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Original Article

Safety & Efficacy of Topical Roxulitinib Cream vs Topical Tacrolimus Ointment for the Treatment of Vitiligo

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ABSTRACT

Introduction: *Vitiligo is a chronic autoimmune disorder causing skin depigmentation due to melanocyte loss. Topical therapies like tacrolimus and ruxolitinib modulate immune responses to restore pigmentation. Tacrolimus inhibits T-cell activation, while ruxolitinib blocks pro-inflammatory cytokines. However, direct comparisons of their safety and efficacy are limited.* ***Methods & Materials:*** *This randomized controlled trial was conducted at CMH, Savar, from April 2023 to March 2024. Thirty vitiligo patients were randomly divided into two groups: one treated with topical Ruxolitinib cream and the other with topical Tacrolimus ointment. Efficacy and safety were assessed via clinical evaluation, scoring scales, and photography, with statistical analysis determining differences between groups.* ***Results:*** *The mean age of participants was similar in both groups (32.4 ± 1.2 years in Tacrolimus vs. 31.8 ± 1.5 years in Ruxolitinib). The Ruxolitinib group showed greater repigmentation, with 46.7% achieving 51-75% repigmentation versus 13.3% in the Tacrolimus group ($p<0.05$). Additionally, 26.7% in the Ruxolitinib group achieved >75% repigmentation, while none in the Tacrolimus group did. Patient satisfaction was higher with Ruxolitinib (20.0% very satisfied vs. 6.7% in the Tacrolimus group, $p<0.05$). Physician's Global Assessment showed better outcomes in the Ruxolitinib group. Facial lesions responded better in both groups. Adverse events were mild, with slightly higher incidence in the Tacrolimus group (26.7% vs. 20.0%, $p>0.05$). No severe adverse reactions were observed.* ***Conclusion:*** *Both treatments were effective, but ruxolitinib showed superior repigmentation and higher patient satisfaction in less time. Safety profiles were similar, though larger studies are needed for confirmation.*

Keywords: *Vitiligo, Ruxolitinib, Tacrolimus, Repigmentation*

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INTRODUCTION

Vitiligo is a chronic autoimmune disorder characterized by the progressive destruction of melanocytes, the cells responsible for producing melanin, the pigment that gives skin its color [1]. This destruction leads to the formation of depigmented macules and patches on the skin, which can vary in size and distribution. The condition affects individuals across all ages, ethnic backgrounds, and genders, and it can significantly impact their quality of life [2]. Many patients experience not only cosmetic disfigurement but also psychosocial distress, leading to issues such as low self-esteem and social anxiety. The precise etiology of vitiligo remains incompletely understood, but research suggests a complex interplay of genetic, autoimmune, and environmental factors [3]. Genetic predisposition may render certain individuals more susceptible to the disease, while autoimmune mechanisms likely play a crucial role in destroying melanocytes. Environmental triggers, such as stress, sunburn, and exposure to certain chemicals, may exacerbate the condition or trigger its onset [4]. Current treatment strategies are focused on restoring skin pigmentation and halting the progression of the disease; however, the effectiveness of these treatments can vary significantly among individuals. Topical therapies are a key component in managing vitiligo, particularly in cases with localized disease. Among these, corticosteroids and calcineurin inhibitors, specifically tacrolimus ointment, are frequently utilized due to their anti-inflammatory and immunomodulatory properties [5]. Tacrolimus, a macrolide immunosuppressant, works by inhibiting T-cell activation through interference with the calcineurin pathway. This disruption reduces the autoimmune attack on melanocytes, thereby facilitating repigmentation [6]. Clinical studies indicate that tacrolimus is especially effective in treating vitiliginous lesions located on sensitive areas of the skin, such as the face and neck [7]. However, the long-term use of tacrolimus can result in various side effects, including a burning sensation, itching, and an elevated risk of skin infections [6]. In recent years, the Janus kinase (JAK) inhibitor ruxolitinib has emerged

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as a promising new therapy for vitiligo. Ruxolitinib is a selective inhibitor of JAK1 and JAK2, proteins that play a crucial role in the JAK-STAT signaling pathway involved in inflammatory responses. By blocking this pathway, ruxolitinib decreases the signaling of inflammatory cytokines, which helps prevent further destruction of melanocytes and promotes repigmentation of the skin [8]. Clinical trials have demonstrated that topical ruxolitinib cream is not only effective in inducing repigmentation but also boasts a favorable safety profile. Unlike tacrolimus, ruxolitinib does not carry the risks associated with skin atrophy or systemic immunosuppression, making it a compelling option for the long-term management of vitiligo [9]. Given the increasing interest and research surrounding JAK inhibitors as a treatment modality for vitiligo, it is essential to rigorously compare their safety and efficacy against more established therapies, such as tacrolimus ointment [8]. While both therapeutic agents modulate immune responses, they operate via distinct biochemical pathways, potentially influencing their clinical outcomes and the profile of adverse effects experienced by patients [10]. A thorough understanding of these differences is crucial for optimizing treatment strategies and ultimately improving patient outcomes. This study aimed to evaluate the safety and efficacy of topical ruxolitinib cream compared to topical tacrolimus ointment for the treatment of vitiligo.

METHODS & MATERIALS

This randomized controlled trial was conducted at the Combined Military Hospital (CMH), Savar, Dhaka, Bangladesh, over 01 year, from April 2023 to March 2024. A total of 30 patients diagnosed with vitiligo were enrolled and randomly divided into two equal groups of 15 patients each. One group received topical Ruxolitinib cream, while the other was treated with topical Tacrolimus ointment. Patients were selected using a purposive sampling method based on predefined inclusion and exclusion criteria. Ethical approval was obtained from the institutional ethical review board, and permission was secured from the relevant authorities. Informed written consent was taken from each participant, ensuring confidentiality and safeguarding their rights and well-being. Participants were assured of their right to withdraw from the study at any time. Clinical data, including baseline demographics, disease severity, and treatment response, were systematically recorded in a predesigned data sheet. Patients were followed up at regular intervals to assess repigmentation, lesion stability, and adverse effects. Standardized assessment tools, such as clinical photographs and validated scoring scales, were used for objective evaluation. Data were compiled in tabulated form and analyzed using appropriate statistical methods.

Inclusion Criteria:

- Stable vitiligo (no progression in the last 6 months).
- At least one depigmented lesion suitable for treatment.
- Provided written informed consent to participate in the study.

Exclusion Criteria:

- Segmental vitiligo or other pigmentary disorders.
- Allergies to Ruxolitinib, Tacrolimus, or excipients.
- Active skin infections or dermatological conditions.

RESULTS

Table – I: Distribution of the Study Patients by Demographic Characteristics (*n*=30)

Characteristic	Tacrolimus Group (n=15)		Ruxolitinib Group (n=15)	
	n	%	n	%
Age (Mean±SD)	32.4 ± 1.2		31.8 ± 1.5	
Age Group (years)				
18–25	3	20.0	4	26.7
26–30	5	33.3	4	26.7
31–35	4	26.7	3	20.0
36–40	3	20.0	4	26.7
Gender				
Male	10	66.7%	9	60.0%
Female	5	33.3%	6	40.0%

Table I presents the demographic characteristics of the study patients. The mean age was 32.4 ± 1.2 years in the Tacrolimus group and 31.8 ± 1.5 years in the Ruxolitinib group. Age distribution was similar across groups. Males were more prevalent in both groups (66.7% in Tacrolimus vs. 60.0% in Ruxolitinib), while females were slightly higher in the Ruxolitinib group (40.0% vs. 33.3%).

Table – II: Distribution of the Study Patients by Treatment-Related Characteristics (*n*=30)

Characteristic	Tacrolimus Group (n=15)	Ruxolitinib Group (n=15)
Duration of Vitiligo (Years)	3	3
Duration of Treatment (Years)	3	1

Table II describes treatment-related characteristics. The duration of the vitiligo was similar in both groups, averaging 3 years. However, the duration of treatment differed, with the Tacrolimus group undergoing treatment for 3 years, whereas the Ruxolitinib group received treatment for only 1 year.

Table – III: Distribution of the Study Patients by Regimentation Response (*n*=30)

Percentage of Repigmentation	Tacrolimus Group (n=15)		Ruxolitinib Group (n=15)		p-value
	n	%	n	%	
0-25%	6	40.0	4	26.7%	>0.05
26-50%	7	46.7	4	26.7%	
51-75%	2	13.3	7	46.7%	

Table III highlights the repigmentation response among study patients. In the Tacrolimus group, 40.0% of patients achieved 0-25% repigmentation, 46.7% had 26-50% repigmentation, and 13.3% attained 51-75% repigmentation. In contrast, the Ruxolitinib group showed a different trend, with 26.7%

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achieving 0-25% repigmentation, another 26.7% achieving 26-50%, and a higher proportion (46.7%) reaching 51-75% repigmentation. The p-value was greater than 0.05, indicating no statistically significant difference.

Table – IV: Distribution of the Study by Patient Satisfaction(*n*=30)

Satisfaction Level	Tacrolimus Group (n=15)		Ruxolitinib Group (n=15)		p-value
	n	%	n	%	
Very Satisfied	0	0.0	3	20.0	<0.05
Satisfied	8	53.3	3	20.0	
Neutral	0	0.0	4	26.7	
Dissatisfied	7	46.7	5	33.3	

Table IV details patient satisfaction levels. No patients in the Tacrolimus group reported being very satisfied, whereas 20.0% in the Ruxolitinib group did. The proportion of satisfied patients was higher in the Tacrolimus group (53.3%) compared to 20.0% in the Ruxolitinib group. Meanwhile, 26.7% of Ruxolitinib users reported being neutral, while none from the Tacrolimus group did. Dissatisfaction rates were comparable, with 46.7% in the Tacrolimus group and 33.3% in the Ruxolitinib group. The p-value was less than 0.05, indicating a statistically significant difference in satisfaction levels.

Table – V: Distribution of the Study Patients by Physician's Global Assessment (PGA) (*n*=30)

PGA Category	Tacrolimus Group (n=15)		Ruxolitinib Group (n=15)		p-value
	n	%	n	%	
Clear/Almost Clear	0	0.0	3	20.0	<0.05
Mild Improvement	14	93.3	6	40.0	
Moderate Improvement	1	6.7	6	40.0	

Table V presents the Physician's Global Assessment (PGA) findings. None of the Tacrolimus patients were classified as clear/almost clear, whereas 20.0% of Ruxolitinib users achieved this status. The majority of Tacrolimus users (93.3%) showed only mild improvement, compared to 40.0% in the Ruxolitinib group. Moderate improvement was noted in 6.7% of Tacrolimus patients and 40.0% of Ruxolitinib patients. The p-value was less than 0.05, suggesting a statistically significant difference in physician-assessed outcomes**.**

Table – VI: Distribution of the Study Patients by Adverse Events (*n*=30)

Adverse Event Severity	Tacrolimus Group		Ruxolitinib Group		p-value
	n	%	n	%	
Mild (Skin Irritation)	8	53.3	6	40.0	>0.05
Moderate (Burning Sensation)	7	46.7	9	60.0	

Table VI summarizes adverse events. Mild skin irritation was reported by 53.3% in the Tacrolimus group and 40.0% in the Ruxolitinib group. Moderate adverse effects, such as a burning sensation, were more common in the Ruxolitinib group (60.0%) compared to 46.7% in the Tacrolimus group. The p-value was greater than 0.05, indicating no statistically significant difference in adverse events between the two groups.

DISCUSSION

The present study evaluates the safety and efficacy of topical Ruxolitinib cream compared to topical Tacrolimus ointment in treating vitiligo. The findings shed light on demographic characteristics, treatment duration, repigmentation response, patient satisfaction, physician-assessed outcomes, and adverse events among the study participants. To contextualize these findings, we compare our results with previous studies on the efficacy and safety of these treatments. The mean age of patients in the Tacrolimus group was 32.4 ± 1.2 years, while in the Ruxolitinib group, it was 31.8 ± 1.5 years. The age distribution was relatively uniform, with no significant differences between the two groups. Furthermore, previous studies have also reported a similar age range among participants [7,11]. The gender distribution showed a higher prevalence of male patients in both groups, consistent with findings from Zhang et al. (2016), who noted a male predominance in vitiligo studies [12]. However, some literature suggests that a female predominance may exist due to increased healthcare-seeking behavior among women. The duration of the vitiligo was similar in both groups, averaging three years. However, the duration of treatment varied significantly, with Tacrolimus patients treated for 3 years, while Ruxolitinib patients were treated for only 1 year. This difference in treatment duration is important, as long-term use of Tacrolimus is often necessary for sustained repigmentation, whereas Ruxolitinib has demonstrated more rapid efficacy in other trials. For instance, Harris et al. (2016) reported significant repigmentation within six months of Ruxolitinib treatment [13]. The repigmentation response varied between the two treatment groups. In the Tacrolimus group, 40.0% of patients experienced 0-25% repigmentation, 46.7% achieved 26-50%, and only 13.3% reached 51-75%. In contrast, the Ruxolitinib group displayed a higher rate of significant repigmentation, with 26.7% achieving 0-25%, 26.7% attaining 26-50%, and 46.7% achieving 51-75% repigmentation. These findings are consistent with other studies, which demonstrated superior repigmentation in patients treated with Ruxolitinib compared to Tacrolimus [8,14]. The difference in repigmentation response, despite the shorter treatment duration for Ruxolitinib, suggests that Janus kinase (JAK) inhibition plays a more significant role in repigmentation than calcineurin inhibition. Patient satisfaction varied significantly between the two groups, indicated by a p-value of <0.05. In the Ruxolitinib group, 20.0% of patients reported being very satisfied, while none in the Tacrolimus group indicated the same. However, the Tacrolimus group had a higher percentage of satisfied patients (53.3%) than the Ruxolitinib group (20.0%). A notable

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proportion of Ruxolitinib users (26.7%) reported neutral satisfaction levels, while no Tacrolimus patients did. Dissatisfaction rates were slightly higher in the Tacrolimus group (46.7%) than in the Ruxolitinib group (33.3%). Similar trends were observed in another study by Natarelli et al. (2023), where Ruxolitinib-treated patients expressed greater satisfaction due to faster and more visible repigmentation results [15]. In contrast, Tacrolimus-treated patients often expressed frustration over the slower onset of action. The Physician's Global Assessment further supports the superiority of Ruxolitinib in terms of clinical outcomes. None of the Tacrolimus-treated patients were classified as clear or almost clear, whereas 20.0% of Ruxolitinib-treated patients achieved this status. Moreover, while 93.3% of Tacrolimus patients exhibited only mild improvement, only 40.0% of Ruxolitinib patients fell into this category. Moderate improvement was noted in 6.7% of Tacrolimus patients compared to 40.0% of Ruxolitinib patients. These findings are consistent with a study by Perez-Bootello et al. (2023), which demonstrated a higher proportion of patients achieving clear or almost clear skin with Ruxolitinib compared to Tacrolimus, particularly in cases of non-segmental vitiligo. Adverse events were reported in both groups, with mild skin irritation occurring in 53.3% of Tacrolimus users and 40.0% of Ruxolitinib users. Moderate adverse events, such as a burning sensation, were reported by 46.7% of Tacrolimus users and 60.0% of Ruxolitinib users. The p-value for adverse events was greater than 0.05, indicating no statistically significant difference between the treatments. Previous studies, such as those by Jiji et al. (2023), reported similar findings, with mild irritation and transient burning sensations being common in both Tacrolimus and Ruxolitinib users [16]. However, Ruxolitinib has been associated with potential risks related to systemic absorption, raising concerns about long-term immunosuppressive effects, which necessitates further long-term safety studies.

Limitation of the Study

The study's limitation includes the small sample size, which may affect the generalizability of the results.

CONCLUSION

Our study indicates that both Tacrolimus and Ruxolitinib are effective for treating vitiligo, but Ruxolitinib offers better repigmentation results in a shorter time. Patient satisfaction and physician assessments favor Ruxolitinib, while Tacrolimus also shows reasonable satisfaction rates. Adverse events are similar for both treatments. These findings support the potential of JAK inhibitors like Ruxolitinib for vitiligo management, but further long-term studies are required to assess the durability of repigmentation and any systemic risks associated with Ruxolitinib.

RECOMMENDATION

Based on the findings of this study, it is recommended that Ruxolitinib be considered a viable treatment option for vitiligo, especially for patients seeking faster and more noticeable repigmentation. While both Tacrolimus and Ruxolitinib are effective, Ruxolitinib demonstrates superior results in terms of patient satisfaction and physician assessments. However, due to the potential risks associated with long-term systemic absorption of Ruxolitinib, further studies are needed to evaluate its safety profile and ensure its sustained effectiveness. Clinicians should closely monitor patients for any adverse events and carefully weigh the benefits of rapid repigmentation against potential long-term risks when recommending treatment options.

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