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Comparison of Efficacy of Oral Tofacitinib (JAK Inhibitor) Combined with Narrow Band UVB Vs Alone Oral Tofacitinib in Patient with Vitiligo at Tertiary Care Hospital, Karachi

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ABSTRACT

Objective: compare the oral Tofacitinib added to NB-UVB phototherapy versus Tofacitinib monotherapy in patients with vitiligo, at a tertiary care teaching hospital in Karachi. **Methods:** After the ethical approval from the institutional review board, this open-label, non-randomized study is conducted at the Department of Dermatology, JPMC, Karachi from April 2024 to Sep 2024. Through non-probability consecutive sampling, 40 patients aged 18 above, both genders, diagnosed of vitiligo with stable lesions for half a year were included in the present study. The patients were divided into groups: Group B patients that received only oral Tofacitinib 5 mg twice a day (n=20) and Group A patients treated with oral Tofacitinib 5 mg twice a day in combination with NB-UVB phototherapy three time weekly (n=20). **Results:** At 12 weeks, the VASI score showed significant improvement in the Tofacitinib + NB-UVB group (36.8 ± 8.3) compared to the Tofacitinib alone group (54.15 ± 9.5, $p < 0.0001$). The percentage improvement in VASI was also significantly higher in the combination therapy group at 57.4 ± 9.7% versus 36.7 ± 9.9% in the monotherapy group ($p < 0.0001$). Furthermore, the efficacy outcome, defined as ≥51% improvement in re-pigmentation, was achieved in 15 patients (75%) in the Tofacitinib + NB-UVB group compared to only 1 patient (5%) in the Tofacitinib alone group, with a highly significant p-value of <0.0001. **Conclusion:** Oral tofacitinib complemented with NB-UVB phototherapy is more effective than Tofacitinib monotherapy in re-pigmentation in vitiligo patients.

INTRODUCTION

Vitiligo is a chronic disease of skin with acquired causes which is caused by the destruction of melanocytes in the skin thus resulting to blanched areas of skin (1). This condition impacts about 1 in 100 to 500 people worldwide, but there might be no preference with race or gender and age (2). As a highly visible disease, the illness affects the psychology and social aspect of patients' lives. However, vitiligo is still difficult to treat, mostly targeting to stop the deterioration of the disease and to repigment the affected skin (3).

Tofacitinib, a Janus kinase (JAK) inhibitor has been recently identified to be effective in the treatment of vitiligo because of suppression of interferon-gamma signaling which leads to melanocyte destruction (4). Oral JAK inhibitor tofacitinib has been effective in repigmentation, preferably in the face and upper limbs area (5). Several research works have shown that within 3-6

months of therapy up to 40-50 % of patient treated with oral Tofacitinib experienced a notable re-pigmentation. Though, the response is suboptimal and frequently requires more than one treatment to achieve the best outcome (6).

NB-UVB phototherapy is now a well-established form of therapy in vitiligo. It acts through promotion of melanocyte proliferation and migration as well as the inhibition of autoimmunity (7). Co administration with Tofacitinib has been evidence to augment the effect of NB-UVB on treatment outcomes. A combination therapy is shown to yield higher re-pigmentation values (≥50% improvement) as compared to Tofacitinib monotherapy, especially on chronic vitiligo skin areas (8).

A study conducted in the United states confirmed that 60-70% of patient who were treated by combined JAK inhibitors and NB-UVB saw significant re-pigmentation as compared to monotherapy, where only 30-40 percent of the patients saw the same new results (9). This makes a call for combination treatments that can easily overcome the barriers of treatment. Considering the promising result of this study, the aim of this work is to evaluate and compare the oral Tofacitinib added to NB-UVB phototherapy versus Tofacitinib monotherapy in patients with vitiligo, at a tertiary care teaching hospital in Karachi.

METHODOLOGY

After the ethical approval from the institutional review board, this open-label, non-randomized study is conducted at the Department of Dermatology, JPMC, KARACHI from april 2024 to sept 2024. Through non-probability consecutive sampling, 40 patients aged 18 above, both gender, diagnosed of vitiligo with stable lesions for half a year were included in the present study. The patients were divided into groups: Group B patients that received only oral Tofacitinib 5 mg twice a day (n=20) and Group A patients treated with oral Tofacitinib 5 mg twice a day in combination with NB-UVB phototherapy three time weekly (n=20). Participants with prior usage of topical treatments were subjected to a 2-week washout period, immunomodulating oral medication 4 weeks, laser and light therapies 8 weeks and biologic agents 12 weeks. Contraindicated conditions are pregnancy and breast feeding, active hepatitis B or C virus infection, HIV, or malignancy, serious liver, renal, or hematological disorders, active vitiligo therapy were excluded from the present study. Basic anthropometric data, gender, Age, BMI, family history, autoimmune comorbidities and duration of vitiligo were collected at baseline. At the initial visit, participants underwent blood tests for CBC, LFTs, RFTs, hepatitis B and C, HIV and IGRA. The overall skin depigmentation was quantified at the baseline and week 12, via the Vitiligo Area Scoring Index (VASI). Pre and post treatment photographs were taken for standardization in order to compare the before and after results. Re-pigmentation was graded between a from 0 to 4; any grade of 3 or more (above 50% of re-pigmentation) was define efficacy. Statistical analysis was done using computer aided software known as Statistical Package for Social Sciences (SPSS) version 26. Age, BMI, and vitiligo duration were presented as mean ± SD or median (IQR) depending on their normality while gender and family history were presented as frequencies and proportions. Descriptive data of patients' outcome according to the treatment they received were analysed using the Chi-square test at 5% significance level.

RESULTS

In this study, the demographic variables, clinical variables, and treatment outcomes were compared between the two treatment groups: Tofacitinib + NB-UVB and Tofacitinib alone, each comprising 20 patients.

For the demographic variables, the mean age of patients in the Tofacitinib + NB-UVB group was 38.82 ± 12.6 years, while in the Tofacitinib alone group, it was 39.45 ± 11.2 years ($p = 0.544$), showing no significant difference between the groups. The gender distribution was identical in both groups, with 12 males (60%) and 8 females (40%) in each ($p = 1.0$). Similarly, the mean BMI was 26.7 ± 4.9 kg/m² in the Tofacitinib + NB-UVB group and 26.4 ± 4.4 kg/m² in the Tofacitinib alone group ($p = 0.144$), indicating no significant difference.

For the clinical variables, the mean duration of vitiligo was 33.5 ± 15.6 months in the Tofacitinib + NB-UVB group and 32.75 ± 12.2 months in the Tofacitinib alone group ($p = 0.323$), which was statistically non-significant. A positive family

history of vitiligo was reported in 14 patients (70%) in the Tofacitinib + NB-UVB group compared to 9 patients (45%) in the Tofacitinib alone group (p = 0.709). The presence of autoimmune comorbidities was higher in the Tofacitinib alone group at 10 patients (50%), compared to 7 patients (35%) in the Tofacitinib + NB-UVB group, with a statistically significant p-value of 0.03.

For the treatment variables, the baseline VASI scores were similar, with 86.8 ± 6.5 in the Tofacitinib + NB-UVB group and 85.7 ± 7.2 in the Tofacitinib alone group (p = 0.526). However, at 12 weeks, the VASI score showed significant improvement in the Tofacitinib + NB-UVB group (36.8 ± 8.3) compared to the Tofacitinib alone group (54.15 ± 9.5, p < 0.0001). The percentage improvement in VASI was also significantly higher in the combination therapy group at 57.4 ± 9.7% versus 36.7 ± 9.9% in the monotherapy group (p < 0.0001). Furthermore, the efficacy outcome, defined as ≥51% improvement in re-pigmentation, was achieved in 15 patients (75%) in the Tofacitinib + NB-UVB group compared to only 1 patient (5%) in the Tofacitinib alone group, with a highly significant p-value of <0.0001.

Table 1

Demographic Variables

Variables	Tofacitinib + NB-UVB (N=20)	Tofacitinib Alone (N=20)	P Value
Age (years)	38.82±12.6	39.45±11.2	0.544
Gender			
Male	12 (60%)	12 (60%)	1
Female	8 (40%)	8 (40%)	
BMI (kg.m2)	26.7±4.9	26.4±4.4	0.144

Table 2

Clinical variables

Variables	Tofacitinib + NB-UVB (N=20)	Tofacitinib alone (N=20)	P Value
Duration of Vitiligo (months)	33.5±15.6	32.75±12.2	0.323
Family History	14 (70%)	9 (45%)	0.709
Autoimmune Comorbidities	7 (35%)	10 (50%)	0.03

Table 3

Treatment variables

Variables	Tofacitinib + NB-UVB (N=20)	Tofacitinib alone (N=20)	P Value
Baseline VASI Score	86.8±6.5	85.7±7.2	0.526
VASI Score at 12 weeks	36.8±8.3	54.15±9.5	<0.0001
Improvement in VASI (%)	57.4±9.7	36.7±9.9	<0.0001
Efficacy Outcome	15 (75%)	1 (5%)	<0.0001

DISCUSSION

The results of this work show that vitiligo patient who receive combined treatment with oral Tofacitinib and NB-UVB has a better therapeutic outcome than the patient who were treated using only oral Tofacitinib. The demographic characteristics such as age, gender distribution and BMI score did not differ significantly between the two groups, when analyzing the treatment results there was a noticeable advantage of combination therapy.

The therapeutic outcome aimed for in this study was measured using the Vitiligo Area Scoring Index (VASI) and showed patients who were under combination treatment had greater re-pigmentation. After 12 weeks of therapy, the mean VASI scores exhibited improvement of 57.4%±9.7% in the combination group as compared to 36.7%±9.9% in the monotherapy group, p < 0.0001. In addition, there was a marked difference in re-pigmentation efficacy, with 75% of the patients in the Tofacitinib + NB-UVB group attaining an efficacy outcome of 51% or more, while only 5% of the Tofacitinib alone group. In line with these observations is growing evidence that immunosuppressive agents such as Janus kinase (JAK) inhibitors exemplified by Tofacitinib may have potential in suppressing immune-mediated melanocyte killing which, when combined with NB-UVB, can further augment melanocyte proliferation and migration thus encouraging re-pigmentation.

According to research conducted by Liu et al. (2017), Tofacitinib is a JAK1/3 inhibitor which lowers interferon-gamma (IFN-γ) signalling, which is fundamental in vitiligo. Thus, although Tofacitinib independently showed modest therapeutic effects, its use combined with phototherapy helped to enhance the density of successfully treated lesions (10). Likewise, Song et al. (2022) showed the effectiveness of adding Tofacitinib in treating vitiligo patients with unresponsive VASI scores to phototherapy. The synergistic effect comes because NB-UVB directly act on melanocytes and interacts with immune system modulating T regulatory cells in combination with Tofacitinib, which helps to suppress cytokine based depigmentation (8).

In this research, the autoimmune comorbidity was significantly higher in Tofacitinib

monotherapy group (50%) compared to the combination group (35%). This raises an important consideration because autoimmune conditions increase the inflammatory process that may interfere with vitilgo and may not respond well to monotherapy. Concerning NB-UVB, its immunomodulatory effects may reverse such processes contrary to what was observed in the combination first group.

The finding of the present study corroborates the studies carried out by Wang et al. (2024), which identified the Tofacitinib as a limited monotherapy intervention for significant re-pigmentation. Their work implied that though JAK inhibitors arrest vitiligo progression, adding phototherapy results in superior and long-lasting response (11). In a very recent meta-analysis, Zhou et al. (2023) have stressed that NB-UVB together with systemic immunomodulators was more effective compared to monotherapies for achieving ≥50 % improvement in terms of VASI (12).

Nevertheless, this study has clear limitations in terms of analysing the clinical response dependent on the family history of the patient. Yet, the positive history of the familial cases of vitiligo in the participants of the combination group was 70%, whereas in the monotherapy group it was 45% and it seems that this factor does not have the effect on the therapeutic outcome (p = 0.709). Further research should address this question of genetic predisposition and determinacy of patients' response to respective treatment.

But it was observed that the results of this research could only be taken for 12 weeks of the experiment and long term studies regarding efficacy and safety are scarce. In a like manner, the authors pointed out that the sample size was small and conducted on participants drawn from a single country at that, thus may be a cause for generalization bias. However, there were highly significant improvements of the VASI scores and re-pigmentation rates in the combination therapy group, which can also support the opinion, that Tofacitinib combined with NB-UVB is much more effective than monotherapy.

CONCLUSION

This study shows that oral Tofacitinib complemented with NB-UVB phototherapy is more effective than Tofacitinib monotherapy in re-pigmentation in vitiligo patients. The combination therapy demonstrated higher level of improvement in VASI scores, more patients reached the re-pigmentation of 51% or more. These findings articulate the advantages of using JAK inhibitors concurrently with phototherapy further endorsing the consideration of the latter as a superior treatment model for vitiligo.

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