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Original Research Article

A Comparative Study of Efficacy of Systemic PUVA and NBUVB in Treatment of Vitiligo

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ABSTRACT

Context: Vitiligo is an acquired pigmentary disorder of unknown etiology which has a great cosmetic significance and psychological impact on affected individuals. A number of therapeutic agents have been used over time with variable results. Systemic psoralen and ultraviolet A (PUVA) has been the mainstay of treatment. Narrowband ultraviolet B (NBUVB) is a comparatively newer and safer modality of recent times. This study was undertaken with objective to compare the efficacy of systemic PUVA and Narrowband UVB therapy in patients of vitiligo.
Aims: To compare the efficacy of Systemic PUVA therapy and Narrowband UVB therapy in patients of vitiligo.
Settings and Design: Prospective study.
Materials and methods: A randomized prospective study was conducted on vitiligo patients attending the Out Patient Department of dermatology, venereology and leprosy, Indira Gandhi Medical College, Shimla, Himachal Pradesh from July 2011 to June 2012. The patients were divided equally into two groups; Systemic PUVA (Trimethylpsoralen) and NBUVB groups and therapy was administered twice per week on nonconsecutive days.
Statistical analysis the data was statistically analyzed using Chi-square and Mann Whitney test.
Results: The mean degree of repigmentation attained after excluding the acral sites (hands and feet) in the NBUVB group was 46.25% over a mean treatment period of 6.1 months, whereas in the systemic PUVA group it was 30.05% in a mean period of 5.9 months (P = 0.01). In NBUVB group the pigmentation was better and side effects were less as compared to systemic PUVA group.
Conclusions: In the treatment of non segmental and non acral vitiligo, NBUVB therapy is superior and better to systemic PUVA therapy.

Key words: NBUVB, systemic PUVA, vitiligo, regimentation.

INTRODUCTION

Vitiligo is an acquired, idiopathic disorder characterized by circumscribed depigmented macules and patches. It is one of the most ancient diseases known to mankind [1] still the treatment remains a goal to achieve which will cover both the cosmetic and psychological aspects. Functional melanocytes disappear from affected skin by a mechanism(s) that has not yet been identified. [2] The extent and distribution of vitiligo often changes during the course of a person's lifetime and its progression is unpredictable. The course of vitiligo is usually of slow progression but it may exacerbate rapidly or may stabilize. Vitiligo occurs worldwide with a prevalence of 0.1% to 2.0%. [3] The available global

data shows that its highest incidence is in India and Mexico. [4] Despite continued progress towards an elucidation of the genetic and immunopathological pathways in vitiligo, a definitive cure remains elusive. The causes of vitiligo are poorly understood and treatment is often unsatisfactory. [5] There are number of therapeutic options currently available, each having certain advantages and disadvantages. The choice of therapy depends on the extent, location, type of vitiligo and activity of disease, the patient's age, skin type and motivation to undergo treatment. [6]

The modern photochemotherapy of vitiligo with PUVA was introduced in 1948 by El Mofty in Egypt which stands for psoralen plus UVA [7] and subsequently in 1997 NBUVB was first used by Westerhof and Nieuweboer-Krobotova. [8] So the study was done to compare the efficacy of systemic PUVA and NBUVB in the treatment of vitiligo. This was for the first time that such comparative prospective study was done in the dermatology department of Indira Gandhi Medical College Shimla, Himachal Pradesh.

MATERIALS AND METHODS

Study design

The prospective study was conducted in the dermatology department of Indira Gandhi Medical College Shimla, Himachal Pradesh on vitiligo patients attending the Out Patient Department over a period of one year from July 2011 to June 2012. The subjects were screened at a preliminary visit and reviews were performed after 8, 16 and 24 weeks of treatment.

Subjects

Forty patients having non segmental and non acral vitiligo affecting more than 2% of the body surface area in age group of 12 to 70 years over a period of one year (July 2011 to June 2012) attending the Out Patient Department were included in the study. The patients with history of photosensitivity or administration of a drug known to cause photosensitization, photosensitizing disorder, previous failure or intolerance to photochemotherapy or phototherapy, treatment within the last 2 months (phototherapy, systemic therapy, topical therapy with corticosteroid agents, vitamin D analogues or tacrolimus), more than 100 sessions of photochemotherapy or phototherapy, history of skin cancer, renal or hepatic disease, aphakia or cataracts, claustrophobia and pregnant or lactating women were excluded from study.

Patients were randomly allocated into two groups: Group A (Systemic PUVA) and Group B (NBUBV). An informed written consent was taken after explaining the procedures. Before starting therapy patients were counseled regarding safety profile, the importance of adherence and compliance and limitation of therapy. The ethical approval for conducting study was also taken.

Group A: (Systemic PUVA)

Patients were treated with PUVA as monotherapy in a whole body phototherapy chamber with 18 UVA lamps, peak wavelength: 366 nm, minimal intensity: 1.020mW/cm^2 at 15 inches, radiation (measured with UVA photometer) at 6 inches is approximately 6mw/cm^2, calibrated twice yearly. Therapy was administered twice per week on non consecutive days. Patients were instructed to ingest Trimethylpsoralen (0.6 mg/kg) with food, 2 hours before exposure on the days of exposure. Standard initial dose of 2J/cm^2 was started on all patients. The irradiation dose was increased by 0.5J/cm^2 for each subsequent visit till minimal erythema occurred in the lesions. The maximum dose of UVA was 10.5J/cm^2

Group B: (NBUVB)

Patients were treated as monotherapy in a whole body phototherapy chamber comprising of 18 NBUVB lamps with emission spectrum 311 nm, irradiance 1800–2000 μW/cm^2, calibrated twice yearly. NBUVB phototherapy was administered twice per week on non consecutive days. Photo testing was not performed and standard initial dose of

0.250J/cm^2 was started on all patients. The dose increment was 20% of the previous dose on subsequent visit. The optimal constant dose was achieved when minimal erythema occurred in the lesions.

During each treatment, patients in both groups were instructed to shield the genitals and uninvolved skin as much as possible with clothing and to put on photo protective goggles. If lesion was present on eyelids, patients were asked to keep eyes closed during treatments without goggles. They were advised to apply sunscreen after treatment on exposed areas and to avoid excessive sun exposure. Dose was adjusted according to the erythema occurring after the previous session, determined by patient self report and by physical examination.

All assessments consist of estimation of the improvement in percentage of body surface area with vitiligo (BSA-V). The first assessment was made by using the rule of nines, subsequent assessments and comparisons were made with the baseline photograph to determine the percentage improvement in BSA-V. At 16, 32 and 48 sessions, regimentation was assessed as Grade 1 (0- 25%), Grade 2 (26 - 50%), Grade 3 (51 -75%), Grade 4 (76-100%) and mean repigmentation in individual patient was calculated by adding the extent of repigmentation achieved in each topographical area after therapy and then dividing the figure with the total number of included topographical areas having vitiligo lesions. Mean repigmentation in the individual group was determined by adding the mean repigmentation of the individual patient divided by the number of patients in each group. Patient compliance was scored as Score A (<16 sessions), Score B (16 -32 sessions), Score C (33 -48 sessions).

Statistical analysis

The data was statistically analyzed using Chi-square and Mann Whitney test.

OBSERVATIONS AND RESULTS

All the patients of NBUVB and systemic PUVA group completed the study period of six months or 48 sessions of phototherapy. Comparing the demographic and disease parameters in the two groups, both the groups were comparable (Table1). Discuss more about table 1.

Table 1: Demographic and patients parameters

Parameters	Systemic PUVA	NBUVB
No. of patients	20	20
Age in years (mean±SD)	25.8 ± 10.8	33.4 ± 8.99
Sex (Male/Female)	14/6	11/9
Disease duration (years)	6.91±5.79	6.91±5.10
Progression (Yes/No)	16/4	16/4
Family history(Yes/No)	0/20	3/17
Leuchotrichia (Yes/No)	9/11	9/11
Kobernization(Yes/No)	3/17	3/17
Associated diseases	1	2
Body Surface Area (mean±SD)	8.25 ±7.41	11.10±9.73
Treatment Duration (mean±SD)	5.9 ±12.3	6.1 ±15.7
Compliance score	C	C

The mean degree of repigmentation attained after excluding the acral sites (hands and feet) in the NBUVB group was 46.25% over a mean treatment period of 6.1 months, whereas in the PUVA group it was 30.05% in a mean period of 5.9 months (Figure 1). The improvement in repigmentation in the two groups at the end of six months of treatment, it was found that grade 4 improvement was seen in 2 (10%) patients in the NBUVB group and none in the systemic PUVA group. The grade 3 improvement was found in 9 (45%) in the NBUVB as compared to 3 (15%) in systemic PUVA group (Figure 2).

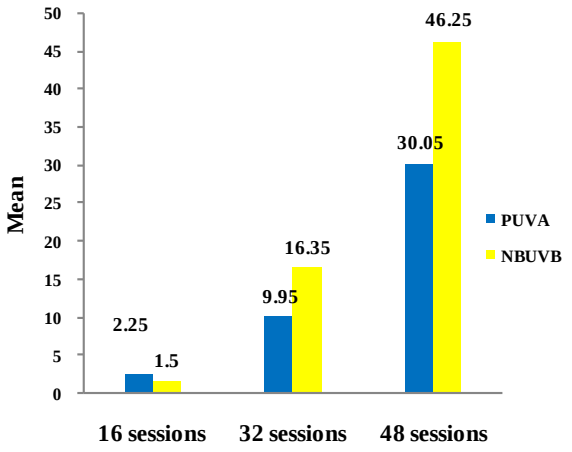

Figure 1: Mean degree of repigmentation achieved in PUVA and NBUVB group

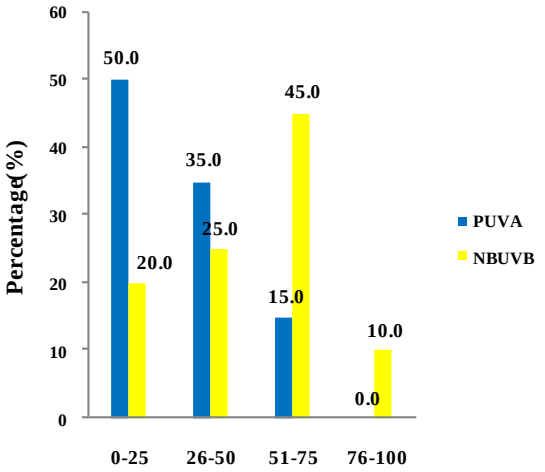

Figure 2: Distribution of grade of improvement among PUVA and NBUVB group.

The colour match was excellent in 7 (35%) in systemic PUVA and 16 (80%) in NBUVB (Figure 3). We found repigmentation in all the patients in both the groups (figure 4-5). The mean dose 8.8J/cm^2 ±1.44 of mild erythema achieved after 16.4±3.55 mean sessions in the systemic PUVA group and mean dose 4.51 J/cm^2 ± 2.67 after 20.45±4.7 mean sessions was achieved in the NBUVB group. The side effects profile was almost similar except for nausea observed in systemic PUVA group and no patients left the treatment because of side effects.

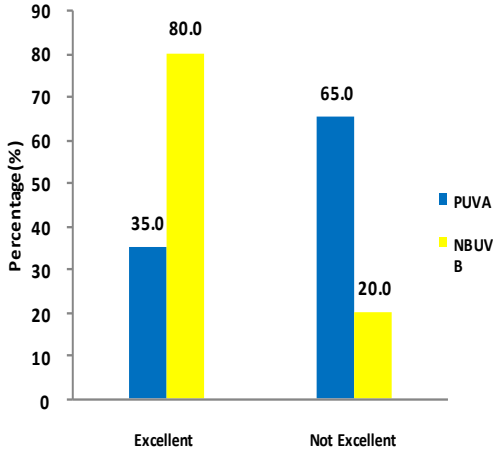

Figure 3: Distribution of colour match among PUVA and NBUVB group.

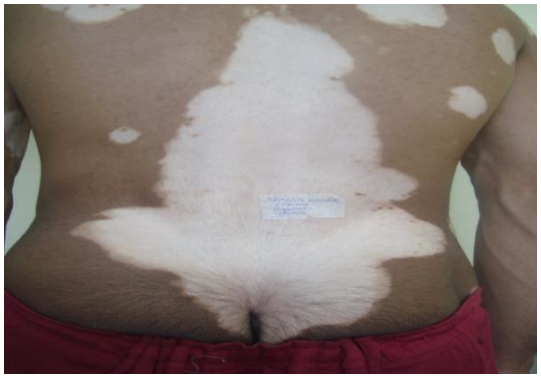

Figure 4 (a) Before NBUVB

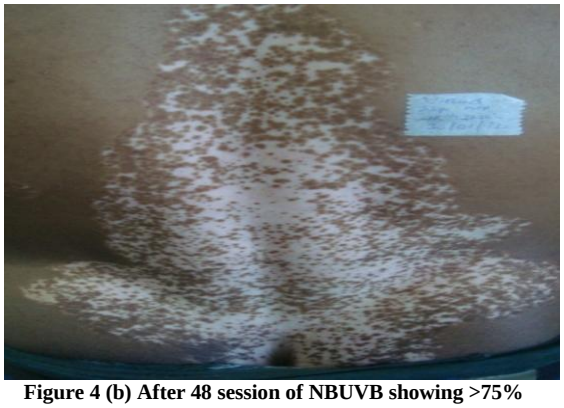

Figure 4 (b) After 48 session of NBUVB showing >75% repigmentation

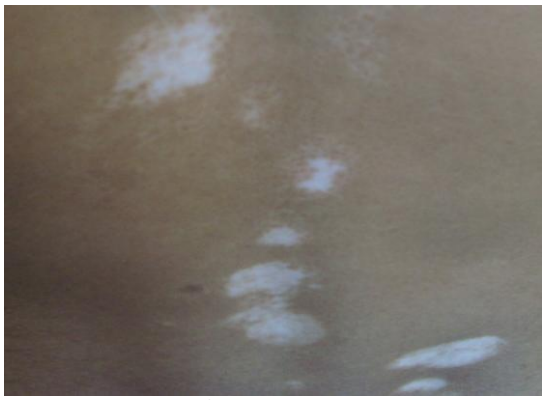

Figure 5 (a) Before Systemic PUVA

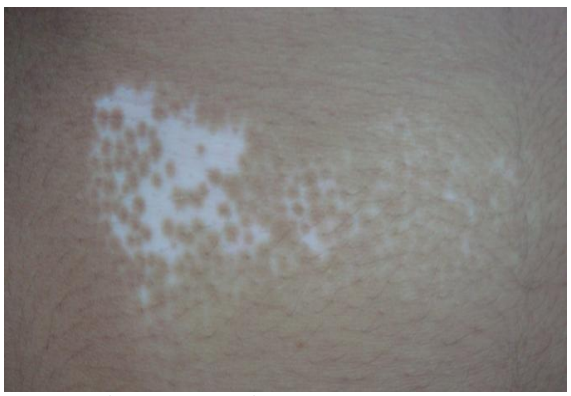

Figure 5(b) After 48 session of Systemic PUVA showing>50% repigmentation

DISCUSSION

The aims of vitiligo treatments are stabilization of the depigmentation process along with stable repigmentation. Although there is still no therapeutic panacea for vitiligo, but many options available may lead to satisfactory results in most of the patients. The photo chemotherapy (PUVA/PUVASOL) is one of the commonest modality used in the past but recent introduction of NBUVB in the treatment of vitiligo has shown better out come. In the study, various confounding factors, like family history, age of onset, disease duration, history of progression, [9] leucotrichia, kobernization, associated other diseases were comparable in both the groups as shown in demographic table.

The use of NBUVB phototherapy for vitiligo was first reported by Westerhof and Nieuweboer-Krobotova [8] who compared twice-weekly topical PUVA with twice-weekly NBUVB phototherapy. The study of Westerhof and Nieuweboer-Krobotova [8] showed that after 4 months of therapy, 67% of patients undergoing NBUVB phototherapy developed repigmentation compared with 46% of patients receiving topical PUVA. The lower cumulative dose and the fewer side effects were considered to be the major advantages of the use of NBUVB over PUVA.

In our study we found that at the end of 8 weeks (16 sessions) the mean repigmentation was similar in both the groups (statistically non significant) but it was 2.25±2.15 little higher in systemic PUVA as compared to 1.5±2.09 in the NBUVB group. It shows that there is earlier repigmentation seen with PUVA. After 16 weeks (32 sessions) the mean repigmentation in systemic PUVA and NBUVB group was 9.95±6.73 and 16.35±11.55 respectively (p value=0.04). The mean repigmentation in systemic PUVA group was 30.05±15.24 over a mean period of 5.9 months and which was 46.25±20.38 in mean period of 6.1 months in NBUVB group (p value=0.01). The colour match was excellent in 7 (35%) patients in systemic PUVA and 16 (80%) patients in NBUVB group. This was in accordance with the study conducted by Bhatnagar et al. [10] (where thrice weekly treatment was given as compared to twice weekly in our study). After excluding the results of therapy resistant sites, the mean degree of repigmentation in the NBUVB group was more 67.57% over a mean period of 6.3 months, whereas in the PUVA group it was 54.2% in mean period of 5.6 months. The colour match with surrounding skin in NBUVB was in 88% patients as compared to 80% in our study, whereas in PUVA group it was 56% as compared to 35% in our study. Hence the NBUVB was found superior to systemic PUVA in the present study.

In our study the improvement in repigmentation at the end of 6 months of treatment, it was found that grade 4 improvement was seen in 2 (10%) patients in the NBUVB group and none in the systemic PUVA group. The grade 3 improvement was found in 9 (45%) in the NBUVB as compared to 3 (15%) in systemic PUVA group. In the retrospective analysis of comparison between NBUVB and PUVA by Parsad *et al.* [11] 41.9% of patients in the NBUVB group and 23.6% in the PUVA group had marked to complete repigmentation after a maximum treatment for one year and colour matching was observed in 86% of the NBUVB patients and only 35% in the PUVA group. It differ from our study as treatment session was three times per week for one year but in our study the treatment session was twice per week for six months. However the study design was different from our study and degree of repigmentation was not directly comparable.

The number of others studies evaluating only NBUVB in the treatment of vitiligo such as Scherchum *et al.* [12] Kanwar *et al.* [13] Anber *et al.* [14] Sitek *et al.* [15] and Kishan Kumar *et al.* [16] has found that repigmentation achieved was acceptable and matched with the surrounding skin with minimal side effects. So in accordance to

these studies, our study also found that the repigmentation achieved was acceptable and matched with surrounding skin with minimal side effects in the NBUVB group.

CONCLUSION

In our experience, NBUVB phototherapy was found better in terms of repigmentation, colour match and less side effects than systemic PUVA in the treatment of vitiligo. Large studies with longer duration of treatment are required to fully establish the efficacy of both systemic PUVA and NBUVB in the treatment of vitiligo.

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