GLUCOCORTICOIDS IN ORAL MEDICINE

M. Nakova[1], A. Sredovska Bozhinov[2], M.Stojanova[3]

[1]*marijanakova@yahoo.com;* [2]*a.sredovska@gmail.com*

[1,2]International Balkan University, Faculty of Dental Medicine
[3]DHI "DentalCair" Skopje

Abstract. *Through, widely known as the body's stress hormone, cortisol has a variety of effects on the different functions of the body; it is mainly been released from the zona fasciculata, a layer of the adrenal cortex. Glucocorticosteroid receptors are present in almost all tissue in the body. Therefore, cortisol is able to affect nearly every organ and system: nervous, immune, cardiovascular, respiratory, reproductive, musculoskeletal, and oral disorders. Cortisol has many functions in the human body, such as mediating the stress response, regulating metabolism, inflammatory responses, and immune function. Steroids are been used as anti-inflammatory, antiallergic, and immunosuppressive drugs in many general and oral diseases. Steroids can be manufactured synthetically as drugs, available in the form of fluid for injections, tablets, ointment, solution, and gels. Steroids are of the most broadly used drugs in dentistry and readily act as an immunosuppressive agent. Corticosteroids have modernized the treatment protocol for several disease conditions inclusive of many oral diseases. These are strong and effective anti-inflammatory drugs resembling cortisol. Their function is to decrease inflammation, particularly when the body inaccurately activates the inflammatory system. Many oral and maxillofacial clinicians apply the usage of corticosteroids established on their effectiveness to control the consequences of any dental procedure or surgery. The present review focused on the pharmacology, use of corticosteroids in oral medicine, and side effects of corticosteroids.*

1. INTRODUCTION

The adrenal cortex consists of the cortex and medulla. The cortex produced steroid hormones including glucocorticoids. Mineralocorticoids and adrenal androgens, and the medulla produce catecholamine, epinephrine, and norepinephrine. (Fig. 1)

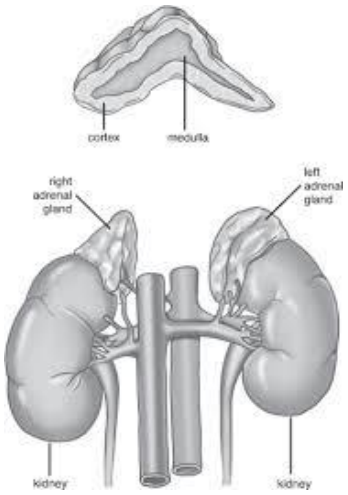

Figure 1. Adrenal Cortex

The adrenal cortex takes part in steroidogenesis, producing glucocorticoids, mineralocorticoids, and androgen precursors. It has three distinct functional and histological zones: the zone glomerulosa, zona fasciculata and zona reticularis. Each layer produces steroid hormones from the precursor cholesterol. The zona glomelurosa produces mineralocorticoids, the zona fasciculata produces glucocorticoids and zona reticularis produces androgen precursors

Endogenous cortisol by the adrenal gland is been controlled by the hypothalamic-pituitary-adrenal axis and occurs in a diurnal and circadian pattern every 24 hours. The hypothalamic-pituitary-adrenal (HPA) axis is involved in the production of glucocorticoids and adrenal androgens from zona fasciculata and zona reticularis. In response to circadian rhythms or stressors, paraventricular neurons (PVN) in the hypothalamus make and secrete a corticotropin-realizing hormone (CRH). CRH binds receptors on the anterior pituitary gland, which leads to the synthesis of ACTH (corticotropin) from pre-pro- opomelanocortin (pre- (POMC). ACTH from the anterior pituitary is been released into the circulation and engages the melanocortin type 2 receptors (MC-2 R) in the zona fasciculata of the adrenal cortex predominantly to induce the synthesis of glucocorticoids. [1, 2]

Circulating glucocorticoids negatively feedback on the hypothalamus and the anterior pituitary, suppressing the release of CRH and ACTH respectively. This is the prevention of the continued rise of glucocorticoid levels. Sl.2

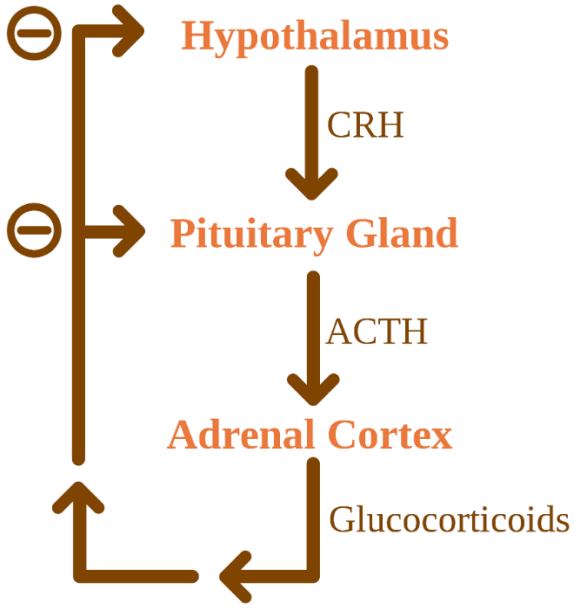

Figure 2.

Cortisol is a major glucocorticoid and increases in response to stress, which activates the HPA axis. Therefore, all of its functions can be thought of as allowing the body to function with increased stress. Upon engaging glucocorticoid receptors, cortisol increases the expression of genes that will regular metabolism, the immune system, cardiovascular function, growth, maintaining blood pressure, the sensitivity of vascular smooth muscle, and suppresses the release of vasodilatation like nitrous oxide.!)Regarding metabolism, cortisol increased gluconeogenesis and decreases peripheral glucose uptake and the next effect is an increase in serum glucose. Generally, growth is inhibited, leading to muscle atrophy, increased bone resorption, and thinking of the skin. [3]

1.1 Pharmacology of Corticosteroids

Corticosteroids are classified into three groups: corticosteroids with short acting; intermediate-acting and long-acting (hydrocortisone, triamcinolone, dexamethasone, clobetasol, and mometasone. (table 1)

Table 1.

Drug	Route of administration	Duration of action (hours)	Equivalent glucocorticoid dose (mg)	Relative potency — anti-inflammatory	Relative potency — mineralcorticoid
Short-acting					
Hydrocortisone	Oral, parenteral	8–12	20	0	++
Cortisone	Oral, parenteral	8–12	25	0	++
Intermediate-acting					
Methylprednisolone	Oral, parenteral	12–36	4	+	0
Prednisone	Oral	12–36	5	+	+
Triamcinolone	Oral, parenteral	12–36	4	+	0
Long-acting					
Dexamethasone	Oral, parenteral	24–72	0.75	++	0
Betamethasone	Oral, parenteral	24–72	0.60	++	0

The corticosteroids may be used systematically administrated (orally intravenously and topical (creams, ointments, nasal oral inhalation, intraarticular injection) the pharmacology efficacy chiefly depends on the anti-inflammatory immune-suppressive and antiproliferative, effect. [4, 5]

The physiologic and metabolic effect of corticosteroids is numerous. Glucocorticosteroids bring inhibition of white blood cells function, and lysozyme membrane stabilization inhibits plasminogen activation and decreases the synthesis of inflammatory mediators like prostaglandins and leukotrienes. These drugs might be directed systematically or topically, are metabolized in the liver after conjugation, and are excreted through urine [9]. Corticosteroids help to decrease inflammation by inhibiting phospholipase A2, consequently blocking the production of prostaglandins, leukotrienes, and other substances associated with thromboxane A2. The production of these end products is a mixture of effective inflammatory mediators and has the capacity to alleviate lysozyme membranes, diminish the discharge of inflammation-causing lysozymes, and reduce the permeability of capillary thus preventing diapedesis. Bradykinin production, which is a powerful vasodilator, is also reduced. [6, 7]

1.2 Immunosuppressive action

Steroids inhibit several in vitro and in vivo T-cells function normally: Reduced lymphokine synthesis.

T-cell's reaction against autologous tissue is mostly eliminated even in physiological concentration. Inhibition of the undefined cytolytic activity of lymphocytes against allogenic cells. Corticosteroids drugs are used in various oral diseases: (topically, sub focal application, or systematically). Topical corticosteroids are frequently used in the management of many oral mucosal. Their use should be based on detailed medical history event intake of any medication and accurate diagnosis of the oral lesion. One of the factors that play a major role in determining the success of the treatment with topical corticosteroids is the amount of time the drug comes indirectly connected with the lesion, which depends on the means used for applying topical corticosteroids. The mode of application most often used in oral pathology is adhesive ointments and aqueous solutions. Among adhesive ointments, the orobase ointment is one of the most commonly used agents. [8]

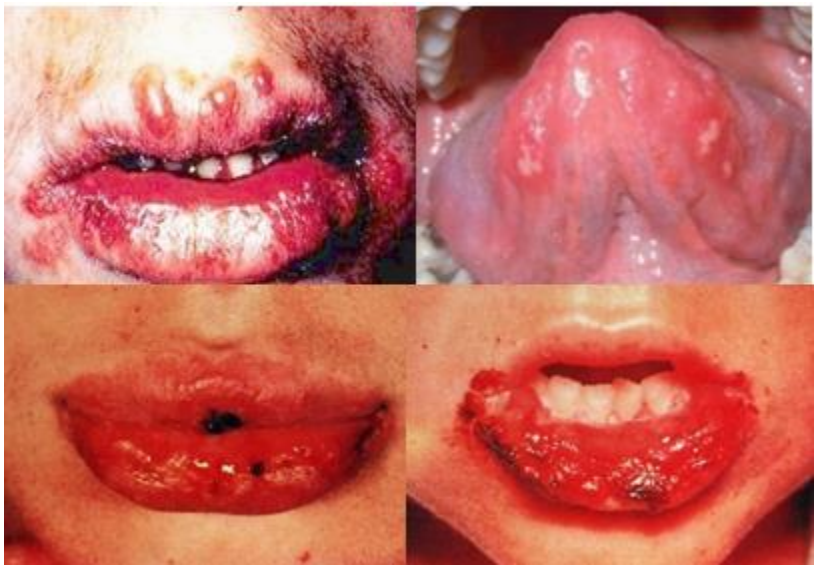

Figure 3. Ulcerative vesicular -bullous disease (aphthous ulcers; Behchte-s disease, erythema multiform, pemphigus)

2. TREATMENT OF RECURRENT APHTHOUS LESION WITH CORTICOSTEROIDS

Recurrent aphthous ulcers top the list of the commonest oral mucosal lesions encountered by any dental practitioners. Generally, this condition is self-limiting and resolves within 2-2 weeks with the exception of major recurrent aphthous ulcers. Despite it being self-limiting the pain and the frequency of recurrence treatment options for recurrent aphthous ulcers are no longer effective in relieving the discomfort caused by these ulcers. (Figure 3)

Corticosteroids are one available treatment option for recurrent aphthous ulcers.

The most commonly used steroids for local application topically are:

- Triamcinolone on acetonide (adhesive paste containing 0.1% of the steroid)
- Hydrocortisone hemisuccinate (pellets 2.2 mg)

Ulcerative that are located in the areas which are inaccessible can be controlled by:

- Topical Dexametason elixir 0.5 mg/5 ml held over the area of applied with a saturated gange pad to the ulcers, 4 times/day for 15 minutes

Betamethasone sodium phosphate rinse by dissolving 0.5 mg in 5 ml water and asking the patients to rine for 2-3 min.

Steroids aerosol Bethamethason disproportionate

A high potency topical corticosteroids such a clobetasol 0.05% in orobase or fluocinonide 0.05% in orobas.Pedersen (5)

Systemic application of corticosteroids in the aphthous lesson:

Major aphthous ulcers commonly require systemic treatment (intralesional application).[9, 10]

Prednisolon therapy 40 mg/day for one weak

- Bechet's syndrome, 40-60 mg prednisolone /day

3. TREATMENT OF ORAL LICHEN PLANUS WITH CORTICOSTEROIDS

Oral lichen planus may exist as a reticular, papillary, atrophic, erosive,bulous, or plaque-like form amongst which the erosive-atrophic forms are symptomatic.

Steroids have been shown to play an imperative role in symptomatic treatment (Kiran) Some options include topical application of corticosteroids and it is reasonably effective in the treatment of oral lichen planus. The use of the most potent corticosteroids is associated with more improvement following therapy. However, the incidence of oral candidiasis also increased in proportion to the potency of corticosteroid used. Carbone et all in 2003 reported that the use of topical corticosteroids can be as effective or even more effective than systemic corticosteroids in the treatment of oral lichen

Topical corticosteroids are reasonably effective in the treatment of the classic form of oral lichen. [11,12,13]

Topical application

- Triamcinolone acetonide 0.1%
- Gel 0.05% Behamethason valerate
- Gell clobetasol propionate 0.05%
- Gell Betamethasone valerate 0.05%
- Gell Fluconanide 0.05%Creame clobestrol 0.1%

Extensive lesions erosive lesion

- Subcutaneous injection of 0.2-0/4 ml a 10 mg/ml solution of triamcinolone acetate
- Intralesion triamcinolone acetonide in dose 0.5-1 ml a 1mg/ml suspension in the form—of weekly injection injections

Systematic steroid therapy

The commonly used systemic corticosteroid is prednisolone which is usually prescribed within the range of 40-80vmg/day to achieve a clinically response to avoid adverse effects of this drug, it is best to prescribe the lowest dose for the shortest duration possible.To achieve this, prednisolone can either be given for a brief period of 5-7 days and stop abruptly or the dose can be tapered down by 5-10 mg/day gradually over a period of 2-4 weak (Al=Hashimi,

- Prednisolon 40-80 mg.day

4. TREATMENT ERYTHEMA EXUDATIVE MULTIFORM WITH CORTICOSTEROIDS

It is an acute,self-limiting inflammatory mucocutaneous disease, that manifests on the skin and mucosal surface namely oral mucosa and genitalia. Erythema multiforme is considered a hypersensitivity reaction, the most common factors being HSV infection or drug reaction to NSAIDS or anticonvulsants (12).

Topical steroid therapy

- Clobetasol propionate (mouthwashes in aqueous solution is commonly used 15)

Systemic steroid therapy

- Prednisolon 20-40 mg/day,4-6 days for erythema exudative multipphorme (minor form)
- Prednisolon 60 mg/day over 6 weak (Erithema exudative multiform (major form)

It is a chronic autoimmune disease to a group of autoimmune, chronic mucocutaneous diseases that cause blisters and erosions of the skin and mucous membrane by intraepidermal acantholytic structure.

Pemphigus is characterized by the rapid appearance of vesicles and bullae, vying in diameter from a few millimeters to several centimeters. These lesions contain a thin, watery fluid shortly after development, but this may soon may purulent or sanguineous. When the bulla rupture, they have a raw eroded surface.

Pemphigus is a serious disease. Prior to the advent of corticosteroids, the mortality rate was approximately 95%, particularly for pemphigus Vulgaris. Today steroids and antibiotics therapy for secondary infection has reduced the mortality so that only 30 to 40 % of patients will die either of the diseases still run an acute course despite treatment and terminate in early death.

Oral mucosal lesions in pemphigus are common and predominantly appear as buccal erosions in the occlusal line, which is most exposed to trauma and also on the palate, gingival, and tongue.

It is important to realize that, while systemic therapy is important to the overall treatment of the disease, topical therapy of both skin and oral lesions is especially necessary because of the pain and discomfort suffered by these patients.

Corticosteroids can be prescribed in the form of the paste, an ointment or a mouthwash administrated as monotherapy or as adjunctive therapy with systemic therapy

Severe cases are advised high doses of pemphigus behind the topical application of corticosteroids: 100-200 mg/per day, un clinical signs decline, and then the dose can be slowly decreased to a maintenance level of 40-50 mg/daily. [14, 15] In the therapy, topical corticosteroids are used in cases where the pemphigus is not extensive and lesions are limited to the oral cavity. [17, 18]

Topical corticosteroid is used in skin and oral mucosa:

- Triamcinolon acetate 0.1% in or base 3 times/day
- Flucononide o.5% ointment,2-3 time/per day
- clobestrol propionate 0.05%%
- halobetasol 0.05%

Intralesional injection:

- Triamcinolonbacetonide (20 micrograms per liter) or
- Paramethason every 7-15 days [15,16]

Chronic treatment with systemic corticosteroids is associated with numerous and significant risks for adverse reactions and toxicities. These agents affect every organ and system and metabolic process in humans. The risk for adverse effects from corticosteroid therapy is related to the dose and the duration of therapy as well the specifics agent used. Historically, short courses of systemic corticosteroids were not thought the cause significant long-lasting toxicities. [14]

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