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Student's Section

Narrowband UVB phototherapy and PUVA photochemotherapy in psoriasis vulgaris

Rakhee Varadarajan Nair^{*}, Sabeena Jayapalan

Department of Dermatology and Venereology, Government Medical College Thiruvananthapuram, Kerala 695011, India

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ABSTRACT

Introduction: Psoriasis is a common papulosquamous skin disease, which presents as a chronic, disfiguring, inflammatory condition of the skin and joints. Most patients require lifetime treatment. Different treatment modalities, both systemic and topical, are available for psoriasis, with varying degrees of effectiveness and safety. Phototherapy is a well-established treatment option for moderate to severe psoriasis. PUVA photochemotherapy is a time-tested treatment option. NBUVB is becoming an accepted modality of treatment. **Methods:** 30 psoriasis patients with PASI > 10, who attended a tertiary care centre, were randomized into two groups to receive PUVA photochemotherapy and NBUVB therapy, respectively to know whether NBUVB therapy was better than PUVA therapy. The outcome measures were PASI 75, number of treatment exposures, adverse effects and non-compliance. Non-parametric tests were used to analyze the data.

Results: 75% of NBUVB-treated and 50% of PUVA-treated patients had disease clearance. The total number of treatment exposures required for disease clearance was 15 for the NBUVB group and 18 for the PUVA group. 25% patients in the NBUVB group and 75% patients in the PUVA group developed the adverse effects and this prevented the patients from continuing the treatment.

Conclusion: NBUVB can be considered as the treatment of choice in this particular group of patients taking into account the higher disease clearance rate, lower number of treatment exposures and lesser adverse effects.

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Psoriasis is a common papulosquamous skin disease with prevalence ranging from 0.5% to 4.6%.^{1,2} The prevalence in India is estimated to be 0.7%.³ This disease is enormously variable in morphology, duration and extent. In majority of the patients, it presents as a chronic, disfiguring, inflammatory condition of the skin and joints. Environmental as well as

genetic factors play a critical role in its pathogenesis.^{4,5} Due to the highly variable disease course, most of the patients require lifetime intermittent treatment. Different treatment modalities are available for psoriasis with varying degrees of effectiveness and safety. Treatment is usually started with topical measures for mild disease. In moderate to severe cases,

^{*} Corresponding author. Tel.: +91 9496888959.

E-mail address: rakheennair8@yahoo.com (R.V. Nair).

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a combination of both topical and systemic treatment is used.⁶ Psoralen ultraviolet A (PUVA) photochemotherapy is an established systemic therapy for psoriasis and narrowband ultraviolet B (NBUVB) is now an accepted upcoming modality of treatment.^{7,8} NBUVB phototherapy has remarkable advantages over PUVA photochemotherapy in that there is no need of a systemically administered medicine, consequent lesser adverse effects, no requirement for post-treatment protection, able to administer in pregnant women, lactating mothers, children and in individuals with hepatic or renal dysfunctions and less chance for malignancy.^{9–11} Many studies have shown PUVA therapy to be more effective than NBUVB therapy. Most of the studies in the field of phototherapy and photochemotherapy have been conducted in I, II and III skin types. These skin types are prone to sunburn whereas types IV, V and VI burn less and tan more. Majority of the skin types in our part of the country belong to type IV, V and VI. Our patients belonged to the higher skin types and mostly work outdoors. We did this study to compare the efficacy, adverse effects, cumulative dose, number of treatment exposures for disease clearance and the compliance of patients to NBUVB phototherapy and PUVA photochemotherapy.

1. Methods

All clinically diagnosed psoriasis vulgaris patients who were 18 years or over, had a PASI score (psoriatic area severity index) of 10 or more and attending the outpatient wing of a tertiary care centre in South Kerala were recruited for the study. Among them, patients with history of photosensitivity, photosensitive disorders, on regular intake of photosensitizing drugs/immunosuppressant therapy, cutaneous malignancies, severe renal, hepatic or cardiovascular dysfunction, cataract/aphakic, pregnant women and lactating mothers, exposed to radiotherapy and on regular systemic treatment for psoriasis were excluded. Explanatory counselling of the therapy was given, and after getting informed consent, the patients were randomized into two groups by block randomization. A washout period of two weeks, with only antihistamines and emollients, was given to all patients. One group received NBUVB phototherapy and the other group PUVA photochemotherapy as per standard protocols. The irradiation cubicle used was V care's Therapy model Surya 440 ANB Opt.1. For NBUVB phototherapy, the initial NBUVB dose was 280 mJ/cm² followed by 10% increment per exposure. Treatment was given thrice weekly on alternate days. If the patient had minimal erythema, the same dose was continued. If there was asymptomatic well-defined erythema, the next exposure was postponed and the increment for each visit was only 5%. If the patient developed painful erythema with or without oedema and bullae, no treatment was given until recovery, and then the dose was reduced by 50% of initial dose, and thereafter, only 5% increment was given during each visit. After disease clearance, maintenance dose of twice weekly for 4 weeks, and thereafter, once weekly for 4 weeks was given and therapy was stopped. For PUVA photochemotherapy, 20 mg of 8-methoxypsoralen (8-MOP) was taken 2 h prior to irradiation. Starting dose of UVA was 2.0 J/cm² followed by increment of 0.5 J/cm² per treatment. The treatment was given

thrice weekly on alternate days. Persistent tenderness or erythema of uninvolved skin required temporary reduction or cessation of treatment. After disease clearance, maintenance dose of twice weekly for 4 weeks followed by once weekly for 4 weeks was given and therapy was stopped. The eyes were protected with UV-blocking goggles during therapy and also post-treatment for PUVA group. The genitalia were protected with thick underwear and uninvolved areas with appropriate clothing and broad-spectrum sunscreen. PASI was used as to measure the response to treatment.¹² Baseline PASI was calculated prior to the initiation of therapy and twice weekly till the achievement of PASI 75. The main outcome measure, PASI 75/disease clearance, was defined as 75% reduction from baseline PASI. The total dose required to achieve PASI 75 was the cumulative dose. The total number of treatment exposures required to achieve PASI 75 was also looked into. Asymptomatic minimal erythema was defined as the minimal perceptible erythema observed by the patient or the physician within 8–24 h after NBUVB exposure and within 48–72 h after PUVA exposure. Symptomatic erythema was defined as painful erythema with or without oedema, bullae or erosions. Erythema and scaling involving 90% or more of body surface area constituted erythroderma. Non-compliance meant missing at least one treatment exposure. The data were entered in Excel and were analyzed by appropriate software. Non-parametric tests were used due to the small sample size. A probability of value of ≤ 0.05 was considered significant.

2. Results

Thirty psoriatic patients were randomized into two treatment groups – the PUVA group (14 patients) and the NBUVB group (16 patients), and the groups were comparable in their baseline characteristics (Table 1).

In the NBUVB group, 12 (75%) patients achieved PASI 75. The median number of treatments to achieve PASI 75 was 15 (range 12–30). The median cumulative dose to achieve PASI 75 was 8390 mJ/cm² (range 6000–23,330). Asymptomatic minimal erythema was seen in 6 patients and they achieved PASI 75. The median dose at which asymptomatic minimal erythema occurred was 968 mJ/cm² (range 800–1065). Adverse effects like erythema and pruritus were seen in 4 (25%) patients and exfoliation in 2 (12.5) patients. The median dose and the median number of treatments at which symptomatic erythema and pruritus occurred were 732 mJ/cm² (410–1172) and 10.5 treatments (5–16). The median dose at which erythroderma developed was 453 mJ/cm² (range 410–496) and the median number of exposures was 6 (range 5–7). All the patients who developed adverse effects did not complete the treatment. 56.3% (9 patients) were non-compliant. The median number of treatments missed was 2. Comparing those patients who achieved PASI 75 and those who did not, the development of adverse effects was found to be a risk factor (p 0.001 by Fisher exact test). There was no significant correlation between the initial PASI and the total number of exposures required for achieving PASI 75 (Spearman's rank correlation 0.40, p – 0.197) and between the initial PASI and the cumulative dose to achieve PASI 75 (Spearman's rank correlation 0.32, p – 0.31).

Table 1 – Baseline characteristics of both groups.

Baseline features		NBUVB (16)	PUVA (14)	p value
Age (median)		41 (26–60)	45.5 (21–61)	0.82 ^a
Gender	Males	11 (68.8%)	10 (71.4%)	0.872
	Females	5 (31.2%)	4 (28.6%)	0.872
Occupation	Manual labourers	9 (56.25%)	10 (71.4%)	0.389
	Homemakers	4 (25%)	3 (21.4%)	0.818
	Others	3 (18.75%)	1 (7.2%)	0.352
Skin type	4	1 (6.25%)	0 (0)	0.342
	5	13 (81.25%)	11 (78.6%)	0.857
	6	2 (12.5%)	3 (21.4%)	0.515
Baseline PASI		28.2 (20.3–38.8)	30.6 (24–38.4)	0.36 ^a

PASI – psoriatic area severity index, PUVA – psoralen ultraviolet A, NBUVB – narrowband ultraviolet B.
^a Mann–Whitney U test.

In the PUVA group, of the 14 patients, 7 (50%) patients achieved PASI 75. The median number of treatments to achieve PASI 75 was 18 (range 12–30) and the median cumulative dose to achieve PASI 75 was 70.5 J/cm² (range 39–112.5). Asymptomatic minimal erythema was seen in 4 (28.6%) patients who achieved PASI 75. The median cumulative dose for asymptomatic minimal erythema was 3.25 J/cm² (range 3–4.5) and the median number of treatments was 3.5 (range 3–6). Adverse effects were seen in 7 (50%) patients and they could not complete treatment. All had erythema and pruritus. Only 3 had exfoliation. Out of 14 patients, 7 (50%) patients developed symptomatic erythema. The median dose and the median number of treatments at which symptomatic erythema, pruritus and erythroderma occurred were 3 J/cm² (2–4.5 J/cm²) and 3 treatments (1–6), respectively. 21.4% (3 patients) were non-compliant and missed one treatment each. The median number of treatments missed was one. Development of adverse effects was found to be a significant risk factor ($p = 0.001$, Fisher exact test) in preventing the patients from achieving PASI 75. There was no significant correlation between the initial PASI and the total number of exposures (Spearman's rank correlation 0.06, p value = 0.91) and between initial PASI and the cumulative dose to achieve PASI 75 (Spearman's rank correlation 0.18, p value = 0.7).

On comparing NBUVB and PUVA, there was no significant difference in the number of patients who achieved PASI 75, who developed asymptomatic erythema, adverse effects like erythema, pruritus, erythroderma and the number of patients who discontinued treatment (Table 2).

3. Discussion

Phototherapy is one of the treatment modalities in patients with moderate to severe psoriasis. PUVA therapy has been in vogue for several years. NBUVB therapy is one of the recent introductions into the phototherapy armamentarium. Several studies have shown PUVA therapy to be more effective than NBUVB. Few contradictory reports are also there. Since PUVA therapy has many adverse effects, including cutaneous malignancies, an alternative phototherapy with less adverse effects is always welcome. As NBUVB is a new introduction in our part of the state, we decided to conduct a comparative study of NBUVB and PUVA therapies.

Thirty patients were randomized into PUVA group and NBUVB group by block randomization with 14 patients in PUVA group and 16 patients in NBUVB group. Both the groups were

Table 2 – Comparison of NBUVB and PUVA therapies.

Outcome measures		NBUVB (16)	PUVA (14)	p value (Fisher exact test)
PASI 75	Achieved	12 (75%)	7 (50%)	0.257
	Not achieved	4 (25%)	7 (50%)	
Treatment exposures for PASI 75 (median)		15 (12–30)	18 (12–30)	0.61 ^a
Asymptomatic erythema	Present	6 (37.5%)	4 (28.6%)	0.709
	Absent	10 (62.5)	10 (71.4%)	
Symptomatic erythema	Present	4 (25%)	7 (50%)	0.257
	Absent	12 (75%)	7 (50%)	
Pruritus	Present	12 (25%)	7 (50%)	0.257
	Absent	4 (75%)	7 (50%)	
Erythroderma	Present	2 (12.5%)	4 (28.6%)	0.378
	Absent	14 (87.5%)	10 (71.4%)	
Discontinued treatment	Yes	4 (25%)	7 (50%)	0.257
	No	12 (75%)	(50%)	

PASI 75 – psoriatic area severity index, PUVA – psoralen ultraviolet A, NBUVB – narrowband ultraviolet B.
^a Mann–Whitney U test.

comparable in the baseline characteristics like age, gender, occupation and baseline PASI. The median age of the patients of both groups (41 and 45.5) was comparable to the age group in a randomized double blind trial (40 and 44).¹¹ As most of the similar studies were conducted in the western population, majority of the skin types ranged from 1 to 4, contrary to our study where the major skin type was 5.^{9–11,13}

PASI 75 was achieved by 75% in the NBUVB group and 50% in PUVA group ($p = 0.257$), showing similar efficacy in both the groups. Similar efficacy was also seen in a study where the efficacy was calculated after a maximum number of 18 exposures.¹⁰ In other studies, the clearance rate was more with PUVA (83% and 84%) than with NBUVB (60% and 65%).^{9,11} The reports of better efficacy of PUVA could be due to the 8-MOP dosage (0.6 mg/kg) instead of our fixed dosage (20 mg 8-MOP). Thrice-weekly NBUVB in our study compared to twice-weekly in other studies could explain the observed higher clearance in NBUVB group.

In the NBUVB group, the median cumulative dose to achieve PASI 75 was 8390 mJ/cm² while in the PUVA group it was 70.5 J/cm². The median cumulative dose for clearance of psoriasis was 35,000 mJ/cm² in NBUVB group and 70.1 J/cm² in the PUVA group in one study.⁹ The reported higher cumulative dose of NBUVB may be due to the twice-weekly schedule, leading to more treatment exposures for clearance. In another study, the median cumulative dose to achieve clearance in the NBUVB group was 12,700 mJ/cm² and in the PUVA group was 40.1 J/cm². The low cumulative dose of NBUVB and PUVA may be because the study was an intra-individual half-body comparison and the endpoint was an improvement in any one side compared to the other and the median baseline PASI (16) was low.¹⁰ In the above study, there was a correlation between baseline PASI and cumulative dose in the PUVA group contrary to our finding.

The median number of treatment exposures to achieve PASI 75 was 15 in the NBUVB group and 18 in the PUVA group. For other studies, median number of treatment exposures were 15, 25, 25.3, 28.5 in the NBUVB group and 15, 19, 16.7, 17 in the PUVA group.^{9–11} This difference may be due to our thrice-weekly NBUVB schedule instead of twice-weekly schedule, which resulted in faster clearance.

Asymptomatic minimal erythema was observed in 37.5% in the NBUVB group and 28.6% in the PUVA group compared to 75% of patients receiving NBUVB therapy and 80% of patients receiving PUVA therapy in another study.¹³ The low asymptomatic erythema in the PUVA group in ours may be due to our low psoralen dosage.

The adverse effects observed in our study like symptomatic erythema, pruritus and erythroderma were similar to the other studies.^{10,13} Nausea, an important adverse effect in other studies, was not reported in ours. This may be due to a lower dose of 8-MOP tablet and patients took their tablets with lunch, as treatment sessions were given post-lunch. Symptomatic erythema was associated with severe pruritus irrespective of the treatment groups. Some patients with symptomatic erythema and pruritus also developed erythroderma. Similar observations were not reported in any other studies. Pruritus due to phototoxicity usually develops without erythema and symptomatic erythema occurs without pruritus. The possible reason for the development of both these adverse effects together could be due to the fact that most of our patients

belonged to lower socioeconomic status and they went out for work in the sun irrespective of our repeated explanations. 25% in the NBUVB group and 50% in the PUVA group developed symptomatic erythema and pruritus. The difference was not statistically significant ($p = 0.257$). Symptomatic erythema and pruritus was found to adversely affect the disease clearance in both the groups ($p = 0.001$). These patients could not complete the treatment schedule. In other studies, symptomatic erythema was more in the NBUVB group than in the PUVA group (73% versus 35% and 49% versus 22%, respectively).^{9,10} The higher cumulative dose required for clearance due to the twice-weekly NBUVB schedule may be the reason for the higher observed symptomatic erythema. 56.3% were non-compliant in the NBUVB group and 21.4% in the PUVA group. This high non-compliance rate may be due to the stringent criteria for non-compliance. Even though 25% in NBUVB group and 50% in PUVA group could not complete treatment due to adverse effects, no patients were lost to follow-up.

Though many studies quote efficacy of PUVA therapy as more compared to NBUVB, the overall efficacy of both the treatments was the same in our study. Low dose of 8 MOP may be the reason for the observed lesser efficacy for PUVA. We chose the lower dose according to our department protocol as we have observed adverse effects with dosage according to body weight. In the present study also, 50% of patients in the PUVA group could not continue treatment due to adverse effects in spite of being given a fixed dose. Small sample size limits the generalization of the study. PUVA photochemotherapy requires the intake of 8-MOP prior to UV-A exposure. This drug gets deposited in the skin and eyes and can sensitize the patient to UV-A in the sunlight causing damage to skin and eyes even after therapy. This can affect the day-to-day activities of the patients and requires photoprotection with broad-spectrum sunscreens and UV-protecting goggles after treatment, which will not be feasible in manual labourers due to the high cost. NBUVB is relatively safe and do not require UV protection after treatment. Thrice-weekly schedule results in low cumulative dose, lesser number of treatment exposures and in turn lessens the risk of development of cutaneous malignancies later in life. Even though the higher disease clearance and the lower observed adverse effects in the NBUVB group did not achieve statistical significance, the fact that the observed values were better than the time-tested PUVA therapy warrants NBUVB therapy as a safe treatment option for moderate to severe psoriasis, especially in patients similar to our study population. Hence, in patients whose occupation is predominantly outdoors, among phototherapy, NBUVB may be considered as the first-line therapy.

Conflicts of interest

The authors have none to declare.

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