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A COMPARATIVE STUDY OF EFFICACY OF HALOBETASOL PROPIONATE (0.05%) OINTMENT AND TACROLIMUS (0.1%) OINTMENT IN LOCALIZED CUTANEOUS LICHEN PLANUS

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ABSTRACT In recent years, calcineurin inhibitors have been used as the first line alternative to topical corticosteroids in the treatment of discoid lupus erythematosus (DLE). We aim to evaluate the efficacy and safety of topical tacrolimus 0.1% vs topical halobetasol propionate 0.05% in patients with localised cutaneous lichen planus. This comparative study was carried out in the Department of Dermatology and Venereology, Nalanda Medical College Hospital (NMCH), Patna between the period of August 2018 to September 2020.Among the 80 patients under study, 42 were males and 38 were females. They were in the age group ranging from 13 years to 69 years with mean age of 34.73 years. The duration of lichen planus ranged from 2 weeks to 2 years with mean duration of 5.5 months. The time interval between the last and the present therapy ranged from 1 to 6 months. None of them had systemic treatment.The present study demonstrated that tacrolimus 0.1% ointment and halobetasol propionate 0.05% ointment had a comparable efficacy in localised cutaneous lichen planus; however, halobetasol showed significantly better improvement regarding itchy, hypertrophic lesions.

KEYWORDS : Localised cutaneous lichen plasnus, halobetasol propionate ointment,Tacrolimus ointment.

INTRODUCTION

Lichen Planus is a unique inflammatory disorder characterized by shiny, violaceous, flat-topped polygonal papules, varying in size from a pin–point to several centimeters purple, polygonal, pruritic, papule are used to describe the clinical appearance of the lesions. White lines known as Wickham's striae may traverse the surface of the papules, and are better visualized with a hand lens after applying oil, water or xyleneand consist with isomorphic response (Koebner response). Lichen Planus is one of the most itchy dermatoses. It is prevalent worldwide with no social or climatic predilection. It affects the skin, mucous membrane, nails and hair. Itching is a constant feature of lichen planus and the lesions heal with pigmentation which may be persistent and intense in dark skinned people. Spontaneous remissions can occur after varying amounts of time.However treatment with medium to high-potency topical corticosteroids is generally recommended as the first-line therapy for localised lichen planus. Topical Tacrolimus in addition to its inhibitory effect on cytokine production causes alterations in epidermal antigen-presenting dendritic cells that may result in decreased immunologic response to antigens.The possible role of activated T cells in the pathogenesis of lichen planus as well as the extensive safety profile makes topical tacrolimus an attractive option for the treatment of cutaneous lichen planus. However, there are no head to head comparisons of corticosteroids and tacrolimus in the treatment of lichen planus.Towards this goal we performed a prospective, randomised, open label clinical trial comparing the therapeutic efficacy of a topical corticosteroid 0.05% halobetasol propionate with a topical calcineurin inhibitor 0.1% tacrolimus in adults with localised cutaneous lichen planus.

MATERIALS AND METHOD

The present study had been undertaken at NMCH College and Hospital, Patna. The study period is from August 2018 to September 2020.

Inclusion Criteria:

1) Patients of clinically diagnosed localised (< 10% of body surface area) lichen planus lesions of both sexes.
2) Subjects who have not been on any form of therapy (oral/ topical/ injectables) for this particular disease for the last 45 days prior to their enrolment in the study.

Exclusion Criteria:

1) Lichen planus with facial/ mucosal involvement.
2) Use of drugs known to produce lichenoid reactions.
3) Pregnant/ lactating women.
4) Children < 12 years of age.
5) Subjects with prior history of hypersensitivity to any of the components of the test medications.

METHOD:

Patients was randomly allocated into the 2 groups and 2 phases.
Phase 1 consists of topical treatment for 2 weeks.
Phase 2 consists of a two month follow-up period without any therapy.

Group 1: Patients in this group was receive 0.05% halobetasol propionate ointment. The patients were advised to apply the ointment only over the lesions twice daily for a period of 2 weeks or until the lesions cleared, whichever is earlier. Assessment was done every 2 weeks.
Patient Visual Analogue Scale for pruritus (VAS) consists of a horizontal line marked 0(= no itching) to 10(= more severe itching)] and Clinician VAS for thickness [0= flat to 10= highly raised] was marked & photographs will be taken at each visit.

Group 2: Patients in this group was receive 0.1% tacrolimus ointment to apply only over the lesions twice daily for a period of 2 weeks or until the lesions clear, whichever is earlier. Assessment was done at weekly intervals. Patient Visual Analogue Scale for pruritus and Clinician VAS for thickness was marked with photographic assessment.

RESULTS

The following observations were made in the present study.Among the 80 patients under study, 42 were males and 38 were females. They were in the age group ranging from 13 years to 69 years with mean age of 34.73 years. The duration of lichen planus ranged from 2 weeks to 2 years with mean duration of 5.5 months. Family history of lichen planus was positive in 6.7% of patients, all had onset < 20 years of age. History of previous topical application was present in 15% of patients. The time interval between the last and the present therapy ranged from 1 to 6 months. None of them had had systemic treatment.

Damographics

Variables	Group 1 Halobetasol	Group 2 Tacrolimus
No. of Patients	40	40
Gender (M/F)	20/20	22/18
Mean duration of lesions	169 days	165 days

Mean Age	32.6 years	36.8 years
Type of lesions		
Classical	22	26
Hypertrophic	12	8
Linear	4	5
LP of Palms/Soles	2	1
Site of involvement		
Upper limb	14	16
Lower Limb	23	21
Trunk	1	2
Palms and soles	2	1

THERAPEUTIC RESPONSE:

Pruritus-Response:

The patient Visual Analogue Scale scores for pruritus

1) In the halobetasol group in weeks 1 and 2 dropped from a mean of 6.13 at baseline to 3.55 at day 7 and 1.53 at day 14 which were both statistically significant($p<0.01$).
2) In the tacrolimus group, the mean had dropped from 6.13 to 4.6 at day 7(statistically significant, $p<0.01$) and 2.6 at day 14(statistically significant, $p<0.01$)

Thickness – Response:

The physician Visual Analogue Scale scores for thickness

1) In the halobetasol group dropped from a mean of 6.48 at baseline to 4.15 at day 7 and 2.37 at day 14 which were both statistically significant.(p value <0.01)
2) In the tacrolimus group, the mean dropped from 6.48 at baseline to 5.42 at day 7(p value >0.05,not statistically significant) and 4.35 at day 14(p value < 0.01,statistically significant)

The difference between the two groups in the mean scores of thickness had a p value of 0.03 at the end of 1 week and 0.0072 at the end of two weeks which were both statistically significant.

7th & 14th day day of clinical assessment of both halobetasol and tacrolimus

	Days 7		Days 14	
	Halobetasol	Tacrolimus	Halobetasol	Tacrolimus
Cleared	1(2.5%)	-	14 (35%)	3(7.5%)
Marked Improvement	11(27.5%)	-	10(25%)	6 (15%)
Moderate Improvement	16 (40%)	10 (25%)	10 (25%)	5 (12.5%)
Slight Improvement	8 (20%)	18 (45%)	6 (15%)	17 (42.5%)
No Change	4 (10%)	12(30%)	-	9 (22.5%)
Exacerbation	-	-	-	-

The difference between the two groups in clearance rates showed a statistically significant difference at the end of 2 weeks with a p value of 0.019

Follow-up:

1) At week 4 of follow-up, 35% of patients in the halobetasol group and 47.5% of patients in the tacrolimus group developed new lesions. Relapse of lesions were found in 7(17.5%) of halobetasol and 2 (5%) of tacrolimus group. No change in existing lesions was found in 22.5% of halobetasol and 27.5 % of tacrolimus group.
2) At week 8 of follow-up, number of new lesions increased in both the groups with 40% of patients in the halobetasol group and 52.5% of patients in the tacrolimus group having new lesions, with no significant difference between the two. Significant difference was seen in the relapse of lesions, with more people in the halobetasol group experiencing relapse compared to the tacrolimus group($p=0.03$ by Fisher's exact test).

Follow-up period

	Halobetasol		Tacrolimus	
	Week 4	Week 8	Week 4	Week 8
New Lesions	14 (35%)	19 (47.5%)	16 (40%)	21(52.5%)
Relapse	7(17.5%)	7(17.5%)	2(5%)	3(7.5%)
Remission	14(35%)	3(7.5%)	11(27.5%)	4(10%)
No change in Existing Lesions	9(22.5%)	8(20%)	11(27.5%)	10 (25%)

Adverse effects:

No serious adverse effects were noted. About 40% of patients in the Tacrolimus group experienced mild burning sensation, more on the first week of treatment. This subsided spontaneously and no patient discontinued treatment. In the halobetasol group, no significant side effect was noted. The most common adverse effect noted was the hypo pigmented halo around the lesions, which was seen in 42.5% of patients.

CONCLUSION

After 2 weeks of study period, topical halobetasol caused a significant reduction in symptoms (p value = 0.017) compared to tacrolimus in localised cutaneous lichen planus.

After 8 weeks of follow-up, topical tacrolimus resulted in lower relapse rates compared to halobetasol (p value = 0.03).

In the halobetasol group, there was no change in rate of response with respect to site of involvement, blood group or duration of lesions.

This is the probably first study comparing topical halobetasol and topical tacrolimus head-to-head. Prospective randomized trials with more subjects are needed before any treatment recommendations can be made based on the conclusions of our study.

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