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COMPARATIVE EVALUATION OF EFFICACY OF TOPICAL CURCUMIN AND CORTICOSTEROID IN TREATMENT OF OLP

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ABSTRACT

Introduction: Oral Lichen Planus (OLP) is a chronic inflammatory mucocutaneous disease affecting the oral cavity which has been associated with severe burning sensation which in turn affects the quality of life of the patients. Its treatment is often symptomatic ad includes topical and systemic corticosteroids. Although corticosteroid therapy is usually successful, but may induce candidiasis and mucosal atrophy. The chronicity and recalcitrant nature of the disease demand the long term use of these drugs with ensuing adverse effects. Turmeric and its active ingredient, "curcumin", have been found to have anti-inflammatory, antioxidant and anticancer properties. Hence, this study was done to compare the efficacy of topical triamcinolone and curcumin in the management of oral lichen planus. **Materials and Methods:** A study was conducted on 36 patients diagnosed with OLP divided into two groups, Group 1 (0.1% triamcinolone acetonide) Group 2 (curcumin oral gel). The Subjects in Group I were asked to apply 0.1 % triamcinolone acetonide and in Group II were asked to apply 1% curcumin oral paste three times a day for three months on the lesion. Patients were recalled for the evaluation of progression of the treatment for 3 months. Follow up was done on the 1st week, 2nd week, 4th week, 12th week of treatment period. At follow up visit curative response of two different treatment modalities for OLP lesions were assessed using reduction in VAS scale and Thongprasom score. **Results:** There was statistically significant reduction in mean VAS score and Thongprasom score (Appearance score) of lesion were seen in both the treatment groups on subsequent follow up. Statistically no significant difference were found between two treatment groups. **Conclusion:** The results of the present study suggested

that local use of curcumin can be effective in improving the symptoms of patients with oral lichen planus without any side effects.

KEYWORDS: Curcumin, Triamcinolone acetonide, Oral Lichen Planus.

INTRODUCTION

Lichen planus is a chronic inflammatory, autoimmune, mucocutaneous disease of unknown etiology.[1-3] It can affect the oral mucosa, skin, genital mucosa, scalp, and nails. Globally, Lichen Planus affects about 1-2 % of population and prevalence in India ranges from 0.1% to 1.5%.[4,5] The world health organization (WHO) has defined OLP as a potentially precancerous disorders, representing generalized state associated with a significantly increased risk of cancer. OLP affects 0.5% to 2.2% and more frequent in women than men, from 2:1 to 3:1. In India prevalence rate of OLP is 2.6%.[6,7]

The exact etiology of OLP is not well understood. It is believed to result from antigen specific mechanism which causes deregulation of T‑Cell mediated immune response in which auto cytotoxic CD8+T Cells trigger the apoptosis of oral epithelium which occurs as a result of migration and activation of T lymphocytes.[4] As the true cause of lichen planus remains poorly defined, it has been associated with so many local and systemic factors. Lichen planus has been most often cited as being of stressful or psychogenic origin, because the disease seems to have a tendency to appear in allegedly ‘high strung’ persons. Other etiological factors include rheumatic collagen diseases, HLA predispositions, mouth irritation and smoking.[3,7-10]

The clinical presentation of OLP ranges from mild painless white keratotic lesions to painful erosion and ulceration. The most common site is buccal and vestibular mucosa followed by lateral borders of tongue and gingiva.[4] Andreasen (1968) classified OLP into six clinical forms Reticular, Papular, Plaque-like, Atrophic, Erosive, Bullous. The reticular form is the most common type and presents as interlacing white keratotic lines or in an annular pattern with an erythematous border.[6,9 -15]

The treatment modalities in oral lichen planus are still experimental. Extensive research and numerous trials have been conducted to determine the most efficacious and safe treatments for OLP, but currently no definite treatment protocol for the management of OLP exists. Contemporary treatment modalities of OLP are primarily symptomatic aiming to reduce pain,

erythema & ulceration. Treatment of OLP patients depends on symptoms, the extent of oral and extra-oral clinical involvement, medical history, and other factors. The most common treatment for OLP is corticosteroids which are administered topically, systemically or intralesional. The chronic and recalcitrant nature of the disease demands the use of these drugs for long durations with subsequent increase in dose. Considering side effects of these drugs there has been a constant search for an alternative herbal drug which could be taken as monotherapy or in combination with the mainstay drugs used in the treatment of lichen planus on a long term basis with minimal side effects.[3,4,12,16,17]

Recently, herbal medicines have been introduced for symptomatic treatment of OLP. Specifically, Curcumin is one of the nutraceuticals that has received a great attention nowadays. Curcumin has been identified as a natural phytochemical and active principle in turmeric. Curcumin exhibits antioxidant, anti-inflammatory, anticancer, and immunomodulatory activities.[18-20]

The present study was undertaken to assess and compare the efficacy of 1% curcumin and 0.1% triamcinolone acetonide in alleviating the symptoms of OLP.

MATERIAL AND METHOD

A clinical study was carried out in Department of Oral Medicine. Ethical clearance was obtained from Institutional Ethical Committee and informed consent was taken from all participants of study. Study included 36 patients who were diagnosed clinically as OLP. The patients of OLP were selected randomly irrespective of age and gender.

Inclusion criteria

All cases were clinically diagnosed as per Modified WHO diagnostic criteria[21] – 2003 irrespective of their complaint. Along with this basic criteria[22], the following criteria, were used for the selection of patients for the study.

- Patients with symptoms like ‘burning sensation’ or ‘itching pain’ of mucosa were selected.
- Patients showing oromucosal changes as diffuse papule, white reticular, plaque, vesicle, ulceration.
- Patients having combined lesions i.e. combination of two different clinical forms of OLP were included in the study.
- Patients having skin lesions of lichen planus.

- Patients with systemic disorders like diabetes and hypertension were also included in study.
- Patients willing to take part in the study.

Exclusion criteria

- Patients with history of topical treatment for OLP in the past two weeks or any systemic treatment for OLP in the past four weeks, taking azathioprine, cyclosporine or receiving Psoralen plus ultraviolet A (PUVA), ultraviolet A (UVA) or ultraviolet B (UVB) radiation in the past month.
- History of allergic reactions to corticosteroids or herbal preparations.
- Evidence of lichenoid reaction and other associated surface lesion in clinical assessment were also excluded.
- Patients on long term corticosteroid therapy or any other immunosuppressants or immunomodulatory for other systemic diseases.
- Pregnant and lactating female patients were also excluded.

All the patients meeting the eligibility criteria were randomly divided into two groups. They were informed about their disease and treatment.

Group I: Topical triamcinolone acetonide 0.1%

Group II: Topical curcumin 1%

Subjects in Group I were asked to apply 0.1 % triamcinolone acetonide and in Group II were asked to apply 1% curcumin oral paste three times a day for three months after meal on the lesion. Patients were advised not to rinse, eat or drink anything for the next half an hour after the application of the oral paste and recalled for the evaluation of progression of the treatment for 3 months. Follow up was done on the 1^{st} week, 2^{nd} week, 4^{th} week, 12^{th} week of treatment period. Subjects in both the treatment group were also given supportive medications. E.g. vitamin B complex and antioxidant tablets.

At follow up visit curative response of two different treatment modalities for OLP lesions were assessed using reduction in VAS scale. (The patients were asked about the degree of pain on a score of 0–10, where 0 indicates no pain and 10 indicates the most severe pain) and Thongprasom score. If any adverse effects occurred during the course of therapy is noted and respective medication is asked to discontinue and appropriate medications are prescribed as per the adverse effect and once it subside patient is asked to continue same medications.

Thongprasom score: was used to evaluate the clinical appearance of lesion as follows,

0: No lesion, normal mucosa

1: Mild white striae, no erythematous area

2: White striae with atrophic area less than 1cm²

3: White striae with atrophic area more than 1cm²

4: White striae with ulcerative area less than 1cm²

5: White striae with ulcerative area more than 1cm²

STATISTICAL ANALYSIS

All the recorded data of patient were subjected to statistical analysis using the SPSS (Statistical package for social science ver. 25.0) package. The demographic data, chief complain, various systemic conditions, different clinical forms of OLP, curative response of different clinical forms of OLP at different sites in both treatment groups were represented in tables. The baseline VAS score and Thongprasom score as well as post treatment VAS score and Thongprasom score between the groups were compared using independent t-test. The pre and post treatment VAS score and Thongprasom score within the groups were compared using paired t-test.

RESULTS

Table 1: Distribution of patients of different forms of OLP according to age.

Age (years)	Clinical forms of OLP						Total (n=36) (100%)
	Reticular (n=15) (41.67%)	Papule (n=0) (0%)	Plaque (n=0) (0%)	Erosive (n=2) (5.55%)	Atrophic (n=2) (5.55%)	Mixed lesions(n=17) (47.23%)	
>30 (n=7)	3 (20%)	0 (0%)	0 (0%)	0 (0%)	1 (50%)	3 (17.65%)	7 (19.44%)
31-50 (n=21)	11 (73.33%)	0 (0%)	0 (0%)	1 (50%)	1 (50%)	8 (47.06%)	21 (58.34%)
51-70 (n=8)	1 (6.67%)	0 (0%)	0 (0%)	1 (50%)	0 (0%)	6 (35.29%)	8 (22.22%)

n= number of patients

17 (47.23%) patients with mixed lesions include Reticular and Papule (1 patient), Reticular and Plaque (6 patients), Reticular, Erosive and Plaque (2 patients), Reticular and Atrophic (3 patients), Reticular and Erosive (3 patients), Reticular, Atrophic and Plaque (2 patients).

Table 2: Distribution of patients of different forms of OLP according to Gender.

Gender	Clinical forms of OLP						Total (n=36) (100%)
	Reticular (n=15) (41.67%)	Papule (n=0) (0%)	Plaque (n=0) (0%)	Erosive (n=2) (5.55%)	Atrophic (n=2) (5.55%)	Mixed lesions(n=17) (47.23%)	
Male (n=10)	4 (26.67%)	0 (0%)	0 (0%)	1 (50%)	0 (0%)	5 (29.41%)	10 (27.77%)
Female (n=26)	11 (73.33%)	0 (0%)	0 (0%)	1 (50%)	2 (100%)	12 (70.59%)	26 (72.23%)

Table 3: Intergroup and Intragroup comparison of mean reduction in VAS score.

Changes in VAS scale	Intergroup comparison			Intragroup comparison		
	Group 1 (n= 19) Triamcinolone (Mean± SD)	Group 2 (n=17) Curcumin (Mean± SD)	P value	Group 1 (n= 19) Triamcinolone (Mean± SD)	Group2 (n=17) Curcumin (Mean± SD)	P value
Baseline	3.84±1.12	3.18±1.07	.078	3.84±1.12	3.24±1.09	.000
1 week follow up	3.21±1.27	2.59±1.23	.146	3.21±1.27	2.59±1.23	
2 week follow up	2.26±1.45	1.76±1.14	.258	2.26±1.45	1.76±1.14	
4 week follow up	1.11±1.25	1.24±.97	.731	1.11±1.24	1.24±.97	
12 week follow up	.63±.90	.76±.75	.634	.63±.90	.76±.75	

Table 4: Intergroup and Intragroup comparison of mean reduction in Thongprasom score (appearance score).

Changes in appearance score	Intergroup comparison			Intragroup comparison		
	Group 1 (n= 19) Triamcinolone (Mean± SD)	Group 2 (n=17) Curcumin (Mean± SD)	P value	Group 1 (n= 19) Triamcinolone (Mean± SD)	Group 2 (n=17) Curcumin (Mean± SD)	P value
Baseline	2.63±1.21	2.65±.93	.966	2.63±1.21	2.65±.93	.000
1 week follow up	2.26±1.19	2.41±.87	.676	2.26±1.19	2.41±.87	
2 week follow up	1.95±1.13	1.88±.78	.844	1.95±1.13	1.88±.78	
4 week follow up	1.53±.84	1.65±.86	.673	1.53±.84	1.65±.86	
12 week follow up	1.11±.74	1.41±.50	.160	1.11±.73	1.41±.50	

DISCUSSION

OLP is a chronic, T cell‑mediated autoimmune disease characterized by periods of exacerbations and remissions. Corticosteroids have been the main drug of choice in these

patients. However, considering the chronic nature of the condition, associated systematic diseases, and frequent use of steroids, the number of patients affected by the complications is uncountable. In addition to the systemic complications, long‑term topical corticosteroids can lead to secondary candidiasis, taste alterations, mucosal atrophy, and burning sensation, further worsening the condition. Therefore, an alternative and safe therapy which could be equally effective or superior to steroids should be explored. One such therapy is the herbal medicines which have been tried for many chronic conditions including OLP.[18-20,23]

In the present study, 36 patients of OLP were studied regarding their clinical, etiological aspects and therapeutic response using 0.1% triamcinolone acetonide and 1% curcumin. In group I, 19 patients of OLP were treated with 0.1% triamcinolone acetonide application three times a day for period of 3 months. In group II, 17 patients of OLP were treated with 1% curcumin in the same way. In both the treatment groups VAS score, appearance score were evaluated at baseline and subsequent follow up visits.

Out of 36 patients of OLP most patients were of 31-50 years of age range. **(Table 1)** The youngest patient was 15 years old and the oldest was 68 years old. According to the literature, the common age at presentation is 30 to 60 years, predominantly involves middle-aged women and younger-aged men. According to Mccarthy and shklar oral mucosal lesion of lichen planus can occur at any age.[3,8,15,22,24,25]

The present study showed female predominance in all different form (Reticular, papule, plaque, erosive and atrophic form) of OLP. (**Table 2)** This is similar to studies by many authors who have reported female predominance. This could be due to the influence of hormones like estrogen.[8,16,22,24] Dudhiya B et. al[9] found that the reticular/linear/annular lesions were more commonly associated with pan/tobacco/betel nut/ gutkha chewing, which is more common among the males than females and erosive form was more commonly associated with stress and hormonal disturbances, which is most frequently seen in females. In mixed lesions there were equal distribution and this may be due to the fact that mixed lesions contain both erosive and reticular type of patients in equal numbers. While, in present study, mixed lesion of OLP were also showed female predominance.

OLP lesions with classical appearance can be diagnosed solely on the basis of clinical appearance of the affected tissue. Though the definitive diagnosis of various forms of OLP depends on histopathologic examination. Performing a biopsy of lesional tissue, particularly

if the OLP is of the erosive form, can be challenging as it is important to obtain an elliptical wedge of mucosa extending beyond the affected area, to avoid stripping the superficial epithelial layer from the underlying connective tissue and also, acquiring a biopsy means creating a wound site and delaying the treatment until the wound heals. [6,26,27] So, in the present study patients were evaluated on the basis of clinical criteria.

Efficacy of topical triamcinolone acetonide 0.1% (Group I) and topical curcumin 1% (Group II) were compared in OLP lesions in present study. There was statistically significant reduction in mean VAS score and Thongprasom score (Appearance score) of lesion were seen in both the treatment groups on subsequent follow up. Statistically no significant difference were found between two treatment groups (**Table 3 and 4)** similar to studies done by Kia et al.,[28] Nosratzehi et al.,[29] and Thomas et al.[16] Kia et al.[28] revealed that there was comparable effect in pain reduction and appearance score in both triamcinolone and curcumin with no statistical significant difference between two groups. Effects were similar to those of topical corticosteroids, and thus, it can be a suitable alternative to corticosteroids. Nozaretzehi et al.[29] stated that curcumin was effective in the treatment of oral lichen planus lesions and resulted in decrease in lesion size, pain and burning sensation without any complications. Thomas et al.,[16] in her study assessed increased reduction of burning sensation observed in triamcinolone acetonide group, followed by curcumin 6 times daily application and curcumin oral gel, applied 3 times a day. Application of curcumin oral gel six times daily was considered equally effective compared to triamcinolone acetonide. These studies showed intragroup significance from baseline comparison to follow-up visits similar to present study. Only 1 patient in treatment group I developed secondary candidiasis attributed to decreased immune response and none of the patients in the Group II developed any adverse effects during the treatment course.

In the present study, all clinical forms of OLP responded better in Group I compared to Group II. According to literature triamcinolone acetonide 0.1% is a safe and effective drug for OLP. The benefit of corticosteroids in management of lichen planus appears to be related to both immunosuppressive and anti-inflammatory properties. In topical curcumin 1% therapy, number of completely cured lesions was less compared to triamcinolone acetonide 0.1% in all forms. With curcumin 1% therapy, partial cure of lesion were seen. Curative response was good in atrophic and erosive form of OLP compared to reticular and plaque form of OLP. Going through literature curcumin had produced generally good results in

patients with OLP.[30,31] Keshari D et al.,[32] concluded curcumin fared better in reducing pain, erythema, and ulceration. Thus, curcumin can be used as an alternative to steroid in the management of signs and symptoms of OLP with minimal side effects as compared to steroids with similar efficacy. Curcumin mediates its anti-inflammatory effects through the down regulation of inflammatory transcription factors, enzymes (such as cyclooxygenase 2 and 5, lipoxygenase) and cytokine. Furthermore, curcumin produces its antioxidant effect through inhibition of free radicals and nitric oxide which can be very well used in treating OLP.[5,33]

CONCLUSION

Despite many studies conducted to find an effective approach for managing OLP, the results have often been unsatisfactory. The results of the present study suggested that local use of curcumin can be effective in improving the symptoms of patients with oral lichen planus without any side effects. It can be used as an alternative to topical corticosteroid therapy in the management of OLP.

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