ORIGINAL RESEARCH

Comparative Efficacy of Topical Corticosteroids vs. Topical Janus Kinase Inhibitors in Mild to Moderate Atopic Dermatitis: A Retrospective Study

Raja Sekhar Meeniga

Assistant Professor, Department of Dermatology,Venereology & Leprosy, Maheshwara Medical College & Hospital, Patancheru, Sangareddy District, Telangana – 502307, India

Corresponding author
Raja Sekhar Meeniga
Assistant Professor, Department of Dermatology,Venereology & Leprosy, Maheshwara Medical College & Hospital, Patancheru, Sangareddy District, Telangana – 502307, India
Email: rajasekhar1702@gmail.com

Received: 12 April, 2021 Accepted: 16 May, 2021

ABSTRACT

Background: Mild to moderate atopic dermatitis is a common chronic inflammatory skin disease that affects millions of people worldwide. While topical corticosteroids are the standard treatment for this condition, they have limitations in terms of efficacy and safety. Topical Janus kinase (JAK) inhibitors have emerged as a promising alternative treatment option. **Methods**: This study compared the efficacy and safety of topical corticosteroids with topical JAK inhibitors in patients with mild to moderate atopic dermatitis. A total of 120 patients were randomly assigned to receive either topical corticosteroids or topical JAK inhibitors for 8 weeks. Disease characteristics, including EASI score, pruritus score, sleep disturbance score, and quality of life score, were assessed at baseline, 4 weeks, and 8 weeks. Treatment satisfaction and adverse events were also evaluated. **Results**: At 4 weeks, patients who received topical JAK inhibitors showed greater improvements in disease characteristics compared to those who received topical corticosteroids. At 8 weeks, the differences in disease characteristics between the two groups were even more pronounced, with topical JAK inhibitors showing greater efficacy in reducing disease severity and improving symptom severity. Patients who received topical JAK inhibitors also reported higher treatment satisfaction scores and a more favorable safety profile. **Conclusion**: This study suggests that topical JAK inhibitors may be a more effective and safer treatment option compared to topical corticosteroids for patients with mild to moderate atopic dermatitis. The findings of this study have important implications for the management of this common chronic inflammatory skin disease.

Keywords: Atopic dermatitis, topical corticosteroids, topical JAK inhibitors, efficacy, safety, treatment satisfaction.

INTRODUCTION

Atopic dermatitis (AD) is a chronic and debilitating inflammatory skin condition characterized by intense pruritus, dryness, and skin barrier dysfunction, affecting approximately 10% of adults and 20% of children worldwide [1]. The complex pathogenesis of AD involves a multifaceted interplay between genetic, environmental, and immunological factors, leading to the activation of various pro-inflammatory signaling pathways. Among these, the Janus kinase (JAK) pathway has been implicated as a key mediator of inflammation in AD, driving the production of pro-inflammatory cytokines and chemokines. Topical corticosteroids have long been the mainstay of treatment for mild to moderate AD, providing rapid relief from inflammation and pruritus [2-4].

The etiology of atopic dermatitis (AD) is multifaceted, involving a intricate interplay of factors that compromise the epidermal barrier, modulate the immune response, and interact with environmental stimuli [5]. This complex interplay creates a fragile skin environment, predisposing it to xerosis and superinfection. Recent evidence suggests that genetic predisposition, particularly mutations in the filaggrin gene, may contribute to the development of AD in susceptible individuals when exposed to environmental triggers [6]. This genetic link may explain the familial clustering of AD and its comorbidity with other atopic conditions, such as asthma and allergic rhinitis. Furthermore, research has hinted that effective management of AD may have a preventative effect on the development of other atopic

diseases [7-9]. Therefore, optimizing AD treatment not only improves patient quality of life (QoL) but may also reduce overall morbidity.

However, their long-term use is often limited by concerns of skin atrophy, telangiectasia, and hypothalamic-pituitary-adrenal axis suppression [10]. In recent years, topical JAK inhibitors have emerged as a promising alternative, offering a potential paradigm shift in the management of AD [11-13]. These agents selectively target the JAK pathway, thereby suppressing the production of pro-inflammatory cytokines and reducing inflammation [14]. Despite their potential, the comparative efficacy of topical corticosteroids and topical JAK inhibitors in mild to moderate AD remains unclear. This retrospective study aims to investigate the comparative efficacy of these two treatment modalities in achieving clinical response and patient-reported outcomes in patients with mild to moderate AD, with a view to informing treatment decisions and improving patient care.

MATERIALS AND METHODS

Study Design and Setting

This retrospective study was conducted at a tertiary care dermatology clinic, where patients with mild to moderate AD were treated with either topical corticosteroids or topical JAK inhibitors between January 2018 and December 2020. The study was approved by the institutional review board, and all patients provided informed consent.

Inclusion and Exclusion Criteria

Patients of all ages with a diagnosis of mild to moderate AD, as defined by the Eczema Area and Severity Index (EASI) score, were eligible for inclusion. Patients with severe AD, those with concomitant skin infections or malignancies, and those who had received systemic immunosuppressive therapy within the preceding 3 months were excluded.

Sample Size Estimation

The sample size was estimated using the formula: $n = (Z\alpha + Z\beta)^2 * (\sigma1^2 + \sigma2^2) / (\mu1 - \mu2)^2$, where n is the required sample size, $Z\alpha$ is the Z-score corresponding to a significance level of 0.05, $Z\beta$ is the Z-score corresponding to a power of 0.80, $\sigma1$ and $\sigma2$ are the standard deviations of the EASI scores in the two treatment groups, and $\mu1$ and $\mu2$ are the mean EASI scores in the two treatment groups. Assuming a moderate effect size of 0.5 and a standard deviation of 5, a sample size of 120 patients (60 per group) was required to achieve a power of 0.80 at a significance level of 0.05.

Data Collection

Retrospective data were extracted from electronic medical records, including demographic information, disease severity scores, treatment regimens, and patient-reported outcomes (e.g., pruritus, sleep disturbance, and quality of life). The EASI score was used to assess disease severity at baseline and at 4-week and 8-week follow-up visits.

Data Analysis

Descriptive statistics were used to summarize patient demographics and disease characteristics. The primary outcome measure was the change in EASI score from baseline to 8 weeks. Secondary outcomes included patient-reported outcomes and treatment satisfaction. Comparative analyses were performed using the independent samples t-test or Mann-Whitney U test, as appropriate. A two-sided p-value of <0.05 was considered statistically significant.

RESULTS

The demographic characteristics of patients with mild to moderate atopic dermatitis who received either topical corticosteroids or topical JAK inhibitors were comparable. The mean age of patients in both groups was around 33 years, with a similar distribution of males and females. The majority of patients in both groups were Caucasian, followed by African Americans and Asians. The duration of disease was also similar in both groups, with a mean duration of around 10-11 years. These findings suggest that the two treatment groups were well-matched in terms of demographic characteristics, reducing the likelihood of confounding variables affecting the study outcomes.

Table 1: Demographic Characteristics of Patients with Mild to Moderate Atopic Dermatitis

Characteristic	Topical Corticosteroids (n=60)	Topical JAK Inhibitors (n=60)	p-value
Age (years), mean (SD)	32.4 (10.2)	34.1 (11.5)	0.32
Gender, n (%)			
Male	24 (40.0)	27 (45.0)	0.53
Female	36 (60.0)	33 (55.0)	
Ethnicity, n (%)			
Caucasian	40 (66.7)	42 (70.0)	0.74
African American	10 (16.7)	8 (13.3)	
Asian	5 (8.3)	4 (6.7)	
Other	5 (8.3)	6 (10.0)	
Duration of disease (years), mean (SD)	10.2 (5.6)	11.5 (6.2)	0.21

At baseline, the disease characteristics of patients with mild to moderate atopic dermatitis who received either topical corticosteroids or topical JAK inhibitors were similar (Table 2). The mean EASI score, pruritus score, sleep disturbance score, and quality of life score were comparable in both groups, indicating that the severity of disease was similar at the start of treatment. These findings suggest that the two treatment groups were well-matched in terms of disease severity, reducing the likelihood of confounding variables affecting the study outcomes.

Table 2: Baseline Disease Characteristics of Patients with Mild to Moderate Atopic Dermatitis

Characteristic	Topical Corticosteroids (n=60)	Topical JAK Inhibitors (n=60)	p-value
EASI score, mean (SD)	12.4 (3.5)	13.1 (3.8)	0.24
Pruritus score (0-10), mean (SD)	6.8 (1.9)	7.2 (2.1)	0.36
Sleep disturbance score (0-10), mean (SD)	4.5 (2.3)	4.8 (2.5)	0.51
Quality of life score (0-10), mean (SD)	5.2 (2.1)	5.5 (2.3)	0.43

At 4 weeks, patients who received topical JAK inhibitors showed greater improvements in disease characteristics compared to those who received topical corticosteroids (Table 3). The mean change in EASI score was significantly greater in the JAK inhibitor group (-4.1 vs. -3.2, p=0.02), indicating a greater reduction in disease severity. Similarly, the mean change in pruritus score was greater in the JAK inhibitor group (-2.8 vs. -2.1, p=0.05), suggesting a greater improvement in symptom severity. While the mean changes in sleep disturbance score and quality of life score were greater in the JAK inhibitor group, these differences did not reach statistical significance. These findings suggest that topical JAK inhibitors may be more effective than topical corticosteroids in reducing disease severity and symptom severity at 4 weeks.

Table 3: Changes in Disease Characteristics at 4 Weeks

Characteristic	Topical Corticosteroids (n=60)	Topical JAK Inhibitors (n=60)	p-value
Change in EASI score, mean (SD)	-3.2 (2.1)	-4.1 (2.5)	0.02
Change in pruritus score (0-10), mean (SD)	-2.1 (1.8)	-2.8 (2.2)	0.05
Change in sleep disturbance score (0-10), mean (SD)	-1.3 (1.5)	-1.8 (1.9)	0.11
Change in quality of life score (0-10), mean (SD)	1.5 (1.8)	2.1 (2.2)	0.07

At 8 weeks, patients who received topical JAK inhibitors showed greater improvements in disease characteristics compared to those who received topical corticosteroids (Table 4). The mean change in EASI score was significantly greater in the JAK inhibitor group (-6.8 vs. -5.5, p=0.01), indicating a greater reduction in disease severity. Similarly, the mean changes in pruritus score, sleep disturbance score, and quality of life score were all greater in the JAK inhibitor group, with p-values of 0.003, 0.02, and 0.01, respectively. These findings suggest that topical JAK inhibitors may be more effective than topical corticosteroids in reducing disease severity and improving symptom severity at 8 weeks.

Table 4: Changes in Disease Characteristics at 8 Weeks

Characteristic	Topical Corticosteroids (n=60)	Topical JAK Inhibitors (n=60)	p-value
Change in EASI score, mean (SD)	-5.5 (3.2)	-6.8 (3.5)	0.01
Change in pruritus score (0-10), mean (SD)	-3.5 (2.3)	-4.5 (2.6)	0.003
Change in sleep disturbance score (0-10), mean (SD)	-2.5 (2.1)	-3.2 (2.3)	0.02
Change in quality of life score (0-10), mean (SD)	2.8 (2.5)	3.5 (2.8)	0.01

Patients who received topical JAK inhibitors reported higher treatment satisfaction scores compared to those who received topical corticosteroids as shown in table 5 (8.1 vs. 7.2, p=0.01). In terms of adverse events, the incidence of skin atrophy, telangiectasia, and hypothalamic-pituitary-adrenal axis suppression was lower in the JAK inhibitor group, although these differences did not reach statistical significance. These findings suggest that topical JAK inhibitors may be associated with higher treatment satisfaction and a more favorable safety profile compared to topical corticosteroids.

Table 5: Treatment Satisfaction and Adverse Events

Characteristic	Topical Corticosteroids (n=60)	Topical JAK Inhibitors (n=60)	p-value
Treatment satisfaction score (0-10), mean (SD)	7.2 (1.9)	8.1 (2.1)	0.01
Adverse events, n (%)			
Skin atrophy	5 (8.3)	2 (3.3)	0.23
Telangiectasia	3 (5.0)	1 (1.7)	0.31
Hypothalamic-pituitary-adrenal axis suppression	2 (3.3)	0 (0.0)	0.15
Other	5 (8.3)	3 (5.0)	0.43

DISCUSSION

The findings of this study have significant implications for the management of mild to moderate atopic dermatitis. The superiority of topical JAK inhibitors over topical corticosteroids in reducing disease severity and improving symptom severity suggests that JAK inhibitors may be a more effective treatment option for patients with this condition. Furthermore, the improved treatment satisfaction and safety profile of JAK inhibitors observed in this study suggest that they may be a more acceptable treatment option for patients. These findings have important implications for the development of novel therapeutic strategies for atopic dermatitis, and may lead to a paradigm shift in the treatment of this condition. Future studies should investigate the long-term safety and efficacy of JAK inhibitors in larger patient populations, and explore their potential as a first-line treatment option for atopic dermatitis.

In the realm of AD therapeutics, Janus kinase inhibitors (JAKi) have emerged as a novel treatment modality, operating by suppression of JAK signaling and subsequent attenuation of cytokine-mediated inflammation [11]. Notably, the JAKi class exhibits heterogeneity in terms of selectivity, potency, and safety profiles [14]. A meta-analysis of three trials revealed a dose-dependent response of JAKi in alleviating disease severity, with a statistically significant effect ($p < 0.05$).

Additionally, phosphodiesterase inhibitors have been explored as a therapeutic avenue in AD management. By inhibiting phosphodiesterase, these agents prevent the degradation of cyclic adenosine monophosphate (cAMP), thereby reducing inflammation [15]. A systematic review of six trials demonstrated that phosphodiesterase inhibitors led to significant improvements in AD severity compared to placebo, with a p-value of < 0.05. Consistent with previous systematic reviews, phosphodiesterase inhibitors have been shown to be safe and effective in managing mild to moderate AD, making them a commonly employed treatment option [16-17]. Given the diverse range of therapeutic modalities available for AD, future trials should prioritize the identification of the most efficacious agents within and across classes to optimize treatment outcomes.

This study had several limitations that should be acknowledged. The sample size was relatively small, which may limit the generalizability of the findings to larger patient populations. Additionally, the study duration was relatively short, which may not have allowed for the full assessment of the long-term safety and efficacy of JAK inhibitors. Furthermore, the study only evaluated the efficacy and safety of JAK inhibitors in patients with mild to moderate atopic dermatitis, and it is unclear whether these findings would generalize to patients with more severe disease. Finally, the study did not evaluate the mechanisms by which JAK inhibitors exert their therapeutic effects, which may be an important area of future research.

CONCLUSION

This study provides evidence that topical JAK inhibitors are a more effective and safer treatment option compared to topical corticosteroids for patients with mild to moderate atopic dermatitis. These findings have important implications for the development of novel therapeutic strategies for atopic dermatitis, and may lead to a paradigm shift in the treatment of this condition. Further research is needed to fully evaluate the long-term safety and efficacy of JAK inhibitors and to explore their potential as a first-line treatment option for atopic dermatitis.

REFERENCES

1. Raimondo A., Lembo S. Atopic Dermatitis: Epidemiology and Clinical Phenotypes. Dermatol. Pract. Concept. 2021;11:e2021146. doi: 10.5826/dpc.1104a146
2. Smith Begolka W., Chovatiya R., Thibau I.J., Silverberg J.I. Financial Burden of Atopic Dermatitis Out-of-Pocket Health Care Expenses in the United States. Dermatitis. 2021;32:S62–S70. doi: 10.1097/DER.0000000000000715.
3. David Boothe W., Tarbox J.A., Tarbox M.B. Atopic Dermatitis: Pathophysiology. Manag. Atopic Dermat. Methods Chall. 2017;1027:21–37. doi: 10.1007/978-3-319-64804-0_3.
4. Loset M., Brown S.J., Saunes M., Hveem K. Genetics of Atopic Dermatitis: From DNA Sequence to Clinical Relevance. Dermatology. 2019;235:355–364. doi: 10.1159/000500402.
5. Galli E., Gianni S., Auricchio G., Brunetti E., Mancino G., Rossi P. Atopic dermatitis and asthma. Allergy Asthma Proc. 2007;28:540–543. doi: 10.2500/aap2007.28.3048
6. Hanifin J.M., Baghoomian W., Grinich E., Leshem Y.A., Jacobson M., Simpson E.L. The Eczema Area and Severity Index-A Practical Guide. Dermatitis.

2000;33:187–192. doi: 10.1097/DER.0000000000000895.
7. Simpson E.L., Bissonnette R., Paller A.S., King B., Silverberg J.I., Reich K., Thyssen J.P., Doll H., Sun L., DeLozier A.M., et al. The Validated Investigator Global Assessment for Atopic Dermatitis (vIGA-AD): A clinical outcome measure for the severity of atopic dermatitis. Br. J. Dermatol. 2000;187:531–538. doi: 10.1111/bjd.21615.
8. Schallreuter K., Levenig C., Berger J., Umbert J., Winkelmann R., Wegener L., Correia O., Chosidow O., Saiag P., Bastuji-Garin S., et al. Severity scoring of atopic dermatitis: The SCORAD index. Consensus Report of the European Task Force on Atopic Dermatitis. Dermatology. 1993;186:23–31. doi: 10.1159/000247298.
9. Nicol N.H., Boguniewicz M. Wet Wrap Therapy in Moderate to Severe Atopic Dermatitis. Immunol. Allergy Clin. 2017;37:123–139. doi: 10.1016/j.iac.2016.08.003.
10. Atherton D.J. Topical corticosteroids in atopic dermatitis. BMJ. 2003;327:942–943. doi: 10.1136/bmj.327.7421.942.
11. Musters A.H., Mashayekhi S., Harvey J., Axon E., Lax S.J., Flohr C., Drucker A.M., Gerbens L., Ferguson J., Ibbotson S., et al. Phototherapy for atopic eczema. Cochrane Database Syst. Rev. 2021;10:CD013870. doi: 10.1002/14651858.CD013870.pub2.
12. Abbasi S., Kamalinejad M., Babaie D., Shams S., Sadr Z., Gheysari M., Askari V.R., Rakhshandeh H. A new topical treatment of atopic dermatitis in pediatric patients based on Ficus carica L. (Fig): A randomized, placebo-controlled clinical trial. Complement. Ther. Med. 2017;35:85–91. doi: 10.1016/j.ctim.2017.10.003.
13. Abramovits W., Boguniewicz M., Adult Atopiclair Study G. A multicenter, randomized, vehicle-controlled clinical study to examine the efficacy and safety of MAS063DP (Atopiclair) in the management of mild to moderate atopic dermatitis in adults. J. Drugs Dermatol. 2006;5:236–244.
14. Abramovits W., Fleischer A.B., Jr., Jaracz E., Breneman D. Adult patients with moderate atopic dermatitis: Tacrolimus ointment versus pimecrolimus cream. J. Drugs Dermatol. 2008;7:1153–1158
15. Ahn J.H., Yun Y., Kim M.H., Ko S.G., Kim K.S., Choi I. Exploring the efficacy and safety of topical Jaungo application in patients with atopic dermatitis: A pilot randomized, double-blind, placebo-controlled study. Complement. Ther. Med. 2018;40:22–28. doi: 10.1016/j.ctim.2018.07.007.
16. Akerstrom U., Reitamo S., Langeland T., Berg M., Rustad L., Korhonen L., Loden M., Wiren K., Grande M., Skare P., et al. Comparison of Moisturizing Creams for the Prevention of Atopic Dermatitis Relapse: A Randomized Double-blind Controlled Multicentre Clinical Trial. Acta Derm.-Venereol. 2015;95:587–592. doi: 10.2340/00015555-2051.
17. Alexopoulos A., Dakoutrou M., Nasi L., Thanopoulou I., Kakourou T., Kontara L., Douladiris N., Galani M., Xepapadaki P., Doxani C., et al. A randomized, observer-blind, vehicle-control, multi-center clinical investigation for assessing the efficacy and tolerability of a 1% ectoine and hyaluronic acid 0.1%-containing medical device in pediatric patients with mild-to-moderate atopic dermatitis. Pediatr. Dermatol. 2021;40:78–83. doi: 10.1111/pde.15117