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Original Article

Comparative Study between Ultraviolet-B Phototherapy Alone and Ultraviolet-B Phototherapy with Topical Tacrolimus in the Treatment of Vitiligo

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ABSTRACT

Objective: To compare the combined effect of Ultraviolet-B plus Tacrolimus Vs Ultraviolet-B alone in the treatment of Vitiligo.
Study Design: Randomized-controlled trial (ClinicalTrials.gov: NCT05577637).
Place and Duration of Study: Department of Dermatology, Combined Military Hospital, Abbottabad Pakistan, May to Nov 2021.
Methodology: Sixty patients aged 20-60 years were enrolled. Patients in Group-A applied 0.03% topical Tacrolimus twice daily on body and 0.01% Tacrolimus twice daily on face with UVB phototherapy thrice weekly. In Group-B only UVB was given thrice weekly for depigmented patches at a dose of 0.021 j/cm^2 after calculating minimal erythema dose and it was incremented by 10% at every visit. The treatment efficacy was determined as percentage of re-pigmentation monthly for three months. By following up categorizing re-pigmentation as excellent (>75%) to poor (<25%).
Results: In Group-A mean age 36.36+9.75 years, and in Group-B mean age were 32.50+9.02 years. The two groups were evaluated in terms of pre-treatment clinical parameters there was insignificant relations between them (p>0.05). The majority 19(63.4%) of Group-A patients and 23(76.7%) Group-B patients had 1-10% depigmentation level and rest of patients had greater than 11%. While comparing the efficacy Group-A 17(56.7%) patients responded effectively as compared to 08(26.7%) patients in Group-B (p-value <0.05).
Conclusions: When compared to UVB alone, the combined effect of UVB plus Tacrolimus 0.03% for body and 0.01% for face, was significantly greater than Tacrolimus alone.

Keywords: Phototherapy, Tacrolimus, Ultraviolet-B phototherapy, Vitiligo.

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INTRODUCTION

Vitiligo is a skin disorder that causes substantial social and psychological distress due to multiple patches of depigmentation.[1] It can happen at any age and appears to affect various parts of the body due to loss of melanin. While the certain reason of the disease remains unknown, it is stipulated that genetic components, autoimmunity, and an increased susceptibility of melanocytes to the damaging effects of toxic metabolites all contribute to its development.[2] It impacts 0.1%-2% of the general population, with a 30% familial prevalence rate.[3]

Vitiligo treatment still presents a challenge for dermatologists despite a variety of therapeutic modalities[4]. Topical steroids, Ultraviolet-B (UVB) phototherapy, and photochemotherapy i.e. Psoralen plus Ultraviolet-A (UVA) are traditional treatment options. Topical calcipotriol and excimer laser are also used. According to research, narrowband UVB (NB-UVB) is effective when used alone.[5]

Topical immunomodulators such as Tacrolimus is considered safe and efficacious for long-term treatments of vitiligo because they do not cause harmful effects accompanying with long-term use of topical corticosteroids.[6] However, one study shows that 61% of patients achieved greater 75% re-pigmentation when managed with Tacrolimus solely twice a day.4 Another study found that when Tacrolimus was combined with NB-UVB, 73% of patients experienced more than 50% repigmentation.[7]

Since this is a disease that can cause significant distress to the patient, and there is a dearth of studies on this topic, the aim of his research was to compare the treatment that might improve the symptoms of vitiligo patients.

METHODOLOGY

The randomized controlled trial was conducted at Dermatology Department of the Combined Military Hospital, Abbottabad Pakistan, from May to

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November 2021 after Ethical Review Board approval (CMHAtd-ETH-26-Derm-22) and RCT registration (Clinical Trials.gov: NCT05577637).

Inclusion Criteria: Patients of either gender diagnosed with vitiligo aged 20-60 years were included.

Exclusion Criteria: Pregnant as well as breastfeeding women having history of light sensitivity or photo-aggravated dermatoses, immunosuppressive drugs and disorders, steroid use, or a history of skin neoplasms were excluded.

The record of patient's registration number in hospital was ensured. Before being selected for the study, the subjects underwent a medical checkup, antibiotic medication, age, gender, and weight were all noted for analysis. Photos were taken for further clinical evaluation.

After getting informed consent, sixty patients aged 20 to 60 years were enrolled. Non-probability consecutive sampling technique was used. The sample size estimated with confidence interval 95%, 80% power of study and the expected cure rate of Tacrolimus with NB-UVB taken as 64% and NB-UVA alone as 25%. The calculated sample size was 52 with 26 each group however sample size of 60 was taken (30 in each group) to increase the validity of the study.[8]

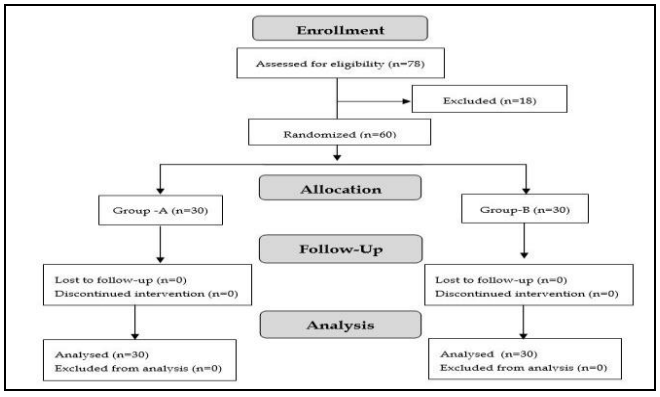

Figure-1: Patient Flow Diagram (n=60)

Randomization was done by lottery method. Patients in Group-A applied 0.03% topical Tacrolimus twice daily on body and 0.01% Tacrolimus twice daily on face with UVB phototherapy thrice weekly. In Group-B only NB UVB was given for depigmented patches after MED calculation by using homemade template with 8 apertures. The starting dose was initiated as 70% of calculated MED and successive doses were incremented by 10% at every visit. Patients were instructed to record any adverse events that occurred during therapy, such as burning, itching, erythema, and so on. When a prior therapy caused severe erythema, no phototherapy was administered in the following session, or the dose was reduced in accordance with the symptoms. Light erythema was deemed tolerable for therapy with the same dosage.

Initially analyzing the proportion of depigmentation, two separate observers assessed the patients monthly for three months during the research period on each follow-up visit. The data was grouped by calculating the mean score or detecting and classifying re-pigmentation as; Excellent (>75%), Good (50-75%), Moderate (25-49%), Poor (< 25%).

Demographic characteristics i.e., age, gender, etc., and frequency and percentages were calculated for qualitative variables by using Statistical Package for Social Science (SPSS) version SPSS 26. To determine pre-and post-treatment effectiveness evaluation, Chi-square test was applied taking a p-value ≤0.05 as significant.

RESULTS

Sixty (60) patients were included in both groups aged 20 to 60 years i.e., 30 in Group-A with mean age 36.36+9.75 years, and 30 in Group-B with mean age 32.50+9.02 years.

Table-I shows clinical baseline parameters of both treatment groups. Both groups were evaluated in terms of pre-treatment, and about clinical parameters there was insignificant relations between both groups (p>0.05). The age of the patients ranged from 20 to 60 years; however, the majority 47(78.3%) patients were less than 40 years of age, with 36(60%) patients having <3 years duration of Vitiligo. The majority of 43(71.7%) reported non-segmental type of vitiligo, while 23(38.3%) patients had Fitzpatrick skin type II (p-value >0.05). The baseline level of de-pigmentation in Group-A majority of 19(63.4%) patients while in Group-B 23 (76.7%) had 1-10% depigmentation level.

In Table-II while comparing the efficacy, in Group-A 17(56.7%) patients respond effectively as compared to 08(26.7%) patients in Group-B (p<0.05). Figure-2 represented the response at end of the 3rd month of treatment. The response was categorized as in Group-A 17(56.7%) patients but only 8(26.7%) patients in Group-B showed excellent response (p-value <0.05), in Group-A 10(33.3%) patients and 13(43.3%) patients of Group-B showed good response and moderate response was seen in 3(10%) patients of Group-A and 5(16.7%) patients of Group-B, hence no poor response was stated in Group-A but 4(13.3%)

Table-I: Clinical baseline Parameters of both Treatment Groups (n=60)

Characteristics		Group-A (n=30)	Group-B (n=30)	Total (n=60)	*p*-value
Age (years)	20-40	21(70%)	26(86.7%)	47(78.3%)	0.209*
	41-60	9(30%)	4(13.3%)	13(21.7%)	
	Mean+SD	36.36+9.75	32.50+9.02	-	
Gender	Male	11((36.7%)	12(40%)	23(38.3%)	0.791
	Female	19((63.3%)	18((60%)	37(61.7%)	
Duration	<3 years	16(53.3%)	20(66.7%)	36(60%)	0.292
	>3years	14(46.7%)	10(33.3%)	24(40%)	
Type of Vitiligo	Segmental	9(30%)	8(26.7%)	17(28.3%)	0.774
	Non-Segmental	21(7-%)	22(73.3%)	43(71.7%)	
FITZPATRICK Skin Type	Type I	2(6.7%)	2(6.7%)	04(6.7%)	0.425
	Type II	9(30%)	14(46.7%)	23(38.3%)	
	Type III	7(3.3%)	7(23.3%)	14(23.3%)	
	Type IV	7(3.3%)	2(6.7%)	9((15%)	
	Type V	5(16.7%)	5(16.7%)	10(16.7%)	
Depigmentation level at baseline	1-10%	19(63.4%)	23(76.7%)	42(70%)	0.518
	11-20%	6(20%)	5(16.7%)	11(18.3%)	
	21-30%	4(13.3%)	1(3.3%)	05(8.3%)	
	>30%	1(3.3%)	1(3.3%)	02(3.3%)	

**Fisher's Exact test*

Table-II: Comparison between Group-A and Group-B (n=60)

Cross Tabulation		Group-A	Group-B	Total	*p*-value
Efficacy	Yes	17(56.7%)	08(26.7%)	25(41.6%)	0.018
	No	13(43.3%	22(73.3%)	35(58.3%)	
	Total	30(100%)	30(100%)	60 (100%)	

patients of Group-B showed poor response. Figure- 3 shows pre-treatment manifestation and post-treatment effect in Group-A which is treated with UVB plus Tacrolimus. The Figure-3 displays before and after treatment photographic recorded data to analyses the effect of UVB therapy alone.

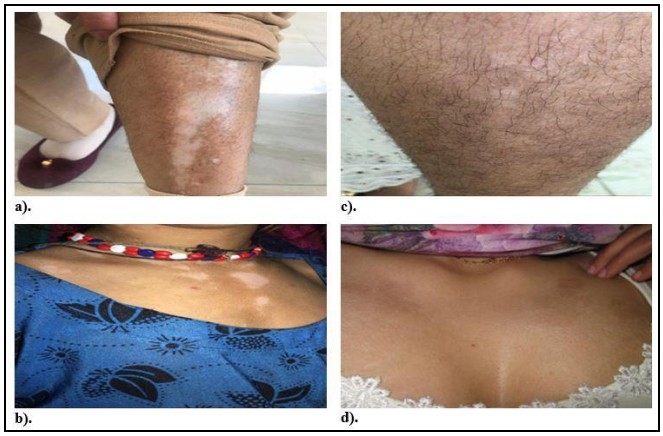

Figure-2: Group-A UVB plus Tacrolimus (a & b) Pre-treatment, (c & d) Post-treatment

DISCUSSION

The result of this study showed that combined effect of Tacrolimus plus UVB is higher as compared to the UVB alone *p*-value <0.05, which is similar to other

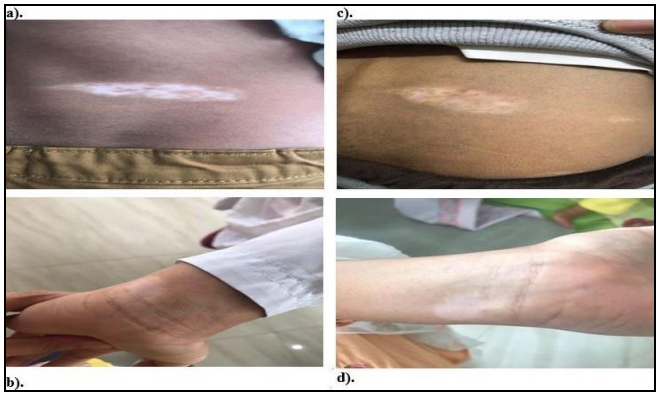

Figure-3: Group-B UVB alone Therapy (a & b) Pre-Treatment, (c & d) Post-Treatment

studies.[10-11] This study showed that the patients 17(56.7%) patients treated with Tacrolimus plus UVB in Group-A but only 8(26.7%) patients in Group-B showed excellent response (>75% re-pigmentation) which is similar to a study from the UK conducted by Utami *et al*.[12] Moreover, Tacrolimus may be beneficial in preventing UVB-induced erythema by inhibiting early-phase inflammatory events.[13,14]

In this study we also assessed that Tacrolimus cream twice daily had an additive effect combined with UVB while treating vitiligo patients and it

concluded that the combination therapy had greater efficacy than Ultraviolet alone in patients suffering from vitiligo. This is in line with multiple other studies.[15,16]

International studies, including a meta-analysis, concluded that age is the predictive factor that influenced the effect of Tacrolimus plus UVB, but in contrast in our study age didn't impact the combination of treatment. Nevertheless, demographic variables such as gender, duration, type of skin, type of vitiligo had also insignificant relationship with combination therapy which is similar to our study results.[7,17,18]

LIMITATION OF STUDY

The study was conducted over a relatively short period of time. Dependent on the chronic nature of the disease, large randomized multicenter trials with relatively long follow-ups are required to further confirm the results for assessing the efficacy of distinctive modes of treatment.

CONCLUSION

The combine effect of UVB plus Tacrolimus was considerably higher as compared to UVB alone in the treatment of vitiligo.

Conflict of Interest: None.

Authors Contribution

Following authors have made substantial contributions to the manuscript as under:

RR & MH: Conception, study design, drafting the manuscript, approval of the final version to be published.

BM & NA: Data acquisition, data analysis, data interpretation, critical review, approval of the final version to be published.

AS & KA: Study design, drafting the manuscript, critical review, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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