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Case Report

Deflazacort Paving its Way in the Treatment of Oral Lesions- Review and A Case Report

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Abstract

Deflazacort is a synthetic corticosteroid characterized by its favorable pharmacokinetic profile, distinct pharmacodynamic properties and a good safety profile when compared to other corticosteroids. Few of the substantial potential properties of this drug include lack of sodium- retaining activity, strong anti- inflammatory/immunosuppressive activity, and lower interference with carbohydrate metabolism and phosphocalcium metabolism in comparison with older corticosteroids. They have always formed an important component of dermatological therapy, but recently has gained importance to be used as a therapeutic drug to treat various oral mucosal lesions. Here, we also reported a case of erosive lichen planus in a 40-year-old man who was treated with deflazacort. He was managed with tapering systemic doses of deflazacort, following which there was complete remission of the lesions.

Keywords: Deflazacort; Adverse Effects; Oral Lichen Planus; Immunosuppressants; Autoimmune; Glucose Metabolism

Abbreviations

DFZ: Deflazacort; OLP: Oral Lichen Planus; CNS: Central Nervous System; RANKL: Receptor Activator of NF- kB ligand; OPG: Osteoprotegrin; BMD: Bone Mineral Density; MRS: Melkerson Rosenthal syndrome; VAS: Visual Analogue Scale; TEN: Toxic epidermal necrolysis; NS: Nephrotic Syndrome

Introduction

Oral lichen planus (OLP) is an autoimmune, chronic inflammatory disease which is known for its recalcitrant nature and hence its management has always posed a challenge. The commonly prescribed corticosteroids come with its share of adverse effects. In this context, the search for a steroid with minimal side effects began. A new glucocorticoid- Deflazacort (DFZ) was introduced in the year 1969 which is a D- ring substituted steroid, otherwise its structure is similar to cortisol. It is a synthetic oxazolone derivative of prednisolone with a molecular formula 11 beta, 21 - dihydroxy - 2'methy - 5' beta- H- pregna- 1,4 - dieno oxazole- 3, 20- dione -21 - acetate [1] and is known to have reduced side effects and this brief review tries to explore and focus on its application for management of Oral lesions.

Pharmacodynamics

Its anti- inflammatory and immunosuppressive effects are used to treat various diseases and are comparable to other anti- inflammatory steroids. The therapeutic dosage ratio has been reported to be 1: 1.2. Clinical studies have indicated the average potency ratio of DFZ to prednisolone is 0.69-0.89 [1,2].

Pharmacokinetics

After oral administration, DFZ is rapidly and completely absorbed in the intestinal tract- peak plasma concentration is reached within 1-2 hours. It is deacetylated at position 21 to form the main

active metabolite- 21- deacetyl deflazacort [3]. It is 40% protein bound and has no affinity for corticosteroid binding globulin and binds to plasma protein and blood cells instead, crossing the blood-brain barrier in very low concentrations. Elimination takes place through the kidneys, 70% of the administered dose is excreted in the urine and the remaining 30% is eliminated through faeces. Due to short pharmacokinetic half-life of its active metabolite, pharmacodynamic effects of DFZ are of shorter duration than those of methylprednisolone and prednisolone [1]. In terms of absolute dosage, it is 25% less potent than prednisolone [4]. It has been accepted that prednisolone 1mg is equivalent in anti- inflammatory effect to 1.2mg DFZ. (British National Formulary)

Why is it superior to other corticosteroids?

- Pharmacodynamic effect of DFZ is of shorter duration [5].
- Biochemical properties prevent early CNS effects that is because DFZ suppresses only cortisol production from the pituitary gland whereas prednisolone suppresses both adrenal and pituitary cortisol production [6].
- The bioequivalence of deflazacort compared to methyl prednisolone is for a longer duration based on phytohemagglutinin- induced T cell proliferation *in vitro* [5].
- DFZ leads to a smaller decrease in serum osteocalcin levels and has less impaired intestinal calcium absorption. And thus, there is favorable RANKL/OPG ratio maintained. (RANKL- Receptor Activator of NF- kB ligand, OPG- Osteoprotegrin) Moreover, because of this DFZ is associated with having less effect on corticosteroid induced osteoporosis when compared to prednisolone [7].
- Fewer effects on glucose metabolism [8].
- DFZ as a maintained therapy prevents fat accumulation and causes minimal impairment of the lipid profile in comparison to prednisolone [9].
- Better corticosteroid to be used in children [1].
- It can be used as long-term therapy in diabetic patients [1].
- DFZ has a wide therapeutic index [1].

Safety profile of DFZ

Several clinical studies have suggested that DFZ is safer than other glucocorticoids. This was postulated owing to its pharmacologic properties of causing less calcium and hydroxyproline excretion [10,11] fewer metabolic effects on glucose balance, [8] and less neuronal degeneration compared to other glucocorticoids [6]. Lippuner., *et al.* [9] in his study showed that treatment with DFZ for several months or more induces less bone loss than other steroids as assessed by photon absorptiometry and bone histomorphometry. Some researchers have claimed that some of the bone sparing effect of DFZ compared to prednisolone could be explained by a less impaired intestinal calcium absorption by DFZ. The BMD (bone mineral density) was reduced in patients treated with prednisolone than in DFZ group according to Luca., *et al.* Fat accumulation is a well-known side effect of glucocorticoid therapy as a consequence of peripheral resistance to insulin with decreased glucose tolerance and increased levels of triglycerides. Luca., *et al*. in his study also showed that the maintenance therapy with DFZ in comparison to prednisolone is associated with an improved linear growth, prevents excessive bone loss, fat accumulation in the population of pre- pubertal patients and contributes to prevent coronary heart disease by lesser impairment of the lipid profile compared with prednisolone [3,9]. DFZ has proven to be advantageous in insulin- treated diabetics who require long term steroid therapy. Various studies have shown that using DFZ in kidney transplant patients helps to prevent fat accumulation and worsening of the lipid profile [1]. The maintenance dose is usually within range 3- 18mg/day. The smallest effective dose should be used and increased if necessary [1].

DFZ withdrawal

Once a daily dose equivalent to 9 mg deflazacort is reached, dose reduction should be slower to allow the HPA-axis to recover. Abrupt withdrawal of systemic corticosteroid treatment that is continued up to 3 weeks is appropriate if it is considered that the disease is unlikely to relapse. Abrupt withdrawal of doses up to 48 mg daily of deflazacort or equivalent for 3 weeks is unlikely to lead to clinically relevant HPA-axis suppression in the majority of patients [1].

Clinical efficacy

Doses and available forms

Tablets are available in various dosages- 6mg, 18mg, 24mg and 30mg.

DFZ oral suspension- Defcort 6mg/5ml in 30 ml.

Applications in oral medicine-oral lichen planus

OLP is the mucosal analogue of lichen planus of skin, although the two demonstrated marked clinical variability. It is a chronic inflammatory disease that is characterized by cytotoxic T- Cell medi-

ated damage of the basal cells of the epithelium and chronic inflammation [12]. Aina., *et al*. in 2020 proposed a guideline for the use of DFZ in OLP. They suggested that DFZ should be advised 30mg 2 days pre-operative, 15mg 3 days post- operative and 7.5mg for 3 more days [13]. They suggested the use of DFZ since it is a synthetic glucocorticoid characterized by high efficacy and good tolerability.

Oral pemphigus

Pemphigus is a rare disease, potentially life threatening autoimmune whose onset is most frequently seen in the oral cavity characterized by blistering that affects stratified squamous epithelium and results in cutaneous or mucosal blistering or both.

Michele., *et al.* treated 16 patients with DFZ being the drug of choice in their therapeutic protocols. The protocol for the initial phase of treatment consisted of systemic DFZ 120mg daily as a single dose in the morning and this dose was maintained for 2-4 weeks. Following clinical remission, the patient's dosage of DFZ was tapered to 6mg every other day. Their study concluded that DFZ was safe and well tolerated by all patients. Pulse therapy with megadose corticosteroids is currently being used for pemphigus for cases which are unresponsive to high doses of oral corticosteroids. Methylprednisolone, cyclophosphamide and DFZ 'pulse therapy' are reserved for such cases [14,15].

Melkerson- Rosenthal syndrome

Melkerson Rosenthal syndrome (MRS) is a triad of facial paralysis, fissured tongue, and oedema. Arantes., *et al*. in 2020 described a case of MRS complicated with intracranial hypertension, where they had treated the patient with alternating use of 10mg prednisolone with 6mg DFZ following which she was relieved of the symptoms and was monitored for intracranial hypertension [16].

Pain

Ravi Kumar., *et al*. had conducted a study to evaluate the efficacy of corticosteroids in relieving pain in the oral cavity. He studied two types of corticosteroid drugs- dexamethasone 4mg and DFZ 30mg. He concluded that DFZ resulted in less pain reduction than dexamethasone during test periods, but the former had least side effects when compared to the latter [17].

Herpes zoster infection

The use of DFZ has also been explored in cases of herpes zoster infection. Rui., *et al.* in 2022 had prescribed valacyclovir and DFZ to manage this viral infection. He concluded that treatment with corticosteroids is still debatable but its use in immunocompromised patient, if done, should be monitored with extreme care due to risk of a further worsening of the viral infection with systemic dissemination [18].

Rheumatoid arthritis

Severe chronic rheumatoid arthritis is often treated with corticosteroids. But such a therapy can cause serious side effects like osteoporosis and vertebral collapse. For such reasons a bone sparing corticosteroid like DFZ would be ideal. Follow- up studies are required for more stronger evidence for its replacement with prednisolone [19].

Case Report

A male patient aged 40 years reported to the department of Oral medicine and maxillofacial radiology, complaining of a continuous burning sensation in the mouth for 2 months. He gave a history of being under stress in the past 6 months. The patient had visited a local dental practitioner for the same who had prescribed him Tab. Wysolone 5mg for 1month, but the burning sensation persisted. The visual analogue scale (VAS) was found to be 10 when reported to us. Intraoral examination revealed mixed red and white lesions on both left and right buccal mucosae, extending approximately 4 X 3 cm in size on left buccal mucosa and 3 X 3 cm in size on right buccal mucosa. We observed diffuse erythematous areas enclosed with pale white lesions with a periphery formed by linear keratotic white papules extending throughout the right and left buccal mucosae, (Figure 1 and 2) suggestive of Erosive Lichen Planus. The lesions on the right buccal mucosa were intermixed with brownish pigmentation suggestive of areas of healed Lichen planus. The gingiva was normal in color, contour and size, there was no sign of Desquamative gingivitis. There was no history of similar lesions on the skin. Clinical diagnosis of Erosive oral lichen planus was made, and a biopsy was avoided due to severe burning sensation in the mouth. Patient was advised Deflazacort 6mg 5 times a day post meal by swish and swallow method for 10 days. Patient was followed up and decrease of VAS scale to 4 was noted, following which tapering of the doses was started. (Figure 3 and 4) He was asked to consume 6mg DFZ 3 times a day for next 10 days and 6mg DFZ 2 times a day for another 10 days. The patient was asked to report after 10 days when we found that he was relieved of the burning sensation and there were no erosive lesions on the buccal mucosae. (Figure 5 and 6) He was followed up after 1 month when the buccal mucosae appeared to be perfectly normal.

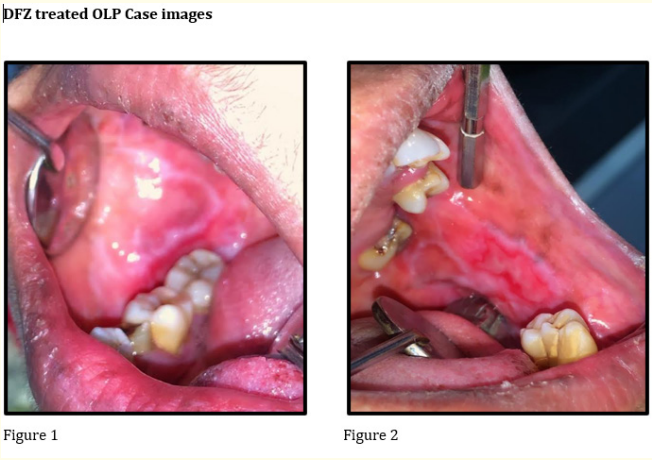

Figure 1 and 2: Showing right and left buccal mucosae with erosive and annular pattern of Oral lichen planus.

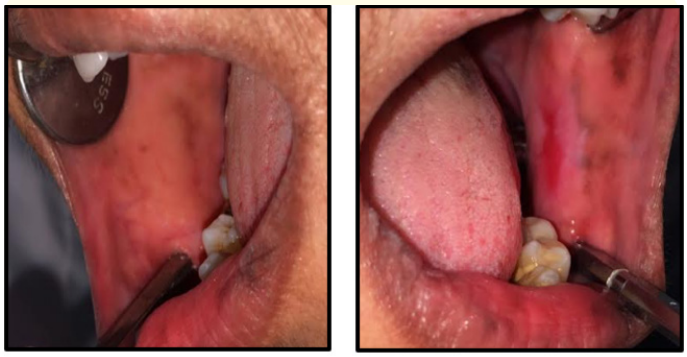

Figure 3 and 4: Showing right and left buccal mucosae after 10 days of treatment with Vitamin D.

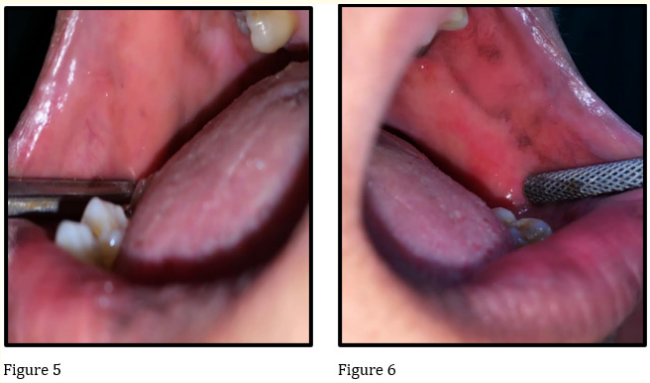

Figure 5 and 6: Showing right and left buccal mucosae after 1 month of treatment showing no lesions.

Adverse effects

Minor adverse events like headache and gastrointestinal disturbances have been reported till now. Lee., *et al*. in 2014 reported two cases of TEN (Toxic epidermal necrolysis) associated with deflazacort (DFZ) with nephrotic syndrome (NS) [20].

Limitations

Unfortunately, very few studies have been performed to study the efficacy of DFZ in treating oral diseases. Therefore, well designed clinical trials are needed, especially to clarify the appropriate ratio of doses for bioequivalence with prednisolone in treating oral diseases.

Conclusion

As learnt from the available literature, it can be stated that DFZ is safe and is a well-tolerated drug. It is worth considering in patients who require long term steroid therapy, who are at higher risk of metabolic side effects and in children as an initial option in those requiring corticosteroid therapies since the adverse effects caused by this class of drugs are minor when compared to the commonly used steroids. DFZ being the drug of choice for the treatment of cutaneous lichen planus and pemphigus, its use should be explored for oral lesions. Long- term studies are required before we can provide any concrete opinion regarding its utility for our domain.

Conflict of Interest

No conflicts of interest.

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