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ORIGINAL ARTICLE

Comparative Efficacy of Topical Tacrolimus Versus Hydrocortisone in the Management of Atopic Dermatitis

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ABSTRACT

Background: Atopic dermatitis is a chronic, relapsing inflammatory skin condition that significantly impacts quality of life. Conventional management with topical corticosteroids, such as hydrocortisone, is effective but associated with potential adverse effects, including skin atrophy. Tacrolimus, a topical calcineurin inhibitor, offers a steroid-sparing alternative with a favorable safety profile.

Objectives: To compare the efficacy and safety of topical tacrolimus 0.1% ointment versus hydrocortisone 1% cream in the management of atopic dermatitis.

Study Design & Setting: Randomized controlled trial conducted at PAF Hospital Rafiqui PAF Base Rafiqui Shorkot cantt.

Methodology: A total of 120 patients aged 18–60 years with clinically diagnosed atopic dermatitis were randomized into two equal groups. Group A received tacrolimus 0.1% ointment, and Group B received hydrocortisone 1% cream, both applied twice daily for 4 weeks. Efficacy was assessed using Eczema Area and Severity Index (EASI) and Visual Analog Scale (VAS) for pruritus at baseline and week 4. Adverse effects were recorded at each visit.

Results: At week 4, mean EASI scores were significantly lower in the tacrolimus group (5.1 ± 1.9) compared to the hydrocortisone group (7.0 ± 2.1; $p < 0.001$). Percentage reduction in EASI was greater with tacrolimus (64.5 ± 10.3%) versus hydrocortisone (50.2 ± 11.6%; $p < 0.001$). Tacrolimus also showed greater reduction in VAS scores (2.6 ± 1.1 vs. 3.5 ± 1.2; $p < 0.001$). Burning sensation was more common with tacrolimus, while skin atrophy occurred only with hydrocortisone.

Conclusion: Tacrolimus was more effective and had a better long-term safety profile than hydrocortisone, making it a suitable option for sensitive skin areas and prolonged therapy.

Keywords: Adverse effects, Atopic dermatitis, EASI score, Hydrocortisone, Pruritus, Tacrolimus, Topical therapy

INTRODUCTION

Atopic dermatitis (AD), also known as atopic eczema, is a chronic, relapsing inflammatory skin disorder characterized by intense pruritus, erythema, and xerosis.[1] It is one of the most prevalent dermatological conditions globally, affecting up to 20% of children and 3% of adults, with a rising incidence over recent decades.[2] The disease has a multifactorial etiology involving complex interactions between genetic predisposition, immune dysregulation, epidermal barrier dysfunction, and environmental triggers. AD significantly impacts quality of life, leading to sleep disturbances, psychological stress, and social impairment, particularly in pediatric populations.[3]

The pathophysiology of AD is marked by immune-mediated inflammation, with a predominance of T-helper 2 (Th2) cytokines in acute phases and a mixed Th1/Th2 profile in chronic stages.[4] Skin barrier impairment due to mutations in the filaggrin gene, reduced ceramide levels, and increased transepidermal water loss contributes to persistent inflammation and heightened susceptibility to allergens and irritants. These mechanisms underpin the rationale for anti-inflammatory and barrier-restoring therapies in disease management.[5]

Topical corticosteroids (TCS), such as hydrocortisone, have been the mainstay of AD treatment for decades due to their potent anti-inflammatory properties.[6] Hydrocortisone, a mild corticosteroid, is often preferred for sensitive skin areas such as the face and intertriginous regions. While effective in controlling flares, long-term corticosteroid use is associated with adverse effects, including skin atrophy, telangiectasia, striae, and tachyphylaxis. These limitations have prompted the exploration of alternative therapeutic agents that can maintain efficacy while minimizing safety concerns.[7]

Topical calcineurin inhibitors (TCIs), such as tacrolimus, have emerged as a promising non-steroidal alternative for AD management. Tacrolimus inhibits calcineurin-dependent T-cell activation, thereby reducing the production of pro-inflammatory cytokines without causing skin atrophy. It is particularly beneficial for long-term use and for application to delicate skin sites. Multiple clinical trials have demonstrated its efficacy in reducing disease severity and preventing relapses, with a favorable safety profile when used appropriately.[8,9]

Comparative study between tacrolimus and hydrocortisone are clinically relevant as they help establish evidence-based treatment algorithms, especially for patients requiring prolonged therapy or those with corticosteroid intolerance.[10] While hydrocortisone offers rapid symptom relief during acute flares, tacrolimus may provide sustained control with fewer chronic adverse effects. However, factors such as onset of action, tolerability, cost, and patient adherence influence treatment choice.[11]

Given the chronic nature of AD and the potential impact of treatment on both short- and long-term outcomes, it is essential to identify the most effective and safe therapeutic approach. This study aims to compare the efficacy of topical tacrolimus and hydrocortisone in the management of atopic dermatitis, focusing on clinical improvement, relapse rates, and adverse effects. The findings may guide clinicians in optimizing individualized treatment plans, balancing efficacy with safety for better patient outcomes.

MATERIALS AND METHODS

This randomized controlled trial was conducted in the Dermatology Department of PAF Hospital Rafiqui PAF Base Rafiqui Shorkot cantt from Jan 2023 to June 2023 after obtaining approval from the Institutional Review Board. A total of 120 patients clinically diagnosed with atopic dermatitis, fulfilling the criteria of the Hanifin and Rajka diagnostic guidelines, were enrolled. The sample size was calculated using the WHO sample size calculator, taking confidence level = 95%, power = 80%, expected efficacy of tacrolimus = 80%, and expected efficacy of hydrocortisone = 60%, resulting in a sample size of 60 patients in each group.

Patients of either gender, aged between 5 and 60 years, with mild to moderate atopic dermatitis involving the face or other

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sensitive skin areas, were included. Patients with severe disease, secondary bacterial or viral skin infections, known hypersensitivity to study drugs, or those who had used systemic immunosuppressive therapy in the preceding four weeks were excluded. Written informed consent was obtained from all adult participants and from parents or guardians of pediatric patients. Participants were randomly allocated into two equal groups using a computer-generated randomization list. Group A was prescribed topical tacrolimus 0.03% ointment, while Group B was prescribed topical hydrocortisone 1% cream. Both medications were applied twice daily on the affected areas for a duration of four weeks. All patients were advised to avoid known triggers, use mild cleansers, and apply a bland emollient twice daily on non-medicated intervals to maintain skin hydration. No other topical or systemic anti-inflammatory agents were allowed during the study period.

Baseline demographic data, disease duration, and severity were recorded. The severity of atopic dermatitis was assessed using the Eczema Area and Severity Index (EASI) score at baseline and at the end of the 4-week treatment period. Pruritus intensity was measured using a Visual Analogue Scale (VAS). Adverse effects such as burning sensation, erythema, or skin atrophy were noted at each follow-up visit. Follow-up visits were scheduled at 2 weeks and 4 weeks after initiation of treatment. Compliance was monitored through patient diaries and by assessing the amount of medication used at each visit. The primary outcome measure was the mean percentage reduction in EASI score from baseline to week 4. Secondary outcomes included changes in VAS pruritus score and the frequency of adverse effects in both groups.

All collected data were entered and analyzed using SPSS version 25. Quantitative variables such as age, baseline EASI score, and percentage reduction in scores were presented as mean ± standard deviation, while qualitative variables such as gender and adverse effects were presented as frequencies and percentages. The independent sample t-test was used to compare mean changes between groups, while chi-square test was applied for categorical variables. A p-value of ≤ 0.05 was considered statistically significant

RESULTS

A total of 120 patients with atopic dermatitis were enrolled, with 60 patients in the tacrolimus group and 60 in the hydrocortisone group. The baseline characteristics of the participants are summarized in Table 1. The mean age was 28.5 ± 10.2 years in the tacrolimus group and 29.2 ± 9.8 years in the hydrocortisone group. Males comprised 56.7% of the tacrolimus group and 53.3% of the hydrocortisone group. The mean disease duration was 3.2 ± 2.1 years in the tacrolimus group and 3.4 ± 2.3 years in the hydrocortisone group. A positive family history of atopy was reported by 36.7% in the tacrolimus group and 41.7% in the hydrocortisone group, while seasonal variation was noted in just over half of patients in both groups. Associated allergic rhinitis and asthma were present in a minority of patients in each group. Baseline EASI and VAS scores were comparable between the two groups.

Changes in EASI and VAS scores after 4 weeks of treatment are shown in Table 2. The mean week 4 EASI score was significantly lower in the tacrolimus group (5.1 ± 1.9) compared to the hydrocortisone group (7.0 ± 2.1) ($p < 0.001$). The mean percentage reduction in EASI score was also greater with tacrolimus (64.5 ± 10.3%) than with hydrocortisone (50.2 ± 11.6%) ($p < 0.001$). Similarly, the mean week 4 VAS score was lower in the tacrolimus group (2.6 ± 1.1) than in the hydrocortisone group (3.5 ± 1.2) ($p < 0.001$), indicating superior improvement in pruritus severity.

The frequency of adverse effects is presented in Table 3. Burning sensation was reported more often in the tacrolimus group (13.3%) compared to the hydrocortisone group (3.3%) ($p = 0.047$). Erythema occurred at similar rates between groups ($p = 0.728$). Skin atrophy was observed only in the hydrocortisone group (8.3%), and this difference was statistically significant ($p = 0.024$). The majority of patients in both groups did not experience any adverse effects.

Efficacy outcomes based on percentage reduction in EASI score are shown in Table 4. A higher proportion of patients in the tacrolimus group achieved an effective response (≥ 60% reduction in EASI) compared to the hydrocortisone group (70.0% vs. 46.7%, $p = 0.009$). Partial efficacy (30–59% reduction) was seen in 23.3% of tacrolimus patients and 36.7% of hydrocortisone patients, with no statistically significant difference ($p = 0.119$). Ineffective treatment outcomes (< 30% reduction) were more frequent in the hydrocortisone group (16.7%) than in the tacrolimus group (6.7%), though this did not reach statistical significance ($p = 0.091$).

Table 1: Baseline characteristics of study participants (n = 120)

Variable	Tacrolimus (n = 60)	Hydrocortisone (n = 60)
Age (years)	28.5 ± 10.2	29.2 ± 9.8
Gender		
Male	34 (56.7%)	32 (53.3%)
Female	26 (43.3%)	28 (46.7%)
Disease duration (years)	3.2 ± 2.1	3.4 ± 2.3
Positive family history of atopy	22 (36.7%)	25 (41.7%)
Baseline EASI score	14.2 ± 2.9	14.0 ± 3.1
Baseline VAS score	7.1 ± 0.9	7.0 ± 1.0

Table 2: Change in EASI and VAS scores after 4 weeks of treatment

Outcome Measure	Tacrolimus (n = 60)	Hydrocortisone (n = 60)	p-value
Week 4 EASI score	5.1 ± 1.9	7.0 ± 2.1	<0.001
Percentage reduction in EASI	64.5 ± 10.3	50.2 ± 11.6	<0.001
Week 4 VAS score	2.6 ± 1.1	3.5 ± 1.2	<0.001

Table 3: Frequency of adverse effects in study participants

Adverse Effect	Tacrolimus (n = 60)	Hydrocortisone (n = 60)	p-value
Burning sensation	8 (13.3%)	2 (3.3%)	0.047
Erythema	5 (8.3%)	4 (6.7%)	0.728
Skin atrophy	0 (0%)	5 (8.3%)	0.024
None	47 (78.3%)	49 (81.7%)	0.648

Table 4: Efficacy comparison between tacrolimus and hydrocortisone after 4 weeks

Efficacy Category	Tacrolimus (n = 60)	Hydrocortisone (n = 60)	p-value
Effective (≥ 60% reduction in EASI)	42 (70.0%)	28 (46.7%)	0.009
Partially effective (30–59% reduction in EASI)	14 (23.3%)	22 (36.7%)	0.119
Ineffective (< 30% reduction in EASI)	4 (6.7%)	10 (16.7%)	0.091

DISCUSSION

Atopic dermatitis is a chronic, relapsing inflammatory skin disease characterized by pruritus, erythema, and xerosis, affecting both children and adults worldwide. It results from a combination of genetic predisposition, immune dysregulation, and epidermal barrier dysfunction.[12,13] Topical corticosteroids, such as hydrocortisone, have long been the standard treatment but carry risks of skin atrophy and other adverse effects with prolonged use. Topical calcineurin inhibitors, such as tacrolimus, offer a non-steroidal alternative with minimal risk of skin thinning, making them suitable for sensitive skin areas.[14] Comparative evaluation of these agents is important to determine optimal treatment strategies. This study aimed to compare the efficacy and safety of topical tacrolimus versus hydrocortisone in the management of atopic dermatitis.

In our study, topical tacrolimus 0.1% ointment demonstrated significantly greater efficacy than hydrocortisone 1% cream in reducing disease severity, as shown by a larger mean percentage reduction in EASI score (64.5 ± 10.3% vs. 50.2 ± 11.6%; $p < 0.001$) and greater improvement in pruritus severity (VAS

reduction: 2.6 ± 1.1 vs. 3.5 ± 1.2; $p < 0.001$). This is consistent with Mohamed et al. (2023), who also found greater clinical improvement with tacrolimus, along with a significantly greater reduction in inflammatory biomarkers IL-10, IL-17, and IL-23 compared to hydrocortisone ($p < 0.05$), and no incidence of skin atrophy in the tacrolimus group.[16] Similarly, Binsaleh et al. (2024) reported that tacrolimus achieved superior biomarker reduction and significant mEASI score improvement compared with hydrocortisone ($p < 0.05$), further supporting our findings.[19] Our efficacy rates also align partially with Rahman et al. (2016), who reported significant improvement in SCORAD components including erythema, edema, and pruritus (all $p < 0.001$) with tacrolimus, although their burning sensation rate (20%) was higher than ours (13.3%).[18] Mandelin et al. (2010) similarly observed that tacrolimus was superior to corticosteroid regimens at 6 months, particularly in head and neck lesions, with long-term efficacy maintained over 12 months.[20]

However, our results differ from Khan et al. (2014), who found no significant difference between tacrolimus and hydrocortisone in percent reduction of severity (69.20 ± 23.41% vs. 74.77 ± 23.30%; $p = 0.360$) or excellent response rates (56.7% vs. 63.3%). The discrepancy may relate to different scoring systems (SCORAD vs. EASI) and study duration.[15] Additionally, Khan et al.'s equal efficacy contrasts with our data showing 70.0% achieving ≥ 60% EASI reduction with tacrolimus compared to 46.7% with hydrocortisone ($p = 0.009$). Adverse effect profiles were consistent with previous literature.[15] We found burning sensation more frequent in the tacrolimus group (13.3% vs. 3.3%; $p = 0.047$), similar to Mohamed et al. ($p < 0.05$) and Rahman et al. (20% vs. 0%). Importantly, no skin atrophy occurred with tacrolimus in our study, consistent with Mohamed et al. ($p < 0.05$) and in contrast to hydrocortisone (8.3%).[16,18]

Lazar's review highlights the need to incorporate quality-of-life and cost-effectiveness assessments, which were not evaluated in our trial, representing an area for future research. Overall, our findings reinforce the superiority of tacrolimus in short-term efficacy and safety, in line with most recent controlled trials.[17]

Follow-up visits were structured to monitor both efficacy and adverse effects closely. However, the relatively short follow-up period of four weeks limits the ability to assess long-term efficacy and relapse rates. The single-center nature of the study may restrict generalizability to other populations. Patient-reported adherence was used, which could introduce recall bias.

CONCLUSION

Tacrolimus demonstrated superior improvement in disease severity and pruritus reduction compared to hydrocortisone over a four-week period. It was associated with fewer long-term adverse effects such as skin atrophy. Tacrolimus may be preferred for prolonged treatment, especially in sensitive skin areas.

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