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Review Paper: Corticosteroids Indications in Oral and Maxillofacial Diseases: Side Effects, Dosage, and Administration

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ABSTRACT

Introduction: Corticosteroid drugs are used to treat many lesions as well as inflammatory and immune-related diseases because of their suppression effect on the immune system and resulting anti-inflammatory reaction. This study aimed to evaluate the use of corticosteroids in oral and maxillofacial diseases as well as their side effects, dosage, and administration.

Materials and Methods: This study was a review study by searching the databases of PubMed, Google Scholar, and Scopus. Articles, published from 2000 to 2018, with the keywords of "steroids", "mouth", "oral", "maxillofacial", "indication", "side effects", and "contraindications" were found and investigated.

Conclusion: These drugs, due to their possible adverse effects like adrenal insufficiency, should be prescribed with caution after an assessment of its risk-reward ratio. Moreover, their nutritional recommendation, discontinuation, and complications should be considered.

1. Introduction

Corticosteroids are naturally secreted by the adrenal glands in the human body. They have important role in regulating the metabolism of fat, carbohydrates, and protein; also the immune response; and salt and water balance. Natural steroids and their synthetic analogs are widely used in medicine. In dentistry, steroids are used as anti-inflammatory agents in the treatment of some oral diseases and also for the relief of pain, edema, and trismus. Hydrocortisone, dexamethasone, methylprednisolone, and prednisolone are some of the most commonly used corticosteroids in dentistry [1]. However, physicians always face challenges in treating

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corticosteroid-responsive disorders with regard to multiple and dangerous side effects of these drugs [2].

This study aimed to review the indications of corticosteroid drugs in the treatment of oral and maxillofacial diseases, and explore their side effects and usage considerations. In this regard, related studies conducted during 2000-2018 were considered for this review. Literature search was done in PubMed, Google Scholar, and Scopus databases by using following keywords: "steroids", "mouth", "oral", "maxillofacial", "Indication", "side effect", and "contraindication".

2. Indications of Corticosteroids in the Treatment of Oral Lesions

Corticosteroid drugs are used in oral and maxillofacial diseases due to their anti-inflammatory and suppressive effects. Most of these disease that corticosteroids are prescribed for are characterized by inflammation. These drugs do not interfere with the early mechanisms of oral and maxillofacial diseases, but are used as "strong painkillers" in the acute phase of the disease, or to control the host's immune system for a long time [2]. These drugs are effective in the treatment of oral diseases such as recurrent aphthous stomatitis, Behçet syndrome, lichen planus, erythema multiforme, pemphigus, bullous pemphigoid, mucous membrane pemphigoid, systemic lupus erythematosus, submucous fibrosis, central giant cell granuloma, mucoceles, hypertrophic scars, keloids as well as treatment of facial pains such as Bell's palsy, temporomandibular joint disorders, Ramsay Hunt syndrome, postherpetic neuralgia, and temporal arteritis [1-8].

The etiology of diseases such as recurrent aphthous stomatitis and lichen planus is still unclear. So far, various treatments have been proposed to reduce pain, inflammation, and disease period, but there is still no definitive treatment for these diseases. In mild cases, they may not require specific treatment or may be treated symptomatically. On the other hand, topical corticosteroids, including triamcinolone, which is commonly used to treat ulcers, has side effects and is contraindicated in some patients [3, 9-11]. Erythema Multiforme (EM) is a mucocutaneous disease that occurs due to a hypersensitivity reaction to infections (e.g. HIV virus) or drugs. In minor EM, there is usually no need for treatment and if needed, mouthwash or local clobetasol propionate cream is useful [4], while for the treatment of major EM, systemic prednisone (1 mg/kg) is recommended [2].

Vesiculobullous diseases such as pemphigus refer to a group of rare chronic mucocutaneous diseases characterized by painful lesions caused by intraepidermal acantholytic structures in the skin and mucous membrane [4]. In patients with severe pemphigus vulgaris, systemic corticosteroid therapy is recommended [3]. It seems that corticosteroid medications do not prevent the binding of pemphigus antibodies to target tissues but by interfering with lymphocyte function, reduce antibody production [2].

Systemic Lupus Erythematosus (SLE) is a classic example of autoimmune disease involving immune complexes [3]. Oral ulcers of SLE are transient and occur with acute lupus flares. Symptomatic lesions can be suppressed with potent topical corticosteroids [2].

Oral Submucous Fibrosis (OSF) is a chronic disease that affects mouth, throat, and two-thirds of the esophagus [3]. Some effects of corticosteroids on the treatment of OSF are preventing inflammatory reactions, reducing proliferation of fibroblasts, and preventing collagen deposition [2]. Corticosteroids are used as ointments or injections at the site of the lesion [2]. Their inhibitory effects on the proliferation of fibroblasts and collagen deposition are used to treat hypertrophic scars and keloids.

It is likely that corticosteroids effectiveness in treating Central Giant-Cell Granuloma (CGCG) is due to the presence of glucocorticoid receptors in multinucleated giant cells and mononuclear stromal cells [6]. Also, triamcinolone acetonide can suppress the angiogenic component of the lesion [1]. The effect of corticosteroids on the treatment of mucoceles may be related to the contraction of salivary glands [7]. The major cause of Bell's palsy is the reactivation of latent herpes simplex in cranial nerve ganglia. Some studies have shown that the use of steroid may prevent denervation, autonomic synkinesis, and progression of paresis to palsy, while other studies suggest that corticosteroids improve the recovery time [2].

It has been proved that intra-articular corticosteroids are useful in reducing pain, swelling and dysfunction caused by inflammatory diseases of Temporomandibular joint (TMJ) disorders [5]. Sometimes it may be necessary to repeat the injection, but injection for the third time should be done with caution as repeated injections may reduce the recovery waiting period. In a controlled study on adults with TMJ arthritis, it was shown that a single injection of methylprednisolone diluted with lidocaine could significantly reduce joint pain and other symptoms for 4-6 weeks [4].

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Ramsay Hunt Syndrome (RHS) is caused by the reactivation of varicella zoster virus infection. Its treatment has not been fully agreed upon. Definitive treatment includes antiviral therapy and sometimes steroids. Adjunctive steroid therapy may be useful in the management of the facial paralysis caused by RHS. However, many experts implement steroid therapy with caution as they fear dissemination of the varicella zoster virus infection, especially to around the eyes [4].

Post-Herpetic Neuralgia (PHN) is a clinical problem that appears after acute herpes zoster in about 25% of patients in the form of persistent neuropathic pain. The most important mechanism for causing chronic and prolonged pain is the repetitive painful stimuli on the central nervous system which can result in central sensitization of the nociceptive system. In these conditions, corticosteroids are used to treat pain and swelling and effectively reduce the recurrence of PHN [4]. Also, glucocorticoids are universally agreed upon as the main treatment of giant cell arteritis, and should be used immediately and aggressively for suppressing inflammation and preventing vision loss and ischemic attacks [4].

3. Contraindication of Corticosteroids

Corticosteroid administration in some cases exacerbates the patient's systemic signs and symptoms and they should not administered in these conditions. Some of the most important contraindications or precautionary use of these drugs include gastric ulcer, diabetes mellitus, hypertension, pregnancy, tuberculosis or other bacterial infections, fungal infections, herpes simplex infections, psychosis, epilepsy, congestive heart failure, renal failure, drug allergy, and osteoporosis [1, 2, 5, 12].

4. Side Effects of Corticosteroids

Topical corticosteroids

Despite the benefits and anti-inflammatory effects of corticosteroids, many side effects have also been reported for these drugs. Side effects of Topical Corticosteroids (TC) vary depending on the drug potency, duration of use, frequency of use, and site of application [4]. According to the review studies, their side effects are as follows: mucosal and skin atrophy; burning mouth syndrome; telangiectasia; purpura; allergic reactions; contact dermatitis; candidiasis; hyperpigmentation; acne form eruptions; striae; hair growth; exacerbation and spread of fungal, bacterial and viral infections; delayed healing; tachyphylaxis; and refractory response [4, 13-15]. The causes of these adverse effects are discussed below:

Mucosal atrophy

Mucosal atrophy may be due to the long-term use of topical steroids, particularly in patients who have lichen planus, where mucosal atrophy is as an intrinsic component of their condition [15].

Refractory response

Refractory response may result from a number of reasons such as poor patient's compliance, wrong instruction use, inappropriate application (for example, not using tray to deliver the drug to gingiva), insufficient drug potency, incorrect diagnosis, and failure to remove any local cause such as amalgam restoration that cause a lichenoid stomatitis [15].

Tachyphylaxis

Tachyphylaxis is skin tolerance and resistance to vascular contraction due to the use of TC. Due to the repeated use of TCs, the capillaries of the skin do not constrict well and require higher doses or more frequent use. The ability of the blood vessels to constrict returns 4 days after discontinuation of the TC use [14].

Percutaneous absorption

Percutaneous absorption depends on several factors. Horny layer of the skin acts as a barrier to percutaneous absorption of the drug into the systemic blood circulation. In a diseased skin, where the horny layer is damaged, there is more percutaneous absorption of the drug. In addition, due to the different thicknesses of the horny layer in different areas of the body, the absorption of the drug is high in some areas (mucous membrane) and low in other areas (palmoplantar skin). In addition, the horny layer acts as a reservoir, and after a single application of the drug, the drug gradually penetrates into the body. Therefore, even a small dose of strong TCs can have systemic side effects. The occurrence of these systemic effects is rare and seen more often in children and the elderly [13].

Systemic side effects

Systemic side effects include suppression of Hypothalamic-Pituitary-Adrenal (HPA) axis, growth retardation in infants and children, and Iatrogenic Cushing syndrome. In a patient with increased level of corticosteroids, signs of iatrogenic Cushing syndrome or hypercor-

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tisolism such as diastolic hypertension, diabetes, buffalo hump, facio-troncular obesity (moon face), hirsutism, striae, telangiectasia, and skin fragility can be observed. According to the studies, all cases of prolonged HPA axis suppression are because of TC overdose caused by long-term daily use for several years or application on larger body surface area. In 48% of the patients treated with potent TCs, transient and reversible reduction of HPA axis function can be observed. In cases who have used relatively low potent TCs, Cushing syndrome was also reported (e.g. triamcinolone acetonide 0.1% with a dose of 38 g/d for 4 years) [13].

Adverse effects of Systemic corticosteroids

There are many side effects for Systemic Corticosteroids (SC), which often occur after long treatment periods or prolonged use of steroids. They are as follows:

Fat redistribution

Central obesity, facio-troncular obesity (moon face), accumulation of fat above the collar bone in neck (buffalo hump).

Weakness of musculoskeletal system

Osteoporosis, bone fractures, weakness, myopathy, proximal muscle atrophy, aseptic necrosis of femoral or humeral head.

Pituitary/gonadal dysfunction

Menstrual disorders, impotence, hypothyroidism, growth retardation, and short stature.

Cutaneous manifestations

Purple striae, hyperpigmentation, hirsutism, acne, ecchymosis, atrophy, and skin fragility.

Endocrine/metabolic disorders

HPA axis suppression, growth retardation in children, insulin resistance, hyperinsulinemia, diabetes, Cushing syndrome-like signs (Central obesity, moon face, buffalo hump, striae, acne, skin fragility), menstrual disorders, impotence, hypokalemia, metabolic alkalosis, and renal calcinosis.

Digestive disorders

Gastric sensitivity, gastric ulcer, acute pancreatitis (rare), hepatic fatty infiltration, and hepatomegaly (rare).

Impaired immune system

Delayed-type hypersensitivity, suppression of the initial antigenic response, suppression of Th1 cell function and dominance of Th2 cells.

Ocular complications

Cataracts, increased intraocular pressure, and glaucoma.

Psychiatric disorders

Sleep disorders and insomnia, irritability, enjoy and depression, mania and insanity, increased intracranial pressure.

Renal impairment

Nephrocalcinosis, kidney stones.

Cardiovascular disorders

Increased arterial pressure, myocardial infarction (rare), cerebrovascular accidents (rare).

It is to be noted that the most common signs and symptoms of endogenous Cushing syndrome are high arterial pressure, acne, hirsutism, menstrual disorders, striae, and ecchymosis, while exclusive signs and symptoms of exogenous corticosteroid use are increased intracranial pressure, glaucoma, cataract, aseptic necrosis of bone, and pancreatitis [16, 17].

5. Drug Interactions With Corticosteroids

The following drugs have interactions with corticosteroids:

Antifungal drugs

They increase the level of corticosteroids and their toxicity.

Macrolides antibiotics

These drugs such as azithromycin and clarithromycin increase the corticosteroids' level in the blood and toxicity.

Antiviral drugs

These drugs increase the corticosteroids' level and toxicity.

Anti-infective drugs

These drugs such as rifampin reduce the effectiveness and level of corticosteroids.

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Anticonvulsants

They reduce the level and function of glucocorticoids.

Anticoagulants

These drugs increase the anticoagulant effect and the risk of gastrointestinal bleeding.

Anti-diabetes drugs

The simultaneous use of these drugs with corticosteroids may be disrupt blood sugar level regulation.

Live vaccines

The simultaneous use of these drugs with corticosteroids increases the risk of life-threatening infections.

Nonsteroidal anti-inflammatory drugs

The simultaneous use of these drugs with corticosteroids increases the risk of gastrointestinal ulcers [17-21].

6. Considerations on Corticosteroids Consumption

Nutritional considerations

The role of proper nutrition in people using corticosteroid for a long time for reducing drugs' side effects and correcting metabolic disturbances is often overlooked. The diet of these patients should be especially rich in protein (1.5 g/kg/d), low in fat (less than 30% calories with mainly unsaturated fatty acids), and based on polysaccharides. In addition, the diet should be low in salt; the patient should use less alcohol and cigarettes and more vitamin D and calcium [4, 22, 23].

Considerations for discontinuation of corticosteroid therapy

Before discontinuing corticosteroid therapy, the patient needs a tapering regime to avoid withdrawal symptoms [24]. An inappropriate discontinuation can reactivate the underlying disease, or because of the HPA axis suppression, the adrenal crisis may appear with anorexia, fatigue, nausea, sudden weight loss, joint pain, muscle weakness and dyspnea, reduced arterial blood pressure, hypoglycemia, fever, and skin desquamation [16, 24].

To avoid these adverse effects, one should follow the following principles: In short-term treatments (less than 10 days), regardless of the dose and type of corticosteroid, corticosteroid therapy can be abruptly stopped. In intermediate-term treatments (10-30 days), corticosteroid should be discontinued within 2 weeks, with dose reduction in every four days. In long-term treatments, the following principles should be observed: changing to short or intermediate-acting corticosteroids, reducing the number of doses to once a day (in the morning), and a gradual reduction in dose. At the end of the dose reduction protocol, HPA axis testing is performed. If the morning cortisol level is greater than 10 µg/dL, corticosteroid therapy is discontinued; and if the dose is lower, the corticosteroid dose is continued to be reduced for additional 2-4 weeks before discontinuation [16].

General considerations to reduce side effects of corticosteroids

The general principles that should be considered in order to minimize the side effects of corticosteroids are as follows: 1. Corticosteroids should be used if they are proved to be necessary; 2. The use of long-acting corticosteroids should be avoided, and short- or intermediate-acting ones should be used instead; 3. Treatment period should be reduced as much as possible; 4. The topical corticosteroids should be used as much as possible; 5. The corticosteroids should be used in association with anti-inflammatory or immunosuppressive drugs in order to reduce dosage and duration of corticosteroid therapy by benefiting from synergism between these drugs; and 6. The minimum effective dose should be used.

7. Conclusion

Corticosteroids are used to treat a wide range of oral and maxillofacial diseases for reducing pain and inflammation, but they sometimes produce severe side effects. These drugs should not be used for trivial reasons, and should be administered with caution and proper considerations for each patient.

Ethical Considerations

Compliance with ethical guidelines

There is no ethical principle to be considered doing this research.

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Authors contributions

Designing the study, Reviewing the literature, and writing the paper: Maryam Basirat and Zahra Dadvar; contribution to writing-up process and revising the article: Seyed Javad Kia and Safa Motavaseli; and reading and approving the final manuscript: All authors.

Conflict of interest

The authors declared no conflict of interest.

References

[1] Sambandam V, Neelakantan P. Steroids in dentistry– A review. International Journal of Pharmaceutical Sciences Review and Research. 2013; 22(2):240-5.

[2] Saravanan T, Subha M, Prem P, Venkatesh A. International Journal of Pharma and Bio Sciences. 2014; 5(4):B439-B446.

[3] Glick M. Burket's Oral Medicine. New York: People's Medical Publishing House; 2014.

[4] Mehdipour M, Zenouz AT. Role of corticosteroids in oral lesions. In: Magdeldin S, editor. State of the Art of Therapeutic Endocrinology. INTECH Open Access Publisher; 2012. [DOI:10.5772/50287]

[5] Panat SR, Upadhyay N, Khan M, Iqubal MA. Corticosteroids used in dentistry: An update. Journal of Dental Sciences and Oral Rehabilitation. 2014; 5(2):89-92.

[6] Osterne RL, Araújo PM, de Souza-Carvalho AC, Cavalcante RB, Sant'Ana E, Nongueira RL. Intralesional corticosteroid injections in the treatment of central giant cell lesions of the jaws: A meta-analytic study. Medicina Oral, Patologia Oral y Cirugia Bucal. 2013; 18(2):e226-32. [DOI:10.4317/medoral.18345] [PMID] [PMCID]

[7] Baharvand M, Sabounchi S, Mortazavi H. Treatment of labial mucocele by intralesional injection of dexamethasone: case series. Journal of Dental Materials and Techniques. 2014; 3(3):128-33.

[8] Luiz AC, Hiraki KR, Lemos CA, Hirota SK, Migliari DA. Treatment of painful and recurrent oral mucoceles with a high-potency topical corticosteroid: A case report. Journal of Oral and Maxillofacial Surgery. 2008; 66(8):1737-9. [DOI:10.1016/j.joms.2008.01.050] [PMID]

[9] Basirat M. The effects of low power lasers in healing of oral ulcers. Journal of Lasers in Medical Sciences. 2012; 3(2):79-83.

[10] Kia SJ, Basirat M, Estakhr L. The effect of oral curcumin on pain and clinical appearance of oral lichen planus. Journal of Dentomaxillofacial. 2017; 6(1):1-7.

[11] Basirat M, Pakfetrat A, Kakaei N, Rohani B, Bashardoust N. Crohn's disease with oral onset - a Case Report. Journal of Research in Dental and Maxillofacial Sciences. 2016; 4(1):45-51.

[12] Mohammadi Z. Systemic and local applications of steroids in endodontics: an update review. International Dental Journal. 2009; 59(5):297-304. [PMID]

[13] Dhar S, Seth J, Parikh D. Systemic side-effects of topical corticosteroids. Indian Journal of Dermatology. 2014; 59(5):460-4. [DOI:10.4103/0019-5154.139874] [PMID] [PMCID]

[14] Rathi SK, D'Souza P. Rational and ethical use of topical corticosteroids based on safety and efficacy. Indian Journal of Dermatology. 2012; 57(4):251-9. [DOI:10.4103/0019-5154.97655] [PMID] [PMCID]

[15] Savage NW, McCullough MJ. Topical corticosteroids in dental practice. Australian Dental Journal. 2005; 50(s2):S40-4. [DOI:10.1111/j.1834-7819.2005.tb00385.x] [PMID]

[16] Longui CA. Glucocorticoid therapy: Minimizing side effects. Jornal de Pediatria. 2007; 83(5):S163-71. [DOI:10.1590/S0021-75572007000700007]

[17] Liu D, Ahmet A, Ward L, Krishnamoorthy P, Mandelcorn ED, Leigh R, et al. A practical guide to the monitoring and management of the complications of systemic corticosteroid therapy. Allergy, Asthma & Clinical Immunology. 2013; 9(1):30. [DOI:10.1186/1710-1492-9-30.] [PMID] [PMCID]

[18] Ajimura CM, Jagan N, Morrow LE, Malesker MA. Drug interactions with oral inhaled medications. Journal of Pharmacy Technology. 2018; 34(6):273-80. [DOI:10.1177/8755122518788809]

[19] Blonna D, Bonasia DE, Mattei L, Bellato E, Greco V, Rossi R. Efficacy and safety of subacromial corticosteroid injection in type 2 diabetic patients. Pain Research and Treatment. 2018; 2018:9279343. [DOI:10.1155/2018/9279343] [PMID] [PMCID]

[20] Reinau D, Schwenkglenks M, Früh M, Signorell A, Blozik E, Meier CR. Glucocorticoids and the risk of peptic ulcer bleeding: Case–control analysis based on Swiss claims data. Drug Safety. 2018; 41(7): 725–30. [DOI:10.1007/s40264-018-0645-3]

[21] Luo PJ, Lin XH, Lin CC, Luo JC, Hu HY, Ting PH. Risk factors for upper gastrointestinal bleeding among aspirin users: An old issue with new findings from a population-based cohort study. Journal of the Formosan Medical Association; 2019; 18(5):939-44. [DOI:10.1016/j.jfma.2018.10.007]

[22] Chrousos G, Pavlaki AN, Magiakou MA. Glucocorticoid Therapy and Adrenal Suppression [Internet]. 2018 [Updated 2018 October 19]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK279156/

[23] Miggiano GA, Migneco MG. [Diet and chronic corticosteroid therapy (Italian)]. La Clinica Terapeutica. 2004; 155(5):213-20. [PMID]

[24] Weinberg MA, Theile CW, Fine JB. Oral pharmacology for the dental hygienist. London: Pearson Higher; 2012.

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