

# TREATMENT OF ORAL LICHEN PLANUS WITH TOPICAL TACROLIMUS AND TRIAMCINOLONE ACETONIDE OINTMENT — A COMPARATIVE STUDY

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## ABSTRACT

*The aim of the study was to compare the efficacy and safety of topical Tacrolimus ointment with that of Triamcinolone Acetonide ointment on patients suffering from oral lichen planus. A total of sixty patients (53 females and 07 males, means age 48 years; 30 patients per groups) were treated with Tacrolimus, a calcineurin inhibitor immunosuppressor drug and Triamcinolone acetonide for three months in a randomized clinical trial.*

*Thirty patients (group I) were treated with topical Tacrolimus (0.1%, 0.003%) ointment four times daily and thirty patients (group II) were treated with Triamcinolone Acetonide 0.1% ointment four times daily. The clinical effects were graded after 1, 2, and 3 months of treatment. Visual analogue scale 0-10 was used to assess the severity of pain before and after treatment. In group I, Sixteen patients showed healed lesion, 10 showed improvement and 4 showed no improvement. In group II, 5 were healed, 9 patients showed 50% improvement and 16 showed no improvement. No side effects of these drugs were reported in these patients.*

*Topical tacrolimus ointment induced a better initial therapeutic response than Triamcinolone acetonide ointment. However, relapse occurred in 12 cases within 6-8 weeks of the cessation of the therapy.*

**Key words:** Oral Lichen Planus, Topical therapy, Tacrolimus ointment, Triamcinolone Acetonide

## INTRODUCTION

Oral lichen planus is a chronic inflammatory, non-infectious muco-cutaneous disease which affects approximately 0.1-4% of general adult population.<sup>1,2</sup> It is more common in women than in men. (4:1).

It affects 44-62.5%<sup>3,4</sup> patients with skin lesions but may occur without skin lesions elsewhere. In mouth, it occurs in six different forms ranging from lacy white streaks to white plaques to eroded ulcers. The white lesions of oral lichen planus are painless while eroded ones elicit burning sensation and soreness. The reticular, atrophic/erosive and plaque type are symptomatic which appear on buccal mucosa, tongue, gingiva, palate, lips and retro molar pad area.

The precise cause of oral lichen planus is unknown but it is considered as an autoimmune disease<sup>5</sup>. Cells called CD<sub>8</sub> +T Lymphocytes and chemical mediators such as cytokine TNF, attach the oral epithelial cells resulting in their death.

The diagnosis of oral lichen planus is based on history, clinical findings and histopathology characterized by variable epithelial thickness, basal cell destruc-

tion, and a band like infiltrate of mononuclear cells in the lamina propria. The treatment of symptomatic OLP is challenging. Various drugs such as corticosteroids cyclosporine, retinoids, griseofulvin, dapsone and hydroxy-chloroquine have been used alone or in combination orally, parentally or topically.

Recently topical tacrolimus was reported effective in the treatment of patients suffering from oral lichen planus in a number of pilot studies.<sup>6,7</sup> The major objection to these studies was non use of adequate control group.

Tacrolimus belongs to macrolide 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.<sup>8</sup> The pharmacological actions of tacrolimus are similar to cyclosporine, although it penetrates deeply in the mucosa, in this form it is said to be 10 to 100 times more potent.<sup>16</sup> Tacrolimus inhibits the activation and proliferation of T-lymphocytes by inhibiting the phosphatase activity of calcineurin and the side effects and remission after the cessation of therapy were also compared.

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## METHODOLOGY

A prospective randomized study was conducted in the Department of Oral Medicine of Khyber College of Dentistry, Peshawar from Oct 2009 to April 2010 on 60 consecutive patients (53 women and 7 men; age range 30-65 years, mean age 48 years). The patients included had oral lesions which gave the appearance and histological appearance of oral lichen planus. The inclusion criteria were clinically, histologically confirmed OLP and Painful lesions.

Exclusion criteria were pregnant or breast feeding women, immunodeficiency or HIV patients, patients using of steroid or other immunosuppressive drugs, known renal or hepatic insufficiency and patients with established allergy to macrolide antibiotics.

The patients were randomly divided into two groups and were provided verbal Information on the study protocol. Study approval was granted by the Institutional Research and Ethics Board (IREB). The severity of OLP was scored at each visit criteria described in the previous study<sup>9</sup> with a score ranging from 0-5: while the pain was assessed by visual analogue scale<sup>10</sup> (0-10).

In group I, thirty patients were treated with topical tacrolimus (Teczem) 0.1%, 0.03% ointment while in group II, same number of patients were treated with topical Triamcinolone Acetonide (Kenalog with orabase) 0.1% ointment which was applied 04 times daily.

The follow up period was 03 months. The treatment was discontinued earlier, if the patient showed complete healing. The clinical affects were graded after 1,2 and 3 months on proforma as shown in Table 1 involving the severity and extent of the disease. The blood sample was not taken for determining the levels of Tacrolimus and Triamcinolone acetone in patients.

TABLE 1: RESULTS OF TREATMENT AFTER 03 MONTHS

Oral lichen planus	Group 1	Group II
Healed	16(53%)	5(16%)
Improvement	10(33%)	9(30%)
No improvement	4(13%)	16(53%)
Worse	Nil	Nil
Side effects	Nil	Nil

TABLE 2: LOCATION OF ORAL LICHEN PLANUS IN THE STUDY GROUPS

Location	Buccal mucosa	Tongue	Retro molar Pad	Lips	Gingiva	Palate
Group I	30	2	9	6	3	3
Group II	25	3	0	3	0	0
Total	55	5	9	9	3	3

## RESULTS

Sixty patients which showed clinical and histopathological features of oral lichen planus were included in this study which had mean duration of 2 years (range 07 days 20 years). The sites of OLP in both groups are presented in Table 2. It can be seen that most of OLP lesions were located on buccal mucosa (n =55) while the gingival and palatal mucosa were the least affected.

Patients in two groups had comparable age and number in term of gender as well as symptoms and the duration of the disease. The relevant data for these are shown in Table 3.

TABLE 3: DEMOGRAPHICS OF SIXTY PATIENTS WITH ORAL LICHEN PLANUS

Female	53(87%)
Male	7(13%)
Age(Range years)	30-65 years
Mean	48 years
Duration of lesion	Mean 2 years (7days – 20 years)
Type of disease	Erosive (EOLP) 42(70%) Reticular (ROLP) 18(30%)

The proportion of patients whose lesions showed the total healing response was in group I; 16 (53%), 10 (33%) showed improvement and 4(13%) showed no improvement. In group 2 the corresponding figures were 5 (16%), 9(30%) and 16(53%) respectively. The data shown in Table 1 indicated that early response to therapy was better in group I patients than that in group 2.

No drug related side adverse effects were observed in patients of both group.

Topical Tacrolimus (0.1%, 0.03%) induced a better initial therapeutic response than Triamcinolone Acetonide 0.1% ointment. However, relapse may occur after stoppage of the treatment with in 6-8 weeks.

## DISCUSSION

This study compared the safety and efficacy of topical Tacrolimus ointment with Triamcinolone Acetonide ointment in patients suffering from Oral

Lichen Planus. The results indicate that both drugs are effective for the treatment of OLP as was the case in other studies.<sup>1,11,12,14</sup>

The demographic characteristic of this study were similar to another study.<sup>9</sup> The positive aspect of the present study was that the included patients responded well to topical tacrolimus.

This study shows that topical tacrolimus (0.1%, 0.03%) ointment applied four times daily induced better therapeutic response than that of Triamcinolone Acetonide .01% ointment. Tacrolimus was found safe and effective in most patients in group I and 53% lesions healed while 33% showed improvement (Table 1).

The study does not support the earlier reports of side effects of tacrolimus such as burning, tingling and irritation. There was not even a single case which showed side effects of this drug.<sup>13</sup>

Tacrolimus, the first macrolide immuno suppressant was discovered in 1984 by a Japanese team, in soil fungus. It was produced by a type of bacterium, streptomyces tsuknbaensis. It suppresses T-cell activation by binding to cytosolic FK-binding protein which in turn interferes with calcium/calmodulin –dependent phosphate calcineurin, which results in the inhibition of cytokine gene transcription including interleukin 2 and TNF- alpha. The pharmacological actions of Tacrolimus are similar to that of cyclosporine.

As an ointment (protopic), Tacrolimus has been recently used in the treatment of eczema particularly atopic dermatitis. The tacrolimus ointment is available in 2 strengths, 0.1% and 0.03%. The topical Tacrolimus has smaller molecule and penetrates better into the skin and mucosa than cyclosporine. It was approved as a safe treatment for atopic dermatitis. The recent most studies have demonstrated the efficacy of topical Tacrolimus in treating the EOLP.<sup>13, 15</sup>

On the other hand, Triamcinolone Acetonide is a synthetic corticosteroid. It is a potent type about 8 times as effective as prednisone and there are only few side effects noted in clinical trials. The efficacy of Triamcinolone Acetonide is mainly due to local anti-inflammatory properties of suppressing T cell function.

## CONCLUSION

Topical Tacrolimus (0.1, 0.03%) ointment is a 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 valuable addition to the already existing therapeutic modalities for treating patients suffering from Oral Lichen Planus. However, this drug has only palliative effects and not the curative one.

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