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Review Article

Role of Steroids in Oral Mucosal Lesions: A Review

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Abstract

From the advent of steroids, they have been an elixir for various diseases. The medicinal benefit of the steroids is due to their anti inflammatory and immunosuppressive properties which are beneficial for the treatment of various oral mucosal lesions. This review article is aimed at understanding the various types of steroids, their chemical structure, the review of various concentrations of steroids used and their effects.

Keywords: Steroids; Oral Mucosal Lesions

Introduction

Steroids, sometimes referred to as corticosteriods, 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 analogues 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 some mucosal lesions.

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 skeletion 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 cyclohedane rings that from skeleton of phenantherene and cyclopentane ring, together called as cyclopentaphenantherene.

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 aor 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 venum 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.

Applications of steroids in oral medicine

Steroids in oral lichen planus

In a randomized, double-blind, placebo-controlled study, the efficacy of the topical application of 0.025% fluocinonide was evaluated in forty patients with OLP. All patients were followed for 3 to 17 months. No adverse effect was noted during the follow-up period. In the group of 20 patients who received the drug, 4 patients (20%) showed complete remission, and 12 patients (60%) had a good or partial response to topical treatment whereas in the placebo-group, there was absolutely no complete remission and only 6 (30%) showed partial remission. In the placebo-group (70%) did not respond at all to the treatment. These results suggest that topical application of fluocinonide in an adhesive base is safe and effective in reducing signs and symptoms in OLP [5,6]. Topical corticosteroids are also first-line therapy for mucosal erosive lichen planus [7]. High-potency corticosteroids applied to the oral mucosa do not appear to cause significant adrenal suppression, even with relatively long-term use. Systemic corticosteroids, such as oral prednisone, should be considered only for severe, widespread oral lichen planus and for lichen planus involving other mucocutaneous sites [7,8]. Rabiyi M., *et al.* [9] reviewed that the use of Triamcinolone acetonide is highly efficacious in the treatment of oral lichen planus. A study conducted by Thongprasom K., *et al.* [10] evaluated fluocinolone acetonide 0.1% in three groups: solution (FAS), Orabase (FAO), and both. The best results were achieved in patients using FAO. Another study conducted by Buajeeb W., *et al.* [11] used fluocinolone acetonide gel 0.1% and fluocinolone acetonide 0.1% in Orabase. There was no significant difference between the 2 groups.

This study did not have any control group and was in the form of a short follow-up. Another study conducted by Carbone M., *et al.* [12] confirmed the efficacy of topical fluocinolone acetonide gel 0.025 %, along with the topical antimicrobial drug chlorhexidine, in treatment of erosive OLP. Topical steroids such as betamethasone showed effectiveness in the treatment of symptomatic OLP in another study [13]. Hydrocortisone hemisuccinate in aqueous solution is often of little benefit in treating OLP [14]. Fluticasone propionate spray and betamethasone sodium phosphate mouthrinse have been used effectively in the short-term management of symptomatic OLP [15]. Topical steroids such as mometasone furoate microemulsion caused a statistically significant reduction in pain in erosive-ulcerative OLP. This treatment significantly reduced the surface area of erythema and ulceration. None of these patients suffered severe adverse effects. Thus, mometasone furoate microemulsion may be safe and effective for the treatment of symptomatic erosive-ulcerative OLP [16]. Clobetasol propionate in various forms such as orabase, ointment or aqueous solution has also been shown to be effective for OLP [17-19]. A study conducted by Gonzalez-Moles MA., *et al.* [20] showed that the application of clobetasol 17-propionate orabase paste 0.05% plus 100,000 IU/ml of nystatin by means of a tray appeared was found to be efficacious for severe erosive gingival lesions and showed complete response in all 33 cases over the 48-week period.Clobetasol-17-propionate in the form of topical application has been reported as an efficacious therapy in atrophic-erosive OLP, without exposing the patient to systemic side-effects. A study by Conrotto D., *et al.* [21] has shown that clobetasol is more effective than cyclosporine in inducing clinical improvement in atrophic-erosive OLP. Triamcinolone acetonide in the forms of mouthwash and orabase were compared in the treatment of 20 cases of OLP [22]. A study was performed by Xia J., *et al* [23]. In this, the patients were instructed to use medication four times daily-after meals and before bed time. The results showed that triamcinolone acetonide mouthwash had a satisfactory shelf life and was well accepted by the OLP patients. Moreover, there was no significant difference in therapeutic efficacy from the commercial paste dosage form in the treatment of OLP in that study. The intralesional triamcinolone acetonide (TA) 0.5 ml (40 mg/ml) injection was employed for the treatment of symptomatic OLP. TA was injected on one side of the buccal mucosa of ulcerative OLP while the other side served as a control in patients with bilateral buccal mucosal lesions. TA injections were shown to be effective and safe in reducing signs and symptoms of OLP. No complication was noted with such TA injections.

The efficacy of topical tacrolimus ointment has been compared with that of triamcinolone acetonide ointment in patients with OLP. Twenty patients in each group were treated with topical tacrolimus 0.1% ointment or triamcinolone acetonide 0.1% ointment 4 times daily. The clinical effect was graded after 6 weeks. The most common side-effects in both groups were temporary burning or stinging at the site of application. Results showed that topical tacrolimus 0.1% ointment showed a better initial therapeutic response than triamcinolone acetonide 0.1% ointment. However, relapses occurred frequently within 3 - 9 weeks of the cessation of the treatment [24]. Rezazadeh Fahimeh., *et al.* conducted a retrospective study in patients with OLP. It was seen that there was a significant relationship between the type of OLP and resistance to corticosteroid, those with ulcerative form of OLP, 31.6 % was resistance to corticosteroid. The prevalence of resistance to corticosteroids was significantly increased by severity of disease [38].

Side effects

Fungal overgrowth of normal oral flora by Candida leading to candidiasis was the only common side-effect arising from topical corticosteroid therapy [25]. However, candidiasis can be controlled or prevented by using anti-fungal therapy (eg, miconazole gel alone or in combination with nystatin suspension) in topical corticosteroids [20,21]. Even though the intralesional injection of corticosteroids can induce the healing of the longstanding lesions and improve the symptoms, it can have a localized side-effect such as mucosal atrophy.

Steroids in pemphigus

Systemic corticosteroids are still the first-line treatment for PV. One of the main concerns in uncomplicated patients is when rapid control of the disease is achieved by monotherapy with corticosteroids. Control of disease activity is usually achieved within several weeks. Complete remission on minimal treatment needs months, while complete remission off treatment often requires several months or even years of therapy [26]. A second debate often concerns whether to start with a low or high dose of corticosteroids. The guidelines by EDF and European Academy of Dermatology and Venereology recommend initial prednisolone dose at 0.5 mg-1.5 mg/kg/d and if controlof the disease is not reached within 2 weeks, a higher prednisolone dose (up to 2 mg/kg) could be administered [27]. A controlled trial conducted by Ratnam KV., *et al*. [28] showed no significant difference regarding the duration of remissions andrelapse rates at 5 years in patients randomized to treatment with either low-dose oral prednisolone (1 mg/kg/d) or highdose oral

prednisolone (2.0 - 2.5 mg/kg/d).Once remission was induced, the dose was tapered by 25% [29]. A recent systematic review that evaluated randomised controlled trials with adjuvant therapy with azathioprine, mycophenolate mofetil (MMF), cyclophosphamide, cyclosporine, intravenous immunoglobulin (IVIG), plasma exchange, and infliximab in PV patients concluded that adjuvants were not beneficial for achieving remission, but were found to collectively decrease the risk of relapse by 29% [30].

Steroids in oralsubmucous fibrosis

James L., *et al*. [31] conducted a study in patients diagnosed with OSMF to assess the efficacy of injection of Hyaluronidase and Dexamethasone in Grade III OSMF. It was seen that improvement in the patient's mouth opening with a net gain of 6 ± 2 mm (92%), the range being 4 - 8 mm. Definite reduction in burning sensation, painful ulceration and blanching of oral mucosa and patient followed up for an average of 9 months and it was concluded that injection of hyaluronidase with dexamethasone is an effective method of managing Grade III OSMF and can possibly eliminate the morbidity associated with surgical management. According to Le PV., *et al*. it was observed that patients receiving hyaluronidase alone showed a quicker improvement in the burning sensation and painful ulceration produced by the effects of local by-products, although combination of dexamethasone and hyaluronidase gave better long-term results than other regimens [32]. In patients with moderate OSF, weekly submucosal intralesional injections or topical application of steroids may help to prevent further damage. Steroid ointment applied topically helps in cases with ulcers and painful oral mucosa. Its therapeutic effects were mainly anti inflammatory and appeared to have a direct healing action. Steroids act as immunosuppressive agents for prevention or suppression of the fibro productive inflammation found in OSF lesions, thus ameliorating this fibro-collagenous condition [33].

Steroids in apthous stomatitis

Topical steroids are reserved for cases that show inadequate success from the combination of local anaesthetics and anti-inflammatory agents. Corticosteroids by their anti-inflammatory action modify, in a minor way, the progress of the ulceration at all stages. In a study by Thompson AC., *et al* [4], they compared the effect of steroids on aphthous ulcers with placebo effect. In both trials there were significant reductions, compared with placebo, in ulcer duration and pain severity and no changes in the frequency of RAU in patients who applied betamethasone gel or beclomethasone aerosol spray to ulcers four times daily for six days to four weeks. The drugs most commonly adopted for local oral application in RAS are hydrocortisone hemisuccinate as 2.5 mg pellets and triamcinolone acetonide in a adhesive paste containing 0.1% of the steroid [34]. In severe minor ulcers unresponsive to these preparations and in major type ulcers it may be necessary to use a more potent steroid preparation such as a betamethasone sodium phosphate rinse (dissolve 0.5 mg in 5 mL of water and rinse for 2 - 3 min), or a high-potency topical corticosteroid, such as clobetasol 0.05% in orabase (1 : 1) or fluocinonide 0.05% in orabase (1 : 1) [35,36]. Crispian Scully stated that most patients of RAS can be managed satisfactorily with the topical steroids. These when used for short period, have a very safe profile and should be the first line of treatment for recurrent aphthous stomatitis [37]. I T Macaphee., *et al*. [38] stated that corticosteroids are the most promising approach to treatment of aphthous ulceration.

Conclusion and Summary

In this article, we have tried to review the use of corticosteroids in the treatment of some oral mucosal lesions. The use of corticosteroids has been seen to be highly successful and when added with other immunomodulatory drugs and LA agents, the results are highly promising. There is no uniform approach in the treatment of these lesions, but the use of corticosteroids either alone or in adjuvant to some other drug has shown improvement in long term success.

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