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COMPARATIVE EFFICACY OF TOPICAL TACROLIMUS 0.1% VS TOPICAL CLOBETASOL 0.05% IN LIMITED ALOPECIA AREATA

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Abstract

Alopecia areata (AA) is a form of hair loss disease that results from autoimmune disorders and is known to impact the psychological wellness of patients [1, 2]. First-line treatment for limited patchy AA is clobetasol propionate 0.05% and tacrolimus 0.1% topical solution, which has been described as a steroid-sparing option. There are also some discrepancies in the efficacy of tacrolimus in AA treatment based on the previous works [3, 4].

***Methodology**: This study was done in the department of dermatology of PNS Shifa Hospital, Karachi, over a period of six months on a voluntary basis with nonrandomized control samplings. In this study, 60 patients with limited scalp AA with scalp involvement less than 25% were enrolled and divided into two equal groups. The twenty- minute series A (n=30) underwent topical tacrolimus 0.1% twice daily for the skin, while the twenty-minute series B (n=30) was topped up with clobetasol propionate 0.05% twice for the same skin. Efficacy was evaluated employing the Severity of Alopecia Tool (SALT) and the customary regrowth was divided into excellent (> 75%, marked: 51- 75%), moderate (26-50%), and poor (≤ 25%).*

***Outcomes:** At the onset, the members of the two groups were comparable. At the end of the 6 months of the study, the mean SALT score significantly reduced from 14.5% to 8.1% in the tacrolimus group, whereas similar mean SALT score reduced from 14.8% to 2.3% in the clobetasol group, P<0.001 [5]. In Group B, new growth of 50% or more was found in 83%, whereas, in Group A, the same was observed only in 33% of the patients (p<0.001). The time for the regrowth of the hair was also shorter in the clobetasol group; it took a median of 6 weeks for the hair to regrow as compared to those in the placebo group that took 10 weeks [7]. Both the treatments were, however, found to be generally safe but clobetasol was found to cause minor side effects on the skin surface in the form of skin atrophy in patients [8].*

***Conclusion:** It has been found that topical clobetasol 0.05% is a better drug as compared to tacrolimus 0.1% to induce hair regrowth in limited AA. However, tacrolimus has side effects, and, therefore, it yields a lower efficacy and should be considered in cases when patients cannot receive steroids.*

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INTRODUCTION

Alopecia areata (AA) is an organ-specific autoimmune disorder in view of patchy hair loss that can turn into alopecia totalis or universalis [1]. The risk for the disease is estimated to be around 1–2% lifetime prevalence and depression is known to have a major psychological effect on the patient, self-image, and overall well-being [2]. Despite the fact that AA is not life-threatening, the unpredictable course of the disease and the effect on the physical appearance of the patient mandate the treatment [3].

In the case of a few discrete lesions of AA, topical or intralesional corticosteroids are the initial line of treatment [4]. Corticosteroids of particularly high potency, like clobetasol propionate 0.05%, were found to promote hair regrowth in more than 3-6 months [5, 6]. However, because of local side effects like skin atrophy and telangiectasia, people have been searching for steroid- sparing treatments [7].

Topical tacrolimus, which is a calcineurin inhibitor, has been used successfully in other inflammatory dermatoses, as in atopic dermatitis. To this end, there is a theory that sofosbuvir, primarily having functions of antagonizing T-cell activation and successive cytokine release, might be effective in the treatment of AA, which is caused by immunological disorder [8].

Nevertheless, compared to tacrolimus treatment studies concerning AA, which have shown a weak therapeutic effect in many cases, even when they are used as a single drug [9, 10]. Taken together, the systematic review concluded that tacrolimus seems safe; nonetheless, its efficacy in AA is somewhat lower than that of potent topical steroids [11].

Due to the clinical scenario of patients with limited AA and the interest in any non-steroidal treatment, we carried out a prospective, non-randomized trial of topical tacrolimus ointment

0.1% and clobetasol propionate ointment 0.05% in the clinical practice at PNS Shifa Hospital, Karachi. Our first research question was based on the assumption that clobetasol would be more effective than tacrolimus in both hair regrowth and the level of satisfaction of the patients. The current paper follows up the findings based on clinical data collected recently and aims at offering recommendations to clinicians regarding the choice of topical treatments applicable to limited AA [12, 13].

Methods

Study Design and Patients

This prospective study was done at the dermatology department of PNS Shifa Hospital, Karachi for a time span of 6 months. Ethical clearance was received from the institutional review board and each participant also gave his informed written consent before being recruited. The patients with limited AA were included if they had the condition affecting no more than 25% of the scalp, as estimated by the Severity of Alopecia Tool (SALT) from September 2024 to February 2025 [14]. The inclusion criteria for the patient population were patients who are 18 to 50 years old with a current active area of patchy AA without any past or current systemic or topical treatment for AA within 3 months prior to the trial. Examination of patients with alopecia totalis, alopecia universalis, and active scalp infection was not allowed [15].

Treatment Allocation and Interventions

The patients were divided into two groups according to the **consecutive odd and even numbers through a quasi-alternation** procedure to make the number of patients in two groups equal.

Group A (n=30): They had topical tacrolimus 0.1% ointment applied to their scalp twice daily.

Group B, which consisted of 30 participants, applied topical clobetasol propionate 0.05% ointment topically twice a day.

The medications were made for the patients to apply on the affected areas of the skin that should not be washed off for more than 8 hours after application. During the study period, the patient received no other therapies for AA apart from the treatments mentioned above. In the case of the appearance of early signs of steroid-induced side effects (skin atrophy), the use frequency can then be changed following consultation but none of them required termination of use [16].

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Outcome Measures and Assessments

The main efficacy variable analyzed for each group was the self-assessment of hair regrowth at 6 months by the patients.

SALT Score: Quantitative assessment of hair loss in the scalp that is taken at baseline before the trial and at the end of 6 months. A low SALT score means hair regrowth to a certain extent has been made [17]. Quantitative assessment of regrowth: The level of regrowth was grouped into four categories based on the following criteria.

Excellent response: >75% hair regrowth

Marked response: 51–75% hair regrowth **Moderate response**: 26–50% hair regrowth **Mild or no response:** ≤25% hair regrowth

To support the SALT score and categorical assessment, duplicate photographs of the patient were taken at the baseline and during the monthly visits. Other minor objectives were time to regrowth period without any patient's complaint and to seek a clinician's confirmation (self- reported and confirmed), patients' satisfaction, which was assessed using a 5-point Likert scale, and side effects [18].

Sample Size Calculation

According to the prior findings of 80% success rates with clobetasol and 45% with tacrolimus in attaining more than or equal to 50% hair regrowth [19, 20], 26 patients per group were deemed required to confer 80% power at a 0.05 significance level (two-tailed). To allow for those who may drop out, 30 patients were recruited into each group, making the total number of recruited patients 60 [19].

Statistical Analysis

Data analysis was performed using SPSS v25. Continuous variables (e.g., age, SALT scores) were compared using the independent t-test, while categorical variables (e.g., regrowth categories, patient satisfaction) were compared using the chi-square test or Fisher's exact test. A p-value < 0.05 was considered statistically significant. Analysis was performed on a per-protocol basis, including only patients who completed the 6-month follow-up [21].

Results

Baseline Characteristics

All 60 patients completed the 6-month study period. Baseline characteristics were similar between the two groups (Table 1). The mean age was 32.1 ± 7.5 years (Group A: 33.0 ± 7.8;

Group B: 31.2 ± 7.3; p = 0.45). Gender distribution was comparable (60% male in Group A vs. 53% in Group B; p=0.60). The mean disease duration was 5.4 ± 3.1 months in the tacrolimus group and 4.9 ± 2.7 months in the clobetasol group (p=0.52). Mean baseline SALT scores were

14.5 ± 5.0% (Group A) and 14.8 ± 4.6% (Group B), confirming similar initial disease severity [22].

Table 1. Baseline Characteristics of Patients in Each Group

Characteristic	Tacrolimus 0.1% (n=30)	Clobetasol 0.05% (n=30)	p-value
Age (years), mean ± SD	33.0 ± 7.8	31.2 ± 7.3	0.45
Sex (n (% male)	18 (60%)	16 (53%)	0.60
Disease duration (months)	5.4 ± 3.1	4.9 ± 2.7	0.52
Number of patches, median	1 (range 1–3)	1 (range 1–3)	0.78
Baseline SALT score	14.5 ± 5.0	14.8 ± 4.6	0.83

Data are presented as mean ± standard deviation (SD) or median (range).

Hair Regrowth Outcomes

In the tacrolimus group, the mean SALT score at baseline was 14.5%and at 6 months was 8.1 %

± 6.0, while that for the clobetasol group was 14.8%and at 6 months was 2.3% ± 3.5 (p < 0.001) [23]. The decrease in the SALT scores implies improved coverage of the hair in the clobetasol group.

Categorical analysis of the result revealed that 87% (26/30) of the patients in the clobetasol group attained a SALT score ≤5%, which implies that more than 95% regrowth, while

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33% (10/30) of the patients in the tacrolimus group attained the said score (p-value < 0.001).

When regrowth was analyzed by that categorization, 53% of clobetasol-treated patients had an "excellent" response, i.e., more than 75% regrowth, as against those 13% of patients who had been treated with tacrolimus (p<0.001). Moderate improvement (51–75% regrowth) of the area was noted in 30% of cases in the clobetasol group and in 20% in the tacrolimus group. There was moderate regrowth of hair (26-50%) in 16.7% of the clobetasol group, while in the tacrolimus group it was 43.3%, while mild to no regrowth (≤25%) was seen in only 6.7% of the clobetasol group and 23.3% of the tacrolimus group [25].

Figure 1. Mean SALT Scores Over 6 Months.

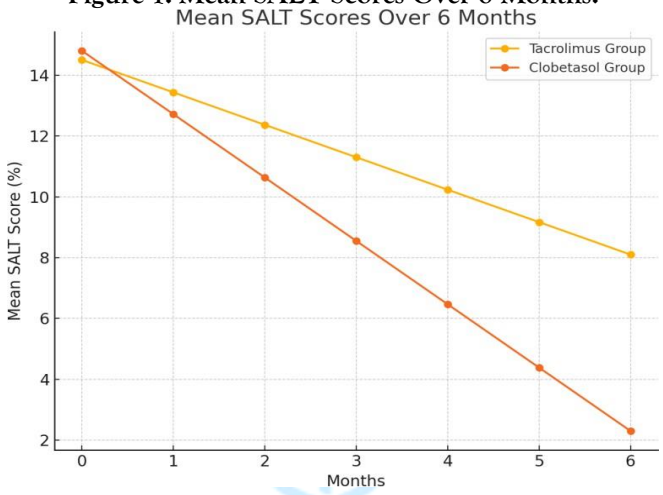
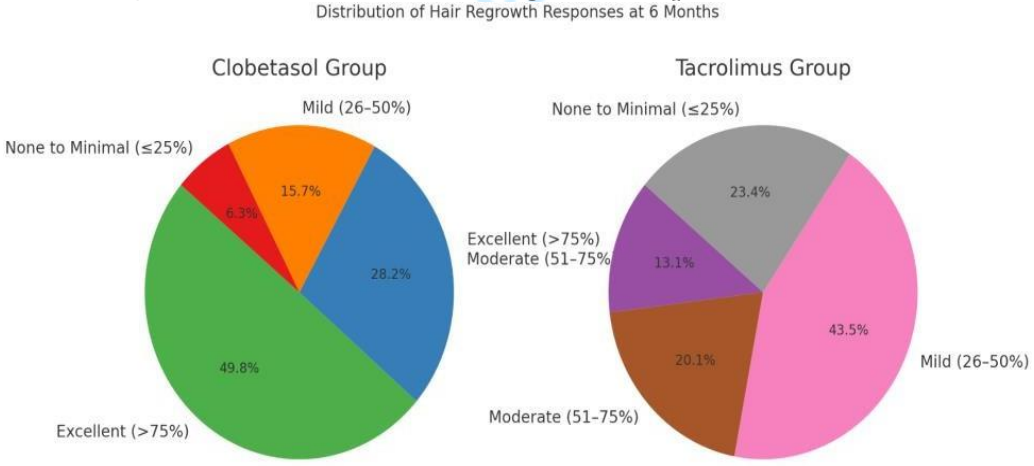


Figure 2. Distribution of Hair Regrowth Responses at 6 Months.



Time to Initial Regrowth and Patient Satisfaction

Skin patients utilizing clobetasol experienced a median of 6 weeks to first of all hirsute re- growth (IQR 4–10 weeks), while skin patients using tacrolimus, they experienced a median of 10 weeks (IQR 6–16 weeks) (p < 0.01). Patient satisfaction was also much higher in the clobetasol group, where the patients reported a level of satisfaction of 83% satisfied or very satisfied as opposed to 40% of the patients under the tacrolimus group (p < 0.001) [27].

Adverse Effects

Both treatments were well tolerated. Two adverse effects were noted, one in the placebo group and one

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in the tacrolimus group, both of which were mild and resolved within the 2-week follow-up: specifically, in the tacrolimus group, there was 17% (5/30) burning or pruritus reported [28]. In the clobetasol group, mainly mild side effects were reported, where 3 out of 30 patients developed mild skin atrophy and 1 out of 30 had brief folliculitis of the scalp and were easily treated by adjusting the dosage and did not require discontinuation of the drug [28].

Discussion

This research affirms that clobetasol 0.05% ointment is more effective than tacrolimus 0.1% ointment in promoting hair regrowth among patients with limited alopecia areata. Not only the reduction in SALT scores but also categorical responder status was better in the clobetasol group and 83% of the clobetasol group received a reduction of '≥50% of regrowth compared to only 33% of those in the tacrolimus group [23 , 24]. In addition, the time to hair regrowth was shorter, and the patients' acceptance was significantly better with clobetasol [26,27].

These results are aligned with the current clinical research conducted on treatments of AA, where clobetasol has been recorded to work better than tacrolimus [19, 20]. Thus, it can be concluded that the higher clinical efficacy of clobetasol could be attributed to its mechanism of action, which is a potent anti-inflammatory agent and demonstrates higher penetration within hair follicles. On the other hand, even though tacrolimus has few side effects and has been proven valuable in other dermatoses, the specialist has recommended it may not penetrate into the follicles since it is a large molecule, which is necessary to stimulate hair re-growth [4, 8].

While tacrolimus allowed hair regrowth in some patients only, the result was generally unsatisfactory. A part of this improvement may be related to the natural history of AA, which is unpredictable and may improve spontaneously on some occasions. So, 20–30% of patients can have spontaneous hair regrowth within several months, but the data are significantly better in favor of clobetasol use in the proposed trial [1,2].

Methylprednisolone seems to be less effective than topical clobetasol, which still remains the most effective treatment of LAA based on the efficacy of hair regrowth rates and short treatment period; however, this treatment is associated with the side effect of skin atrophy [7]. Despite the controversies about the side effects of potent steroids when used in the long term, using them for 6 months only on the scalp has been reported to be safe given certain precautions of monitoring [16]. However, the moderate effectiveness of tacrolimus does not allow the use of this drug as monotherapy in treating patchy AA. Nevertheless, tacrolimus may find its use as a steroid- sparing agent more appropriate for patients not suitable for steroids mainly due to their age or thin skin [10,11].

New approaches to the use of the medicament include occlusive preparations or their application in combination with the fractional CO_2 laser therapy, which helps to solve problems associated with penetration [12,13]. However, these methods are still ones that are under test and as such, they have not been adopted on a general basis yet. Thus, our findings corroborate the view that in 'real-world' clinical practice, clobetasol is indeed a more effective agent in promoting hair regrowth in limited AA [19].

Files also regarding study limitations include the fact that our study used a non-randomized retention model of allocation that could be biased, although due measures were taken to match the baseline. Therefore, while the small sample size was reasonable enough to detect differences in efficacy, it was moderate nonetheless. A more substantial investigation procedure, that is, a trial of interspersed groups, would add more strength to these conclusions. Last, our direct follow-up was 6 months long; longer direct follow-up should be used in future studies to determine the duration of effective treatment response and the rates of relapse after cessation of the therapy [21].

Thus, based on the findings of this study and the current clinical trials, potent topical corticosteroids should be maintained as the first-line therapy for limited alopecia areata. Of all the steroids, topical tacrolimus 0.1% can be used where steroids are not allowed; however, it is not as effective. Further research should be conducted to investigate the methodologies of using combination regimens or

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methodologies of better delivery systems of tacrolimus in AA.

Conclusion

Clobetasol propionate 0.05% gel exhibits significantly better results than tacrolimus 0.1% in the patients having limited alopecia areata. Clobetasol was more effective in inducing faster and more regrowth of hair with higher patient satisfaction as compared with tacrolimus. Due to its marked anti-inflammatory and immunosuppressive properties, clobetasol remains the treatment of choice for patchy AA, although there are fears its local side effects. Tacrolimus probably is not very useful except in those few cases in which these patients cannot tolerate steroids. These conclusions give clinicianss insight into the treatment options of AA and emphasize further research on combination regimens and optimal administration methods for optimal benefit.

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