IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

Treatment Of Oral Lichen Planus With Topical Tacrolimus And Triamcinolone Acetonide Ointment- A Comparative Study

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Abstract

Aim: To compare the efficacy of topical tacrolimus ointment with that of triamcinolone Acetonide ointment in patients with symptomatic oral lichen planus.

Methods and Material: In this prospective randomized comparative study, 30 consecutive patients with oral lesions consistent clinically and histologically with OLP were recruited. The patients were divided into 2 groups to receive topical triamcinolone acetonide 0.1% or tacrolimus 0.1% ointment and treated for 6 weeks. The clinical effect of treatment in the patients were graded after 6 weeks by the treating physician using an ordinal score and recorded as worse, unchanged, improved or healed. Statistical analysis was done between no improvement and improvement-Healing group with Fisher's Exact Test.

Results and conclusion: The results of this study allow the conclusion 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.

Key words: Oral Lichen Planus, Tacrolimus, Triamcinilone Acetonide

Introduction

Oral lichen planus (OLP) is a chronic inflammatory condition that affects the oral mucous membranes with a variety of clinical presentations, including reticular, papular, plaque-like, atrophic, and ulcerative lesions. OLP affects between 0.1% and 4% of the population. It is a disease of the middle-aged population and is more common among women.[1] Treatment of symptomatic OLP is challenging. Several drugs have been used with varying efficacy.[2, 3] Specific treatment includes corticosteroids (topical, intralesional or systemic), retinoids, cyclosporine, psoralen plus ultraviolet A light (PUVA), griseofulvin, hydroxychloroquine and dapsone. [2, 3]

Tacrolimus, also called FK 506, is an immunosuppressant macrolide lactone antibiotic produced by streptomyces tsukubaensis.[4] Recently, there have been a few case reports and trials of successful use of tacrolimus in the treatment of OLP.[5] 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.[6] Topical corticosteroid therapy are common and conventional therapy for treatment for OLP.[1]

Materials and Methods

In this prospective randomized comparative study, 30 consecutive patients with oral lesions consistent clinically and histologically with OLP were recruited. The patients were divided into 2 groups to receive topical triamcinolone acetonide 0.1% or tacrolimus 0.1% ointment and were treated for 6 weeks. The patients were divided in such a way that patients in two groups had comparable age and number in term of gender as well as symptoms and the duration of the disease. The clinical effect were graded after 6 weeks. The study was approved by the Institutional Ethical Committee and consent form was taken from the study participants.

In group I, fifteen patients were treated with topical tacrolimus (Tacroz) 0.1%, ointment while in group II, same number of patients were treated with topical Triamcinolone Acetonide (Tess) 0.1% ointment applied 4 times daily.

The clinical effect of treatment in the patients were graded after 6 weeks by the treating physician using an ordinal score and recorded as worse, unchanged, improved or healed. The ordinal (ranked) scoring involved assessing the severity and the extent of the disease. An improvement of less than 30% in the extent and the severity of the lesion was scored as unchanged. An improvement of more than 30% in the extent and the severity of the lesions was scored as improved and as healed when the lesion had resolved completely.

Statistical analysis of the results was done at the end of the study.

Results

1. Age distribution: (Table 1)

Age distribution of the Group I and Group II was made at the intervals of 10yrs, starting from 21-30 yrs, 31-40 yrs, 41-50 yrs, 51-60 yrs and 61-70 yrs.

The Mean Age difference between the OLP patients (Group A) and Controls (Group C) was non-significant with t=0.28 and p=0.052. (Table 1, Graph 1)

Table1: Age Distribution

AGE GROUP (YEARS)	**STUDY GROUP I TRIAMCELONONE N (%)**	**STUDY GROUP II TACROLIMUS N (%)**
21-30	3(20.0%)	3(20.0%)
31-40	8(53.33%)	6(40.0%)
41-50	2(13.33%)	3(20.0%)
51-60	1(20.0%)	2(13.33%)
61-70	1(6.67%)	1(6.67%)
TOTAL	15	15
MEAN AGE ±SD RANGE	**37.33** ± 10.13	**38.4** ± 10.7

t=0.28, p= 0.781

The Mean Age difference between both Study I and Study II is statistically non-significant

2. Gender Distribution : (Table II)

Total number of male patients observed among both the Group I and Group II were 7 (46.67%) and female patients were 8 (53.33%). (table 2, graph 2)

GENDER	**STUDY GROUP I TRIAMCELONONE N (%)**	**STUDY GROUP II TACROLIMUS N (%)**
MALE	7(46.47%)	7(46.47%)
FEMALE	8(53.33%)	8(53.33%)
TOTAL	15	15

3. Clinical Pattern/ Forms Of OLP (Table III and IV)

All subjects included were further categorized into Nonerosive and Erosive Categories. Nonerosive category included Reticular, Annular, Papular and Plaque-type. Erosive category included Erosive, Ulcerative and Vesiculo-bullous types of OLP.

Group I: 12(80.0%) patients were Nonerosive, among them 6(40.0%) were male and 6(40.0%) were female. Erosive pattern was noted in 3(20.0%) among them 1(6.67%) was male and 2(13.33%) female patients.

Group II: 12(80.0%) patients were Nonerosive, among them 6(40.0%) were male and 5(33.35%) were female. Erosive pattern was noted in 3(20.0%) among them 1(6.67%) was male and 2(13.33%) female patients.

Fisher's Exact Test done to find out statistical difference between in distribution of erosive and nonerosive pattern distribution of OLP patients Study group I and Study group II. **Two Tailed p=1.000.** There is no statistical difference in distribution of erosive and nonerosive pattern distribution of OLP patients in Study group I and Study group II.

Table 3 Clinical types in study group I

Pattern	Age range (years)					Gender		Total (N%)
	21-30	31-40	41-50	51-60	61-70	Male	Female	
Non erosive	3	6	1	1	1	6 (40.0%)	6 (40.0%)	12(80.0%)
Erosive	0	2	1	0	0	1(6.67%)	2(13.33%)	3(20.0%)
Total	3	8	2	1	1	7(46.67%)	8(53.33%)	15

Table 4 Clinical types in study group II

Pattern	Age range (years)					Gender		Total (N%)
	21-30	31-40	41-50	51-60	61-70	Male	Female	
Non erosive	3	5	1	1	1	6 (40.0%)	5(33.35%)	11(73.37%)
Erosive	0	1	2	1	0	1(6.67%)	3(20.0%)	4(26.68%)
Total	3	6	3	2	1	7(46.67%)	8(53.33%)	15

Fisher's Exact Test - Two Tailed p=1.000

There is no statistical difference in distribution of erosive and nonerosive pattern distribution of OLP patients in Study group I and Study group II.

4. Treatment Results In Group I And Group II (Table 5)

In Group I patients 5(26.68%) had no improvement, 6(40.0%) showed Improvement and 4(33.35%) patients showed healing results. 11

In group II patients none of the patients showed no improvement, 7(40.0%) showed Improvement and 8(53.33%) patients showed healing results

The treatment results of Group II are better than Group I.

For statistical analysis Improvement and Healing group were combined together.

Fisher's Exact Test - p=0.042

Table 5: Treatment outcomes of patients in Group I and Group II

	GROUP I	GROUP II
No Improvement	5(26.68%)	0
Improvement	6(40.0%)	7(46.67%)
Healed	4(33.35%)	8(53.33%)

Discussion:

Tacrolimus, also called FK 506, is an immunosuppressant macrolide lactone antibiotic produced by streptomyces tsukubaensis.[4] This macrolide is produced by Streptomyces tsukabaensis, a bacterium found in the soil near Tsukuba, Japan.[1]

The first successful use of topical tacrolimus in patients with atopic dermatitis was reported by Nakagawa et al. in 1994 and 6 years later the U.S. Food and Drug Administration (FDA) approved tacrolimus ointment as a promising treatment for atopic dermatitis. Additionally, tacrolimus was investigated for a wide variety of inflammatory skin diseases beyond atopic dermatitis; particularly for conditions recalcitrant to other forms of therapy. [7]

In this study, topical tacrolimus 0.1% was found to be significantly more effective than topical triamcinolone acetonide 0.1%. 5(26.68%) of the patients treated with triamcinolone showed no improvement in size of mucosal lesions while all the patients treated with tacrolimus had an improvement in size of mucosal lesions. This study showed that rate of change in size of the lesion initially was faster in tacrolimus group than in triamcinolone group. This is in accordance with the study conducted by R. Laeijendecker et al [5] and which suggested that the treatment with topical tacrolimus ointment 0.1% four times daily induced a better initial therapeutic response than triamcinolone acetonide 0.1% ointment in patients with symptomatic OLP. Similar study done by Preeti Arora et al 7 found same results with comparison of topical tacrolimus 0.03% and triamcinolone acetonide 0.1% ointment.

In this randomized comparative double-blind study done by Lida Radfar at el[8] the profiles of mean lesion sizes and mean pain measures did not differ between the tacrolimus and clobetasol treatment groups. In this study clobetasol ointment was used which is more potent steroid than triamcinolone acetonide.

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.[6] Better treatment results from tacrolimus topical ointment as in this study may be because of its more potent action.

Several studies have reported the relapse of the lesion after the cessation of both the treatments. It is probable that tacrolimus acts to suppress the disease rather than inducing a long term remission, and it may offer control of the condition in patients who do not respond to topical steroid therapy.[9]

In our study duration of the treatment period which was too brief to identify the possible relapse after cessation of the treatment and adverse events due to long term use of tacrolimus but follow up of patients will be done after submission of thesis.

Conclusion:

The results of this study allow the conclusion 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.

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.

Research Funding:

The present research was funded by Indian Council of Medical Research (ICMR), New Delhi. Ref No 2011-02049.

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