Narrow-band ultraviolet B is a useful and well-tolerated treatment for vitiligo

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Background: The treatment of vitiligo remains a challenge.

Objective: The purpose of this article is to review our results and experience with narrow-band ultraviolet (UV) B phototherapy for vitiligo.

Methods: This is a retrospective analysis of our experience and results with patients with vitiligo who were treated with narrow-band UVB between November 1998 and November 1999. Narrow-band UVB phototherapy was given as monotherapy 3 times a week. The starting dose was 280 mJ/cm^2, with 15% dose increments at each subsequent treatment.

Results: Seven patients were able to be evaluated for the purposes of this analysis. Their ages ranged from 19 to 59 years (mean, 37.6 years). Three patients had Fitzpatrick skin phototype IV and V, and 4 had phototypes II and III. Five of the 7 patients achieved more than 75% repigmentation with a mean of 19 treatments; the mean duration of disease was 13 months. The remaining two patients had 50% and 40% repigmentation after 46 and 48 treatments, respectively. Their mean duration of disease was 132 months. Adverse effects were mild erythema and pruritus.

Conclusion: This treatment protocol resulted in rapid repigmentation in many patients, including those with skin phototypes IV and V. In accordance with previous studies, this report indicates that narrow-band UVB is a useful and well-tolerated therapy for vitiligo. (J Am Acad Dermatol 2001;44:999-1003.)

Vitiligo is an acquired cutaneous disorder of pigmentation with a 1% to 2% incidence worldwide, without sex or skin color predilection. The clinical presentation is characterized by solitary or multiple depigmented macules or patches that may arise in a localized, segmental, or generalized distribution.

Various treatment modalities have been described in the literature. The surgical modalities consist of autologous transplantation and include split-thickness epidermal grafting, epidermal blister grafting, and grafting of cultured melanocytes. The nonsurgical modalities, considered first-line therapy, include corticosteroids (oral, topical, and intralesional), oral or topical psoralens plus ultraviolet A (PUVA), and recently, narrow-band ultraviolet (UV) B therapy.

PUVA is a well-described therapy for vitiligo; its limitations include acute side effects such as nausea and phototoxic reactions, as well as long-term carcinogenic risk.[1] In the past few years, two studies on narrow-band UVB for vitiligo have been published, both from a single center in Europe, and one of them specifically evaluated the efficacy and safety in children.[2,3] We present our experience with narrow-band UVB phototherapy as further evidence of its utility in the treatment of vitiligo.

PATIENTS

All of the patients were seen in the dermatology clinic, Henry Ford Hospital, Detroit, Michigan. Patients with localized, segmental, or generalized vitiligo who initiated treatment over a 12-month period (November 1998-November 1999) were included in this data analysis. Eleven patients (6 men, 5 women) were included in the study. The ages of these 11 patients ranged from 19 to 59 years (median, 40 years). The patients were assessed for Fitzpatrick skin phototypes, overall disease duration, and history of previous therapy.

METHODS

This article reports a retrospective review of our experience with narrow-band UVB phototherapy for vitiligo. All 11 patients were treated with nar-

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Table I. Profile of patients

Patient No.	Age (y)/Sex	Skin type	Duration of disease	Disease phase	Previous therapy
1	53/M	II	6 mo	Latent	Topical corticosteroids
2	25/M	V	3 y	Progressive	Topical corticosteroids
3	24/F	III	1 y	Latent	Topical corticosteroids
4	59/F	IV	8 mo	Progressive	None
5	54/M	V	5 mo	Progressive	None
6	29/F	II	10 y	Regressive	Topical corticosteroids, PUVA
7	19/M	II	12 y	Latent	Topical corticosteroids

Table II. Clinical response

Patient No.	% Repigmentation	No. of treatments for repigmentation	Cumulative dose (J/cm^2)	Side effects
1	>75	11	7.4	Mild erythema
2	>75	19	11.1	Mild erythema
3	>75	20	14.7	Pruritus
4	>75	25	26.6	Mild erythema
5	>75	22	18.8	None
6	50	46	77.0	None
7	40	48	63.8	Mild erythema

row-band UVB as a monotherapy from November 1998 to November 1999. All patients were treated in a phototherapy unit (Ultralite 6809 Phototherapy Process Controller, Lawrenceville, Ga) containing a bank of 48 fluorescent tubes (TL-100W/01, Phillips, Eindhoven, The Netherlands) with peak emission at 311 to 312 nm. Therapy was administered 3 times a week, on nonconsecutive days. Affected segments of the body were exposed during each treatment. The genital area was shielded in all cases. Phototesting was not done as the lesional skin of all patients was considered to be Fitzpatrick skin phototype I. A minimal erythema dose (MED) of 400 mJ/cm^2 was predetermined for this skin phototype. The initial fluence for each patient was 70% of the MED, or 280 mJ/cm^2. The irradiation dose was increased by 15% for each subsequent treatment. If the patient reported mild erythema or pruritus, the irradiation dose was held constant for the subsequent treatment, or until resolution of symptoms. If symptomatic erythema (burning, pain) or blistering developed, the irradiation dose was decreased by 15%. A physician (L. S., J. J. K., or H. W. L.) examined patients every 2 weeks. Once 75% repigmentation was achieved, the frequency of treatments was tapered to twice a week for 4 weeks, then weekly for 4 weeks. Lesional photography was performed at the initial pretreatment visit and monthly thereafter.

RESULTS

Profile of patients

Of the 11 patients, 4 were lost to follow-up because of scheduling difficulties. None of these patients experienced any adverse effects from phototherapy that warranted discontinuation of the phototherapy. Seven patients completed a course of therapy or were continuing to receive therapy as of April 2000. As shown in Table I, the age range was 19 to 59 years, with a mean of 37.6 years. Three of the 7 patients had skin phototypes IV and V, and the rest had skin phototypes II and III. Disease duration ranged from 5 months to 12 years. By history, previous therapies, including topical corticosteroids (n = 5) and oral PUVA (n = 1), had failed in 5 of the 7 patients.

Treatment outcome

The outcomes are presented in Table II. Five of 7 patients showed greater than 75% repigmentation after a mean number of 19 treatments (Fig 1). The mean duration of disease among these 5 patients was 13 months (Table III). Two of 7 patients failed to show repigmentation of greater than 75% after 46 and 48 treatments, respectively, although they did exhibit 50% and 40% repigmentation. The mean duration of disease in these two patients was 132 months.

Repigmentation in 6 cases was follicular in nature; it was most prominent in the center of each lesion. In one case (localized vitiligo of the right temporal area),

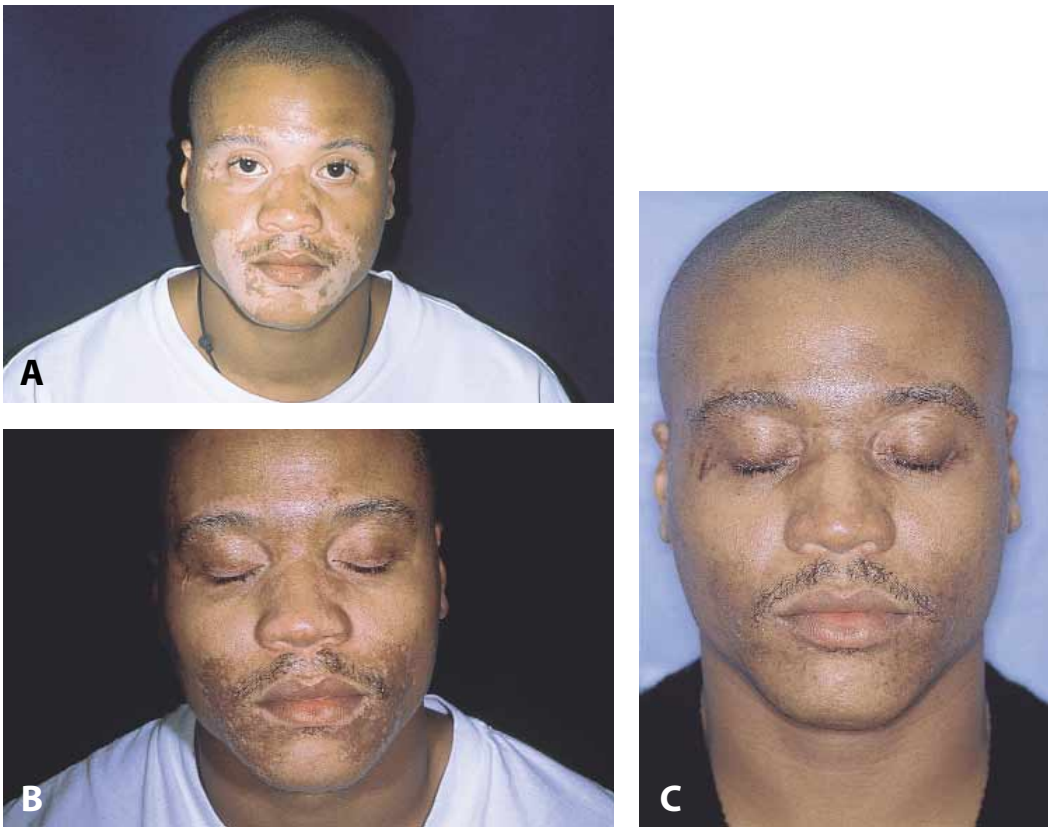

Fig 1. A, Pretreatment photograph of a 25-year-old African American man with a 3-year history of vitiligo. Note depigmentation at periorbital and perioral areas. **B,** Complete repigmentation after 19 treatments, with darker color compared with the surrounding skin. **C,** Normalization of color intensity of the repigmented areas after 26 treatments.

observed repigmentation occurred from the periphery (Fig 2). Of note, most patients experienced initial repigmentation that was darker than surrounding nonlesional skin. This darker pigmentation was especially prominent in patients having skin phototypes IV and V. In all cases, the color intensity normalized over several weeks, providing a good cosmetic result without any ancillary intervention, even while patients continued to receive therapy (Fig 1).

Six of the 7 patients continue to be followed up in the dermatology clinic, whereas one was lost to follow-up. In the assessment of duration of response, 4 patients have retained their repigmentation. In fact, one subject has remained completely repigmented 11 months after phototherapy was discontinued. By contrast, two patients experienced a loss of pigmentation. Approximately 4 months after phototherapy was discontinued, several depigmented macules and patches in previously uninvolved skin developed in one of these two patients. The second patient experienced a loss of pigment in newly repigmented areas when phototherapy was tapered to twice a week. In both cases, repigmentation occurred after narrow-band phototherapy treatments were reinitiated at 3 times a week.

Table III. Correlation between therapeutic response and disease duration

% Repigmentation	Disease duration
>75	13 mo
<75	132 mo

Adverse effects

Adverse side effects were minimal. Four patients reported mild asymptomatic erythema and one patient reported pruritus, which resolved spontaneously. No patients experienced symptoms that warranted suspension or discontinuation of narrow-band UVB phototherapy.

DISCUSSION

In 1981 Parrish and Jaenicke[4] found that 311-nm wavelength UVB radiation was most effective for the

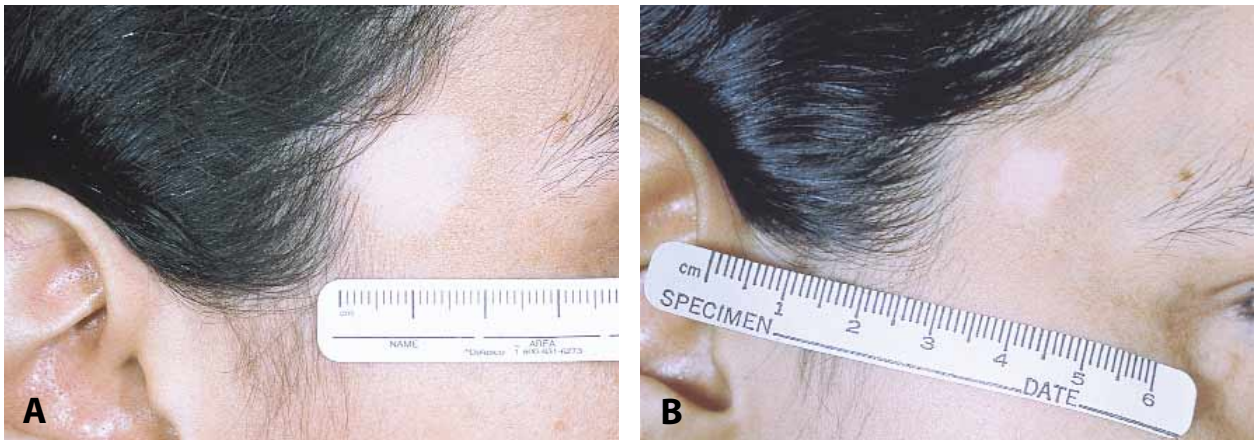

Fig 2. A, Pretreatment photograph of a 24-year-old Middle Eastern woman with a 1-year history of vitiligo. Note that the depigmentation extended into the hairline. **B,** Marked improvement after 18 treatments.

treatment of psoriasis. This finding provided the impetus for developing the Phillips TL-01 fluorescent bulb, the narrow-band UVB light source. Currently, there are several clinical indications for narrow-band UVB phototherapy, including psoriasis,[5-11] atopic dermatitis,[12] desensitization (hardening) therapy for photodermatoses,[13-15] and patch-stage cutaneous T-cell lymphoma.[16]

The use of narrow-band UVB phototherapy for vitiligo was first reported by Westerhof and Nieuweboer-Krobotova[2] in 1997. These investigators compared twice-weekly topical PUVA to twice-weekly narrow-band UVB phototherapy. They showed that after 4 months of therapy, 67% of patients undergoing narrow-band UVB phototherapy showed repigmentation compared with 46% of patients receiving topical PUVA. The extent and rates of repigmentation among patients receiving narrow-band UVB were further examined in a separate subset of patients. In this subset, 8% of patients repigmented greater than 75% after 3 months of treatment and 63% did so after 12 months. It was concluded that compared with topical PUVA phototherapy, narrow-band UVB was equally, if not more, effective and was associated with fewer side effects.

There are several key differences between the findings of Westerhof and Nieuweboer-Krobotova[2] and ours. Their study design was a two-arm treatment trial, whereas ours is a report of prescribed therapy. The starting dose in this previous study was 75 mJ/cm^2, and treatment frequency was twice weekly. In contrast, we used a starting dose of 280 mJ/cm^2, and treatment was given 3 times per week. Eighty-six percent of the patients in the previous study had skin types II and III, whereas the corresponding percentage in our patients was 57% (4/7 patients). Five of our 7 patients had more than 75% repigmentation after a mean of 19 treatments (ie, 6-7 weeks), a response rate that was faster and higher than that reported previously.[2] Whether the differences in the treatment protocols and in the distribution of skin types between the two analyses have contributed to the different response remains to be investigated.

Potential limitations of narrow-band UVB phototherapy are the scheduling difficulties and time commitment. At our center, phototherapy treatments are initiated on a 3-times-weekly schedule. Multiple visits are required for successful repigmentation. At present, in the United States, narrow-band UVB phototherapy is only available in a few centers; therefore patients often have to commute long distances for treatment. In fact, 4 of our initial 11 patients, or 36%, discontinued narrow-band UVB phototherapy because of time and schedule restraints. Issues with insurance coverage are also germane since the therapy is not covered by all insurance carriers.

In a recent meta-analysis of nonsurgical therapies for vitiligo by Njoo et al,[17] corticosteroid therapy was reported to have a success rate of 56% in localized disease. However, the high incidence of cutaneous side effects makes corticosteroid therapy undesirable for long-term use; it is also impractical in cases involving large body surface area. In the same analysis, high success rates in the treatment of generalized vitiligo were seen with oral PUVA (51%), broad-band UVB (57%), and narrow-band UVB (63%). Our results extended these previous observations by demonstrating that rapid repigmentation occurs in patients with skin types IV and V. A noteworthy observation in our patients is that longer duration of disease seems to correlate with less successful repigmentation (Table III). The mean duration of disease

among the best responders (>75% repigmentation) was 13 months, compared with 132 months among the poor responders (<75% repigmentation). Thus those patients who had more than 75% repigmentation had a 10-fold shorter disease duration than the patients who repigmented less than 75%. This correlation has not been previously reported; it is difficult to say whether these data represent a significant finding or reflect our small sample size (n = 7). However, this observation suggests that it may be best to initiate narrow-band therapy in the early stages of the disease process.

The mechanism of action of narrow-band phototherapy in vitiligo has not been completely understood. Vitiligo is characterized by the selective destruction of melanocytes; the cause is unknown, but is generally believed to be an autoimmune process. Repigmentation, when it occurs, begins at the hair follicle, where dopa-negative, amelanotic melanocytes in the outer root sheaths are somehow activated to proliferate, produce melanins, and migrate outward to surrounding depigmented skin.[18] Melanocyte mitogenesis, melanogenesis, and melanocyte migration have been shown to be induced by various cytokines and inflammatory mediators, including interleukin (IL)-1, tumor necrosis factor–α, and leukotriene C_4. IL-1α stimulates the synthesis of endothelin-1, a potent vasoconstrictive peptide that has mitogenic and melanogenic properties. Imokawa, Miyagishi, and Yada[19] found that expression of endothelin-1, IL-1α, and tyrosinase in human keratinocytes in vitro and in vivo were increased after UVB irradiation, suggesting a possible mechanism of UVB-induced repigmentation.

Another new approach in the treatment of vitiligo comes from recent investigations on the effect of oxidative stress in vitiligo. Schallreuter et al[20] reported low epidermal catalase in lesional and nonlesional skin, resulting in the accumulation of hydrogen peroxide. They demonstrated that application of topical pseudocatalase, a nonenzymatic complex capable of degrading hydrogen peroxide to water and oxygen after photoactivation with narrow-band UVB, resulted in repigmentation.

In summary, our findings extend previous observations that narrow-band UVB is a useful and well-tolerated treatment option for patients with vitiligo. It is clear that much still needs to be elucidated at both the clinical and molecular levels in the pathogenesis of and therapy for this disease.

REFERENCES

1. Morison WL, Baughman RD, Day RM, Forbes PD, Hönisgmann H, Krueger GG, et al. Consensus workshop on the toxic effects of long-term PUVA therapy. Arch Dermatol 1998;134:595-8.
2. Westerhof W, Nieuweboer-Krobotova L. Treatment of vitiligo with UV-B radiation vs topical psoralen plus UV-A. Arch Dermatol 1997;133:1525-8.
3. Njoo MD, Bos JD, Westerhof W. Treatment of generalized vitiligo in children with narrow-band (TL-01) UVB radiation therapy. J Am Acad Dermatol 2000;42:245-53.
4. Parrish JA, Jaenicke KF. Action spectrum for phototherapy of psoriasis. J Invest Dermatol 1981;76:359-62.
5. Alora MBT, Taylor CR. Narrow-band (311 nm) UVB phototherapy: an audit of the first year's experience at the Massachusetts General Hospital. Photodermatol Photoimmunol Photomed 1997;13:82-4.
6. Coven TR, Burack LH, Gilleaudeau P, Koegh M, Ozawa M, Krueger JG. Narrowband UVB produces superior clinical and histopathological resolution of moderate-to-severe psoriasis in patients compared with broadband UV-B. Arch Dermatol 1997;133:1514-22.
7. Gupta G, Long J, Tillman DM. The efficacy of narrowband ultraviolet B phototherapy in psoriasis using objective and subjective outcome measures. Br J Dermatol 1999;140:887-90.
8. Storbeck K, Hölzle E, Schürer N, Lehmann P, Plewig G. Narrowband UVB (311 nm) versus conventional broad-band UVB with and without dithranol in phototherapy for psoriasis. J Am Acad Dermatol 1993;28:227-31.
9. Picot E, Meunier L, Picot-Debeze MC, Peyron JL, Meynadier J. Treatment of psoriasis with a 311-nm UVB lamp. Br J Dermatol 1992;127:509-12.
10. Green C, Ferguson J, Lakshmipathi T, Johnson BE. 311 nm UVB phototherapy: an effective treatment for psoriasis. Br J Dermatol 1988;119:691-6.
11. Van Weelden H, Baart De La Faille H, Young E, Van Der Leun JC. A new development in UVB phototherapy of psoriasis. Br J Dermatol 1988;119:11-9.
12. Grundmann-Kollmann M, Behrens S, Podda M, Peter RU, Kaufmann R, Kerscher M. Phototherapy for atopic eczema with narrow-band UVB. J Am Acad Dermatol 1999;40:995-7.
13. Bilsland D, Geoge SA, Gibbs NK, Aitchison T, Johnson D, Ferguson J. A comparison of narrow band phototherapy (TL-01) and photochemotherapy (PUVA) in the management of polymorphic light eruption. Br J Dermatol 1993;129:708-12.
14. Man I, Dawe RS, Ferguson J. Artificial hardening for polymorphic light eruption: practical points from ten years' experience. Photodermatol Photoimmunol Photomed 1999;15:96-9.
15. Collins P, Ferguson J. Narrow-band UVB (TL-01) phototherapy: an effective preventative treatment for the photodermatoses. Br J Dermatol 1995;132:956-63.
16. Hofer A, Cerroni L, Kerl H, Wolf P. Narrowband (311nm) UV-B therapy for small plaque parapsoriasis and early-stage mycosis fungoides. Arch Dermatol 1999;135:1377-80.
17. Njoo MD, Spuls PI, Bos JD, Westerhof W, Bossuyt PMM. Nonsurgical repigmentation therapies in vitiligo: meta-analysis of the literature. Arch Dermatol 1998;134:1532-40.
18. Cui J, Shen LY, Wang GC. Role of hair follicles in the repigmentation of vitiligo. J Invest Dermatol 1991;97:410-6.
19. Imokawa G, Miyagishi M, Yada Y. Endothelin-1 as a new melanogen: coordinated expression of its gene and the tyrosinase gene in UVB-exposed human epidermis. J Invest Dermatol 1995;105:32-7.
20. Schallreuter KU, Moore J, Wood JM, Beazley WD, Gaze DC, Tobin DJ, et al. In vivo and in vitro evidence for hydrogen peroxide (H_2O_2) accumulation in the epidermis of patients with vitiligo and its successful removal by a UVB-activated pseudocatalase. J Invest Dermatol Symp Proc 1999;4:91-6.