Original Paper

Efficacy of Narrow-Band Ultra Violet B versus Narrow-Band Ultra Violet B with Topical Tacrolimus Ointment (0.1%) in the Treatment of Vitiligo

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Abstract

Introduction: Several treatment options e.g. topical corticosteroids, phototherapy like narrow-band ultra violet B (NB-UVB) and psoralen+ultra violet A (PUVA) etc are available for vitiligo. But none is so effective in single but combined one is more effective and superior.

Objective: To compare the efficacy of NB-UVB vs NB-UVB with topical Tacrolimus ointment (0.1%) in the treatment of Vitiligo.

Materials and Methods: This descriptive cross-sectional study was conducted in Combined Military Hospital, Dhaka from October 2015 to April 2016. Total 100 patients with vitiligo were divided into 2 groups of 50 patients. NB-UVB was given for 04 weeks to Group-A. In Group-B patients, topical Tacrolimus ointment (0.1%) twice daily was advised with simultaneous NB-UVB. The patients were followed-up at the baseline of the 4th, 8th and 16th week.

Results: Majority (46%) of the patients were from 25-34 years of age with a mean age of 27.4±12.6 years. Among all risk factors, Family history of Vitiligo was the most common risk factor and common skin type (Fitzpatrick) was Type IV (40%). At the end of 4th week, maximum cases of Group-B showed good response (score 3) with a mean score of 1.74. Whereas, maximum cases of Group-A showed poor response (score 1) with a mean score of 0.86. End of the 16th week, maximum cases of Group-B improved successfully. In the end, 20% patients of Group-A showed an excellent result; but it was 42% from Group-B.

Conclusion: It is revealed from this study that patients treated with a combination of NB-UVB with topical Tacrolimus ointment (0.1%) showed better treatment outcome, more effective and becomes a new mode of treatment.

Key-words: Vitiligo, Narrow-band ultra violet B (NB-UVB), Tacrolimus ointment (0.1%).

Introduction

Vitiligo is a dermatological problem which is affecting the social, psychological status and quality of life of the patients all over the world and is becoming a global burden day by day. In this condition, melanocyte cells die or are unable to perform physiological activity. It may arise from autoimmune, genetic, oxidative stress, neural, or viral causes. A variety of therapeutic options are available. But combined treatment with NB-UVB and topical 0.1% Tacrolimus ointment is more effective and superior to other treatment option, e.g. NB-UVB with placebo control[1]. Tacrolimus ointment is commonly prescribed medication in vitiligo. It acts mainly by prevention of T-cell and pro-inflammatory cytokines in vitiligo. Therapeutic success rate is increased when other treatment modalities, e.g. NB-UVB micro-phototherapy, helium-neon laser or narrow-band excimer laser are combinedly used with Tacrolimus[2].

On genetic hypothesis, TYR gene was proposed to be the responsible factor. Tyrosinase protein is not associated with the immune system but is an enzyme of the melanocyte that catalyzes melanin biosynthesis, and a major autoantigen in generalized vitiligo. Among the environmental risk factors sunburns, irritation, radiation exposures are proposed to be important factors. Common autoimmune and inflammatory diseases include- type 1 diabetes mellitus, psoriasis, rheumatoid arthritis, Addison's disease, scleroderma, pernicious anemia, Hashimoto's thyroiditis, alopecia areata and systemic lupus erythematosus are associated with vitiligo[3].

A variety of therapeutic agents have been tried on vitiligo but none is uniformly effective. Application of steroids with a combination of ultraviolet light has been suggested as best treatment option[4]. The United Kingdom's National Health Service suggests that phototherapy can only be used if primary treatments are ineffective as there is risk of skin cancer[5]. Exposing the skin to light from UVB lamps is the common treatment option for vitiligo. Ultraviolet light

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broadband and narrowband is used in this technique[6,7]. Studies suggest that combination therapy with UVB phototherapy and other topical treatments improve clinical outcome, repigmentation. Tacrolimus is a very effective agent for treatment of any form of dermatitis when compared with steroids it has several benefits.

Tacrolimus prevents the release of cytokines, inflammatory mediators in mast cells by degranulation. Lotti T et al found in his study that Tacrolimus is an effective pharmacological agent where 61% of patients showed more than 75% repigmentation when treated with Tacrolimus alone[9].

Materials and Methods

A descriptive cross-sectional study was conducted in the outpatient department of Dermatology and Venereology, Combined Military Hospital, Dhaka from October 2015 to April 2016. A total of 100 patients diagnosed with vitiligo having criteria of well circumscribed milky white cutaneous macules and patches by Wood's lamp with Fitzpatrick skin type IV-VI were enrolled for the study. Simple random sampling method was applied to sampling population. Patients with any contraindication to phototherapy like skin cancer or pre-malignant skin conditions, photoinduced or photo aggravated dermatoses like SLE, Photodermatitis, etc. and photosensitivity or allergy to Tacrolimus ointment were excluded from the study. Patients were allocated into two groups (Group-A and Group-B). After approval from the hospital ethical committee, the informed consent of the selected patients was obtained. Patients in treatment Group-A was given Narrowband UVB (NB-UVB) and those in Group-B was given Narrowband UVB (NB-UVB) with topical Tacrolimus ointment (0.1%) twice daily for vitiligo patches over the affected area. Response to treatment was measured as percentage of repigmentation and was calculated at 4th, 8th and 16th week. On initial visit, the total vitiliginous area was measured in centimeters. Calculated value (cm) was considered as 100% hypothetically for respective patients and this initial depigmentation values in percentage was referred to as baseline depigmentation. On subsequent visits, the percentage of depigmentation was reassessed and calculated by this formula: % depigmentation =Present depigmentation÷Baseline depigmentationx100. Then improvement or repigmentation was calculated by 100-% depigmentation. The results were scored as-

- No response: dermatological symptoms remain unchanged (0% improvement or no repigmentation).
- Poor response: dermatological symptoms slightly improved (1-25% improvement or repigmentation).
- Moderate response: dermatological symptoms improved (26-50% repigmentation).
- Good response: dermatological symptoms markedly improved (51-75% repigmentation).
- Excellent response: dermatological symptoms mostly disappeared (76-100% repigmentation). On each follow-up day, naked eye skin examination and photographic evaluation were done to see improvement.

The data were analyzed using SPSS and MS Excel.

Results

No significant difference in age was observed between two groups. While studying the distribution of cases by age it was found that majority of the patients i.e. 46% were between 25-34 years of age, 39% were between 14-24 years of age. Mean age was found to be 27.4±12.6 years (Table-I).

Table-I: Distribution of patients by treatment group and age(n=100)

Age (years)	No of patients		%
	Group-A (n=50)	Group-B (n=50)	
14-24	19(38%)	20(40%)	39.0
25-34	25(50%)	21(42%)	46.0
35-44	5(10%)	8(16%)	13.0
45-54	0(0%)	1(2%)	1.0
>54	1(2%)	0(0%)	1.0
Mean ± S.D.	27.4±12.6		

Table-II: Distribution of patients by the duration of symptoms (n=100)

Duration	No of patients	%
1-2 years	29	8.0
3-4 years	56	56.0
>5 years	15	15.0
Total	**100**	**100**

Duration of symptoms ranged from 5 months to maximum 7 years. Out of 100 cases, the majority of cases (56%) attended hospital with the history of vitiligo for 3-4 years duration (Table-II). Common Skin type (Fitzpatrick) was IV (40%), followed by type-V (31%) and type-VI (29%) (Figure-1). Among common risk factors, family history of vitiligo was the most common risk factor present in 29% cases followed by smoking 26% and obesity 19%.

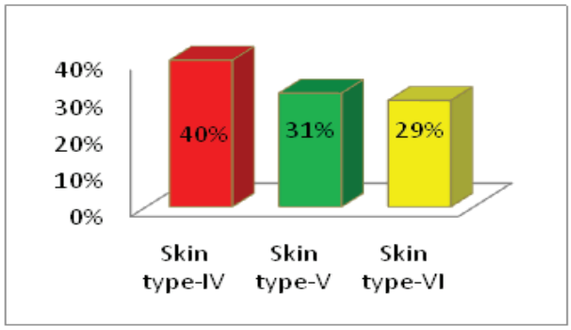

Fig-1: Distribution of patients according to skin type (Fitzpatrick) (n=100)

Follow up and assessment was done in three sessions. At the end of 4th week, maximum cases of Group-B showed good response (score 3) to poor response (score 1) with their current treatment; mean score was 1.74. On the other hand, maximum cases of Group-A showed poor response (score 1) to no response (score 0) with a mean score of 0.86. At the end of 16th week, comparatively maximum cases of Group-B improved successfully (almost normal skin to slight depigmentation). Among both groups, 20% cases and 42% cases showed excellent results in Group-A and Group-B respectively; mean score of two groups being 2.56 and 3.22 respectively (Table-III).

The present study suggested that patients of Group-B who were treated with a combination of NB-UVB with topical Tacrolimus ointment (0.1%) showed excellent treatment outcome than Group-A who were treated with NB-UVB alone. In this study, score range was from 3.22 to 0.86 (normal score range is 0 to 4). Line graph demonstrated that upward direction of the curve implied gradual improvement of vitiligo. After treatment with NB-UVB with topical Tacrolimus ointment (0.1%), repigmentation level was higher steadily in Group-B than Group-A who were treated with NB-UVB alone. So the effectiveness of NB-UVB with topical Tacrolimus ointment (0.1%) combination treatment is proven.

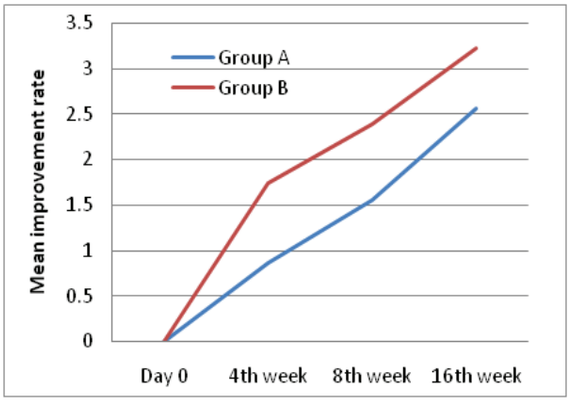

Fig-2: Comparison of efficacy between Group-A and Group-B patient (n=100)

Table-III: Evaluation of vitiliginous area and response to treatment during the course of treatment (n=100)

Duration	At 4th week			At 8th week			At 16th week		
	No of patients		%	No of patients		%	No of patients		%
Response	Gr-A	Gr-B		Gr-A	Gr-B		Gr-A	Gr-B	
No response	19	6	25.0	8	0	8.0	0	0	0
Poor response	21	13	34.0	19	12	31.0	7	0	0
Moderate response	8	19	27.0	10	14	24.0	18	10	28.0
Good response	2	12	14.0	13	17	30.0	15	19	34.0
Excellent response	0	0	0	0	7	7.0	10	21	31.0
Mean score	**0.86**	**1.74**		**1.56**	**2.38**		**2.56**	**3.22**	

Discussion

This study design raised a number of important methodological issues, including patient selection, sample size and the prospective identification of efficacy of therapy, all of which may have exerted a powerful influence on the results. The study showed that the frequency of vitiligo was highest in young age i.e. 25-34 years age group, mean age was found to be 27.4±12.6 years. The disease can appear at any age but more frequently seen in individuals of less than 20 years of age. It affects about 0.1%-2% of general population and familial incidence is about 30%[11]. Present study demonstrated that duration of symptoms ranged from 5 months to maximum 7 years. Out of 100 cases, the majority of cases (56%) attended the hospital with the history of vitiligo for 3-4 years. Bilal A reported that duration of disease was of < 3 years in 60% and 53.3% cases in Group-A and Group-B, respectively as observed in their study[1].

All of the present study findings correlate with the result of other studies. NB-UVB has shown a number of advantages in vitiligo patients in addition to its excellent, efficacy. These advantages include its extremely low side-effect profile particularly on the systemic front, its established use in children and adults and also considered safe in pregnant females[12]. Majid[13] in his study mentioned the effect of combining topical Tacrolimus and NB-UVB therapy in inducing repigmentation in vitiligo lesions and concluded that addition of topical Tacrolimus increases the extent of overall repigmentation achieved with NB-UVB therapy in vitiligo and also reduces the cumulative NB-UVB dose needed to achieve a therapeutic benefit in affected patients of vitiligo. Moreover, the use of Tacrolimus may be useful to prevent UVB induced erythema by inhibiting early-phase events of the inflammatory process[14-16].

Satyanarayan HS et al[17] reported that in their study seven (33%) patients with the NB-UVB and Tacrolimus combination treatment and 6(28%) with only the NB-UVB treatment, lesions had >75% repigmentation. Though repigmentation was slightly better in the lesions treated with a combination of NB-UVB and Tacrolimus. A recent study by Nordal et al found the combination of NB-UVB and Tacrolimus ointment (0.1%) to be more effective than UV treatment alone in patients with vitiligo[18]. However, NB-UVB was administered for a minimum 3 months and probably, more patients treated with NB-UVB alone arm would have achieved better re-pigmentation, if phototherapy was given for a longer duration. Other studies with smaller sample size have found better pigmentation in NB-UVB and Tacrolimus arm although the difference was not statistically significant[19,20].

The present study suggested that Group-B cases or patients treated with a combination of NB-UVB with topical Tacrolimus ointment (0.1%) showed excellent treatment outcome than Group-A. In this study, the score range is from 3.22 to 0.86 (normal scored range is 0 to 4). Line graph demonstrated that upward direction of the curve implied gradual improvement of vitiligo. When using NB-UVB with topical Tacrolimus ointment, repigmentation level was higher steadily than that of Group-A. So the effectiveness of NB-UVB with topical Tacrolimus ointment (0.1%) combination treatment is proven.

Another study by Fai et al[10] evaluated the efficacy and tolerability of combined treatment with NB-UVB and topical Tacrolimus in vitiligo. Their study demonstrated 42 years as a common age group; repigmentation was evident on more than 70% of lesions and clinical response (re-pigmentation more than 50%) was observed. A recent study by Nordal et al[19] assessed the additive effect of Tacrolimus ointment (0.1%) once daily in vitiligo patients treated with NB-UVB and concluded that the combination of NB-UVB and Tacrolimus ointment (0.1%) was more effective than NB-UVB treatment alone in patients with vitiligo.

Conclusion

The present study revealed that combined treatment with NB-UVB along with topical Tacrolimus ointment (0.1%) in vitiligo patients is more effective and becomes a new mode of treatment which will be beneficial to the patients of vitiligo. It may also cause quick symptomatic improvement thus decreasing the psychological stress of patients due to cosmetic disfigurement caused by vitiligo.

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