Comparison of Efficacy of Combination of Acitretin and Narrow Band Ultraviolet B versus Narrow Band Ultraviolet B Alone in the Treatment of Chronic Plaque Psoriasis

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Abstract

Objective: To compare the efficacy of combination of narrow band ultraviolet B (NBUVB) and Acitretin (ReUVB) versus NBUVB alone in the treatment of moderate to severe plaque psoriasis.

Method: This randomized clinical trial was conducted at the Department of Dermatology Services Hospital, Lahore from October 2020 to April 2021. After getting approval from Ethical Review Committee, 100 patients of moderate to severe plaque psoriasis were enrolled. They were divided into two groups of fifty patients each. Group A patients received both acitretin and NBUVB therapy while group B received NBUVB therapy alone for 8 weeks. PASI 50 was set as the efficacy end point. PASI scores and photographs taken before and after treatment were analysed.

Results: Mean age of patients was 34.99 ± 9.28 years. In group A, 46 (92%) patients achieved PASI 50 while in group B, 19 (38%) patients achieved PASI 50. Therefore, the efficacy of combination of acitretin and NBUVB was significantly higher compared to NBUVB alone. Statistically significant effect of age, gender, body mass index and duration of disease was found on efficacy.

Conclusion: Narrow band Ultraviolet-B therapy is a useful treatment modality in moderate to severe psoriasis. However, combining it with acitretin can significantly enhance its efficacy.

Keywords: Efficacy, Acitretin, Narrow band Ultraviolet-B, Chronic plaque psoriasis

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Introduction

Psoriasis is a common skin disorder caused by an aberrant immune system. Its prevalence varies from 2 to 3% in different parts of the world.[1] Due to the disability caused by the disease and cost of the therapeutic modalities used to cater them, there is significant impact on healthcare system.[2] Therefore, choice of therapeutic options as well as strategies to improve their efficacy is of utmost importance in management of this chronic debilitating disease.

The major pathogenetic factors leading to manifestations of psoriasis involve an aberrant innate and acquired immune system that leads to release of cytokines that damage target tissues including skin and joints. This leads to activation of nuclear factor-κB (NF-kB) signalling pathway and leads to differentiation of T helper cells toward Th1 and/or Th17 cells.[1] To counter this complicated cascade, various topical and systemic agents are in use worldwide depending on disease severity and patient factors. Among these, Phototherapy especially narrowband Ultraviolet-B (NBUVB) is very useful, since it lacks systemic toxicity and can be used in combination with other topical and systemic agents safely.[3] NBUVB (311nm) replaced the broadband UVB (290-320nm) due to its ability to target only the diseased skin and sparing the normal tissues.[4] The mechanism of action of UVB in clearing psoriatic plaques is still uncertain. However, immunomodulation caused by UVB has been postulated to induce death of diseased epidermal cells and T cells. This has been suggested

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by reduced amounts of cytokines and interleukins of Th-17 pathway after treatment with NBUVB.[5,6] The usual dosage of NBUVB is started with minimal initial dose that is 50% of the minimal erythema dose (MED) administered thrice a week.[7] Acitretin is a second-generation retinoid and active metabolite of etretinate.[8] It selectively agonises retinoic acid receptor (RAR) leading to suppression of inflammation and regulation of keratinocyte differentiation and proliferation.[9] It also suppresses vascular endothelial cells of dermal vessels and migration of neutrophils.[10]

Combination of acitretin and NBUVB (ReUVB) therapy has been shown to be superior in treating psoriasis than either modality alone.[11] The combination has been proposed to regulate release and expression of Matrix metalloproteinase 13(MMP13) which is a key modulator of inflammation and epidermal proliferation in psoriasis.[12] However, there is little clinical data on the efficacy of the combination of the two modalities in our part of the world. We conducted this study to evaluate the role of the two treatment options in our population as it may reduce the dose of either modality and its side effects and help in earlier and better management of patients.

Material and Method

After getting approval from Ethical Review Committee, this randomized clinical trial was carried out in the Department of Dermatology, Services Hospital Lahore from October 15, 2020 to April 15, 2021. Patients of both genders and ages between 18 and 50 years, having moderate to severe psoriasis (PASI > 10) diagnosed clinically, were included after taking written informed consent. Patients were selected by non-purposive consecutive sampling. Patients less than 18 years of age, pregnant or lactating females, females of child bearing age not willing for contraception, patients having renal, hepatic, lung or neurological disease, photosensitivity or photo aggravated diseases or cutaneous malignant or premalignant lesions were excluded. Patients who had received oral retinoids, phototherapy or other immunosuppressive agents in last two months were also excluded. Detailed history and thorough physical and cutaneous examination of all patients was done. Pretreatment Psoriasis Area and Severity Index (PASI) scores were calculated and photographs were taken. Relevant serological tests including renal and liver function tests and fasting lipid profiles were carried out to rule out contraindications to acitretin.

The patients were randomly divided by lottery method into two equal treatment groups as follows. Group A was given acitretin at a dose of 0.5mg/kg daily along with NBUVB thrice weekly using whole body exposure chamber of Daavlin Phototherapy Unit, fitted with 12 Philips 100 W TL-01 lamps (FDA approved device) for eight weeks. Minimal erythema dose (MED) was tested on upper back of every patient before starting treatment. Group B was treated with NBUVB alone using the same protocol for eight weeks. Post treatment assessment was done at the end of eighth week, PASI scores were calculated and photographs were taken. Demographic and clinical data was recorded on a predesigned proforma. Efficacy was defined as achievement of PASI 50 i.e. at least 50% reduction in PASI score after treatment.

Data was entered and analysed using IBM Corp. Released 2020. IBM SPSS Statistics for Windows, Version 27.0. Armonk, NY: IBM Corp. Numerical variables like age, body mass index (BMI), baseline and post treatment PASI scores were presented as mean±standard deviation. Qualitative variables like gender and efficacy were presented as frequencies and percentages. Data was stratified for age, gender, duration of disease and BMI to evaluate the role of effect modifiers. Post stratification Chi-square test was applied to check the significance with p-value≤0.05 as significant.

Results

This randomized therapeutic trial was carried out with the aim of comparing efficacy of combined treatment with acitretin and NBUVB versus NBUVB alone. Total 100 patients were enrolled; fifty each were allocated randomly to each treatment group. The mean age of all the patients was 34.99 ± 9.28 years, while the mean ages in group A (oral acitretin and UVB therapy) and group B (NBUVB therapy) were 34.72±9.20 years and 35.26±9.45 years respectively. In group A, 50% patients (25) were males and 50% were females. In group B, 21 patients (42%) were males and 29 (58%) were females. The mean BMI in group A was 30.62 ±4.05 and in group B was 30.26±4.71. The mean PASI score at baseline in group A was 42.14±13.18 and in Group B was 39.64±11.66. At the end of 8th week the mean PASI score in group A was 14.84 ± 8.86 and in group B was 23.38 ±11.38. In group A, 46(92%) patients achieved PASI 50 and in group B, it was achieved in 19(38%) of the cases, this difference was statistically significant (p-value≤0.001). It is evident that combination of acitretin and UVB led to significantly better disease

clearance than UVB alone (Table 1, Fig 1). Data stratification indicated that efficacy was also affected by age, gender, BMI and duration of disease since p-values were either significant (≤0.05) or highly significant (≤0.001).

Table 1: *Demographic Data of Patients*

			No. of Patients (n = 194)	
			n	%
Gender	Group A	Male	25	50
		Female	25	50
	Group B	Male	29	58
		Female	21	42
Age	Group A	18–34 years	22	44
		35-50 years	28	56
	Group B	18–34 years	21	42
		35-50 years	29	58
Body mass index	Group A	Obese	15	30
		Non-obese	35	70
	Group B	Obese	18	36
		Non-obese	32	64
Duration of disease	Group A	< 2 years	34	68
		≥2 years	16	32
	Group B	< 2 years	33	66
		⩾2 years	17	34

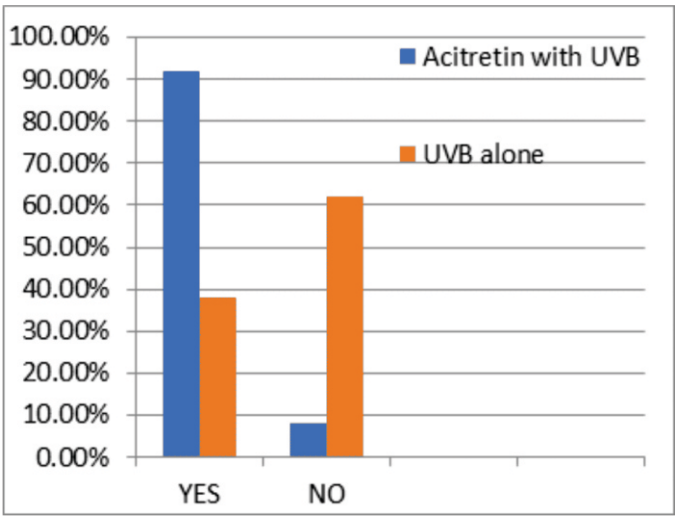

Fig-1: *Comparison of Efficacy between Treatment Groups*

Discussion

Due to the chronicity and significant psychosocial distress associated with psoriasis,[13] many treatment modalities have been used and developed over time for effective and timely cure of the disease. Phototherapy is a cost effective and relatively safe option among them. However, due to the potential theoretical risk of

Table 2: *Comparison of Efficacy between Treatment Groups*

Demographic parameter		Efficacy (PASI 50 Achieved)	Groups		Total	Chi-square	p-value
			Group-A (Acitretin plus UVB)	Group-B (UVB)			
Overall Efficacy		Yes	46(92%)	19(38%)	65(65%)	32.044	<0.001
		No	4(8%)	31(62%)	35(35%)		
Age (years)	18-34	Yes	18(18%)	5(23.8%)	23(23%)	14.532	<0.001
		No	4(18.2%)	16(76.2%)	20(20%)		
	35-50	Yes	28(100%)	14(48.3%)	42(42%)	19.655	<0.001
		No	0(0%)	15(51.7%)	15(15%)		
Gender	Male	Yes	25(100%)	8(38.1%)	33(33%)	21.573	<0.001
		No	0(0%)	13(61.9%)	13(13%)		
	Female	Yes	21(84%)	11(37.9%)	32(32%)	11.803	0.001
		No	4(16%)	18(62.1%)	22(22%)		
Body Mass Index	Obese	Yes	12(80%)	7(38.9%)	19(19%)	5.661	0.017
		No	3(20%)	11(61.1%)	14(14%)		
	Non-obese	Yes	34(97.1%)	12(37.5%)	46(46%)	27.633	<0.001
		No	1(2.9%)	20(62.5%)	21(21%)		
Duration of disease	< 2 years	Yes	33(97.1%)	12(36.4%)	45(45%)	27.973	<0.001
		No	1(2.9%)	21(63.6%)	22(22%)		
	⩾2 years	Yes	13(81.2%)	7(41.2%)	20(20%)	5.544	0.019
		No	3(18.8%)	10(58.8%)	13(13%)		

P-value ⩽0.05=significant

developing skin cancer associated with it,[14] patient compliance may be reduced. Combining it with retinoids, may reduce this risk because of tumour suppressive effects of retinoids.[15]

We found that significantly higher proportion of patients in the combination (ReUVB) group achieved efficacy end point (92%) compared to patients getting UVB alone (38%). Similar results were documented by Saeed et al in Chinese population who reported efficacy in 82.5% patients treated with ReUVB versus 55% patients treated with UVB alone.[16] They reported 80 to 100% improvement in clinical disease. Mean age of their patients was similar to our patients. However, they didn't find any significant effect of age or gender on efficacy. This can be attributed to different ethnicities of the study populations.

Iest et al disease clearance in 89% patients following ReUVB therapy compared to 62.5% patients treated with UVB alone.[17] Spuls et al reported more than 75% clearance in 72.5% patients after ReUVB in American patients.[18] Ruzicka et al compared the efficacy of ReUVB versus placebo and UVB in Wst Germany. They found a reduction in PASI of 79% in ReUVB group versus 35% in patients receiving placebo and UVB. This efficacy was achieved with significantly lower dose of UVB.[19] Therefore, the combination therapy may help in dose reduction of both treatments leading to a better safety profile of both modalities.

Kampitak et al also reported marked improvement in the ReUVB combination group in their study in Thailand.[11] Lebwohl also highlighted better efficacy of combination of acitretin and UVB along with reduction in doses and duration of both treatment modalities.[20]

We found combination of acitretin and UVB therapy more effective than UVB alone in management of moderate to severe psoriasis. However, the patients' compliance to the treatment might be hampered because of frequent visits to hospital for phototherapy, which might weaken his/her confidence in the therapy and the treating dermatologist. This can be countered by using home-based phototherapy devices which have given promising results in many studies.[2]

Conclusion

The combination of acitretin and NBUVB has many advantages including better and faster improvement in clinical disease achieved with lower dosage of both treatment options. This leads to better safety profile and more compliance. Hospital-based phototherapy may lead to reduced compliance especially for patients who live far from the source. They may benefit from home-based phototherapy devices. Combination therapy may also benefit those in whom other treatment options like biologics or methotrexate are contraindicated. Better and faster disease clearance with the combination therapy may increase patient compliance, satisfaction and adherence to treatment, which is inevitable in treating diseases like psoriasis.

Conflict of interest *None*

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Authors Contribution

FQ, SA: Conceptualization of Project
FQ: Data Collection
FQ: Literature Search
FQ: Statistical Analysis
SA, HT: Drafting, Revision
HT: Writing of Manuscript