# **Original Research Article**

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# Triamcinolone acetate vs combination of triamcinolone acetate and isotretinoin in treatment of oral lichen planus: a comparative study

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#### **ABSTRACT**

**Background:** There are many treatment modalities being practiced for oral lichen planus and many are under trial. However, none has been able to provide a complete permanent cure. This study aims to see if combination therapy with topical triamcinolone acetate and isotretinoin is superior to topical triamcinolone acetate alone, in treating oral lichen planus.

**Methods:** Patients were randomly divided into 2 groups to receive either triamcinolone (0.5%) only (group A) or 0.5% triamcinolone with 0.1% isotretinoin (group B). Patients applied medication thrice daily and were followed up at, 2 week, 1st month, 2nd month and 3rd months. Size of lesion and symptoms were assessed at each visit. The data was analysed by chi square test.

**Results:** Patients in group B (combination therapy) showed significantly better improvement in symptoms at the end of 2<sup>nd</sup> week and 1<sup>st</sup> month as compared to group A. Decrease in lesion size was also better in group B with p values of 0.012, 0.004 and 0.022 at 2 weeks, 1<sup>st</sup> month and 2<sup>nd</sup> month respectively. Complete resolution of lesion was obtained in 53.33% people in group B and 26.67% people in group A.

**Conclusions:** Combination of 0.5% triamcinolone acetate and 0.1% isotretinoin is superior to 0.5% triamcinolone acetate alone in treatment of oral lichen planus. It causes quicker relief in symptoms and decreases lesion size faster. Complete resolution of the lesions is also more when combination therapy is used.

**Keywords:** Oral lichen planus, Triamcinolone acetate, Isotretinoin, Burning sensation, Oral cavity

### INTRODUCTION

Lichen planus of the oral cavity is a chronic inflammatory disease with an incidence of about 0.5- 2% in the general population It is more common in women with a male-female ratio of 1:1.4 and usually presents in the 4<sup>th</sup> decade.¹ Different types are described like reticular, plaque like, popular and erosive, of which reticular type is the commonest. It is thought to be idiopathic although certain factors like stress, depression, anxiety, diabetes may influence it. Another school of thought is that it is an autoimmune disease, mediated by T-cells (CD8+ T Cells), that causes apoptosis of the oral epithelium's basal layer.² Diagnosis is usually made by

history and clinical findings,but biopsy is confirmatory. Oral lichen planus on histology shows projections of the epithelium in the form of sawtooth and Civatte bodies.<sup>3</sup>

Currently there are a large number of treatment modalities being tried for this condition, but none is established as definitely curative. Corticosteroids are in the forefront, followed by antibiotics, retinoids, tacrolimus, cyclosporine, dapsone, hydroxychloroquine, mycophenolate mofetil etc. PUVA, Photodynamic therapy and lasers are also being tried. On this background, we thought of combining the two commonly used agents namely steroids and retinoids. There is ample data on these individual drugs, but works with the

combination therapy is minimal. Here we used topical treatment with the steroid triamcinolone acetate and the retinoid isotretinoin. Steroids act by modulating the immune response and inflammation.<sup>4</sup> Retinoids act via immunomodulatory, anti inflammatory, anti keratotic properties and they increase the macrophage concentrations intralesionaly.

#### **METHODS**

This is a prospective single blinded study conducted in a tertiary care hospital from November 2016 to October 2017. Patients who presented to the ENT outdoor department with oral lesions characteristic of oral lichen planus, were biopsied. Those patients whose histopathology report confirmed lichen planus were taken up for the study after getting proper informed consent. The ethical committee clearance was obtained for the study. Thorough history of the participants was taken.

The inclusion criteria included a histopathology report of oral lichen planus with no evidence of any malignancy, age more than 18 years, of both sexes, were willing to come for follow up. We excluded patients younger than 18 years, those with features of malignancy, inconclusive diagnosis, those with uncontrolled immunodeficiency, pregnancy, breast feeding, those who have received previous treatment and those with history of allergy to triamcinolone or isotretinoin. The selected patients (n=60) were divided into 2 groups using a random number table. Group A (n=30) received topical 0.5% triamcinolone acetate alone and Group B (n=30) patients received topical 0.5% triamcinolone acetate and 0.1% isotretinoin. Initial size of the lesions was noted with the help of calipers and photography. Severity of symptoms (pain, burning sensation) was noted in a 10 point visual analogue scale. Participants were instructed to apply the medication topically thrice daily after food for three months continuously. They were followed up at the end of 2 weeks, 1 month, 2 months and 3 months. At each visit they were re-evaluated. A decrease in size of the lesion by 25% or more of the initial, and an improvement by 2 points or more in the visual analogue scale for symptoms were taken as positive responses. Further, at the end of study, we calculated the number of patients who had complete resolution of their lesions, those who had partial resolution and those with resistant lesions. Findings were recorded and the results of the two groups compared using chi square test

# **RESULTS**

There were 16 males and 14 females in group A and 19 males and 11 females in group B (p=0.432, no significant difference). Both the groups had maximum patients in the 30-50 year age group (Table 1). When we evaluated the improvement in symptoms (pain and burning sensation), we saw that 73.3% of patients in group A and 93.3% in group B showed improvement at the end of two weeks (p=0.037). This increased to 86.6% and 96.6% in group A and group B respectively by end of 1 month (p=0.044). On further follow up at 2<sup>nd</sup> month all patients in group B had relief in their symptoms where as only 90% had improvement in group A (p=0.3). At the end of the study period at 3 months, 3 patients in group A had persistent symptoms (Table 2).

Table 1: Age distribution.

Age in years	Number of participants		
	Group A	Group B	
<30	5	8	
30-50	18	12	
>50	7	10	
Total	30	30	

In case of decrease in the lesion size, group B patients showed much more improvement compared to group A. This difference was statistically significant during 2<sup>nd</sup> week, 1<sup>st</sup> month and 2<sup>nd</sup> month, with p values of 0.012, 0.004 and 0.022 respectively. However, this difference was not significant when evaluated at the end of 3<sup>rd</sup> month (Table 3).

Table 2: Patients showing improvement in their symptoms.

Group	2 weeks	1 month	2 months	3 months
Group A- 0.5% Triamcinolone acetate	22 (73.3%)	26 (86.6%)	27 (90%)	27 (90%)
Group B- 0.5% Triamcinolone acetate and 0.1% isotretinoin	28 (93.3%)	29 (96.6%)	30 (100%)	30 (100%)
P value	0.037	0.044	0.3	0.3

Table 3: Patients showing decrease in size of the lesion.

Group	2 weeks	1 month	2 months	3 months
Group A- 0.5% Triamcinolone acetate	17 (56.6%)	19 (63.3%)	23 (76.6%)	26 (86.7%)
Group B- 0.5% Triamcinolone acetate and 0.1% isotretinoin	25 (83.3%)	28 (93.3%)	29 (93.7%)	30 (100%)
P value	0.012	0.004	0.022	0.16

Table 4: Degree of response of lesions in each group.

Response	Group A (%)	Group B (%)
Complete response	8 (26.67)	16 (53.33)
Partial response	19 (63.33)	14 (46.67)
No response	3 (10)	0
Total number of patients	30 (100)	30 (100)

There were 26.67% and 53.33% patients with complete resolution of lesions in group A and group B respectively, with a p value of 0.035, that was statistically significant. Partial response was seen in 60% in group A and 47% in group B. When all patients responded with at least 25% decrease in the lesion size in group B, 10% in group A were resistant with no improvement in their lesions (Table 4).

There were no significant adverse effects noted during the study, except for an irritation on initial application of isotretinoin, that subsided by itself after some time. This did not require discontinuation of medication in any patient.

# **DISCUSSION**

Recently, stress is being given for local treatment of lesions of oral lichen planus as opposed to systemic ones. This is because of the fear of side effects if treatment is given systemically. But in case of recalcitrant lesions it may become necessary. This study shows that topical triamcinolone acetate is effective in controlling the symptoms and clinical lesions of oral lichen planus, but if isotretinoin topical formulation is added to it the effects may be better. A randomized control study in 2007 showed that 50% of the patients with oral lichen planus who were treated with 0.1% triamcinolone acetate achieved symptom free state at the end of 6 months.<sup>5</sup> In contrast, in the present study, 90% patients treated with 0.5% triamcinolone acetate were symptom free. This increased effect may be due to the higher concentration (0.5%) of the drug used. Le Cleach et al recommended topical steroids as the first line treatment for oral lichen planus.<sup>6</sup> Kar et al compared the effect of topical isotretinoin and steroids in oral lichen planus. There was an improvement in the average symptom score from 3.4 to 1 in patients treated with 0.05% isotretinoin as compared to a symptom score from 3.6 to 2.1 in the topical steroid group. This study concluded that isotretinoin was more effective than triamcinolone in controlling symptoms.7 However Buajeeb et al observed an opposite effect in his study where the steroid fluocinolone acetate showed significant improvement than isotretinoin.8 A placebo controlled study by Boisnic et al showed that 0.1% topical isotretinoin applied 4 times daily was superior and that it decreased lesions in 97% patients compared to 21% in the placebo group. A similar study conducted by Giustina et al that used 0.1% of the drug for 8 weeks showed attenuation of the lesions in 90%. 10 The

100% response that we observed in our study group B may be attributed to the fact that we had combined the drugs. In the present study, patients in the combination group (group B) showed quicker and much better response when compared to those treated with triamcinolone acetate alone. This can be seen from the statistically significant difference between the 2 groups in the initial periods of the study.

The final lesion size was graded as complete response (no clinically detectable lesion), partial response (clinically detectable lesion with decrease in size by 25% or more) or no response (less than 25% change). In group A (triamcinolone), 26.67% showed complete response and 63.3% showed partial response. Thongprasom et al study recorded an equal number (50%) of complete and partial responses. 11 In yet another study, these figures were 16% and 30% respectively for complete and partial response. 12 Out of 10 patients, Pietalli et al observed that 4 (40%) showed complete response and 6 (60%) showed partial response of their lesions in oral cavity when treated with 0.1% isotretinoin.<sup>13</sup> The present study revealed a complete response in 53.33% and partial response in 46.67% of study population treated with combination therapy. It showed a significantly better result (p=0.035) when compared to the triamcinolone alone group in case of complete resolution. In 2010 a study was done to compare the effect of mouthwash containing triamcinolone and isotretinoin with mouth wash containing triamcinolone alone. The authors concluded that combining both drugs enhanced the outcome in cases of oral lichen planus. 14 Data from our study is comparable with this observation.

Due to the continuing research in this field, a number of newer treatment options are continuously being suggested for treatment of oral lichen planus. In this context, combining two already proven effective drugs would be beneficial. It will be a cost effective and affordable alternative as newer modes of treatments are costlier. His study shows that patients treated with a combination of 0.5% triamcinolone acetate and 0.1% isotretinoin responded faster and better than those treated with 0.5% triamcinolone acetate alone. The combination was also found to cause complete resolution of lesions much better than triamcinolone acetate alone.

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