

EVALUATION OF THE EFFICACY AND SAFETY OF 0.05% HALOBETASOL PROPIONATE OINTMENT AND 0.05% CLOBETASOL PROPIONATE OINTMENT IN CHRONIC, LOCALIZED PLAQUE PSORIASIS

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ABSTRACT

Objective: To compare the efficacy and tolerability of halobetasol propionate (HP) and clobetasol propionate ointment in chronic localized plaque psoriasis in Indian patients.

Methods: This study was conducted in 202 patients from 6 centers after taking the Ethics Committee Approval. The patients were randomly assigned to either of two groups: Group X- 0.05% clobetasol propionate; Group Y-0.05% HP for 14 days after taking written informed consent. The assessment was done at days 7 and 14. Serum cortisol levels were measured in a random selection of 40% of patients at day 0 and 14.

Results: In both treatment groups, the local plaque severity index scores were significantly reduced at the end of treatment which was comparable in both treatment groups X and Y ($p > 0.05$). The physician's global evaluation rating at day 14 of almost total clearing of lesion (Grade 4) was reported in 19.2% and 32% patients, marked improvement (Grade 3) in 47.5% and 50.5%, moderate improvement (Grade 2) in 30.3% and 17.5%, and mild improvement (Grade 1) in 3% and 0% for clobetasol and halobetasol groups, respectively. The difference between the two groups for physicians' global evaluation was found to be statistically significant ($p = 0.019$). 19.2% and 27.2% patients in clobetasol and halobetasol, respectively, showed >75% improvement in photographic assessment ($p = 0.521$). There was a significant difference in the cosmetic acceptability ($p = 0.042$) and in the ease of application ($p = 0.019$) between the two groups. No significant difference was found in serum cortisol levels, in both groups ($p = 0.074$).

Conclusion: This study reaffirms that halobetasol has better efficacy and good tolerability profile compared to clobetasol.

Keywords: Psoriasis, Halobetasol, Clobetasol.

INTRODUCTION

Psoriasis is a common, chronic, inflammatory, multisystem disease involving the skin and joints. It accounts for 2.3% of the total dermatology outpatients in India [1].

Corticosteroids are extremely useful in the treatment of inflammatory skin disorders. Corticosteroids have an important role in skin diseases because of their anti-inflammatory [1], immunosuppressive [2], and anti-proliferative effects [3] on the keratinocytes.

Topical steroid applications are the most effective treatment for all types of psoriasis [4]. Several factors influence the treatment of psoriasis such as the site of lesions, treatment history, cost consideration, and co-morbid conditions. Psoriasis, localized to certain areas of the body (e.g. scalp, nails, palms, and soles), calls for special intervention, and remains difficult to control for various reasons such as unrealistic expectations of the patients, time-consuming applications, side-effects, cosmetic non-acceptability, restricted bioavailability of drugs, and problems of adherence to treatment. These sites have been referred to as the difficult locations in literature.

Topical corticosteroids are commonly used in the short-term management of psoriasis and other inflammatory skin disorders. Clobetasol 0.05% ointment and halobetasol 0.05% ointment are both synthetic Class I super-potent topical corticosteroids with anti-

inflammatory, antipruritic, and vasoconstrictive properties commonly prescribed for the treatment of psoriasis.

Halobetasol propionate (HP) ointment contains 0.05% 6- α -fluoro-clobetasol 17-propionate, trihalogenated, ultra high-potency corticosteroid as the active ingredient. Its chemical structure is similar to that of clobetasol 17-propionate, which has been the most potent dermato-corticosteroid used in clinical practice since 1974. In addition, HP has an extra fluorine atom in the 6- α position that increases its topical anti-inflammatory and anti-proliferative properties.

There are very few studies available showing the comparative efficacy and safety of halobetasol and clobetasol.

In a double-blind, parallel-group, multicenter trial in 134 patients with severe, localized, plaque psoriasis, the success rate (described as "healed" or "marked improvement") at the end of the study was 96% in the HP group and 91% in the clobetasol propionate group. A significantly larger proportion of patients treated with halobetasol had no disease or mild disease after 14 days compared with those treated with clobetasol (86% vs. 70%, $p = 0.023$). Healing within 24 days of starting treatment was noted in 69% and 56% of patients treated with halobetasol and clobetasol, respectively [5].

In another study by Mensing, *et al.*, the patient acceptance of HP ointment, based on cosmetic acceptability and ease of application, was

significantly better ($p=0.02$) than that of betamethasone dipropionate ointment [6].

Due to limited availability of data in Indian patients, the present study was conducted to compare the efficacy and tolerability of HP and clobetasol propionate ointment in chronic localized plaque psoriasis in Indian patients.

METHODS

This randomized, multicentric, and double-blinded study was carried out in 202 patients from 6 different centers. The approval of the Institutional and Independent Ethics Committee was obtained and written informed consent was taken from the patients. The patients were recruited as per the inclusion and exclusion criteria.

Inclusion criteria

1. Subjects between 18 and 60 years (treatment naïve patients or patients receiving treatments, such as corticosteroids, methotrexate or psoralen, and ultraviolet radiation, were given a washout period of 10 days)
2. Clinically diagnosed localized, plaque psoriasis vulgaris, or palmoplantar psoriasis affecting maximum up to 10-20% of the total body surface area. The size of lesion selected is approximately 4-10 cm²
3. Subjects must provide written informed consent and comply with the protocol.

Exclusion criteria

1. Subjects with psoriatic erythroderma generalized Pustular psoriasis
2. Pregnancy and lactation
3. Concomitant tuberculosis
4. Syphilis
5. Uncontrolled Diabetes mellitus
6. Leukemia.

Methodology

The study was conducted in accordance with the principles of ICH GCP guidelines. Written informed consent was obtained from subjects recruited for the study. Patients with clinically diagnosed localized, mild to moderate plaque psoriasis vulgaris, or palmoplantar psoriasis were recruited for the study. The enrolled patients were randomly assigned to either of the two groups.

- Group X - 0.05% Clobetasol propionate ointment application without occlusion for 14 days
- Group Y - 0.05% HP ointment application without occlusion for 14 days.

The study drugs were applied twice daily, once in the morning and the other application in the evening on the target lesion according to fingertip unit [FTU] method.

Patients were carefully instructed to apply a half FTU [7] of the ointment, twice daily on the selected patch according to their group allocation. On the other lesions, patients were allowed to continue applying the emollients/moisturizer.

Serum cortisol levels were measured in a random selection of 40% of patients at visit 1 and visit 3.

Parameters of assessment

The investigator's clinical assessment was done to evaluate the reduction of erythema, scaling, and thickness. These parameters were evaluated according to local plaque severity index (LPSI) scores for 14 days (Grade 0 = none; Grade 1 = slight; Grade 2 = moderate; Grade 3 = marked; and Grade 4 = very marked).

Subject's assessment of pruritus was graded on the 5 point Likert scale during the 3 visits for 14 days (0 = no pruritus; 1 = minimal pruritus;

2 = pruritus present but not requiring medications to control itching; 3 = pruritus present and requires medication to control itching; and 4 = pruritus present not subsiding with medications).

Global evaluation was assessed on a 4-point scale for 14 days (1 = slight or mild improvement [0-25%]; 2 = moderate improvement [25-50%]; 3 = marked improvement [50-75%]; and 4 = almost clear/clear [more than 75%]).

The subject's observation on cosmetic acceptability and ease of the application was noted at visit 2 (day 7) and 3 (day 14). Grading was done on a 4 point rating scale (Grade 0 - poor; Grade 1 - average; Grade 2 - good; and Grade 3 - very good).

Photographic assessment by the investigator was done at baseline and at visit 3 (day 14) and was rated on a 4 point scale (1 = slight or mild improvement [0-25%]; 2 = moderate improvement [25-50%]; 3 = marked improvement [50-75%], and 4 = almost clear/Clear [more than 75%]).

Serum cortisol levels were measured in a random selection of 40% of patients at 8 am to assess the extent of adrenal suppression after application of medication at visit 1 and visit 3.

The patient compliance was rated as average, good, or excellent. Furthermore, a note was made of the number of missed applications. Follow-up visits were on day 7 and day 14. For judging compliance, patients were asked to bring the used/empty tubes. Post-treatment, the patients were called for follow-up in every 2 weeks interval, i.e. in the 2nd, 4th, and the 6th weeks. Telephonic interviews were conducted with patients who did not come for follow-up visits.

At each visit, or study assessment, adverse events that might have occurred since the previous visit or assessment were elicited from the patient and documented in the AE initial notification form.

RESULTS

The change in LPSI scores

The change in LPSI score from baseline to the end of treatment was compared between the two treatment groups. The change in LPSI scores was comparable in the two treatment groups (Table 1). The LPSI scores at the end of treatment were significantly reduced as compared to baseline scores in both the treatment groups ($p>0.05$).

Pruritus scores

At baseline (visit 1), in the clobetasol and halobetasol groups, 7.1% and 10.1% of patients did not have pruritus, respectively. However, at the end of treatment visit (day 14), 58.6% and 59.2% patients did not have pruritus in clobetasol and halobetasol groups, respectively.

Global evaluation scores

The physicians' global evaluation rating of marked improvement (Grade 3) or almost total clearing of the lesion (Grade 4) was reported at the end of treatment visit (day 14) in 47.5% and 19.2% patients, respectively, in the clobetasol group, while in the halobetasol group, it was 50.5% (Grade 3) and 32.0% (Grade 4), respectively.

Comparison of global evaluation scores between treatment groups demonstrated significant differences between the two groups (Fig. 1) ($p=0.013$)

Table 1: Comparative evaluation of LPSI scores between the two treatment groups

Group	N	Mean reduction in LPSI scores	p value
Clobetasol	99	-4.1±2.3	$p>0.05$
Halobetasol	103	-4.2±2.0	$p>0.05$

LPSI: Local plaque severity index

Cosmetic acceptability

There was a significant difference in the cosmetic acceptability between the two groups (p=0.042) (Fig. 2).

Photographic assessment

The photographic assessment was comparable between the two treatment groups (p=0.521) at visit 3 (day 14) (Figs. 3 and 4). However, many of the patients had more than 75% score.

Ease of application

There was a significant difference in the ease of application between the two groups (p= 0.019) (Fig. 5).

Serum cortisol levels

No significant difference was found in serum cortisol levels from visit 1 (baseline) to visit 3 (day 14), in both the groups (p=0.074).

No adverse events were encountered in the study.

DISCUSSION

Psoriasis, a chronic skin disorder, can have a profound impact on the quality of life of patients. The availability of numerous topical agents,

systemic agents, and phototherapy has complicated the treatment of psoriasis. Among the topical preparations available today, the ultra-high potency, also referred to as Class I steroids, have an important role in treating psoriasis. They are used most appropriately for the treatment of plaque psoriasis in regions excluding the face, axilla, groin, and genitals [7].

HP 0.5% ointment and cream are examples of Class I topical corticosteroids [8]. The efficacy of HP is consistently superior to other super-potent topical corticosteroids. Local adverse events associated with topical HP have been found to be similar to those experienced with other super-potent corticosteroids.

In the current study, the efficacy of halobetasol ointment 0.05% was comparable to that of clobetasol ointment 0.05%. It was observed that the change in LPSI scores was comparable between the two treatment groups. However, it was found that halobetasol ointment scored better than clobetasol ointment on various factors, including physicians' global rating and cosmetic acceptability. The photographic assessment also showed better results in Halobetasol group as compared to Clobetasol group. This study confirms the results from

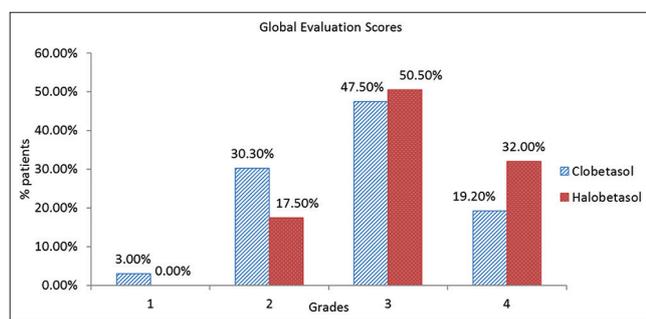


Fig. 1: Comparison of global evaluation values of clobetasol and halobetasol

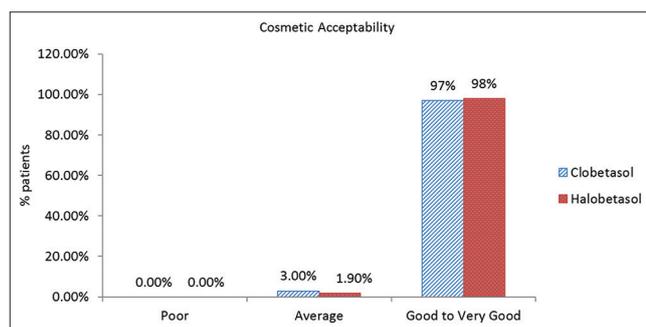


Fig. 2: Comparison of cosmetic acceptability at visit 3 (day 14) between clobetasol and halobetasol

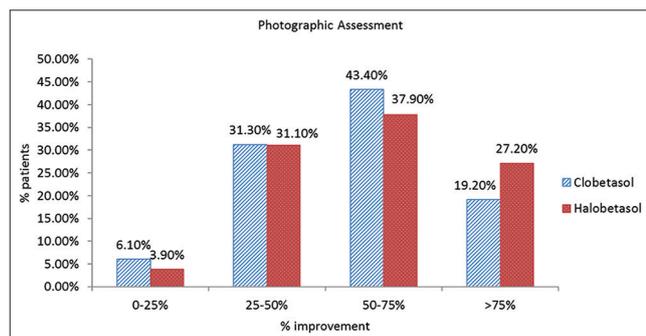


Fig. 3: Comparison of photographic assessment of respondents between clobetasol and halobetasol



Fig. 4: Photographic assessment at visit 1 (baseline) and visit 3 (day 14) for Halobetasol group

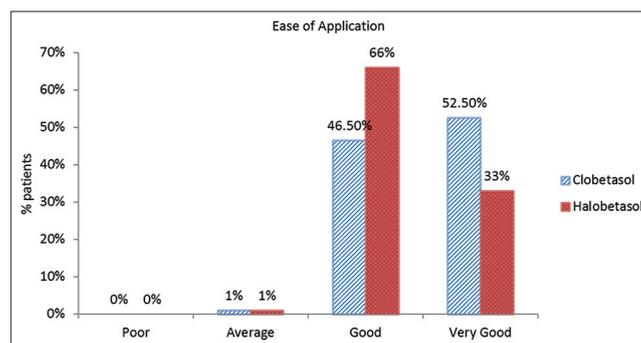


Fig. 5: Comparison of ease of application between clobetasol and halobetasol

earlier studies in terms of efficacy and safety of Halobetasol and Clobetasol.

CONCLUSION

The current study reaffirms the efficacy and good tolerability profile of halobetasol as compared to clobetasol. Our results confirm the findings of earlier published studies that halobetasol 0.05% is effective and well-accepted Class I steroid for the management of chronic plaque psoriasis.

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