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Narrow band Ultraviolet B 311 nm in the treatment of vitiligo: two right–left comparison studies

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Aim: **Evaluation of narrow band ultraviolet B (NB UVB 311 nm) in the treatment of vitiligo by two independent studies. The first study compared NB UVB with a well-established therapeutic modality, psoralen ultraviolet A (PUVA), and the second study was conducted to find out whether psoralen might add to its efficacy.**

Methods: **In the first study, 15 patients were exposed on the left half of their body to UVB 311 nm and then exposed on their right half to UVA after ingestion of psoralen. In the second study, 20 patients were exposed to UVB 311 nm on the left side of the body, followed by ingestion of psoralen and exposure to NB UVB 311 nm 90 min later to the right side of the body. In both studies, while exposing one side, the other was protected by an UV-proof gown. Thus two right–left comparative studies were carried out simultaneously, namely: UVB 311 nm vs. PUVA and UVB 311 nm vs. PUVB 311 nm.**

Results: **In the first study, comparison of PUVA and NB UVB 311 nm showed no difference either in the degree of response or in the incidence of complications. In the second study, comparison of PUVB and UVB showed equal clinical improvement on both sides. The cumulative dose needed to achieve the same response on the PUVB side was lower than that on the UVB side, but the difference was not statistically significant. The incidence of phototoxic reactions was significantly higher on the PUVB treated body half.**

Conclusion: **NB UVB 311 nm has similar repigmentary effects as PUVA. The addition of psoralen does not increase its efficacy.**

Key words: **comparison; NB UVB 311 nm; PUVA; PUVB; vitiligo.**

Different lines of phototherapy have been used in the treatment of vitiligo and the most classic being psoralen ultraviolet A (PUVA) (1). During the past few years, narrow band ultraviolet B (NB UVB, 311 nm) (TL01) has established itself in the field of phototherapy and has shown particular effectiveness in psoriasis (2). It results in less irritation and erythema compared with broadband UVB, and is more superior as a treatment with a better benefit risk ration (3). In addition to its efficacy in controlling psoriasis (2), NB 311 nm was found to have a beneficial therapeutic response in several inflammatory dermatoses such as prurigo nodularis (4), lichen planus (5), photodermatoses and atopic eczema (6). Multiple trials were carried out to evaluate its efficacy in vitiligo.

With the development of NB UVB, it was found that it offer a potential for the management of childhood vitiligo (7), and was considered as an effective and safe therapeutic option in adult patients with vitiligo that may significantly improve the quality of life (8). UVB 311 nm was also found to be at least as effective as topical PUVA in the treatment of vitiligo (9).

The potential of NB UVB psoralen photochemotherapy has been investigated in psoriasis (2). Some authors reported that the efficacy of NB UVB could be enhanced by oral or topical psoralen in the treatment of psoriasis (10–12). It could be accordingly postulated that the effect of using psoralen plus NB UVB 311 nm is superior to the effect of using NB UVB (311 nm) alone in the treatment of other diseases including vitiligo. The use of psoralen with NB UVB was found to be as effective as PUVA in the treatment of vitiligo (13). The exact mechanism of action of psoralen ultraviolet B (PUVB) phototherapy is unknown. It seems likely to be through both a direct therapeutic effect of 311 nm radiation on melanocytes, as well as through psoralen-mediated photochemical responses, namely: increasing tyrosinase activity, as

demonstrated in melanocyte culture of vitiliginous skin (14).

In this study, we aimed to evaluate the use of NB UVB in the treatment of vitiligo, by comparing it with a well established phototherapeutic modality as PUVA (group A), and finding out whether oral psoralen could add to its efficacy in the treatment of vitiligo (group B).

Patients and methods

Patients

Thirty-five patients with bilateral and symmertrical vitiligo randomly selected from vitiligo patients attending the Phototherapy Unit, Dermatology Department, Cairo University, were the subjects of both studies collectively.

The exclusion criteria were as follows.

- Patients with localized and unilateral lesions.
- Chidren under 12 years.
- Aphakia.
- Pregnancy.
- Hepatic impairment.
- History of cutaneous malignancy.
- Photosensitivity.

Each patient was subjected to:

- detailed history taking;
- CBC, liver and kidney function tests;
- ophthalmological examination;
- examination of the lesions; and
- photography before and after the duration of the study.

Treatment protocol

Patients were randomly divided into two study groups: the first study group A included 15 patients, and the second study group B included 20 patients.

Group A: The left half of each patient was exposed to UVB 311 nm at a starting dose of 0.74 J/cm^2 and the right half was covered with a protective gown. This was followed by oral administration of 0.7 mg/kg 8-methoxypsoralen (Ultra Meladinin 10 mg capsules, Memphis Chemical Company, Cairo, Egypt) on a full stomach. After 2 h, the right half of the body was exposed to UVA. The starting dose was 1 J/cm^2 and increments of $\frac{1}{2}$ J/cm^2 were made every other session according to the patients' response and degree of erythema.

Evaluation: Appearance of perifollicular pigmentation was considered an initial response.

Assessment was performed at sessions 20, 40, and 60 for the degree of repigmentation and any side effects using the following grading response:

(1) *Poor*: (0–40%) repigmentation.
(2) *Moderate response*: (40–60%) repigmentation.
(3) *Good*: (60–75%) repigmentation.
(4) *Very good*: (75–100%) repigmentation.

Patients were monitored for the appearance of new lesions during treatment.

Phototoxicity was managed by stopping sessions for 1–2 weeks. Oral antihistamines and emollients were used for itching and xerosis.

Group B: Patients were treated by UVB 311 nm on the left half of the body. Immediately thereafter, the patients received 8 MOP/Ultra Meladinine capsules (Memphis Chemicals Company, Cairo, Egypt) orally at a dose of 0.7 mg/kg. Two hours after receiving oral psoralen, the right half of the body was exposed to UVB 311 nm, while covering the previously treated side by a UV-proof gown.

The starting dose was 0.74 J/cm^2, and an increment of 15% was made, guided by the UVB schedule supplied by the manufacturer and modified according to the patients' response.

Evaluation: Patients were evaluated weekly, for the incidence of erythema and the extent of repigmentation. A report was filled at sessions 16, 32, and 48 for each case as regards the cumulative dose and the degree of response (assessed the same as in group A).

In both groups:

- Treatment sessions were performed three times weekly.
- Male genitalia were covered.
- Eyes were protected using goggles.

The UV source

The machines used were as follows:

- PUVA 1000 (Waldmann Medizintechn, Villingen-Schwenningen, Germany): Waldmann lighting cabin equipped with 20 UVA lamps having a radiation spectrum of 315–400 nm, with a peak at 365 nm used for PUVA therapy; and
- UVB 100 (Waldmann Medizintechn, Villingen-Schwenningen, Germany): two Waldmann lighting cabins equipped with 16 UVB lamps having a radiation spectrum extending from 310 nm to 315 nm, with a peak of 313 nm used for NB UVB.

Statistical analysis

The data were coded and analyzed using the statistical package SPSS for Windows 5.02. The mean and the standard deviation were used as suitable statistical

Table 1A. Summary of the clinical demographic data of group A patients

Number of patients	15
Age	Range: 12–60 Mean: 26.9 ± 15.8
Sex	Males: 4 patients (26.7%) Females: 11 patients (73.3%)
Disease duration	Range: 4 months to 11 years Mean: 4.8 ± 3.5
Skin type	III: 5 patients (33.3%) IV: 4 patients (26.7%) V: 6 patients (40%)
Type of vitiligo	Generalized: 7 patients (47%) Localized: 8 patients (53%)
Extent of surface area (%)	Range: 30–70% Mean 39.67 ± 13.3

Table 1B. Summary of the clinical and demographic data of group B patients

Number of patients	20
Age	Range: 15–55 Mean ± SD = 31.50 ± 11.41
Sex	Males: 7 (35%) Females: 13 (65%)
Duration	Range: 1–20 years Mean ± SD = 7.98 ± 6.33
Extent of the lesions	Range: 5%–85% Mean+SD = 27.75 ± 21.61
Skin type	II: 1 (5%) III: 4 (20%) IV: 11 (55%) V: 4 (20%)

Table 2. Comparison of clinical response in group A (PUVA and NB UVB)

	Number (%) of patients		
	PUVA	NB UVB 311 nm	*P*-value
At 20 sessions			
Poor response	10 (66.7)	10 (66.7)	0.574
Moderate response	5 (33.3)	4 (26.7)	0.574
Good response	−(0)	1 (6.7)	
At 40 sessions			
Poor response	5 (33.3)	7 (46.7)	0.757
Moderate response	5 (33.3)	4 (26.7)	0.757
Good response	5 (33.3)	4 (26.7)	0.757
At 60 sessions			
Poor response	4 (28.6)	4 (28.6)	1
Moderate response	2 (14.3)	2 (14.3)	1
Good response	8 (57.1)	8 (57.1)	1

*Statistically significant (*P*-value <0.05).
NB UVB, narrow band ultraviolet B; PUVA, psoralen ultraviolet A.

parameters to summarize the data. Frequency tables using the percent were used to describe the data.

Pearson χ^2 was used to statistically test the difference between quantitative data. The two groups were considered significantly different when *P*-value was less than 0.05.

Because of the small number of the 'good' and 'very good' responders in each group, both degrees of response were included in the 'good' grade for statistical reasons.

Results

Clinical and demographic data for all patients in groups A and B studies are outlined in Tables 1A and 1B, respectively.

Group A

The difference between the two sides as regards the response category was statistically insignificant at 20, 40 or 60 sessions (Table 2):

At the end of the 60 session the cumulative dose of UV radiation was calculated. On the PUVA side, it was $129.8 \pm 52.35\,J/cm^2$ in poor responders, $150 \pm 15.2\,J/cm^2$ in moderate responders and $133.65 \pm 45.4\,J/cm^2$ in good responders. On the NB UVB side, the cumulative dose was $113.23 \pm 44.55\,J/cm^2$ in poor responders, $142.17 \pm 70.7\,J/cm^2$ in moderate responders and $94.57 \pm 37.42\,J/cm^2$ in good responders.

Side effects: As regards the incidence of side effects, there was no statistically significant difference in the occurrence of complications between both sides (blisters, erythema, and appearance of new lesions) (Table 3). Nausea occurred in 3 (20%) patients after ingestion of oral psoralen.

In this study group, no significant relations were found between the extent of repigmentation and variables such as age, sex, skin type, and duration of disease on either PUVA or UVB 311 nm-treated sides.

Group B

Both sides were compared with respect to the following:

Table 3. Comparison of complications in group A (PUVA and narrow band UVB)

	PUVA		UVB-311 nm		
Comparison of ttt	No. of patients (Total = 15)	Percentage (%)	No. of patients (total = 15)	Percentage (%)	*P*-value
Erythema	10	66.6	11	73.3	0.69
Blisters	2	13.3	1	6.6	0.5
New lesions	8	53.3	8	53.3	1.0

NB UVB, narrow band ultraviolet B; PUVA, psoralen ultraviolet A.

(1) *Erythema:* the erythema started earlier on the P UVB side but this apparent difference was statistically non-significant.
(2) *Pigmentary response:* comparison of the number of sessions and cumulative doses achieving similar clinical response showed that

- the initial response (perifollicular pigmentation) started earlier on the PUVB side but with no statistical significance;
- the number of sessions needed to achieve 40–60% pigmentation was less on the PUVB treated side, but the difference was statistically insignificant;
- cumulative doses needed to achieve similar effects were less on the PUVB treated side, but the difference was statistically insignificant;
- the difference between the two sides as regards the response category was statistically insignificant at 16, 38 or 42 sessions (Table 4); and
- pigmentation on both sides occurred in a perifollicular pattern, however tanning in the form of diffuse grayish brown pigmentation of vitiliginous patches was also observed on both sides in two of our patients, one in each group.

Table 4. Comparison of clinical response in group B (UVB and PUVB)

	Number (%) of patients		
	UVB (%)	PUVB (%)	*P*-value
At 16 sessions			
Poor response	18 (90)	19 (95)	0.54
Moderate response	2 (10)	1 (5)	
Good response	– (0)	–(0)	
At 32 sessions			
Poor response	9 (50)	10 (55.6)	0.691
Moderate response	7 (38.9)	6 (33.3)	
Good response	2 (11.1)	2 (11.1)	
At 48 sessions			
Poor response	7 (38.9)	9 (50)	1
Moderate response	4 (22.2)	2 (11.1)	
Good response	7 (38.9)	7 (38.9)	

Statistically significant (*P*-value < 0.05).
UVB, ultraviolet B; PUVB, psoralen ultraviolet B.

(3) *Side effects*: the incidence of phototoxic reactions was more on the PUVB side with a significant *P*-value (Table 5). Nausea occurred in 13 (65%) of cases after ingestion of oral psoralen.

Discussion

In the present work, the use of NB UVB 311 nm in the treatment of vitiligo has been evaluated in two independent studies.

In the first study (group A), where UVB 311 nm was compared with PUVA in 15 vitiligo patients

At 40 sessions, although the number of good responders was more on the PUVA side, the difference was statistically insignificant. In another study (6), it was found that after 32 bi-weekly sessions, NB UVB was equally, if not, more effective than topical PUVA in the treatment of vitiligo and was associated with fewer side effects.

At 60 sessions, a good response was observed in 57.1% patients on both sides. This suggests that, pigmentary response to PUVA might be faster at the beginning but later on NB UVB 311 nm can achieve similar results. A second study showed more or less comparable results, showing 75% overall pigmentation in 53% of patients over a period of 75 sessions (7). In one study only, more than 75% repigmentation within a mean of 19 treatments of NBUVB was obtained in five out of seven cases (15). In a third study of a longer duration, complete repigmentation was achieved in 71.4% Indian vitiligo patients after 1 year of three weekly sessions treatment, and they recommended long-term maintenance to establish the stability of repigmentation (8).

The incidence of erythema was documented at various stages during the course of treatment in 66.6% of patients on the PUVA-treated side and in 73.3% of patients on the UVB 311 nm treated side. A Similar observation was made while making a randomized comparison of NB UVB and PUVA for psoriasis (16). The incidence of erythema can be reduced

Table 5. Comparison of complications occurring in group B (UVB and PUVB)

	UVB		PUVB		
	Number total: 20	Percentage (%)	Number total: 20	Percentage (%)	*P*-value
Phototoxic reaction	12	60	17	85	0.019*
Erythema	11	55	15	75	
Blistering	1	5	2	10	
New lesions	7	35	7	35	1

*Statistically significant (*P*-value <0.05).
UVB, ultraviolet B; PUVB, psoralen ultraviolet B.

by using lower doses of NB UVB, but this will concomitantly increase the number of sessions required to achieve the desired response.

Although of no statistical value, the incidence of skin thickening was higher on the PUVA treated side in contrast to the NBUVB-treated side. A similar observation was obtained on comparing NB UVB with topical PUVA (9).

The use of UVB 311 nm could therefore be considered an effective line of treatment for vitiligo. Its therapeutic effect is equal to but not superior to PUVA.

In the second study (group B), where the effect of adding psoralen was compared with NB UVB alone in 20 patients in treating vitiligo.

The good and very good responders on both sides were equal (38.9%) showing that psoralen did not really add any benefit to UVB 311 nm with regard the clinical response after 48 sessions (four months). The initial pigmentary response represented by perifollicular pigmentation occurred earlier and with a lower cumulative dose on the P UVB side but this difference was not statistically significant when compared with UVB 311 nm.

Comparison of the mean number of exposures and the mean cumulative dose required to achieve a certain response grade whether erythema, initial response 40% and 70% pigmentation showed no statistically significant difference between the UVB and PUVB sides. Based on our observation in this study it seems that psoralen dose not increase the pigmentary effect of NB UVB in vitiligo.

The incidence of phototoxic reactions was significantly higher on the PUVB side i.e., PUVB was more erythemogenic than UVB alone. This stands in contrast to Sakantubhai *et al.* (1993) (10), who noticed a better response without increase incidence of erythema the P UVB side, compared with UVB alone in the treatment of psoriasis. However, this difference may be explained by the fact that vitiliginous skin is more liable to sunburn and the higher starting dose in our study.

There was a positive correlation between disease duration and the good response to treatment on both sides, a finding that could be explained by the stabilization of the autoimmune process in disease of long duration. This was in contrast to the findings of another study, which reported a lower percentage of pigmentation in patients with a very long duration of vitiligo, compared with those with a shorter duration of the disease (15).

Apart from a significantly better response in males, no other factors, namely: skin type, extent of lesions, previous treatment, positive family history, pre-disposing factors or patient compliance showed any correlation to the response.

According to the results in both studies, we can conclude that NB UVB 311 nm is an effective, well-tolerated line of management for vitiligo. Its efficacy is equal to, but not superior, to PUVA. The addition of oral psoralen to NB UVB 311 nm reduces the cumulative dose of UVB exposure, but increases its phototoxic hazards and does not improve its therapeutic pigmentary capabilities in the treatment of vitiligo.

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