Treatment of Oral Inflammatory Diseases with a New Mucoadhesive Prednisolone Tablet Versus Triamcinolone Acetonide Paste

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Abstract

Background: The existing clinical trials have shown that topical corticosteroids are often effective in the management of oral inflammatory diseases. The purpose of this study was to compare the effectiveness and safety of a new mucoadhesive prednisolone tablet with that of triamcinolone acetonid paste in the management of oral lesions such as RAS-EM -pemphigus vulgaris-recurrent intraoral herpes -OLP and chemical burn.

Methods: In this randomized comparative study, 60 consecutive patients with oral lesions were recruited. The patients were divided into 2 groups, one receiving topical triamcinolone acetonid 0.1% paste and the other prednisolone 5 mg mucoadhesive tablet for 2 weeks.

Results: The profiles of mean lesion sizes and mean pain measures did not show any difference between the prednisolone and triamcinolone groups.

Conclusion: It was found that prednisolone 5mg table is useful as triamcinolone paste in the treatment of oral inflammatory lesions with minimal side effects.

Keywords: Treatment; Oral inflammatory diseases; Prednisolone; Triamcinolone acetonide

Introduction

Corticosteroids have been in regular clinical use for a range of inflammatory and immune mediated conditions for over 50 years. Glucocorticosteroids have both anti-inflammatory and immunosuppressive effects. Both are seen most clearly with the systemic use of the agents, but there is potent activity in both areas with topical use. More importantly, there is a dramatic difference in the incidence of adverse reactions when used topically or systemically.1

Corticosteroids play a central role in the treatment of vesiculoeosive lesions. However, the frequency and severity of the adverse effects associated with the use of systemic corticosteroids have led to the increased use of topical corticosteroids (TCS). In contrast, evidence for the efficacy of TCS in oral medicine is limited.2

The therapeutic efficacy of corticosteroids is now known to derive from their anti-inflammatory and immunosuppressive properties. The anti-inflammatory action of glucocorticoids is based on a range of actions involving glucocorticoid receptors, the glucocorticoid-responsive genes, the release of anti-inflammatory molecules such as lipocortin-1, interleukins IL-10, IL-1, and nuclear factor-kB, by macrophages, eosinophils, lymphocytes, dendritic cells, neutrophils, and endothelial and epithelial cells.2 Lipocortin-1, a member of annexin super-family of proteins, is one of the “second messengers” of anti-inflammatory action of glucocorticoids, acting through inhibition of prostaglandin formation as well as playing a major regulatory role in systems such as cell growth regulation and differentiation, neutrophil migration, CNS response to cytokines, neuroendocrine secretion, and...
neurodegeneration. Glucocorticoids also induce the transcription of the gene, encoding the inhibitor of factor Kappa B subtype α (IkBa), which reduces the amount of NF-κB that translocates to the nucleus and the secretion of pro-inflammatory cytokines. The immunosuppressant effect of corticosteroids is derived mainly from the suppression of antigen-driven T-cell proliferation through the inhibition of interleukin-1 release from monocytes. At higher doses, they can also interfere with antibody formation.

Corticosteroids can, therefore, reduce the migration of leukocytes and exudation of plasma constituents, thereby eliminating the edema and maintaining the integrity of cell membranes. They also help avoid the excessive swelling of cells, inhibit the release of lysozymes from granulocytes and phagocytes, and stabilize the membrane of the intracellular lysosomes, thereby avoiding the further release of hydrolytic enzymes, intracellular digestion, and spread of the inflammatory process. Corticosteroids also inhibit fibroblast proliferation suppressing fibrosis.

Severe erosive disease of the oral mucosa is one of the main challenges facing oral medicine today. It is often chronic, rarely remits spontaneously, causes intense pain, and interferes with the usual daily activities of the patient (eating, drinking, talking and maintaining normal relationships). Treatment of these lesions frequently involves the administration of systemic corticosteroids, which is often problematic because of its chronic nature and the associated risk of adverse effects.

Topical corticosteroids are often the mainstay in the treatment of oral inflammatory diseases. Several studies have shown the efficacy of such treatment in the management of oral lesions such as oral lichen planus (OLP), herpes labialis (in combination with famciclovir), recurrent aphthous stomatitis (RAS), pemphigus vulgaris (PV), and benign mucous membrane pemphigoid (BMMP). Traditionally, anti-inflammatory and analgesic topical therapy in the oral cavity is confined to very limited formulations such as mouthwash, sprays, gels, or lozenges, which cannot be used successfully since they do not adhere well, are washed away by saliva, and hence are quickly removed. In the recent years, the development of mucoadhesive buccal delivery systems has been the subject of intensive research in order to increase the retention of the drug in the oral cavity.

The purpose of the present study was to evaluate the response of patients with severe oral erosive lesions to treatment with new formulated mucoadhesive prednisolone tablets in comparison with their response to the treatment with triamcinolone acetonide paste.

**Material and Methods**

Sixty patients with previously untreated severe erosive lesions of the oral mucosa were recruited from patients referred to the Oral Medicine Clinic and Dermatology Department of Faghihi Hospital affiliated to Shiraz University of Medical Sciences in southern Iran for the diagnosis and treatment of oral lesions. The daily activities of the patients were affected by the disease. The study group consisted of 60 patients (38 women and 22 men) aged between 14-68 years (mean=37±14.2). 20 patients suffered from OLP, 19 patients presented with RAS, 3 presented with chemical burn, 10 had PV, 5 patients had EM and 3 patients suffered from recurrent intraoral Herpes (Table 1). In all the patients, the diagnosis was based on medical history, clinical examination and routine histopathologic study of a representative biopsy specimen. The approval of the local ethics committee was obtained before the trial started and all the patients gave written informed consent.

The patients were randomly divided into two groups. The first group received mucoadhesive prednisolone (5 mg tablet), the pharmaceutical characteristic of which was established (Iranian product) (G1 group), whereas the second group of patients (G2) received triamcinolone acetonide (0.1% paste; ADOCORTYL in ORABASE™). Prednisolone (5 mg tablet) was placed on the lesion and pressed for a few seconds for local fixation 2 times daily (after breakfast and dinner). The triamcinolone acetonide (0.1% paste) was spread on the lesions 3 times daily. Both medications were applied for 3 days in recurrent

| Table 1: Frequency of the oral lesions in both study groups |
|---------------------------------|-------------------|-------------------|-------------------|-------------------|
| **Type of oral lesion**       | **OLP** | **RAS** | **Chemical burn** | **PV** | **EM** | **Intra oral Herpes** |
| No                         | 20   | 19     | 3                 | 10    | 5     | 3                        |
| %                          | 33.3 | 31.7   | 5.0               | 16.7  | 8.3   | 5.0                       |


intra-oral herpes, major aphthous stomities and chemical burns, 5 days for EM and 2 weeks for OLP and PV. Every variable (pain, atrophy, ulceration and interference in daily life) was evaluated independently by the same experienced clinician at 2-6 follow ups (the first one 48 hours after the beginning of treatment). The treatment was assessed as complete remission, excellent, good, and poor or failed (no response). The patients were warned not to discontinue or modify the treatment on their own decision. At every visit, the patient was examined for the presence of adverse effects related to topical corticosteroids treatment.

The data on the post-treatment evaluation of pain, ulceration, atrophy and interference in daily activities were recorded and analyzed by chi-square and two sample t-tests.

Results

Although many patients dislike the bitter taste of topical prednisolone mucoadhesive tablet, it is well tolerated when topically applied. It resulted in reduction in pain, and burning sensation within 3-5 days of application in major aphthous ulcer and chemical burn. All the patients with RAS (19 patients) in both groups had an excellent response to the treatment. One out of five patients in G1 and two out of five patients in G2 with pemphigus vulgaris had a good response to topical treatment. Nine patients out of eleven in G1 (Figure 1 and 2) and eight out of nine patients in G2 with erosive and atrophic lichen planus responded to the treatment (fair to good). Two patients out of 2 in G1 and one patient out of one in G2 with chemical burn caused by sodium hypochlorite had excellent responses to topical corticosteroids. Two patients out of 2 in G1 and 3 patients out of 3 in G2 with erythema multiforme had good to excellent response to topical corticosteroids. One patient out of one in G1 and 2 patients from 2 in G2 with recurrent intra-oral herpes had a good to excellent response to these medications (Figure 3). Both groups showed significant improvement in the measured efficacy. There was no significant difference between changes from the baseline median values of G1 and G2 groups after treatment. ($p = 0.919$).

Discussion

Topical prednisolone (5 mg tablet) was used to treat severe erosive lesions in comparison to triamcinolone acetonide (0.1% paste; ADCORTYL in ORABASE™). By using this medication, most of the patients showed partial to complete resolution of pain and ulceration at the end of treatment. More than 80% of those in the prednisolone group (G1) and 86.7% of triamcinolone group (G2) had complete absence of ulceration and full recovery of daily activities. With respect to the results of the present study, such treatments with topical steroids was found to be efficacious and relatively rapid to control severe erosive diseases of the oral mucosa. Lozada -Nur and Zhong Huang,10 and Lozada -Nur11 treated patients with severe erosive disease, using clobetasol propionate mixed in an adhesive paste. They reported a complete response in 62.5% of the series (15 patients), an excellent response in 29.7% (7 patients), and a failed response in 8.3% (2 patients). They concluded that
their treatment was efficacious and safe. Our better outcomes are probably related to the improved access of the new formulated adhesive prednisolon tablets to all lesional area. Although orabase is adhesive, mouth movement can soon alter the initial placement of the paste. Nevertheless, we regard orabase as a good means for topical corticoids when it can be kept in contact with all the lesions for the prescribed time. It is of particular use when a dental tray can be used for the application, especially for lesions of the gingiva and palate. Arash and Shirin reported a successful management of mild to moderate benign mucous membrane pemphigoid with topical corticosteroids alone.\textsuperscript{12} It has been reported by Scully that four out of 32 patients with localized oral lesions of pemphigus vulgaris were controlled by topical corticosteroids only;\textsuperscript{13} this finding is similar to what we obtained.

We observed a complete absence of response in 2 patients with oral lichen planus in G1 and one patient in G2. Four patients with pemphigus vulgaris in G1 and 3 patients in G2 did not respond to such treatments. Corticosteroids had no the adverse effects in any patients, but the bitter taste of the adhesive prednisolon tablet was the main problem of G1.

Our result suggests that potent topical corticosteroid such as new formulated adhesive prednisolone may control oral inflammatory lesions in most cases, with no significant adverse effect. Among all modalities of topical treatment, application of mucoadhesive corticosteroid seems to be more specific and highly effective in the management of oral ulcers. The novel formulation of this new mucoadhesive prednisolone tablet was safe and demonstrated statistically significant pain reduction and may be an effective alternative to systemic corticosteroids without any important side effect. This formulation released 90% of 5 mg prednisolone in 6 hours after application on oral mucosa. The main advantage of prednisolone mucoadhesive tablet is the ease of administration and the patient's ability to eat and talk normally during the administration of this medication.

**Acknowledgement**

We wish to thank the Office of Vice Chancellor for Research of Shiraz University of Medical Sciences for financial support and Center for Development of Clinical Studies at Nemazee Hospital for editorial assistance.

**Conflict of interest:** None declared.

**References**


