



Steroids in Dentistry - A Review

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ABSTRACT

Steroids are cycloalkane based compounds that are naturally produced by the body. They are also artificially produced for pharmacotherapeutics, wherein they are used to control pain, anxiety and for the management of some oral diseases. They may be administered topically or systemically. They are also immunosuppressive and hence their use should be with caution after weighing the risk-benefit ratio. This review discusses the pharmacology of steroids and its applications in dentistry.

Keywords: oral mucosa, oral surgery, orthodontics, root resorption, steroids, vesiculobullous lesions.

INTRODUCTION

Steroids, sometimes referred to as corticosteroids, are substances that are naturally produced in our body. They are produced by the adrenal glands and help to regulate many functions in our body like the way body uses fats, proteins and carbohydrates. They regulate our immune system and the salt-water balance and water in our system. They help to reduce inflammation.¹

Steroids can be manufactured synthetically as drugs, available in the form of fluid for injections and tablets. There are different types of steroids and they all have different effects on the body. Steroids that are commonly used are hydrocortisone, dexamethasone, methyl prednisolone, prednisolone etc. In dentistry, steroids are used as anti-inflammatory drugs to control pain, relieve anxiety and also for the treatment of some oral diseases. Members of steroid family are ubiquitous, occurring in plants, protozoa, yeast and higher forms of life. Steroids exhibit a variety of biological function, from participation in cell membrane structure to regulation of physiological events. Naturally occurring steroids and their synthetic analogs are used extensively in medical practice. Steroids are important in biology, chemistry and medicine.¹

Dental patients with a history of corticosteroid use may require special consideration prior to receiving dental treatment. The purpose of this clinical review understands the use of steroids in dentistry and the special considerations or the dental patients who present with a history of corticosteroid use.

Structure, Classification, Synthesis and Metabolism

Chemical structure

Steroid is a type of organic compound that contains a characteristic arrangement of four cycloalkane rings that are joined to each other. The configuration of nucleus, the nature of the groups attached to it and their positions distinguish different steroids. Examples of steroids include sterols (cholesterol), hormones (estradiol and

testosterone), bile acids, oral contraceptives and anti-inflammatory drugs such as dexamethasone). The core steroid is composed of twenty carbon atoms bonded together that take the form of four rings: three cyclohexane rings (designated as rings A, B and C) and one cyclopentane ring (D ring).²

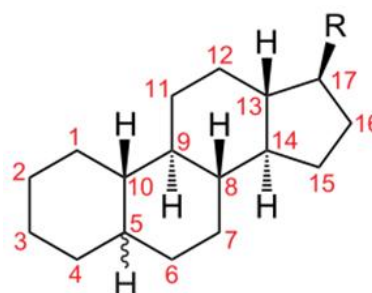


Figure 1: Basic structure of steroid

Steroids are a class of organic compounds with a chemical structure that contains the core of gonane or a skeleton derived there from. Commonly, steroids have a methyl group at the carbons C-10 and C-13 and an alkyl side chain at C-17. Further they vary by the configuration of the side chain, the number of additional methyl groups, and the functional groups attached to the rings. For example, sterols have a hydroxyl group attached at position C-3 and a skeleton derived from Cholestane.² Gonane is the simplest possible steroid and is composed of seventeen carbon atoms, bonded together to form four fused rings. The three cyclohexane rings that form skeleton of phenanthrene and cyclopentane ring, together called as cyclopentaphenanthrene.

Classification

The classification of steroids is based on chemical structure and on the nature of the physiological effect or function. There are eight groups of steroids.³

Group 1- Sterols, contain side chain R having 8-10 carbon atoms. They are components of plant and animal lipids.

The most important sterol is cholesterol participates in the biosynthesis of hormones.

Group 2 – Vitamin D – is made up of unsaturated isomers of sterols (with ring B open). These isomers act to regulate calcium metabolism and formation of skeleton in vertebrates.

Group 3- Bile alcohol and bile acids which contain a hydroxyl or carboxylic group in the side chain with 5 or 8 carbon atoms, aid in the digestion of food in the intestines of vertebrates.

Group 4 - Aglycones (genins) of steroid saponins and steroid glycoalkaloids. Typical representative of this group are diosgenin and solasodine. They are surface active and haemolytic properties.

Group 5 - Steroid alkaloids possessing bactericidal and amoebicidal action, some of them like Cortidoxic are reported highly toxic.

Group 6 - Cardiac genins, 5 (cardenolides) or 6 membered (bufodienolides) which can strengthen the cardiac muscles by inhibiting ATPase activity. Bufodienolides are found in venom of toads.

Group 7 - Steroids sex hormones of male and female and the product of hormone conversions, a hydroxyl or carboxylic group replaces the side chain in androgens and estrogens.

Group 8 - Hormones of adrenal cortex – corticosteroids which regulate the balance of electrolytes and the metabolism of carbohydrates in vertebrates. Certain triterpene antibiotics like cephalosporin P and other triterpenes are similar to steroids.

It is also possible to classify steroids based on their chemical composition. Mesh performs this classification as follows:

Table 1: Classification of steroids based on chemistry

Class	Examples	No of C atoms
Cholestanes	Cholestrol	27
Cholanes	Cholic acid	24
Pregnanes	Progesterone	21
Androstanes	Testosterone	19
Estranes	Estradiol	18

Applications of steroids in medicine - overview

Some examples of diseases treated with naturally occurring or synthetic steroids are allergic reactions, arthritis, some malignancies, and diseases resulting from hormone deficiencies or abnormal production. In addition, synthetic steroids that mimic an action of progesterone are widely used oral contraceptive agents. Other synthetic steroids are designed to mimic stimulation of protein synthesis and muscle building action.⁴

Uses of Corticosteroids in Dentistry

Corticosteroids have wide range of uses in dentistry. Steroids are used in intracanal medicaments such as Ledermix to reduce pulpal inflammation and prevent root resorption; widely used in oral medicine such as in vesiculobullous diseases, orofacial granulomatosis, temporal arteritis and other oral mucosal disorders.⁵

In oral surgical procedures, steroids are commonly used to limit post-operative inflammation. Hooley and Hohl described several instances of steroid use in prevention of post-operative oedema and topical use on the lips and corners of the mouth to prevent ulceration and excoriation as a consequence of retraction during surgery.⁶ They are also used in the prophylaxis of adrenal crisis in patients with secondary adrenal insufficiency. Corticosteroids are immunosuppressive and anti-inflammatory drugs very widely administered to treat pathological process in medial and dental practice.

For a dental patient taking large dose of steroid supplementation, requiring less than two weeks for minor dental procedure with minimal stress, no alteration of drug therapy is indicated. However, for more than two weeks for extensive major or stressful dental procedure, the daily dose must be doubled the day before, the day of and the day after surgery and patient should be asked to resume normal maintenance dose post operatively for 2 days.

If the patient has received at least 20 mg of cortisol for more than 2 weeks within one year, then 60 mg of cortisol should be taken the day before and the day of surgery in the morning; 40 mg cortisol on the first two days post operative post op days, and then 20 mg cortisol until 6 days postoperative.

The uses of steroids in dentistry may be summarized as below

Topical use: non infections, ulcerative diseases in oral cavity, inhibit the inflammatory reaction, redness and edema

Systemic use: third molar extraction, pre-prosthetic surgery, reconstructive oral surgery, orthognatic surgery.

Corticosteroids in Orthodontic Tooth Movement

The biology of orthodontic tooth movement comprises the study of cellular, biochemical and molecular phenomena occurring in the periodontal ligament and alveolar bone. It has been shown that orthodontic movement can be affected by administration of pharmacological agents.⁷ Patients under orthodontic treatment may present variations in normal bone remodeling due to these drugs.⁸

Orthodontic tooth movement is characterized by a multiple biological process involving sequential reactions of the periodontal tissue in response to biomechanical forces. In the periodontal ligament, light or heavy mechanical force in traction zone leads to formation new

bone or alveolar wall where as the alveolar bone is directly resorbed under light force by osteoblasts. The arachidonic acid metabolites also play an important role in the process of bone remodeling during tooth movement.⁹

It is reported that the upon treatment with hydrocortisone at a dose of 10 mg/kg/day for 7 days on rats followed by observed for 20 hours; the teeth showed lower amount of tooth movement. Hence, it is essential that the patients are reviewed of their prior history of corticosteroids use. Orthodontic treatment may have to be differentiated and longer interval between treatments will help to understand any possible changes in bone.^{10,11} Study on tooth movement in humans will have a better understanding as animal studies have limitations.

Steroids in endodontics

Steroid administration influences the occurrence of root resorption. The percentage of root resorption has been found to be more on treatment with corticosteroids.⁸ However steroid-antibiotic combinations like Ledermix have also been used as intracanal medicaments for management of root resorption with reasonable success. Steroids like hydrocortisone are also mixed with zinc oxide eugenol to be used as root canal sealers. It appears that the action of steroids on root resorption is chemistry dependent.

Corticosteroids in oral and maxillofacial surgery

Use of corticosteroids plays an important role in treatment of diseases, disorder and also during the oral and surgical treatment of the maxillofacial area and other related structures due to local expression of systemic problems. Group of corticosteroids with glucocorticoid activity such as betamethasone, dexamethasone, triamcinolone and prednisolone are being used extensively in controlling pain, allergy, inflammation, and also alter immune conditions. Temporomandibular Disorders (TMDs) are clinical problems involving temporomandibular joints (TMJs), the masticatory muscles or both. It is a common musculoskeletal disorder causing orofacial pain. The most common signs and symptoms of TMDs are pain, altered mandibular movements and the elicitation of joint noise.

Treatment of TMDs varies based on their etiology. Based on the severity of the disorder, surgical or a combination of treatment like splint application, thermal application, physiotherapy etc treatment is recommended. Various corticosteroids are used in treatment of TMDs, which have dramatic effects in controlling hypomobility, pain, inflammation especially associated with TMJ problems. For a short term treatment (tapering dose for 5-7 days) oral corticosteroids are being used mainly for acute TMJ discomforts. Long term use of corticosteroids may result in acute adrenal crisis, hypertension and electrolyte anomalies, even diabetes even formation of osteoporosis that includes TMJ also. It is also reported that intra articular injections of corticosteroids (like triamcinolone

acetanide) cause damage to fibrous layer, cartilage and bone of TMJ.¹³

Table 2: Application of steroids in dentistry

Condition	Administration
Apthous ulcer	Topical
Dentin hypersensitivity	Topical
Desquamative gingivitis	Topical, Systemic
Oral lichen planus	Topical, Systemic
Post Extraction	Systemic
Pulp capping	Topical
Pulpotomy	Topical
Severe allergy	Systemic
TMJ arthritis symptoms	Systemic
Oral pemphigus	Topical, systemic

Table 3: Steroids in the management of TMD

Drug	Alternative name	Usual dose
Hydrocortisone	Hydrocortone	20-240 mg /day
Prednisone	Deltasone, Orasone	5 0=60 mg/day
Dexamethasone	Decadron	0.75 – 9.0 mg/day
Betamethasone	Celestone	0,6 – 7.2 mg/day

Corticosteroids are effectively used in treating several ulcerative and vesiculobullous lesions involving the oral cavity and perioral areas including recurrent aphthous stomatitis (RAS), Behcet's syndrome, pemphigus vulgaris, bullous pemphigoid, mucous membrane pemphigoid, erythema multiforme and Stevens-Johnson syndrome.¹⁴

Recurrent aphthous stomatitis

These are superficial ulcers creating severe pain commonly occurring in the oral cavity. Ulcers which are less than one cm are considered to be minor form having 1-5 ulcers and they persist for one to two weeks and heal spontaneously without sequelae. The ulcers larger than 1 cm are considered as major aphthous ulcers and persist for months. In such cases, Corticosteroids either alone or in combinations with other drugs is administered for treatment based on severity.¹⁵

Topical and injectable (intralesional) corticosteroids are useful for large and painful lesions. Systemic administration of corticosteroids is reserved for severe cases to prevent lesion formation or to reduce the number of lesions. Systemic corticosteroids should be prescribed in short courses, provided severe outbreaks or cases not respond to injectable or topical corticosteroids.¹⁴

Pemphigus Vulgaris

It is severe in nature and also potentially life threatening vesiculobullous disease. Oral cavity is involved in 80% of the patients affecting skin and mucous membranes. If not healed by corticosteroids, will be administered using systemic corticosteroids, with immunosuppressive

agents, in order to achieve disease control with lower dose of steroids.¹ Systemic administration of corticosteroids at doses of 1-2 mg/kg/day is effective for principal treatment of pemphigus vulgaris. Topical corticosteroids can be given to maintain remission, allowing reduction in systemic dose. Isolated lesions can be treated with injectable corticosteroids.¹⁴

Behcet's Syndrome

The treatment for this syndrome is similar to the treatment of severe or major Recurrent Aphthous Stomatitis (RAS).¹⁴

Bullous and Mucous membrane pemphigoid

Based on the clinical severity, disease progression and site of involvement systemic steroids are choice of initial treatment, followed by addition of steroid-sparing agents for long term maintenance.¹⁷ Topical and injectable corticosteroids are useful for treatment of mild or localized oral lesions.

Erythema Multiforme (EM) and Stevens-Johnson syndrome (SJS)

It has been proved that corticosteroids are very effective on EM and SJS, if treated in high doses for a short time

with proper tapering of dosages^{18, 19}. Treatment protocols such as early therapy by giving systemic prednisone (0.5 to 1.0 mg/kg/day or pulse methyl prednisolone (1mg/kg/day for 3 days), intravenous pulsed dose methyl prednisolone (3 consecutive daily infusions of 20-30 mg/kg to a maximum of 500 mg given over 2 to 3 hours), and dexamethasone pulse therapy (1.5mg/kg over 30-60 minutes on 3 consecutive days), all have been shown to be effective.¹⁸⁻²⁰

Keloid and hypertrophic scars

These generally represent pathologic over-healing conditions that are caused due to excess production of fibrous tissue following healing of skin injuries. Keloid produces more collagen than hypertrophic scars (HS). Contributory factors for more keloid production are due to inflammation, tension, and genetic background also. Keloids and HS have different clinical features. Keloids extend beyond the confines of the original wound, develop months after injury and rarely regress, whereas HS is a raised scar that remains confined to the area of the injury, normally occur within weeks, and may regress without any intervention.

Table 4: Steroids used in management of vesiculobullous lesions

Drug	Beclomethasone	Betamethasone	Clobetasol	Halobetasol	Fluocinonide
Indications	Severe recurrent aphthous stomatitis, Behcet's syndrome, Pemphigus vulgaris, Pemphigoid				
Administration	Inhaler spray topically to mucosal lesions	Topical intraoral cream or gel, soluble tablets as mouth wash	Topical intraoral cream or gel	Topical intra oral cream or ointment	Topical intraoral cream
Usual dosage	50-100 microgram sprayed onto oral Lesions	0.1% cream or 0.05% gel applied thinly bid; 0.5 mg 2-4 times daily as mouth wash	0.05% cream or gel applied thinly bid	0.05% cream or ointment applied thinly bid	0.05% cream applied thinly bid
Contraindications	Untreated infections				
Common side effects	Oral candidiasis				
Unusual side effects	Adrenal suppression if doses exceeded				

Table 5: Topical corticosteroids that are administered for oral lesions

Drug	Prednisone (Tablets)
Indications	Severe recurrent aphthous stomatitis, Behcet's syndrome, pemphigus vulgaris, emphigoid, erythema multiforme
Usual dosage	Dosage of 30-40 mg daily after breakfast for 4-5 days 1-2 mg/kg/day after breakfast until disease controlled 1-2 mg/kg/day, then maintenance of 2-5 to 15 mg daily 20-40 mg daily for 7-10 days at onset of lesions or until resolve 60 mg daily for 2 days; then 50, 40, 30, 20 and 10 mg for every 2 days
Contraindications	Hypersensitivity to corticosteroids, systemic infection, peptic disease, live vaccines
Common side effects	Dyspepsia, candidiasis, myopathy, osteoporosis, adrenal suppression, Cushing's syndrome, euphoria, depression
Unusual side effects	Peptic ulceration with perforation, Cushingoid side effect increasingly likely with the does above 7.5 mg daily

Various methods have prescribed for prevention and treatment of keloid and HSs such as pressure therapy, silicone gel sheeting, topical flavonoids, corticosteroids therapy, radiotherapy and surgery. Triamcinolone acetonide is the most commonly used steroid for the treatment of HS and keloid. It is used at a concentration of 10-20 mg/ml and can go upto 40 mg/ml for a tough and bulky lesion. The concentration depends upon the size, and site of the lesion and age of the individual²¹. Side effects of steroid injection include hypopigmentation, telangiectasia, dermal atrophy and cushingoid effect due to systemic absorption.²² Cushing's syndrome secondary to injection of triamcinolone acetonide for the treatment of keloids have been reported by several investigators.²³

Central giant cell granuloma

It is a lesion having benign tumor in jaws made up of loose fibrous connective tissue stroma most often occurs among young adults and children the characteristic of the tumor is with interspersed proliferating fibroblasts, aggregations of multinucleated giant cells and foci of hemorrhage. Both surgical and non-surgical treatments are administered based on the severity of lesion. Intracellular corticosteroid injections are generally given for non surgical treatment. Triamcinolone acetonide is found to be effective, and may act by suppressing any angiogenic component of the lesion.²⁴

Other uses

Corticosteroids are successfully used in the treatment of acute trigeminal nerve injuries, traumatic facial nerve paralysis, chronic facial pain and allergic diseases involving maxillofacial area.

Contraindications of steroids

Topical corticosteroids are contraindicated in the treatment of primary bacterial infections and in patients with hypersensitivity

Side effects

Side effects are dependent on type and dosage of drug, length of treatment. It includes weight gain, impaired growth, adrenal insufficiency, increased susceptibility to infection, myopathy, osteoporosis, osteonecrosis, cataract, glaucoma, fractures, hypertension, insomnia, diabetes, peptic ulcer.²⁵

Topical treatments cause adverse effects such as skin atrophy, hypo-pigmentation contact dermatitis, oral thrush, sub cutaneous fat wasting and cushingoid effect from systemic absorption. Inhaled corticosteroids cause side effects including oropharyngeal candidiasis, dysphonia, reflex cough, bronchospasm and pharyngitis.²⁶

CONCLUSION

Corticosteroids are used for treatment of various diseases affecting oral and maxillofacial area to control pain, edema especially after surgery. They have widest applications in chronic and acute conditions of allergic,

inflammatory etc. It also carries the potential side effects sometimes very severe. Non steroidal drugs are prescribed to minimize dosage of steroids to minimize side effects. The use of steroids should be viewed careful in dentistry.

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