



Review Article

Effectiveness of Tacrolimus over Triamcinolone Acetonide in The Treatment of Oral Lichen Planus

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ABSTRACT

Aim: The aim of the review article was to compare the efficacy of topical Tacrolimus ointment with that of Triamcinolone acetonide ointment on patients suffering from oral lichen planus.

Materials and method: A review study was done to analyse the efficacy of topical Tacrolimus ointment with that of Triamcinolone acetonide ointment on patients suffering from oral lichen planus. Over 5 articles were referred from Pubmed and Google database meeting our eligibility criteria (August 2006 - December 2016). A total of 240 patients who were clinically diagnosed with Oral Lichen Planus from a total of 5 studies with 3 randomized control trials and 2 clinical trials were included for this review.

Result: Tacrolimus belongs to macrolide family and is caused by streptomycin tukubaensis. It inhibits the activation and proliferation of T-lymphocytes by inhibiting the phosphatase activity of calcineurin. The articles used for the review conclude that the application of Topical Tacrolimus helps in the alleviation of all clinical symptoms in over 80% of the patients under study.

Key words: Tacrolimus, Triamcinolone acetonide, oral lichen planus

Introduction

Oral Lichen Planus (OLP) is a chronic inflammatory, non-infectious, muco-cutaneous disease characterised by a cellular inflammatory infiltrate enriched in CD4+ cells, by the presence of acidophilic bodies that may represent apoptotic epithelial cells and by vacuolating degeneration of the basal epithelial layer. This disease affects 0.5 – 2% of the population and has a female predilection (4:1). It occurs in six different forms ranging from lacy white streaks to white plaques to eroded ulcers. The white lesions are painless while eroded ones elicit burning sensation and soreness. The reticular, atrophic/ erosive and plaque type are symptomatic which appears on buccal mucosa, tongue, gingiva, palate, lips and retromolar pad area. OLP is characterised histopathologically by variable epithelial thickness, basal cell destruction, and a band like infiltrate of mononuclear cells in the lamina propria. Although the pathogenesis of Oral Lichen Planus is still an area of active investigation, it is well documented that OLP represents the cell mediated immune response with the infiltrating cell population composed of both T4 and T8 lymphocytes. There is no curative treatment for OLP. Therapy is aimed at alleviation of symptoms and consists generally of topical corticosteroids. Systemic corticosteroids are not preferred due to their adverse effects.

The treatment of symptomatic OLP is challenging. Various drugs such as corticosteroids cyclosporine, retinoids, griseofulvin, dapsone and hydroxyl-chloroquine have been used alone or in combination orally, parentally or topically. Recently topical tacrolimus was reported effective in a number of pilot studies. Tacrolimus belongs to macrolide family and is caused by Streptomycin tukubaensis. It inhibits the activation and proliferation of T-lymphocytes by inhibiting the phosphatase activity of calcineurin. The purpose of this review article is to compare the efficacy of tacrolimus 0.1% with triamcinolone acetonide 0.1% in the treatment of OLP.

Methodology

The following sources were searched from August 2006 to December 2016, in Pubmed and Google database. The keywords that were used are oral lichen planus, triamcinolone acetonide, tacrolimus and corticosteroid therapy. The primary focus of this search were clinical trials and randomised control trials which used corticosteroids namely tacrolimus and triamcinolone acetonide in the treatment of Oral Lichen Planus (OLP). The outcome of all the studies showed improvement in the clinical signs like soreness and regression of lesion in 3-4 weeks.

Results

This review article was compiled using 5 studies that met the selection criteria (3 randomised control trials and 2 clinical trial) for assessing the efficacy of tacrolimus over triamcinolone acetonide in the treatment of OLP. 4 studies compared tacrolimus (study group) with triamcinolone acetonide (control group) and one study compared tacrolimus with triamcinolone acetonide and placebo group. 220 patients were divided into the study and control groups and 40 patients were divided into study, control and placebo groups. The parameters evaluated were the clinical signs (area of erythema, ulceration and white striation) and adverse effects. Study and control group were administered 0.1% topical tacrolimus in orabase and 0.1% triamcinolone acetonide in orabase respectively, 4 times a day for a mean duration of 3 weeks to 3 months. The lesion was clinically graded by a 6 score scale and their pain was assessed using visual analogue scale (VAS). The scale used for the analysis of the efficiency of drugs were done by the student paired t-test, fisher's exact test and exact χ^2 trend test. The Kruskal – Wallis sample test was used for the analysis of the pain severity scores. On an average, 73% of the study population showed improvement of clinical signs and the pain severity in study and control group was 8.2 and 7.8 at the beginning of treatment, and 3.5 and 3.2 at the treatment respectively. There was statistically significant reduction in pain severity in both groups. Tacrolimus also proved to have better therapeutic results when compared to the placebo group over a period of 9 weeks. Tacrolimus is available in concentration of 0.1% and 0.03%, however the formulation of 0.1% was found to be more effective. Adverse effects like burning sensation at the site of application of ointment, transient taste disturbance and hyperpigmentation was noticed in the study group. Recurrence of lesions were also noticed in the study and control groups over several weeks after cessation of treatment. The data obtained from reviewing the articles were statistically significant in proving that topical Tacrolimus showed better therapeutic effects as compared to topical Triamcinolone acetonide.

Discussion

Oral Lichen Planus (OLP) is a chronic, autoimmune, mucocutaneous disease. It can affect the oral mucosa, skin, genital mucosa, scalp and nails. The clinical history confirms the relationship between OLP and oral cancer, although the degree of the risk involved is controversial. Therefore, OLP should be considered a precancerous lesion, emphasizing the importance of periodic follow-ups in all the patients. Oral Lichen Planus (OLP) is characterised by burning sensation, painful, thickened

patches on the tongue, inflammation of tongue and erosive or ulcerative lesions in cases of symptomatic OLP. Various treatment modalities have been elucidated to alleviate the symptoms of OLP, although a definitive cure has not yet been found. This article reviews the efficacy of topical tacrolimus with topical triamcinolone acetonide in the treatment of OLP.

Cell mediated immunity seems to play a critical role in the pathogenesis of lichen planus. Although the specific antigens, responsible for the activation of T-cells has not been identified, studies have demonstrated the interaction of T-cells and mast cells in a cyclical nature via the production of cytokines, such as RANTES (regulated on activation, normal T-cell, and Secreted) and TNF- α , which may explain the chronic nature of the disease. Investigations have demonstrated the production of RANTES and the presence of specific RANTES receptors such as CCR1. This suggests that RANTES, CCR1 and TNF α may be involved in the accumulation of inflammatory cells in OLP.

Tacrolimus belongs to macolide family and is caused by the streptomycin tukubaensis. It was initially used to prevent solid organ allograft rejection while topical formulations of tacrolimus were developed for the use of atopic dermatitis. The pharmacological actions of tacrolimus is similar to cyclosporine although it penetrates deeply in the mucosa, in this form it is said to be 10-100 times more potent. It suppresses T- cell activation by binding to cytosolic FK-binding protein which in turn interferes with calcium/ calmodulin. This ultimately results in the inhibition of cytokine gene transcription including interleukin 2 and TNF- α . Very recently there have been topical tacrolimus in concentration of 0.1%, 0.3% and 0.03% in orabase. The formulation of 0.1% is found to be more effective.

Triamcinolone acetonide on the other hand is a synthetic corticosteroid. It is 8 times as effective as prednisone and there were few side effects like skin redness, burning and itching. The efficacy of Triamcinolone acetonide is mainly due to local anti-inflammatory properties of suppressing T cell function.

In the studies done in 2006 and in October – December 2012, during the follow-up evaluation 40% of patients treated with tacrolimus revealed side effects like burning sensation at the site of application, transient taste disturbance, intermittent headaches and melanin pigmentation at the site of the lesion indicating the healing phase of LP. Maximum incidence of pigmentation was seen in patients with erosive LP. The fact is substantiated

by increased melanocytic activity at the basement membrane during the healing and post-healing phase.

All the studies concluded that treatment with topical tacrolimus 0.1% ointment four times daily induced a better initial therapeutic response than triamcinolone acetonide 0.1% ointment in patients with symptomatic OLP. However relapses occurred frequently in both groups within several weeks after cessation of both the treatments. Prolonged or intermittent use of topical tacrolimus ointment in patients with symptomatic OLP may be useful, but remains to be clearly established in large, well designed clinical studies. Nonetheless, at present, topical tacrolimus may be a valuable addition to the already existing therapeutic modalities for treating patients with OLP.

Conclusion

Treatment of symptomatic oral lichen planus remains a challenging problem. Various treatment modalities have been tried including topical and systemic steroid, retinoids, immunosuppressive drugs, surgery, lasers and photochemotherapy. According to the studies reviewed, topical tacrolimus ointment is safe, well tolerated and effective therapy for OLP recalcitrant to traditional

therapies and may be used for those cases which are resistant to conventional treatment. It may be a valuable addition to the already existing therapeutic modalities for treating patients suffering from OLP. However this drug has only the palliative effect and not the curative one.

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