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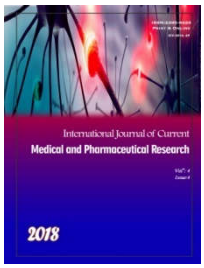

EFFICACY OF TOPICAL CURCUMIN COMPARED TO TOPICAL TRIAMCINOLONE IN TREATMENT OF ORAL LICHEN PLANUS-A RANDOMIZED CLINICAL TRIAL

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ABSTRACT

Objectives: Oral lichen planus is a T-cell mediated autoimmune chronic inflammatory mucocutaneous disease that mostly affects the buccal mucosa, tongue and the gingiva. Systemic & topical corticosteroids are the mainstay and most common drug for OLP management but because of the side effects of long-term use, thus trends toward drugs of natural or herbal origin with antioxidant and anti-inflammatory properties. The aim & objectives of the study was to compare the efficacy of topical curcumin with topical triamcinolone in the treatment of oral lichen planus.

Materials & Methods: In this study 60 patients were included into 2 groups as one group consists of 30 patients which were included in the study group remaining 30 patients in the control group. Each group received 0.1% triamcinolone or 1% curcumin oral paste two times daily for 2 months and patients from both groups were subjected to post treatment follow-up visit after complete and partial remission for a duration of minimum 6 months. Assessment of the appearance score and severity of burning sensation was done at baseline and after 15th day, 30th day, 45th day and 2 months, recorded in the patients' questionnaires. The data were analyzed by SPSS version 18 software using the Mann-Whitney and Spearman's correlation tests. $P<0.05$ was considered statistically significant.

Results: 22 patients in the curcumin group and 24 patients in the triamcinolone group showed complete remission in respect to reduction of burning sensation. 12 patients in study group and 10 patients in control group showed complete remission with respect to the appearance score. No statistically significant difference was noted between the two groups.

Conclusion: Topical application of curcumin is suggested for the treatment of oral lichen planus because of its significant anti-inflammatory, anti-oxidant, anticarcinogenic effects and insignificant side effects.

INTRODUCTION

Lichen planus is a T-cell mediated autoimmune chronic inflammatory mucocutaneousdisease that affects the skin and the mucus membrane. Oral Lichen Planus (OLP) is the mucosal counterpart of cutaneous lichen planus. It presents frequently in the fourth decade of life with women predilection.[1] Reticular, papular, plaque-like, erosive, atrophic or bullous types are the clinical features of OLP. The most involved areas of the mouth are the buccal mucosa, tongue and the gingiva. [2]

The etiology of OLP is still uncertain, some evidences indicate that a dysregulation of T-cell mediated immunity leads to the attack of activated CD8+ lymphocytes on basal keratinocytes, has an important role in the pathogenesis of OLP. [3]Studies have reported higher level of anxiety, greater depression and increased psychic disorders oral lichen planus. [4]

Although various treatments have aimed to improve the lesions and reduce the associated burning sensation, corticosteroids are the mainstay and most common drug for OLP management. Calcineurin inhibitors, retinoids, dapsone, hydroxychloroquine, mycophenolatemofetil and enoxaparin are also applied for OLP treatment. But because of the side effects of long-term corticosteroid therapy such as secondary candidiasis, telangiectasia, hypothalamic–pituitary–adrenal suppression, muco-cutaneous atrophy and increased potential of systemic absorption, it may be better to avoid their long-term use. [5] Thus trends toward drugs of natural or herbal origin with antioxidant and anti-inflammatory properties, with or without corticosteroids, have been considered for the treatment of OLP. [6]

As a natural product, curcumin is nontoxic and has diversified effects in various oral diseases. Curcumin has been identified as a natural phytochemical and active principle in turmeric, the ground powder of the rhizomes of Curcuma longa. Curcumin

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exhibits antioxidant, anti-inflammatory, antimicrobial, and anticarcinogenic activities. Moreover, curcumin is safe even at very high doses. [7] Curcumin mediates its anti-inflammatory effects through the down regulation of inflammatory transcription factors (such as nuclear factor-kappa B), enzymes (such as cyclooxygenase 2 and 5, lipoxygenase) and cytokines (such as TNF-α, IL-1, IL-6 and IL-8). Furthermore, curcumin produces its antioxidant effect through inhibition of free radicals and nitric oxide. [8]

Despite the progress in researches on OLP, the successful treatment is still difficult to obtain. As control and reduction of symptoms is the main purpose for OLP treatment, in the present study we attempted to evaluate the efficacy of topical curcumin and topical triamcinolone acetonide administration in treatment of OLP and compare the response rate before and after treatment.

MATERIALS AND METHODS

A Randomized Clinical Trial was conducted in the Department of Oral Medicine and Radiology, DivyaJyoti College of Dental Sciences and Research, Modinagar, Ghaziabad, Uttar Pradesh, India. The study consisted of clinical case series of 60 patients of both genders and with wide age groups (24 yrs.-65 yrs.) having Oral Lichen Planus involving different regions of the oral cavity diagnosed on the basis of thorough history, proper clinical examination. 60 patients were included into 2 groups one group consists of 30 patients as study group remaining 30 patients in the control group. The age of the subjects in the Study group ranged from 26 years to 61 years and in the Control group ranged from 24 years to 65 years

The exclusion criteria were Pregnancy and lactating mothers, history of hypersensitivity to curcumin, patients with anaemia and blood dyscrasias, co-existing systemic illnesses or any debilitating diseases, current use of anticoagulants or antiplatelet agents, any existing malignancy or viral infections in the mouth, history of topical treatment for OLP in the past two weeks or any systemic treatment for OLP in the past four weeks, Patients who were unwilling to come for regular follow ups for 6 months' duration.

After confirmation of diagnosis burning sensation assessment was done by Visual Analogue Scale (VAS). [17] The VAS consists of a straight line with the end points defining extreme limits such as 'no burning sensation at all' and 'burning sensation as bad as it could be.' If descriptive terms like 'mild', 'moderate', 'severe' or a numerical scale is added to the VAS, one speaks of a Graphic Rating Scale. Zero usually represents 'no burning sensation at all' whereas the upper limit represents the worst burning sensation ever possible. We used Visual Analogue Scale score ranging from 0 to 10 for pre-treatment burning sensation assessment for the subjects in the study group and control group.

Appearance Score (Sign Score) was recorded in the study group and the control group based on the criteria given by Thongprasom K.[9] Score 0 = no lesion normal mucosa, Score 1 = mild white striae only, Score 2 = white striae with atrophic area < 1 cm^2, Score 3 = white striae with atrophic area > 1 cm^2, Score 4 = white striae with erosive area < 1 cm^2, Score 5 = white striae with erosive area = 1 cm^2

Study group comprised of 30 patients with OLP who received Curcumin ointment (Curenext®, Abbott, India) containing Curcuma longa extract 10 mg per gram (1%) applied twice daily for a period of 2 months. Patient was educated to replicate the instructions at home and advice to avoid solid and liquid diet for 15 minutes after application. The patients were asked to report every 15th day till 2 months of their treatment plan and once in a month during 6 monthperiod for post treatment follow-up.

Control group comprised of 30 patients with OLP who received topical triamcinolone acetonide 0.1% (Kenacort®, Abbott, India) orabase twice daily for 2 months. All the patients were recalled every 15 days during the treatment till 2 months and patient was asked to visit once in a month during 6 month period for post treatment follow-up.

The patients in either group were followed up after 15th day, 30th day, 45th day and 2 months from commencement of the treatment. The severity of the clinical sign and symptoms were entered in the set proforma based on appearance score in each patient from either group. The VAS score after 15th day, 30th day, 45th day and 2 months from commencement of the treatment of the respective therapies were recorded. The data was collected tabulated and analysed by SPSS version 18 software using the Mann-Whitney and Spearman's correlation tests. $P<0.05$ was considered statistically significant. Adverse reaction was observed.

RESULTS

Sixty subjects participated in the study, comprising of 30 subjects in the study group and 30 subjects in the control group. In the study group 9 (30%) males and 27 (70%) females and in the control group 8 (26.7%) males and 22 (73.3%) females clinically diagnosed with oral lichen planus based on history, thorough clinical examination.

Pre-treatment Burning Sensation Assessment: Pre-treatment Visual Analog Scale (VAS) among study group ranged from 3-9 with a mean of 3.8, SD = 1.44 whereas the pre-treatment VAS among control group ranged from 2-9 with mean of 3.9, SD = 1.36. **(Table 1)**

Table 1 Pre-treatment Burning Sensation Assessment

	Burning sensation assessment (VAS)		
	RANGE	**MEAN**	**SD**
Study group	3-9	3.8	1.44
Control group	2-9	3.9	1.36

60 days' Post-Treatment Burning Sensation Assessment: 60 days Post-treatment Visual Analog Scale (VAS) among study group ranged from 0-7 with a mean of 1.2, SD = 0.44 whereas the 60 days Post-treatment VAS among the control group ranged from 0-8 with a mean of 1.4, SD = 1.04. (Table 2)

Table 2 60 days' Post-Treatment Burning Sensation Assessment

	Burning sensation assessment (VAS)		
	RANGE	**MEAN**	**SD**
Study group	0-7	1.2	0.44
Control group	0-8	1.4	1.04

In our study the difference between the pre-treatment burning sensation assessment score among the study group and the control group is not significant (p=0.107), the difference between the 15 days post-treatment burning sensation assessment score among the study group and the control group is not significant (p=0.141), the difference between the 30 days and 45 days post-treatment burning sensation assessment score among the study group and the control group is not significant (p=0.132, p=0.124 respectively) in each and the difference

between 60 days post-treatment burning sensation assessment score among the study group and the control group is not significant (p=0.181). (Table 3)

Table 3 Comparison of VAS Score among Study and Control Groups

Duration	Mean ±SD		Probability of "t"	P value	Significance
	Study	Control			
Pre-treatment	3.8±1.22	3.9±1.37	0.0034	P=0.107	Not Significant
15 days post-treatment	3.3±1.22	3.2±1.37	0.0056	P=0.141	Not Significant
30 days post treatment	2.7±1.01	2.5±1.55	0.0087	P=0.132	Not Significant
45 days post treatment	1.9±0.98	2.1±1.41	0.0033	P=0.124	Not Significant
60 days post treatment	1.2±0.89	1.4±1.38	0.0084	P=0.181	Not Significant

Pre-treatment appearance score: Pre-treatment appearance score among study group ranged from 2-5 with a mean of 3.2, SD = 1.22 whereas the Pre-treatment appearance score among the control group ranged from 2-5 with a mean of 3.4, SD = 1.37. (Table 4)

Table 4 Pre-treatment Appearance Score

	Appearance Score		
	RANGE	MEAN	SD
Study group	2-5	3.2	1.22
Control group	2-5	3.4	1.37

60 days' Post-treatment appearance score: 60 days' Post-treatment appearance score among study group ranged from 0-3 with a mean of 1.2, SD = 0.89 whereas the 60 days' Post-treatment appearance score among the control group ranged from 0-5 with a mean of 0.9, SD = 0.17**(Table 5)**

Table 5 60 days Post-TreatmentAppearance Score

	Appearance Score		
	RANGE	MEAN	SD
Study group	0-3	1.2	0.89
Control group	0-5	0.9	0.17

In the present study the difference between the pretreatment mean appearance score among the study group and the control group is not significant (p=0.133), the difference between the 15 days post-treatment mean appearance score among the study group and the control group is not significant (p=0.361), the difference between the 30 days and 45 days post-treatment mean appearance score among the study group and the control group are not significant (p=0.232, p=0.181 respectively) in each whereas the difference between 60 days post-treatment mean appearance score among the study group and the control group is not significant (p=0.129). **(Table 6)**

Table 6 Comparison of Appearance Score among Study and Control Group

Duration	Mean ±SD		Probability of "t"	P value	Significance
	Study	Control			
Pre-treatment	3.2±1.24	3.4±1.17	0.0048	P=0.133	Not Significant
15 days post-treatment	2.7±1.81	2.8±1.37	0.0066	P=0.361	Not Significant
30 days post treatment	2.4±1.01	2.3±1.55	0.0031	P=0.232	Not Significant
45 days post treatment	1.9±0.98	2.1±1.41	0.0017	P=0.181	Not Significant
60 days post treatment	1.2±0.89	0.9±0.27	0.0001	P=0.129	Not Significant

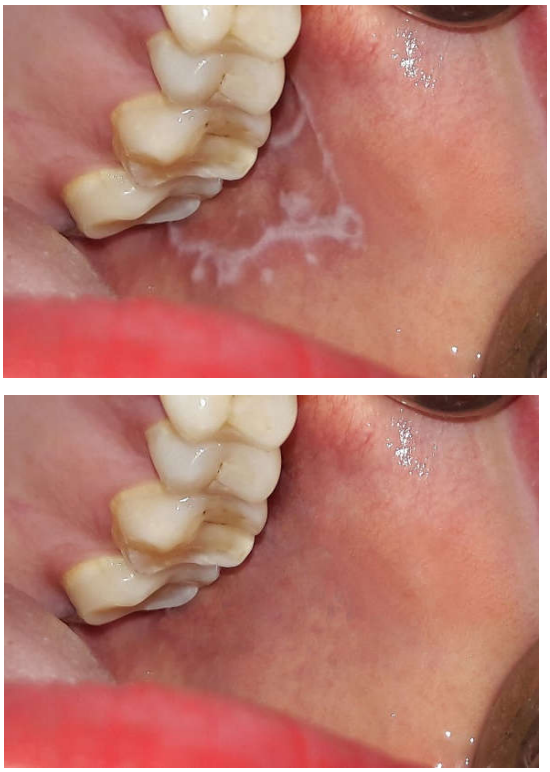

Fig 1 Pre-treatment & post-treatment reticular oral lichen planus in left buccal mucosa (study group)

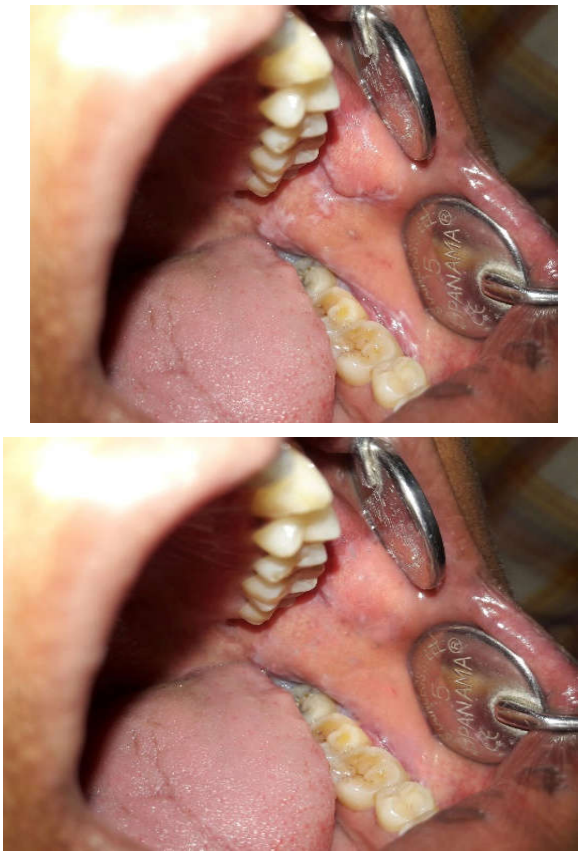

Fig 2 Pre-treatment & post-treatment reticular oral lichen planus in left buccal mucosa (control group)

Out of 30 patients who were included in the study group, 22 patients showed complete relief from burning sensation post curcumin ointment application after 2 months. Out of 30 patients who were included in the control group, 24 patients showed complete relief from burning sensation immediately post triamcinolone acetonide application after 2 months. The difference in the mean reduction in the VAS score for burning

sensation was not significant among the study group and the control group.

Similarly, out of 30 patients who were included in the study group, 12 patients showed complete relief from the appearance of lesion in the oral cavity as assessed by appearance score post curcumin ointment application after 2 months. Out of 30 patients who were included in the control group, 10 patients showed complete relief from appearance of lesion in the oral cavity as assessed by appearance score post triamcinolone acetonide application after 2 months. The difference in the mean reduction in the appearance score was not significant among the study group and the control group. In this study 6 patients have developed candidiasis in the control group whereas no such reaction was noticed in the study group.

DISCUSSION

Lichen planus was first described by Wilson in1869. Its etiology has not been understood well but its incidence is attributed to the immune response mounted by T cells. This lesion can cause oral discomfort and even in some cases, transform into squamous cell carcinoma. Therefore, OLP is considered to be a potentially dangerous and malignant disease and has attracted the attention of clinicians. [3]

There is no known treatment available for lichen planus and all the treatments are empirical. A corticosteroid regimen is the standard treatment for oral lichen planus because it disrupts the activity of the immune system and is used locally within the erosion or in a systemic manner. However, these medications have some disadvantage and if they are administered for more than two weeks, they result in the atrophy of the mucosa and causes candidiasis. In addition, they might be absorbed systemically.It would be better to find an alternative treatment. [10]

Curcumin has been shown to mediate anti-inflammatory effects through the inhibition of different macromolecules involved in inflammation including phospholipase, cyclooxygenase2, lipooxygenase, prostaglandins, interleukins 1 and 2 and tumor necrosis factor. [12]

Curcumin is a strong anti-oxidant agent, comparable to vitamins C and E, which has significant preventive and curative effects in a number of diseases such as cancer, diabetes and arthrosclerosis.

Apart from direct antioxidant action, curcumin also exhibits indirect antioxidant properties by potentiating the other antioxidant systems of body. Curcumin inhibits lipid peroxidation by using linoleate. Curcumin also raises the levels of glutathione, a significant antioxidant. [11]

In the current study, we used curcumin; its safety, anti-inflammatory and antioxidant effects have been confirmed in many previous studies. The clinical efficacy of curcumin was compared with that of a topical corticosteroid, which is the standard treatment for OLP.

Chainani-Wu *et al.* (2007) used curcumin for treatment of 20 consecutive eligible patients of OLP in a placebo controlled clinical trial. Curcuminoids were prescribed as tablets, at a dosage of 2000mg/day for seven weeks. They concluded that systemic administration of curcumin was not successful for treatment of OLP [13]. Systemic administration of curcumin was different from its topical administration in the current study; the topical administration increases the efficacy of the drug. Finding of our study depicted reduction in burning sensation and appearance score which was not in accordance with this study.

Results of our study were at par with the study conducted by Patil*et al* (2012), who evaluated different modalities for the treatment of oral lichen planus. They reported the anti-inflammatory effects of curcumin. In addition, they reported that at doses over 6000 mg daily, the symptoms and signs of the disease are controlled and diarrhea was one of the dose-dependent side effects of curcumin [14]. The difference in our study was that they had used curcumin systemically whereas we had topically applied curcumin ointment 1% in concentration two times daily for about 2 months.

Singh V*et al*. (2013) evaluated 10 patients of oral lichen planus. They used the extract of turmeric in the ointment form twice a day for three months. Decrease of VAS in all participants and improvement in clinical symptoms in nine patients were reported after 3 months [15]. These results were at par with our study that curcumin is effective in managing oral lichen planus.

Prasad *et al* (2014) reported the treatment of a 22 years' male patient with oral lichen planus, who had already received local corticosteroids. Curcumin capsules were administered for 4 weeks and the patient became free of symptoms on the third week. [16] In our study there was no overlapping of corticosteroids with curcumin.

An interesting finding of our study was the insignificant difference between the two groups in the reduction of burning sensation and appearance score (there was no statistically significant difference between the two groups). The number of patients reporting reduction in appearance score in the study group (40%) was more than that in the control group (33%); but the number of patients reporting reduction in the burning sensation in the control group (80%) was more than that of the curcumin group 73%.

The results of the present study suggested that local use of curcumin can be effective in improving the lesions of patients with oral lichen planus without any side effects. Though the results of curcumin are comparable to topical corticosteroids but the side effects like candidiasis due to the latter predispose the use of former therapy over the other.

Further studies are recommended with longer sample sizes and higher oral doses, a longer period of treatment, mouth rinses, orabase and mucoadhesive pastes. In addition, long follow-ups and control of psychological factors can assist in the treatment of oral lichen planus.

CONCLUSION

Many treatment modalities have been tried in the past for the management of Oral Lichen Planus with varied success. The topics pertaining to the appropriate treatment modality for the management of OLP still remain as a never ending debate in the field of dentistry. Till now corticosteroid are the leading choices in the management of Oral Lichen Planus over the other existing treatment modalities. But considerable about of adverse effects associated with it shifts our focus towards other herbal preparation like curcumin which has negligible adverse effect due to its localized effects resulting in no harm to the adjacent tissues and no systemic toxicity. It is non-invasive with good patient compliance having no mutagenic effects and can repeatedly be used without risk. Hence, it was concluded

that corticosteroids as the conventional treatment for OLP may lead to noticeable side effects and development of other conditions like oral candidiasis. Further studies are recommended with large sample sizes, higher oral doses, a longer period of treatment and other forms of curcumin with improved bioavailability may be considered in future studies.

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