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Original Research Article

A randomized triple-blind clinical trial to compare the effectiveness of topical triamcinolone acetonate (0.1%), clobetasol propionate (0.05%), and tacrolimus orabase (0.03%) in the management of oral lichen planus

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Received : 06-04-16
Review completed : 28-04-16
Accepted : 06-05-16

ABSTRACT

Background: Oral lichen planus (OLP) is believed to result from an abnormal T-cell mediated immune response. The most useful agent in the treatment is corticosteroids. The present study will be aimed at evaluation of therapeutic efficiency of two corticosteroids triamcinolone acetonate (0.1%) and clobetasol propionate with tacrolimus orabase (0.03%), an immunomodulator in the management of OLP. **Aim:** To compare the effectiveness of topical triamcinolone acetonate (0.1%), clobetasol propionate (0.05%), and tacrolimus orabase (0.03%) in the management of OLP and also to compare which has less recurrence. **Study Design:** The study comprises 30 patients, all were diagnosed with OLP clinically and histopathologically. They are randomly divided into three groups: Group A - triamcinolone acetonate (0.1%), Group B - clobetasol propionate (0.05%), and Group C - tacrolimus (0.03%). A formal informed consent was obtained from all of them who participated in the study. **Results and Conclusion:** Subjects in the Group A (triamcinolone 0.1%) and Group B (clobetasol 0.05%) show a significant reduction in lesion size than that of Group C (tacrolimus 0.03%). Group B (clobetasol 0.05%) shows a better significant reduction in lesion size than that of Group A (triamcinolone 0.1%). The overall treatment response was significant better in the Group B (clobetasol 0.05%). No recurrence was observed in any of the three groups at the end of 3 months. It is concluded that clobetasol propionate 0.05% ointment has higher efficacy when compared to triamcinolone acetonide 0.1% ointment and tacrolimus ointment 0.03% in the management of OLP. It was also inferred that triamcinolone 0.1% has better effects than tacrolimus 0.03%.

KEY WORDS: Clobetasol propionate, oral lichen planus, tacrolimus, triamcinolone acetonate

Oral lichen planus (OLP) is a common benign inflammatory disease affecting mainly middle-aged and elderly people, with a prevalence of approximately 0.5–2%. The disease has a female:male ratio of approximately 2:1 and may persist for many years.[1] The diagnosis of OLP is based on a combination of characteristic clinical findings, history, and histopathological examination. The hyperkeratotic (white) variant of OLP is often symptomless. The atrophic or the erythematous (red) variant and

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Quick Response Code:

Website: www.jpbsonline.org

DOI: 10.4103/0975-7406.191976

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How to cite this article: Sivaraman S, Santham K, Nelson A, Laliytha B, Azhalvel P, Deepak JH. A randomized triple-blind clinical trial to compare the effectiveness of topical triamcinolone acetonate (0.1%), clobetasol propionate (0.05%), and tacrolimus orabase (0.03%) in the management of oral lichen planus. J Pharm Bioall Sci 2016;8:S86-9.

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the erosive or the ulcerative (yellow) variants of OLP generally have persistent symptoms.[1-5] Treatment of symptomatic OLP is challenging. Several drugs have been used with varying efficacy.[1,3] Specific treatment includes corticosteroids (topical, intralesional, or systemic), retinoids, cyclosporine, psoralen plus ultraviolet A light, griseofulvin, hydroxychloroquine, and dapsone.[1,3] Recently, topical tacrolimus was reported to be effective in the treatment of patients with OLP in a number of pilot studies.[2-6] The aim of this prospective randomized study was to compare the efficacy of topical tacrolimus 0.1% ointment with that of triamcinolone acetonide 0.1% ointment and clobetasol propionate (0.05%) in patients with symptomatic OLP. The side effects of the treatment in each group and the periods of remission after the cessation of therapy were also compared.

Materials and Methods

Randomized study in management of OLP patients was planned and conducted during the period of September 2012 to July 2013 in the Department of Oral Medicine and Radiology, Rajah Muthiah Dental College and Hospital, Annamalai University, to compare the effectiveness with topical triamcinolone acetonide 0.1%, clobetasol propionate 0.05%, and tacrolimus in orabase 0.03%. A formal ethical clearance to conduct this study was obtained from the Ethical Clearance Committee of the college. The patients for the study were selected among the outpatients who visited the Department of Oral Medicine and Maxillofacial Radiology. A total of 30 subjects were randomized using randomization chart and divided into three groups.

- Group I -10 patients with clinically and histologically confirmed OLP subjects were recruited to receive topical triamcinolone acetonide 0.1% for 6 weeks
- Group II -10 patients with clinically and histologically confirmed OLPsubjects were recruited to receive topical clobetasol propionate 0.05% for 6 weeks
- Group III -10 patients with clinically and histologically confirmed OLP subjects were recruited to receive topical tacrolimus 0.03% for 6 weeks.

Inclusion criteria were clinically symptomatic oral lesions confirmed by histologically to be OLP and exclusion criteria were patients who had underwent treatment for OLP within 4 weeks before the study, pregnant or nursing women, skin lesions and lesion extending to soft palate, and tonsils are excluded from the study. A formal informed written consent was obtained from all the subjects. A detailed case history was recorded for all patients, its nature, duration, and associated with skin lesions are noted. All the patients were subjected to a thorough general physical and oral clinical examination and details were recorded on a standard pro forma. In provisionally diagnosed OLP patients, lesion size was measured based on staging given by Farzaneh Agha-Hosseini *et al*. [Table 1]. After establishing the clinical diagnosis, the patients were subjected to routine blood investigations to rule out any systemic ailments. For the histopathological confirmation of the subjects with OLP, an incisional biopsy was done at the lesional site. All the three groups were instructed to apply the topical ointments on the lesional site. Topical agent is applied 4 times a day for 6 weeks and subjects were checked at 1st, 3rd, and 6th week for the remission lesion. Subjects were also checked after 3 months as follow-up. Statistical analysis of the data was carried out with SPSS for Windows 9.0 software (SPSS, Inc., Chicago, IL, USA). Kruskal–Wallis test was used for the statistical evaluations, whereas Mann–Whitney test was used to compare the effectiveness between these three drugs.

Table 1: Staging system for lichen planus lesion size

Score	Inference
0	No lesion
1	White striae only
2	White striae and erosion <1 cm^2
3	White striae and erosion >1cm^2
4	White striae and ulceration <1 cm^2
5	White striae and ulceration >1 cm^2

Inference

After the end of 1st week, Group A and C (triamcinolone 0.1% and tacrolimus 0.03%) show no changes, whereas in the Group B (clobetasol 0.05%), three subjects with white striae with erosion >1 cm is reduced to white striae with erosion <1 cm.

Lesion size

In all the three group A, B, and C, there are 10 subjects. Of 10 patients, 7 subjects in each group are in Stage 1 (white striae only) and 3 patients are in Stage 3 (white striae with erosion more than 1 cm).

Inference 1

After the end of 3 weeks in Group A (triamcinolone 0.1%), 1 subject shows no lesion. In Group B (clobetasol 0.05%), 7 subjects show no lesion and three subjects show white striae only. In Group C (tacrolimus 0.03%), 1 subject from white striae with erosion >1 cm is reduced to white striae with erosion <1 cm.

Inference 2

At the end of 6 weeks in Group A (triamcinolone 0.1%), 7 subjects show no lesion and 3 patients show white striae only. In Group B (clobetasol 0.05%), all the 10 subjects show no lesion. In Group C (tacrolimus 0.03%), 3 subjects show no lesion, 5 subjects show white striae only, and 2 patients show no improvement (white striae with erosion more than 1 cm).

Inference 3

There is a significant difference in all the three groups in the 3rd and 6th week. As there is evident of significant difference in all three groups in the 3rd and 6th week, we carried out Mann–Whitney tests on each pair of groups and used the Bonferroni correction (that is, significance level/number of pairwise tests) to compare the *P* value. We used 5% level of significance for three treatments, hence compared the *P* value for each Mann–Whitney test with 0.05/3 = 0.017. If

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the significance value is less than the 0.017, then we infer the treatments have the difference.

Discussion

OLP is a T-cell-mediated chronic inflammatory oral mucosal disease of unknown etiology, but it is believed to result from an abnormal T-cell-mediated immune response in which basal epithelial cells are recognized as foreign because of changes in the antigenicity of their cell surface. It is a relatively common disorder that is estimated to affect 0.5–2.0% of the general population. OLP affects primarily middle-aged adults, and the prevalence is greater among women. In this study, we included patients in the age range of 18–65 years. Age distribution table [Table 2] shows that the maximum percentage of patients included in the study falls in the range of 30–50 years and the mean age of patients in the group is 39.77 years. Our results are consistent with the another study who reported the typical age of presentation is between 30 and 60 years, but its occurrence in younger people and children is not uncommon.[7]

This study shows that the incidence was higher in females (60%) when compared to males (40%). Similar observations were found in some of the previous studies[8] found that in a study of 30 OLP patients, 56.7% were females and 43.3% were males [Table 3]. Probable reason for the increased incidence of OLP in females may be due to greater psychological stress as a consequence of activities of hormones.

OLP exists in many clinical forms. However, in the present study, only two clinical forms could be recorded: Reticular and erosive. In the current study, the incidence of reticular form of OLP is more frequent (21 out of 30 patients), followed by erosive OLP (9 out of 30 patients). Similar observation was made in another study.[9]

The lesion size was also reduced in the clobetasol propionate (mean rank of 9.0) when compared with triamcinolone acetonide 0.1% (mean rank of 12.0). This was proved another study[10] that clobetasol propionate compared with triamcinolone acetonide provides a more immediate clinical response [Table 4]. The lesion size was also reduced in the triamcinolone acetonide 0.1% (mean rank of 8.20) when compared with tacrolimus 0.03% at the end of 6 weeks (mean rank of 12.80) [Tables 5-7]. This is in contrast to the study[11] who found tacrolimus 0.1% ointment induced a better initial therapeutic response than the triamcinolone acetonide 0.1%. This can be because the concentration of tacrolimus (0.1%) they used is more than that of our study which is 0.03%. The lesion size was also reduced in the clobetasol propionate (mean rank of 7.0) when compared with tacrolimus 0.03% (mean rank of 14.0) at the end of 6th week [Table 8]. This was supported by another study done[12] who reported that clobetasol propionate 0.05% ointment was found to be more useful than tacrolimus 0.1% in the treatment of OLP. This is in contrast to the study done by[13] who found tacrolimus to be as useful as clobetasol in the treatment of OLP.

The other study[14] evaluated the effect of different formulation of clobetasol with other corticosteroids in the treatment of OLP and emphasized that clobetasol had better effects. This result was also supported by other studies. As there were few studies done to compare the effectiveness of corticosteroids with tacrolimus in the treatment of OLP, this study was undertaken.

In this study, we infer that clobetasol propionate 0.05% is useful in effectively reducing the lesion size at the end of 6 weeks in OLP subjects, and also that clobetasol propionate 0.05% has got the better therapeutic effect when compared with triamcinolone acetonide 0.1% and tacrolimus ointment 0.03% [Tables 9 and 10]. However, for increasing the strength of the study, a detailed blinded, randomized trial with a large sample size could be pursued.

Conclusion

It is concluded that clobetasol propionate 0.05% ointment has higher efficacy when compared to triamcinolone acetonide 0.1% ointment and tacrolimus ointment 0.03% in the management of OLP. It was also inferred that triamcinolone 0.1% has better

Table 2: Distribution of age

Age group	Number of patients
10-20	2
21-30	5
31-40	7
41-50	8
51-60	5
61-70	3

Inference: Most commonly affected subjects are in the age group of 30-50 with the mean of 39.77

Table 3: Frequency distribution table for gender

	Frequency	Percentage
Male	12	40
Female	18	60
Total	30	100

Table 4: Treatment progression (lesional) after the end of 1st week

	Treatment			Total
	Group A	Group B	Group C	
White striae only	7	7	7	21
White striae with erosion <1 cm	0	3	0	3
White striae with erosion >1 cm	3	0	3	6
Total	10	10	10	30

Table 5: Treatment progression (lesional) after the end of 3rd week

	Treatment			Total
	Group A	Group B	Group C	
No lesion	1	7	0	8
White striae only	6	3	7	16
White striae with erosion <1 cm	0	0	1	1
White striae erosion with >1 cm	3	0	2	5
Total	10	10	10	30

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Table 6: Treatment progression after the end of 6th week

	Treatment			Total
	Group A	Group B	Group C	
No lesion	7	10	3	20
White striae only	3	0	5	8
White striae erosion >1 cm	0	0	2	2
Total	10	10	10	30

Table 7: Comparing all three Groups A, B, and C

	Lesion 1st week	Lesion 3rd week	Lesion 6th week
χ^2	0.242	12.901	11.163
df	2	2	2
Asymptotic significant	0.886	0.002	0.004

[a]Kruskal–Wallis test, [b]Grouping variable: Treatment

Table 8: Test statistics for Groups B and C

	After 1st week	After 3rd week	After 6th week
Mann–Whitney U-test	45.500	10.500	15.000
Wilcoxon *W*	100.500	65.500	70.000
Z	−0.421	−3.271	−3.139
Asymptotic significant (two-tailed)	0.674	0.001	0.002
Exact significant (2×[one-tailed significant])	0.739[a]	0.002[a]	0.007[a]

Inference: In comparing B and C group there is a highly significant difference in 3rd and 6th week. [a]Not corrected for ties

Table 9: Test statistics for Groups A and B

	After 1st week	After 3rd week	After 6th week
Mann–Whitney U-test	45.500	15.500	35.000
Wilcoxon *W*	100.500	70.500	90.000
Z	−0.421	−2.839	−1.831
Asymptotic significant (two-tailed)	0.674	0.005	0.067
Exact significant (2×[one-tailed significant])	0.739[a]	0.007[a]	0.280[a]

Inference: In comparison of A and B group there is a significant difference in 3rd week. [a]Not corrected for ties

Table 10: Test statistics for Groups A and C

	After 1st week	After 3rd week	After 6th week
Mann–Whitney U-test	50.000	48.000	27.000
Wilcoxon *W*	105.000	103.000	82.000
Z	0.000	−0.179	−1.929
Asymptotic significant (two-tailed)	1.000	0.858	0.054
Exact significant (2×[one-tailed significant])	1.000[a]	0.912[a]	0.089[a]

Inference: No significant difference is found in A and C group at the end of 3rd week. [a]Not corrected for ties

effects than tacrolimus 0.03%. Recurrence was not reported in any group after 3 months of follow-up.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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