EVALUATION OF NARROW-BAND UVB PHOTOTHERAPY FOR VITILIGO

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ABSTRACT: Vitiligo is an acquired de-pigmenting skin condition that results from destruction of melanocytes. There are very few studies from south India regarding the efficacy and safety of narrowband ultraviolet B (UVB) photo therapy in vitiligo which lead to the This prospective open non randomized study was conducted at a tertiary healthcare centre of south India between January 2011 and December 2011 to determine the efficacy and safety of narrowband ultraviolet B (UVB) photo therapy in vitiligo. A total of 62 patients of vitiligo attending the dermatology outpatient department were enrolled in the study. Patients were treated with narrow band UVB phototherapy. Majority of our patients (29%) were in the age group of 31-40 years. Duration of vitiligo varied from 4 months to 18 years, with a mean of 6.2 years. Percentage of body surface area involved by vitiligo varied from 2-80% with a mean of 12.8%. Out of the various body sites, the most satisfactory re-pigmentation was seen on the face and the least was on the extremities. At the end of 6 months percentage area of re-pigmentation varied 60-90% on the face, 10-95% on upper limb, 15-90% on the trunk and 15-80% on lower limbs. Out of 62 patients, all had itching, which responded to oral antihistaminic. The phototoxic reactions were mild which were treated with topical steroid. This study emphasized the utility of narrow band UVB phototherapy as an effective modality of therapy for vitiligo.

KEYWORDS: Erythema; Melanocytes; Phototherapy; Vitiligo.

INTRODUCTION: Vitiligo is an acquired de-pigmenting skin condition that results from destruction of melanocytes. It is visibly striking in India because the depigmentation of vitiligo contrasts with the darker skin colour of Indians. Vitiligo remains the bugbear of dermatologists because of varied response to the therapy. Prevalence of vitiligo in India varied from 0.46% in Kolkata to 1.13% in Surat.^{1,2} No single method is completely successful or satisfactory. PUVA and topical corticosteroids are the most frequently used modalities. Surgical treatment helps in transferring normal skin or melanocytes to the vitiligo affected skin.

Narrow band UVB (NBUVB) phototherapy was first studied by Westerhof W and Nieuweboer-Krobotova.³ During recent times narrow band UVB phototherapy is being increasingly used for this disorder since the shorter wavelengths of UVB radiation have higher energy and are mostly responsible for the development of erythema, less erythema is induced following exposure to 311nm UVB source (narrow band UVB) while treatment response remains high. There are only few published data available regarding the treatment for vitiligo. This study was conducted to determine the efficacy and adverse effects of narrow band UVB phototherapy.

MATERIALS AND METHODS: Patients with generalized and focal vitiligo presenting in the dermatology outpatient department of a tertiary healthcare centre of south India were the subjects

of this study. A total of 62 patients were enrolled for the study. It was conducted for a period of one year from January 2011 to December 2011. In all these patients name, age, sex, occupation and stability were noted. Family history, any precipitating factors and previous therapies tried by the patients and their effects were noted. The patients were examined completely for the sites involved and type of vitiligo. The patients with one of the following were included in the study.

Patients with vitiligo of either sex who had, 1) Generalized vitiligo, involving > 10% of body surface area, 2) Generalized vitiligo, involving <10% of body surface area with more than five sites involved excluding acral sites, lips and genitals or more than ten lesions (at distant sites) size of lesions more than one centimeter, 3) Segmental vitiligo, involving > 10% body surface area. All the patients with above 5 years of age and vitiligo which is stable for minimum period of one month were included in this study. Patients with lack of response to previous PUVA therapy, intolerance to psoralens were also included in the study. Patients with photosensitive disorders or history of cutaneous malignancy were excluded from the study. A washout period in which patient should be off other treatments in the form of systemic steroids / PUVA for 1 month and topical steroids for 15 days was recommended. Pretreatment & post treatment photographs (3 & 6 months) were taken. Parental consent was obtained for the children and informed consent was taken from the rest.

Whole body narrow band phototherapy (DermaIndia) unit with twelve narrow band fluorescent tubes (Philips TL 100W/01) measuring 6 feet in length with a spectrum of 310 to 315nm and a maximum emission wavelength of 311nm was used for the treatment. Narrow band UVB therapy was given twice weekly even while ensuring that it was not administered on two consecutive days. During the treatment the eyes were protected by UV-blocking goggles. If significant depigmentation was present on the eyelids and patients or their guardians insisted on treating these areas, patients were told to keep their eyes shut during the treatment and not to wear goggles. All the patients kept their clothing on to shield the genitals from narrow band UVB exposure.

The initial starting dose was 100mJ (whole body) and the dose was subsequently increased by 20% each time, till the development of persistent erythema (in the vitiligo patches) i.e. just perceptible erythema or an erythema with sharp margins after 24 hours of exposure and persisting at 72 hours after the exposure. Additional exposure of 10%, 20%, and 30% of the whole body dose was given to the upper and lower extremities in successive sittings and was thereafter maintained at 30% of the corresponding whole body dose. If erythema was painful, one dose was omitted and the patient was reassessed after 72 hours. The persistent erythema dose was continued for 6 months. The total duration of the treatment was 6 months after achieving persistent erythema dose in a vitiligo patch.

RESULTS: A total number of 62 patients were included in the study. Table 1 gives age wise distribution of the patients. The age of the patients in this study varied from 6-60 years and mean age was 29 years + 12.8 standard deviation. Majority of the patients (29%) were in age group of 31-40 years. Out of 62 patients 28(45%) were males and 34(55%) were females. Duration of vitiligo varied from 4 months to 18 years, with a mean of 6.2 years. None of the patients had a family history of vitiligo. Stable means no expansion of existing lesions or no appearance of new lesions. Duration of stability varied from 1 month to 5 years with a mean of 9.4 months. Percentage of body surface

area involved by vitiligo varied from 2-80% with a mean of 12.8% (Graph 1). Out of 62 patients of vitiligo, 56(90.4%) were of generalized type and six (9.6%) were of focal type.

Out of the various body sites, the most satisfactory re-pigmentation was seen on the face and the least was on the extremities. Out of total 62 patients, 34 showed first sign of re-pigmentation after 6-10 sittings of narrow band UVB phototherapy. At the end of 3 months, the percentage area of repigmentation varied from 30-70% on the face, 5-80% on upper limbs, 10-80% on the trunk and 10-60% on lower limbs (Graph 2). At the end of 6 months percentage area of re-pigmentation varied 60-90% on the face, 10-95% on upper limb, 15-90% on the trunk and 15-80% on lower limbs (Table 2, Graph 2). Out of the 62 patients, two stopped the treatment after 31 and 32 sittings due to financial compulsions and another two patients stopped after 18 and 24 sittings due to the poor response and constraints in visiting the hospital, and four patients failed to show any re-pigmentation at the end of three months of therapy.

The persistent erythema dose (PED) varied from 120mJ/sq cm to 1278mJ/sq cm with a mean of 531.7mJ/sq cm (Table 3). The cumulative dose varied from 7.1J/sq cm to 61.8J/sq cm with a mean of 26.65J/sq cm. Out of 62 patients, all had itching, which responded to oral antihistaminic (Table 4). The phototoxic reactions were mild which were treated with topical steroid. No correlation could be found with regards to duration of disease and re-pigmentation. Best results of re-pigmentation were obtained when the disease was stable for 1 month to 6 months. It was clinically observed that among patients with less than 10% body surface area involvement and having lesser re-pigmentation (<30% and 30-50%) had smaller patches mainly on areas of bony prominence and less hairy region.

DISCUSSION: Phototherapy continues to be one of the first lines of treatment in vitiligo. Now NB-UVB is preferred as it is safe and effective in treating vitiligo even in pregnancy and children.^{4,5,6} The age of the patients in this study varied from 6-60 years and the mean age was 29.9 years. Majority of the patients (29%) were in age group of 31-40 years. Four patients were aged between 5-10 years. The age distribution in the study by Kishan kumar et al⁷ and Westerhof et al was similar to our study.⁸ Duration of vitiligo in the present study the duration of vitiligo varied from 4 months to 18 years with a mean of 6.2 years. The average duration of the disease in the Westerhof study was 13.3 months and in the Njoo's study it was 4 years.^{8,9}

The duration of stability in our study varied from 1 month to 5 years the average being 9.4 months. In the study by Westerhof et al all the patients had active vitiligo.⁸ Out of the 51 patients in Njoo's study, 8 had active disease in the past 6 weeks, 20 in the past 3 months, 16 in the past 6 months, 5 in the past year and 2 were stable for at least 1 year.⁹ Njoo's study also revealed that 80% of the patients stabilized after 1 year of therapy while in the current study approximately 90% of the patients stabilized after 6 months of therapy.⁹ Percentage of body surface area involvement varied from 2-80% with a mean of 12.8% in our patients. The extent of depigmentation in Westerhof's⁸ study varied from 10-50%. In Njoo's study the mean percentage of depigmentation was 15.9%.⁹ Thus the severity of the disease in the present study correlates well with that of Njoo's study.⁹

Out of the 44 patients in our study, who had facial lesions of vitiligo, 22 (50%) patients had first re-pigmentation on the face. A significant proportion i.e. 58.6% of the patients had first re-pigmentation after 6 to 19 sittings. 34.5% of the patients had initial re-pigmentation after 1-5 sittings. Earliest re-pigmentation was seen after 3rd sitting in our patients. In

the Westerhof's study, re-pigmentation started about 6 weeks after the initiation of treatment.⁸ In the current study re-pigmentation had started earlier than the Westerhof's study.⁸ This may be by virtue of the darker skin type of Indian patients, which may respond more favorably than lighter skin types.^{6,10,11}

In our study at the end of 3 months after achieving the persistent erythema, a significant proportion (54.5%) of the patients showed 45-60% of re-pigmentation on the face. In the Westerhof's study, 48% of the patients showed 25-75% re-pigmentation.⁸ In the current study at the end of 6 months, percentage area of re-pigmentation varied from 60-90% on the face which was observed in other studies also. Thus the most gratifying response was achieved with lesions located on the face and trunk. Lesion located on the breast, back, arms and legs responded with more than 75% re-pigmentation while the joints such as knee and elbows seldom showed more than 75% re-pigmentation. Most lesions on the hands, digits, feet and toes only showed minor to no re-pigmentation. These findings are consistent with the Njoo's and Westerhof's studies.^{8,9} In Njoo's study 72% of lesions on the face and 74% of lesions on the neck showed more than 75% re-pigmentation at the end of 1 year.²⁸ Hamzavi I et al noted best response over legs followed by trunk, arms, hands and feet (without considering face).¹²

Persistent erythema dose is the lowest radiation exposure to ultraviolet radiation sufficient to produce either, just perceptible erythema on exposed lesional skin after 24 hours or an erythema with sharp margins after 24 hours and persisting at 72 hours after the exposure¹³. The persistent erythema dose in the present study varied from 120 mJ/sq cm to 1278 mJ/sq cm with a mean of 531.7 mJ /sq cm. In the study by Westerhof et al⁸ minimal erythema dose of lesional skin was between 200 and 450 mJ/sq cm. In Westerhof's⁸ study the patients were from Netherlands, where the sun exposure is less. While in India, higher sun exposure may be responsible for more, natural photo protective mechanism leading to higher persistent erythema dose as seen in our patients. Serish and Srinivas CR reported that 300 mJ/sq.cm (NBUVB) was the mean minimal erythema dose (MED) for the Indian skin.¹⁴

The cumulative dose in the current study varied from 7.1 J/sq cm to 61.8 J/sq cm with a mean of 26.65 J/sq cm. In the Westerhof's study cumulative dose at 12 months varied from 9.58 to 128.01 J/sq cm with a mean of 32.34 J/sq cm.⁸ In the Njoo's study average cumulative dose was 91.3 J/sq cm at 12 months of treatment.⁹ Cumulative dose reported by Kishan Kumar YH et al was 46.8+25.2 J/sq cm to achieve 25-75% of re-pigmentation.⁷ Thus Indian skin requires less number of exposures to NBUVB to achieve re-pigmentation.^{6,10,11}

Out of the 62 patients in the current study, all the patients had itching, which was treated with emollients and some with an oral antihistaminic. It usually started after 2-5 sittings after initiating the therapy. Itching was also reported by Westerhof et al, Njoo et al and Dogra S but in the Njoo's study 8% and Kishan Kumar YH et al 7% of the patients had itching.^{7,8,9,11} The higher incidence of itching in the study may be related to the higher dose of irradiation. Tanning was seen in 30 of our patients. Most of these patients received a higher dose of irradiation. Phototoxic reaction was seen in 10 patients in the current study, which was mild and was treated with topical steroid with omission of the irradiation till tender erythema disappears. In the Njoo's study there was no phototoxic reaction. In our study the irradiation dose that was maintained was persistent erythema dose (PED), rather than minimum erythema dose in the Westerhof's and Njoo's studies.^{8,9} There was only a very narrow range between persistent erythema dose and the phototoxic dose. Thus this may

explain the cause of higher phototoxic reaction in the current study. Four patients developed photo hardening (thickening of skin on the photo exposed skin) over the vitiligo patches on the knuckles. In the Westerhof's study there was no hyperkeratosis even after long-term irradiation.⁸ Herpes labialis was seen in two of our patients which was not seen in the Westerhof's and Njoo's studies.^{8,9}

No correlation could be found with regards to duration of disease and re-pigmentation in the current study, which is consistent with Njoo's study where also no such correlation could be found.⁹ Best results were obtained when the disease was stable for 1 month to 6 months. Our patients with less than 10% body surface area involvement and having lesser re-pigmentation (<30% & 30-50% re-pigmentation) had smaller patches mainly on areas of bony prominence & less hairy regions. Thus even the small vitiligo patches on the bony prominences and on less hairy regions show poor re-pigmentation. No significant relationship was found between re-pigmentation grades and the variables age, sex and type of vitiligo in the present study, which was consistent with the Njoo's study.⁹ Thus NB-UVB is the most cost effective among the UV based therapies.¹⁵

CONCLUSIONS: Narrow band UVB phototherapy is an effective modality of therapy for vitiligo. Adverse effects are minimal and transient. At higher doses UVB also induces tanning. In view of continuing and incomplete re-pigmentation at the end of 6 months of phototherapy it may be advisable to continue the treatment further, up to a year. Shorter treatment sessions and twice-weekly exposure is a convenient O.P.D. basis therapy, are particularly suited to a busy metropolis. Narrow band UVB phototherapy improves quality of life particularly in children, compared to PUVA therapy, which required outdoor activity restriction to reduce psoralen induced photo toxicity. Cost of therapy may limit its widespread use in developing countries. Being a very useful treatment option for vitiligo, which is a cosmetic embarrassment to a disaster in dark skinned patients; further studies are required with long-term follow up for optimum duration of therapy, pigment retention after stopping treatment and long-term side effects.

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Age group (years)	No. of patients (%)
5-10	4(6.6)
11- 20	14(22.5)
21 - 30	12(19.3)
31- 40	18(29)
41-50	12(19.3)
51- 60	2(3.3)
Total	62(100)

Table 1: Age wise distribution of the study subjects

Results	Number of Patients (%)
Poor (< 30% re-pigmentation)	2(3.2%)
Fair (30-50% re-pigmentation)	12(19.3%)
Good (50-75% re-pigmentation)	40(64.5%)
Excellent (> 75% re-pigmentation)	0(0%)
Failure (No response at the end of 3 months)	4(6.5%)
Failure to follow up	4(6.5%)
Total	62

Table 2: Result at 6 months after NBUVB phototherapy among the study subjects (n=62)

PED in mJ	Number of patients (%)
0-150	14(22.6)
150-300	6(9.7)
300-450	16(25.8)
450-600	8(12.9)
600-750	10(16.1)
750-900	4(6.5)
900-1050	0(0)
1050-1200	2(3.2)
1200-1350	2(3.2)
Total	62(100%)

Table 3: Persistent erythema dose (PED) in mJ/cm² among the study subjects (n=62)

Adverse reaction	No. of patients (%)
Itching	62(100)
Tanning	30(48.3)
Phototoxic reaction	10(16.1)
Photo hardening	4(6.4)
Herpes labialis	2(3.2)

TABLE 4: Adverse reactions following NBUVB phototherapy among the study subjects (n=62)

Graph 1: Percentage of body surface area involvement by vitiligo among the study subjects (n=62)

Graph 2: Area of re-pigmentation at 3 and 6 months

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