MORBIDITIES ASSOCIATED WITH MAXILLOFACIAL SURGERIES:

The expected sequelae of oral and maxillofacial surgeries are facial pain, edema, ecchymosis and limitation of mouth opening. The post-operative complications affects the ability of patient return to the day today life activities, and the quality of life of patient. Many modalities are widely used to reduce the sequelae in the oral and maxillofacial surgery which includes use of ice pack, pressure dressing, surgical drain, and drugs. Corticosteroids are widely recommended to control post-operative morbidities and to promote the comfort for patients. However, there are no definite protocols available regarding the molecules, doses, schedules, and routes of administration. The widely administered types of corticosteroids are betamethasone, dexamethasone, and methylprednisolone, these are administered intravenously, orally or by injection directly into the masseter muscle. The morbidity-management protocol varies depending on the type of surgery that is performed (Kalkwarf, 1982). For many years corticosteroids has been advocated to decrease post-rhinoplasty edema. In a study by Gurlek et al., it was concluded that high dose methylprednisolone was more effective in preventing and minimiseg both the periorbital ecchymosis and edema in open rhinoplasty. At the same time, Kargi et al., and Kara and Gokalan concluded that the perioperative application of corticosteroids helps in reducing edema and ecchymosis that are associated with rhinoplasty surgery. In contrast, Hoffmann et al. did not find any increase either in the edema or the ecchymosis after rhinoplasty surgery. Regarding orthognathic surgery, investigations showed that preoperative corticosteroid administration significantly reduced the post-operative inflammation and edema. In contrast, Munro et al. did not find any significant decrease in postoperative edema even if the highest doses and the longest durations of corticosteroid treatment are recommended.

## OTHER USES OF CORTICOSTEROIDS IN ORAL AND MAXILLOFACIAL SURGERY:

In addition to the above mentioned indications, corticosteroids are used in the management of acute trigeminal nerve injuries, traumatic facial nerve paralysis, chronic facial pain, and allergic diseases which involves the maxillofacial area (Zandi, 2012).

## ROUTES OF ADMINISTRATION

**The main routes of administration of corticosteroids are:**

- ) Oral (by ingestion through the mouth) e.g., prednisone, prednisolone, methylprednisolone, betamethasone, hydrocortisone, dexamethasone
- ) Parenteral (intravenous or intramuscular) e.g., methylprednisolone, triamcinolone, dexamethasone
- ) Inhalation (e.g. aerosol in asthma) e.g., beclometasone, budesonide, flunisolide, fluticasone
- ) Topically (e.g. application to skin) e.g., beclometasone, betamethasone, clobetasol
- ) Corticosteroids can also be administered by intra-articular, ocular, nasal, rectal (enema), in ear or spinal methods (Larsen, 2018).

## GUIDELINES FOR USAGE IN ORAL AND MAXILLOFACIAL SURGICAL PROCEDURES:

Key information must be first elicited in the medical history to identify the patients who may have problems because of

pituitary-adrenal suppression. All the patient undergoing dental therapy must answer these questions: (1) Are you taking glucocorticoid drugs? (2) Have you taken glucocorticoid drugs within the past year?. If it is found out that the patient is currently taking a systemic glucocorticoid medication, additional extra information regarding the dosage, the route of administration, the frequency of doses, and the duration of therapy should be asked.

If at all the patient is not presently using glucocorticoids but has the history in the past, then the length of time since the medication was last received should be asked. Patients receiving glucocorticoids in doses which is greater than or equivalent of 30 mg. of cortisone daily for a period of one week or longer have a high possibility of developing adrenal crisis. Persons who have already discontinued the therapy within the past year are also at high risk. The higher the daily dosage, the longer the period of administration, or the shorter the period since discontinuation, the higher the potential risk of adrenal crisis.

Because of the primary inherent management problems with the very high-risk patient, the elective procedures should be postponed if there is a high possibility of changes in the patient's adrenal status. It is mandatory to get physicians consent if it is decided that dental procedures must be performed.

If the patient has a high risk of adrenal crisis, two precautions must be undertaken: they are (1) stress reduction and (2) increased administration of glucocorticoids. Many regimens for the management of high risk patient during dental therapy have been recommended. Most are them are nonspecific or tend to underestimate the degree of greater stress that are associated with the dental treatment. Dentists must be very careful in evaluating the extent of dental procedures and in estimating the apprehension of patients before the discussion of the corticosteroids recommendations with physicians. The following guidelines may be used to categorize management:

- ) Routine noninvasive dental therapy (examination, impressions, etc.)
- ) A nonapprehensive patient
- ) Slight risk of pituitary-adrenal suppression.
- ) No steroid prep is required.
- ) Light sedation is optional.
- ) Routine invasive dental therapy (restorations, routine endodontics, scaling and root planing, biopsy) or
- ) A moderately apprehensive patient or
- ) Relatively greater risk of pituitary-adrenal suppression.
- ) A steroid prep consisting of doubling' the daily dosage of glucocorticoid prior to the procedure followed by gradually reducing the dose each day for 3 days back to the normal dosage.
- ) Light to moderate sedation.

Combination of two or three factors from Category II or Extensive invasive dental therapy (long restorative or endodontic procedures, multiple extractions, periodontal or endodontic surgery) or An extremely apprehensive patient or Severe risk of pituitary-adrenal suppression.

- ) A steroid prep consisting of quadrupling'9 the daily dosage of glucocorticoid prior to the procedure

followed by gradual reducton over a 2- or 3-day period to the normal dosage.

- ) Moderate to heavy sedation.

Combination of two or more of the situations in Category III or a long surgical procedure.

- ) Hospitalization of the patient where administration of extensive doses of glucocorticoids, heavy sedation, and appropriate monitoring can be provided.

All administration of steroid prescription must be by mutual agreement with the physician in charge of glucocorticoid therapy. If there is any doubt in managing the patient, one should always choose the most rigorous protocol. It is always safer to over administration of prophylactic steroid preps than to underadminister.

**CONTRAINDICATIONS OF STEROIDS:** The main contraindication of topical corticosteroids are the treatment of primary bacterial infections and mainly the patients with hypersensitivity.

## SIDE EFFECTS

Side effects are purely dependent on the type and dosage of the drug and length of the treatment. The common side effects includes weight gain, impaired growth, adrenal insufficiency, increased susceptibility to infection, myopathy, osteoporosis, osteonecrosis, cataract, glaucoma, fractures, hypertension, insomnia, diabetes, and peptic ulcer. Topical treatments are responsible for severe adverse effects like skin atrophy, hypopigmentation contact dermatitis, oral thrush, subcutaneous fat wasting, and cushingoid effect from systemic absorption. Inhaled corticosteroids causes oropharyngeal candidiasis, dysphonia, reflex cough, bronchospasm, and pharyngitis.<sup>4</sup>

## CONCLUSION

Glucocorticoids are recommended, singly or in combination with other drugs, for the treatment of many diseases which affects the oral and maxillofacial area. They are often used to reduce the expected post-operative morbidities like pain and edema after surgeries. Due to anti-inflammatory and anti-allergic actions of glucocorticoids, they are responsible for the management of acute and chronic conditions. However, corticosteroids carry the increased risk of side effects which are sometimes very severe and can be life threatening. Therefore, benefits derived from corticosteroids should be always weighed against their potential risks in each and every patient. It is very essential to prescribe the minimal dose and the least potent type of corticosteroids for the therapeutic effect, it is also necessary for the simultaneous use of non-steroidal agents to minimise the dose of corticosteroids, and administrating corticosteroids for a short period of time are some strategies to reduce the adverse effects of corticosteroids.

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