Original Article

Efficacy and Safety Of Tofacitinib And Narrow-Band UVB In The Treatment Of Vitiligo

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Abstract

Background: Vitiligo is a common acquired disorder of pigmentation which is often emotionally ruinous for patients. At present, only few satisfying treatments modalities are available. The efficacy of daily oral tofacitinib combined with twice weekly narrow-band UVB in the treatment of vitiligo remain less elucidated. **Objective:** The study was conducted to see the safety and efficacy of combined treatment with oral tofacitinib and NB UVB in vitiligo. **Methods:** The prospective clinical trial was conducted on 75 patients of vitiligo, attended at the department of dermatology and venereology, combined military hospital (CMH), Dhaka after taking a formal ethical clearance from the ethical committee of armed forces medical institute. Each individual patient was treated with one tablet tofacitinib (5 mg) taken orally once daily at morning and narrow band ultra violet B (NB UVB) phototherapy twice weekly for 4 months. Photograph of each lesion was taken at every visit. Efficacy (color change) and side effects were assessed at week 4, 8 and 16. **Results:** Mean age of the subject was 36.43(±11.89) years with female predominance (M:F-0.70:1). Vitiligo was first present in lower limb (26.70%), face (18.70%), upper limb (13.30%), hand (13.30%), feet (12.0%), trunk (13.30%) and genital areas (2.7%). Of all, 35% cases had Fitzpatrick skin type IV, 42% cases had Fitzpatrick skin type V and 23% had Fitzpatrick skin type VI. Majority (62.70%) had excellent response, 28% had good response, 08% had moderate response and 1.30% had poor response. Common cold was the most (8%) common adverse effects followed by dryness, loss of appetite, yellow discoloration of eye, skin and urine and headache. **Conclusion:** Combined treatment of once daily oral tofacitinib and twice weekly NB UVB is excellent in two thirds of the cases of vitiligo with unremarkable side effects.

Keywords: Tofacitinib, Narrow band Ultraviolet B, Vitiligo.

Introduction:

Vitiligo is an acquired cutaneous depigmentation distinguished by loss of melanocytes from the epidermis affecting 0.1-4% of the world's population.[1] It is a psychologically devastating disease with a significant impact on the patient's quality of life.[1] Though there are multiple hypotheses regarding the etio-pathogenesis of vitiligo, most evidences support autoimmune, cytotoxic, oxidative stress and neuro-humoral mechanisms. Current treatment modalities attempt to address one or more of these possible etiologies.[2] Recent advances relate vitiligo as a T-helper (Th1)

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Email: shameem_101166@yahoo.com
Received: 12 June 2022 Accepted: 16 June 2022 Available Online: 30 July 2022

Cite this Article:
Khan MMI, Khan MAL, Chowdhury MAI, Chowdhury SN. Efficacy and Safety Of Tofacitinib And Narrow-Band UVB In The Treatment Of Vitiligo. J Ban Acad Dermatol. 2022; 02 (02): 67-71

Available at: www.jbadbd.com
An official publication of Bangladesh Academy of Dermatology (B.A.D.)

cell-mediated disease with excess IFN-γ and describe chemokines CXCL9 and CXCL10 responsible for depigmentation.[2]

Psoralen and ultraviolet A (PUVA) introduced in 1948, remained the mainstay in the treatment of vitiligo, until Westerhof and Nieweboer-Krobotova introduced narrow-band ultraviolet B (NB UVB) in 1997.[3] NB UVB has effectively replaced PUVA therapy due to its superior efficacy and better side-effect profile. Lately, targeted phototherapy (excimer laser), and helium-neon laser (low-level laser therapy), especially for localized vitiligo, have come into use.[3] Narrow-band UVB is considered the gold standard of treatment for vitiligo covering more than 20% of the body surface area. Narrow-band UVB uses the portion of the UVB spectrum from 311-312 nm. This region has been determined to help stimulate pigment cells to produce melanocytes in less time than it takes to burn the skin. Any kind of light therapy has a suppressive effect on the immune system, so it can possibly stop new areas from forming as well. The long term treatment with NB UVB is safe. It has the least carcinogenic effect in all skin types.[4] Side effect of NB UVB is mainly phototoxicity.[4] It is proposed that the treatment of vitiligo should be a two-step process where the first part involves suppressing the immune system, followed by stimulation of the melanocytes to repigment the affected areas. It is emphasized the importance of combined treatment of light therapy with JAK-inhibitors in the treatment of vitiligo.5The current study was aimed to investigate the efficacy and safety of tofacitinib and NB UVB therapy in the treatment of long standing vitiligo.

Materials and methods:

It was a prospective clinical trial to see the safety and efficacy of once daily oral tofacitinib 5 mg tablet along with twice weekly NBUVB phototherapy in vitiligo. The study was conducted among adult patients with vitiligo who attended at the dermatology and venereology, combined military hospital, Dhaka. Sampling method was consecutive sampling and sample size was 75. Patients of 18 years or older, diagnosed case of vitiligo, Fitzpatrick skin type IV-VI and in good general health were enrolled. Before commencement of the study, formal ethical approval was taken from Ethical review committee (ERC) of armed forces medical institute and informed written consent was taken from each patient.

After selecting a patient detail history including demographic profile, drug history, occupation and comorbid conditions were taken. Thorough physical examination and Wood's light examination were done to confirm the diagnosis and relevant laboratory tests were done according to history and physical examination. All collected data were checked and rechecked for omissions, inconsistencies and improbabilities, data were analyzed by SPSS version 21 (Statistical Package for the Social Sciences).

Each enrolled patient was treated with tab tofacitinib 5 mg daily along with twice weekly phototherapy with NB UVB for 4 months. Patients were followed up after 4 weeks of initial assessment, then after 8 weeks and finally at 16 weeks. Photograph of each target vitiliginous patch was taken at baseline and at each visit. Response of the treatment was assessed by the patient's remark and measuring the change of size and color of the target lesions at every visit. Efficacy was measured by percentage of repigmentation of target lesions which was graded into five stages as no response (1 to 25% improvement), moderate response (26 to 50% improvement), good response (51 to 75% improvement), and excellent response (76 to 100% improvement). In every visit blood CBC, liver function test, renal function test, fasting blood sugar and urine routine examination was done.

Result:

Total 75 patients were included into the study. The mean age of the patients was 36.43(±11.89) years. Maximum 33.30% cases were in 18-30 years age group, 29.30% were in 31-40 years age group, 22.70% were in 41-50 years age group, 9.30% were in 51-60 years age group and 5.30% were in >60 years age group.

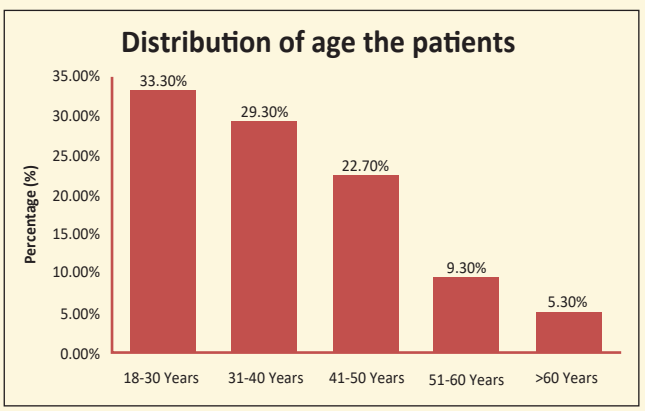

Figure-1: Distribution of age of the patients (n=75).

Among the study cases 41% were male and 59% female. Male female ratio was 0.70:1.

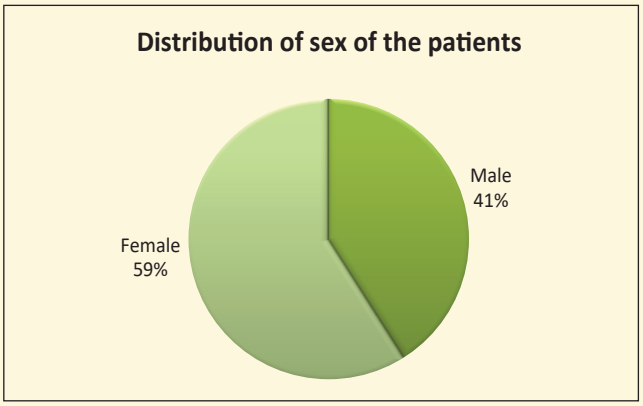

Figure-2: Distribution of sex of the patients (n=75).

Among the study cases vitiligo was first present in lower limb, face, upper limb, hand, feet, trunk and genital areas in 26.70%, 18.70%, 13.30%, 13.30, 12%, 13.30% and 2.70% cases respectively.

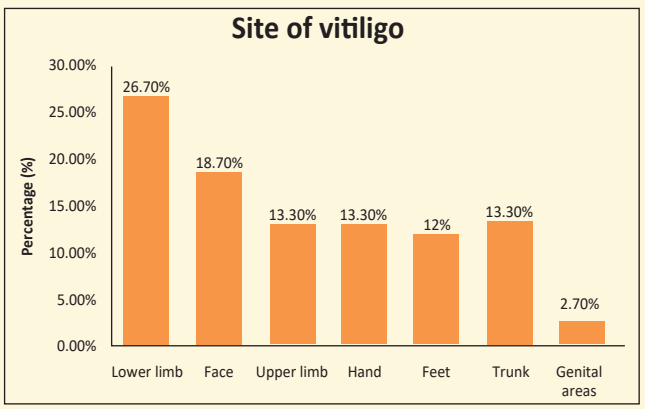

Figure-8: Site of vitiligo among the patients (n=75).

Among the study cases in 68% cases duration of vitiligo was between 1-5 years, in 22.70% cases duration of vitiligo was >5 years and in 9.30% cases duration of vitiligo was <1 year.

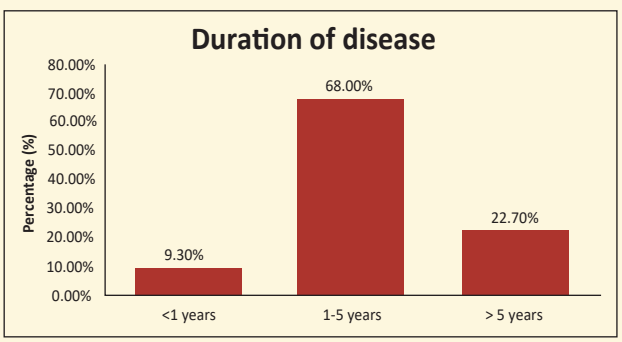

Figure-9: Duration of disease among the patients (n=75).

Among the study cases 35% cases had Fitzpatrick skin type IV, 42% cases had Fitzpatrick skin type V and 23% had Fitzpatrick skin type VI.

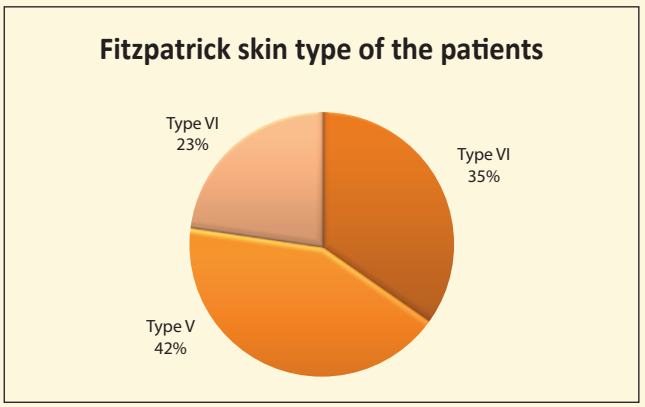

Figure-10: Distribution of different type of skin among the patients (n=75).

Among the study cases following treatment 62.70% had excellent response, 28% had good response, 08% had moderate response and 1.30% had poor response.

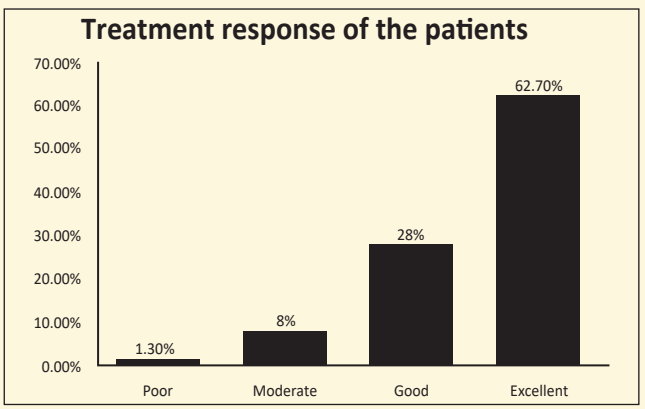

Figure-11: Treatment response among the patients (n=75).

For different sites of vitiligo response of treatment was statistically similar (p=0.138).

Table I: Treatment response according to site of vitiligo (n=75).

Site	Response			
	Poor	Moderate	Good	Excellent
	n(%)	n(%)	n(%)	n(%)
Face	00 (00)	01 (7.14)	01 (7.14)	12 (85.71)
Trunk	00 (00)	00 (00)	03 (30)	07 (70)
Upper limb	00 (00)	01 (10)	03 (30)	06 (60)
Lower limb	00 (00)	02 (0)	09 (45)	09 (45)
Hand	01 (10)	00 (00)	03 (30)	06 (60)
Feet	00 (00)	02 (22.22)	02	05 (55.56)
			(22.22)	
Genital areas	00 (00)	00 (00)	00 (00)	02 (100)
Total	01 (1.33)	06 (08)	21 (28)	47 (62.67)

Among the study cases erythema, pruritus, dryness, cold symptoms, tiredness, loss of appetite, yellow discoloration of eye, skin and urine, diarrhea, vomiting and headache was present in 04%, 5.30%, 6.70%, 08%, 5.30%, 6.70%, 6.70%, 04%, 5.30% and 6.70% cases.

Table 2: Side effects of treatment among the patients (n=75).

Side effects	Percentage (%)
Erythema	04
Pruritus	5.30
Dryness	6.70
Cold symptoms	08
Tiredness	5.30
Loss of appetite	6.70
Yellow discoloration of eye, skin and urine	6.70
Diarrhea	04
Vomiting	5.30
Headache	6.70

Discussion:

Vitiligo is a depigmenting disorder which causes disfigurement and severe disturbance in well being of affected cases. It is an autoimmune diseases that negatively affects persons quality of life and self-esteem.[1] It is the commonest depigmanting disorder, which affects 0.5-2% of the world population.[5-8] There are several options for treating vitiligo including topical creams (topical corticosteroids and calcineurin inhibitors), systemic medications (systemic corticosteroid, minocycline, statin, methotrexate, tofacitinib citrate etc), ultraviolet light therapy and monochromatic excimer light (MEL) therapy.[6,9] The main aim of this study is to find out the efficacy and safety of Tofacitinib and NB UVB in the treatment of vitiligo. The mean age of the cases was 36.43±11.89 years which is consistent with a study by Singh et al. where the mean age was 33.23±16.67 years.[7] Another study also found mean age of their vitiligo cases 36.70 years.[10] Among the study cases 59% were female and 41% were male with a male female ratio 0.70:1; it is consistent with Singh et al.. Sixteen percent had family history of vitiligo. Vora et al. found positive family history in 20.40% cases.[9]

Here lower limb is the commonest site of onset of vitiligo followed by face, upper limb, hands, feet, trunk and genital areas respectively. According to Vora et al. lower limb is the commonest site of vitiligo.10 Among the study cases, maximum 68% cases had duration of vitiligo between1-5 years, 22.70% cases had duration of vitiligo>5 years and in 9.30% cases had duration of vitiligo<1 years. This finding is almost similar to the findings of Patil et al..[11] In their series 5.5% had disease duration <1 years, 55.50% cases had disease duration 1-5 years and rest had disease duration >5 years.[11] In 2015, considering the hypothesis of common immunopathogenesis of alopecia areata and vitiligo Craiglow et al. reported the first case of vitiligo treated with oral tofacitinib where about 10% of body surface area was affected.[12] The 50 years lady had rapidly progressing vitiligo resistant to topical 0.1% triamcinolone ointment, 0.1% tacrolimus ointment and narrow band UVB; however experienced a rapid repigmentation with oral tofacitinib 5 mg taken once daily.[12] Another patient who was on treatment for rheumatoid arthritis and associated vitiligo for two years; reported partial repigmentation on her associated vitiligo patches on the hands, the face, the chest and the cervical areas

without sun exposure.[13] Narrow band UVB is an established treatment modality in vitiligo.[14] Liu et al. hypothesized that for good and sustained repigmentation sun exposure is needed along with JAK inhibitor.[6] Tofacitinib will cause immunosuppression and phototherapy will stimulate melanocytes.[6] A child with a treatment resistant segmental vitiligo on the face was treated with topical tofacitinib and narrow band UVB photoptherapy and was completely cured after 6 months of treatment.[15] Kim et al. reported rapid pigmentation of vitiligo patches of two patients treated with oral tofacitinib with narrow band UVB phototherapy. One case experienced nearly complete repigmentation after 3 months and another more than 75% color change after 6 months.[16] In the current study more than ninety percent patients had excellent to good response. Only few patients experienced minor adverse effects including erythema, pruritus, dryness, cold symptoms, tiredness, loss of appetite, yellow discoloration of eye, skin and urine, headache, diarrhea and vomiting.

Conclusion:

Combination of Tofacitinib along with NB UVB phototherapy is an effective and safe treatment modality for vitiligo. It may also cause symptomatic improvement, thus decreasing the psychological distress of patients due to cosmetic disfigurement caused by vitiligo. Side effect profile was unremarkable except cold symptoms. However, further RCT is recommended before drawing any conclusion.

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