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Comparison of Efficacy of Tofacitinib versus Betamethasone Pulse Therapy in the Treatment of Vitiligo

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ABSTRACT

Vitiligo is a chronic autoimmune skin disorder characterized by depigmentation due to melanocyte destruction, significantly impacting patients' quality of life. Emerging treatments, including Janus kinase inhibitors like tofacitinib, offer promising alternatives to conventional therapies such as corticosteroids. **Objective:** To compare the efficacy of tofacitinib with betamethasone pulse therapy in achieving re-pigmentation in vitiligo patients. **Methods:** This quasi experimental study was conducted on 42 patients of vitiligo of either gender with ages between 12 and 65 years and had a history of vitiligo for over one year with a body surface area affected by vitiligo exceeding 5%, and a vitiligo area scoring index score of more than 10 were included in the study. Patients were divided into 2 equal groups using alternate assignments. Group A were treated with betamethasone pulse therapy of 4mg twice a week. Group B were treated with tofacitinib at a dose of 5 mg twice a day. **Results:** Optimal recovery (vitiligo area scoring index decrease ≥20% from baseline) was observed in 14 (66.7%) of the tofacitinib group compared to 6 (28.6%) in the betamethasone group, highlighting tofacitinib's superior efficacy in achieving significant vitiligo area scoring index reduction. Over three months, the BSA affected by vitiligo decreased in both groups, with a significantly greater reduction in Group B (tofacitinib) compared to Group A (betamethasone). **Conclusions:** It was concluded that tofacitinib may be more effective than betamethasone pulse therapy in reducing both the extent and severity of vitiligo.

INTRODUCTION

Vitiligo is an idiopathic skin condition that causes permanent, non-contagious loss of melanocytes resulting in depigmented patches on the skin. Affecting nearly 1% of people around the world, it has significant effects on quality of life from a cosmetic point of view and social stigma. The precise aetiopathogenesis of vitiligo is unknown, but it appears to be multifactorial with contributions from genetic, environmental and autoimmune aspects that ultimately result in dysregulation followed by apoptosis of the melanocyte [1, 2]. Several approaches to treating it are designed to halt disease progression or facilitate re-pigmentation, but no universally effective therapy is available. The pathogenesis of vitiligo involves IFN-γ production by CD8+ T cells, leading to CXCL9/10 expression by keratinocytes, which recruits additional CD8+ T cells, ultimately destroying melanocytes. Janus kinase (JAK) inhibitors, such as tofacitinib, target this pathway and show promise in managing vitiligo [3-5]. Recently developed JAK inhibitors (immune-modulating agents) introduce new options for treating vitiligo and have brought significant changes to its management. Humanitarian compassionate treatment with pulse therapy has been widely practiced for vitiligo using betamethasone, a highly potent corticosteroid, due to its strong anti-inflammatory and immunosuppressive effects which inhibit melanocyte destruction [6, 7]. Pulse therapy is characterized by the use of high doses in a short period, and mitigates adverse effects related to long-term administration of corticosteroids. A dose-pulse of betamethasone can achieve re-pigmentation in patients with vitiligo, but prolonged use may have side effects including skin atrophy, hyperglycemia and further

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susceptibility to infections [8]. Tofacitinib (JAK inhibitor) is a new alternative for the treatment of vitiligo. Tofacitinib is an inhibitor of the Janus kinase/signal transducers and activators of transcription (JAK-STAT) pathway that may provide targeted immunosuppression by inhibiting a key driver of immune response and inflammation, with fewer side effects compared to those associated with corticosteroids [9]. It is proven to stabilize vitiligo and induce re-pigmentation, particularly with concomitant phototherapy [10]. In contrast to corticosteroids, JAK inhibitors target cytokine signalling involved in autoimmune pathways and therefore would be expected to have an improved safety profile for long-term management [11]. Comparative studies on the efficacy of tofacitinib and betamethasone pulse therapy are limited, but some evidence suggests that JAK inhibitors could be a valuable alternative, particularly for patients experiencing adverse effects with corticosteroid-based therapies.

This study aimed to compare the efficacy of tofacitinib with betamethasone pulse therapy in achieving re-pigmentation in vitiligo patients.

METHODS

This quasi experimental study was conducted from March 2023 to August 2023 at the Skin Out Patient Department (OPD) of Liaquat University Hospital, Hyderabad, on 42 patients with vitiligo. Patients of either gender with ages between 12 and 65 years and had a history of vitiligo for over one year with a body surface area (BSA) affected by vitiligo exceeding 5%, and a Vitiligo Area Scoring Index (VASI) score of more than 10 were included in the study. Pregnant and lactating women and patients receiving chemotherapy or other immunosuppressive treatments were excluded from the study. The sample size was calculated via Open Epi Sample Size Calculator by taking the means of VASI in betamethasone treatment as 10.57 ± 4.03 at 3 months with that of tofacitinib as 7.08 ± 3.90 with 80% power of the study and 95% confidence interval [12]. The study was approved by the Ethical Review Committee of Liaquat University of Medical and Health Sciences, Jamshoro vide letter no. NO. LUMHS/REC/-189. The sampling technique was convenient and all the included patients were divided into 2 equal groups using alternate assignments. Informed written consent was taken from every participant. Group A was treated with betamethasone pulse therapy (betamethasone sodium phosphate) of 4mg twice a week orally. Group B were treated with tofacitinib given as tofacitinib citrate, at a dose of 5 mg twice a day orally. The total duration of treatment for both groups was 3 months. Both groups were advised to have daily sun exposure for 30 minutes in the morning. Participants underwent monthly follow-ups over three months from the date of enrollment. At each visit, the VASI and BSA scores were measured at baseline and the end of the first, second, and third months. A decrease in VASI of ≥10% at each visit from baseline was considered indicative of effective treatment, and a final VASI decrease of ≥20% from baseline was regarded as optimal recovery. SPSS version 22.0 was used for the analysis of data. Quantitative data were measured as mean + SD. Categorical data was measured using frequency and percentages. Independent T-test was used to measure the difference in mean in VASI and BSA between both groups.

RESULTS

Group A (betamethasone) and Group B (tofacitinib) had similar mean ages (35.6 ± 14.2 vs. 34.8 ± 13.6), as well as similar gender distributions, with 57% of participants in Group A and 52% in Group B being male. Baseline measures of disease extent, such as BSA (8.5 ± 2.1 vs. 8.7 ± 2.3) and VASI scores (12.4 ± 3.2 vs. 12.3 ± 3.1),were also closely matched (Table 1).

Table 1: Descriptive Statistics Regarding Study Participants

Variable	Group A (Betamethasone)	Group B (Tofacitinib)	p-value
Age (Mean ± SD)	35.6 ± 14.2	34.8 ± 13.6	0.85
Gender			
Male	12 (57%)	11 (52%)	-
Female	9 (43%)	10 (48%)	
Duration of Vitiligo (Years)	2.8 ± 1.4	3.1 ± 1.2	0.64
Baseline BSA (%)	8.5 ± 2.1	8.7 ± 2.3	0.85
Baseline VASI	12.4 ± 3.2	12.3 ± 3.1	0.92

Over three months, the Body Surface Area (BSA) affected by vitiligo decreased significantly more in the tofacitinib group (Group B) than in the betamethasone group (Group A). At baseline, the mean BSA was similar (p=0.84). By month one, reductions in BSA were 8.2% in Group A and 25.3% in Group B (p=0.47). By month two, Group B showed a significantly greater reduction (40.2% vs. 18.8%, p=0.2). This trend persisted at month three, with reductions of 46.0% in Group B and 25.9% in Group A (p=0.01), demonstrating the superior efficacy of tofacitinib (Table 2).

Table 2: Comparison of Body Surface Area (BSA) At Baseline and Over 3 Months

Follow Up	Group A (n=21) (Betamethasone BSA%) (Change in % from Baseline)	Group B (n=21) (Tofacitinib BSA%) (Change in % from Baseline)	p-value
Baseline	8.5 ± 2.1	8.7 ± 2.3	0.84
End of Month 1	7.8 ± 2.0 (8.2%)	6.5 ± 1.8 (25.3%)	0.47
End of Month 2	6.9 ± 1.9 (18.8%)	5.2 ± 1.7 (40.2%)	0.2
End of Month 3	6.3 ± 1.8 (25.9%)	4.7 ± 1.5 (46.0%)	0.01*

Over the three-month follow-up, the reduction in VASI percentage was consistently greater in Group B (tofacitinib) compared to Group A (betamethasone). At the end of month one, the VASI reduction in Group B was 27.6%, compared to 9.7% in Group A (p=0.32). By month two, the reductions were 43.1% and 21.8% for Groups B and A, respectively (p=0.71). At the end of month three, Group B achieved a significantly greater VASI reduction of 54.5%, compared to 33.9% in Group A (p<0.001), demonstrating the superior efficacy of tofacitinib over betamethasone in improving vitiligo. (p<0.001*)(Table 3).

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Table 3: Comparison of Vitiligo Area Scoring Index (VASI) At Baseline and Over 3 Months

Follow Up	Group A (n=21) Betamethasone VASI Change in % from Baseline	Group B (n=21) Tofacitinib VASI Change in % from Baseline	p-value
End of Month 1	9.7%	27.6%	0.32
End of Month 2	21.8%	43.1%	0.71
End of Month 3	33.9%	54.5%	< 0.001*

Optimal recovery among both groups was analyzed (Table 4).

Table 4: Optimal Recovery among Both Groups

Optimal Recovery	Group A (n=21) Betamethasone	Group B (n=21) Tofacitinib	p-value
Achieved	6 (28.6%)	14 (66.7%)	1.34
Not Achieved	15 (71.4%)	7 (33.3%)	

Optimal recovery (VASI decrease ≥20% from baseline) was observed in 14 (66.7%) of the tofacitinib group compared to 6 (28.6%) in the betamethasone group, highlighting tofacitinib's superior efficacy in achieving significant VASI reduction (Figure 1).

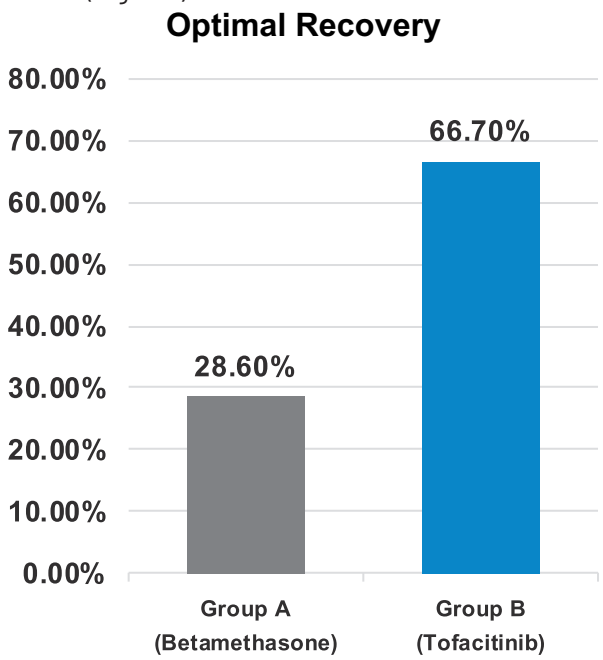

Figure 1 : Outcome in Terms of Optimal Recovery in Both Groups

DISCUSSION

In this study, we observed significantly faster and more consistent re-pigmentation in vitiligo patches treated with tofacitinib compared to betamethasone. The tofacitinib group demonstrated a greater reduction in VASI and BSA scores over three months, achieving the study's primary objective of optimal recovery. Jabbari et al., reported enhanced re-pigmentation with tofacitinib combined with sun exposure, particularly in sun-exposed areas [13]. However, our study did not measure the difference in recovery in sun-exposed areas vs un-exposed areas (which is one of the limitations of our study). Custurone et al., described a case of significant facial vitiligo that showed improvement after one-month treatment with tofacitinib 5 mg twice daily [14]. Various studies support the effectiveness of betamethasone therapy as a treatment of vitiligo [15, 16]. Likewise, in our study, betamethasone pulse therapy showed a modest reduction in both VASI and BSA scores, indicating its effectiveness in managing vitiligo. However, its efficacy was significantly lower compared to tofacitinib, particularly in achieving faster and greater re-pigmentation. While a case of a 17-year-old boy with stable non-segmental vitiligo showed promising results with topical tofacitinib [17]. Rapid and nearly complete facial re-pigmentation was also observed with oral tofacitinib and low-dose Narrowband-Ultra-Violet B (NB-UVB) [18]. Our study aligns with these findings, demonstrating fast and consistent re-pigmentation with oral tofacitinib combined with natural sun exposure [19]. Additionally, a case report by Kim et al., highlighted a 40-year-old female with comorbid rheumatoid arthritis and vitiligo who achieved significant re-pigmentation using tofacitinib without sun exposure [20]. However, in our study, tofacitinib showed significant efficacy in both sun-exposed and sun-protected areas, further supporting its utility as a robust therapeutic option. Overall, the results of this study add to the growing body of evidence supporting the use of tofacitinib in vitiligo treatment. However, future studies with longer follow-up periods and larger sample sizes are required to confirm the durability of re-pigmentation and assess outcomes following treatment discontinuation.

CONCLUSIONS

It was concluded that tofacitinib may be more effective than betamethasone in reducing both the extent and severity of vitiligo.

Authors Contribution

Conceptualization: HSM
Methodology: HSM, HBA, AM, MS, NM, BBK
Formal analysis: NM
Writing review and editing: HBA, AM

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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