

Narrowband UVB Treatment Increases Serum 25-Hydroxyvitamin D Levels in Patients With Chronic Plaque Psoriasis

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PRACTICE POINTS

- The 25-hydroxyvitamin D (25[OH]D) levels are increased by narrowband UVB (NB-UVB) treatment in psoriasis patients.
- The number of sessions of NB-UVB is associated with increased 25(OH)D levels.

The aim of this study was to investigate the effects of narrowband UVB (NB-UVB) phototherapy on serum 25-hydroxyvitamin D (25[OH]D) levels and related parameters in patients with psoriasis. Forty-nine participants with moderate to severe plaque-type psoriasis were included in this study and were treated with NB-UVB therapy 3 times weekly for 6 months or until psoriasis area and severity index (PASI) 75 was achieved. Participants' serum 25(OH)D, calcium, phosphorus, parathyroid hormone (PTH), and alkaline phosphatase (ALP) levels were measured at baseline and completion of treatment, along with PASI scores. We observed that the serum 25(OH)D levels increased after NB-UVB treatment, but the only correlation that was found was the number of sessions of NB-UVB. There was no relationship between patient age, Fitzpatrick skin type, PASI score, or maximum NB-UVB dose and serum 25(OH)D levels.

Cutis. 2017;99:431-435.

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The authors report no conflict of interest.

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Psoriasis is a chronic, inflammatory, T-cell-mediated skin disease. Phototherapy, which consists of light used at various wavelengths, is a well-established treatment method for psoriasis vulgaris. Although successful results have been obtained with phototherapy in psoriasis, its mechanism of action is not fully understood. UV light has been shown to have an effect on T-lymphocyte function as well as various components of the natural and acquired immune response. It also has a suppressive effect on the immune system caused by many independent effects.¹ Phototherapy currently is available using broadband UVB (290–320 nm), narrowband UVB (NB-UVB)(311–313 nm), 308-nm excimer laser, UVA1 (340–400 nm), psoralen plus UVA, and photopheresis.² Narrowband UVB treatment with light sources that peak at 311 to 313 nm have been used with high efficacy and a low side-effect profile, becoming the standard phototherapy method for chronic plaque-type psoriasis.³

More than 90% of vitamin D synthesis is formed in the skin following UV exposure, and the wavelengths and the solar spectrum that stimulate vitamin D synthesis have been a focus of research.⁴ 7-Dehydrocholesterol (provitamin D₃) is first converted to previtamin D₃. Although the necessary UV wavelength for previtamin D₃ synthesis is 295 to 300 nm, it is known that production stops below 260 nm and above 315 nm.⁴⁻⁶ Previtamin D₃ is unstable and is quickly converted to vitamin D₃ in the skin and then to the biologically active

form of 1,25-dihydroxyvitamin D₃ (calcitriol) following hydroxylation in the liver and kidneys. Calcitriol shows its effect by binding to the special nuclear receptor for vitamin D.⁷ Many tissues including the keratinocytes, dendritic cells, melanocytes, and sebocytes in the skin have been shown to possess the enzymatic mechanism necessary for 1,25-dihydroxyvitamin D₃ production. Vitamin D also is known to have paracrine, autocrine, and intracrine effects on immunomodulation, cell proliferation, differentiation, and apoptosis, in addition to its role in calcium metabolism.⁵⁻⁹ Topical vitamin D and its analogues are used effectively and safely in psoriasis treatment with these effects.¹⁰ A correlation between low serum vitamin D levels and chronic inflammation severity has been shown in psoriasis patients in some studies.^{11,12}

In this study, we sought to evaluate the effect of NB-UVB on vitamin D status and related metabolic markers in patients with psoriasis.

Methods

This prospective, single-center study included patients living in or around Eskişehir, Turkey, who were 18 years of age or older and had been diagnosed with chronic plaque psoriasis with a psoriasis area and severity index (PASI) score of 5 or higher. Permission was granted by the local ethics committee. Patients provided written informed consent prior to enrollment. Patients were excluded if they were younger than 18 years; were pregnant or breastfeeding; stayed in open environments for more than 2 hours per day during the summer months (May through September); used drugs affecting calcium metabolism in the last 8 weeks (eg, barbiturates, anticonvulsants, corticosteroids, vitamin D supplements, bisphosphonates); used systemic treatment for psoriasis in the last 8 weeks; used phototherapy or sunbathing in the last 8 weeks; used topical vitamin D analogues in the last 4 weeks; or had a history of psoriatic arthritis and other inflammatory disorders, renal disease, known calcium metabolism disorders, granulomatous disorders, thyroid disease, diabetes mellitus, skin cancer, or abnormal photosensitivity and known lack of response or hypersensitivity to phototherapy.

Clinical Evaluation and Laboratory Studies—The participants' age, gender, Fitzpatrick skin type, disease duration, dairy intake and vitamin supplement levels, hours of sun exposure per week, detailed medical history, and medications were obtained and documented in the medical records.

Serum 25(OH)D levels were measured using high-performance liquid chromatography/mass spectrometry, serum calcium and phosphorus levels

using colorimetric analysis, serum alkaline phosphatase (ALP) levels using the enzymatic colorimetric method, and serum parathyroid hormone (PTH) levels using electrochemiluminescence at baseline and after PASI 75 was achieved with treatment. Vitamin D levels were classified in 3 groups: (1) deficient (<20 ng/mL); (2) inadequate (20–30 ng/mL); and (3) adequate (>30 ng/mL). The PASI scores at baseline and posttreatment were calculated by the same dermatologist (S.S.).

Treatment Protocol and Patient Follow-up—Narrowband UVB treatment was started at 70% of the minimal erythema dose (MED). Phototherapy was administered 3 times weekly for 6 months or until PASI 75 response was achieved. An increase of 20% to 30% from the prior dose was made according to the participants' clinical status at each treatment session, and the dose was stabilized once the maximum dose was achieved according to skin type—up to 2000 mJ/cm² for Fitzpatrick skin types I and II, 3000 mJ/cm² for skin types III and IV, and 5000 mJ/cm² for skin types V and VI. Participants were allowed to use low- and moderate-potency topical corticosteroids and moisturizers containing urea during the course of treatment. The study physician (S.S.) clinically evaluated participants every 4 weeks for 6 months or until PASI 75 was achieved, and the clinical improvement was calculated as the percentage decrease in PASI score.

Statistical Analysis—The Shapiro-Wilk normalcy test was used for the continuous variables in the study. Variables with a normal distribution were analyzed with the paired *t* test and 1-way analysis of variance test and presented as mean (SD). Variables without a normal distribution were analyzed with the Wilcoxon *t* test and the Kruskal-Wallis test and presented as the median and 25th and 75th quartiles. The serum 25(OH)D levels were evaluated according to the seasons with the Kruskal-Wallis test. Categorical variables were expressed as frequency and percentages. The Pearson and Spearman correlation analysis and regression analysis were used to show the relationship between the variables (ie, age, Fitzpatrick skin type, PASI score, maximum NB-UVB dose, and number of sessions). The statistical significance level was set at $P \leq .05$. Statistical analyses were performed using SPSS software version 21.

Results

A total of 49 participants (30 [61.22%] males; 19 [38.78%] females) were included in the study. The mean age (SD) was 40.27 (14.62) years (range, 19–74 years). Three (6.12%) participants were

Fitzpatrick skin type I, 15 (30.61%) were skin type II, and 31 (63.27%) were skin type III.

The baseline median PASI score for the 49 participants was 10.20 (7.85–13.65). Baseline serum 25(OH)D levels were noted to be deficient in 40 participants (81.63%) and inadequate in 9 participants (18.37%). The distribution of the serum 25(OH)D levels of the participants according to the season was evaluated with the Kruskal-Wallis test and no association was found between serum 25(OH)D levels and seasonal changes ($P=.685$). Comparison of 25(OH)D basal values with Fitzpatrick skin type revealed a statistically significant relationship between skin type and vitamin D level ($P=.024$). The basal serum 25(OH)D levels were significantly lower in Fitzpatrick skin type II versus skin type I ($P=.039$).

Thirty-two (65.31%) participants achieved PASI 75 by the end of treatment. The baseline median PASI score (25th–75th quartiles) for the 32 patients was 10.45 (8.20–13.83) and the posttreatment PASI score was 1.95 (1.20–3.55), a statistically significant decrease following treatment ($P<.001$) (Table 1). Mean (SD) baseline serum 25(OH)D levels were 14.14 (6.70) ng/mL and posttreatment levels were 46.42 (15.51) ng/mL in these participants, which demonstrated a statistically significant increase during NB-UVB treatment ($P<.001$). None of the participants reached the toxicity levels (>80 ng/mL) for serum 25(OH)D. There were no significant changes in serum calcium or phosphorus levels

posttreatment (Table 1), but statistically significant decreases in serum ALP and PTH levels were noted ($P=.001$ and $P=.019$, respectively) (Table 1).

Participants who completed the study ($n=32$) received an average (SD) of 30.09 (7.53) sessions of NB-UVB treatment and the mean (SD) MED was 611.88 (240.14) mJ/cm². The mean (SD) maximum dose was 2090.09 (341.78) mJ/cm² (Table 2).

Posttreatment serum 25(OH)D levels were compared with the number of NB-UVB phototherapy sessions and the maximum dose values. We found that the posttreatment serum 25(OH)D levels correlated with the number of sessions ($P=.031$) but not with the maximum dose ($P=.498$).

Using regression analysis, we also evaluated the effect of the increase in vitamin D levels—posttreatment serum 25(OH)D level minus baseline serum 25(OH)D levels—on the decrease in PASI scores—baseline PASI score minus posttreatment PASI score—and found no effect of serum 25(OH)D level increase on PASI decrease ($P=.530$). There was no correlation between increased serum 25(OH)D levels and age, Fitzpatrick skin type, or baseline PASI score.

Comment

The most effective UV wavelength for vitamin D synthesis is 295 to 300 nm, and therefore broadband UVB is frequently studied when determining the relationship between phototherapy and serum vitamin D levels.⁴ The current study demonstrated

Table 1.

Comparison of Baseline and Posttreatment Laboratory Values in Patients Who Achieved PASI 75 ($n=32$)

Laboratory Value	Baseline	Posttreatment	P Value
Median PASI score (25th–75th quartiles)	10.45 (8.20–13.83)	1.95 (1.20–3.55)	$<.001^a$
Mean (SD) serum 25(OH)D level, ng/mL	14.14 (6.70)	46.42 (15.51)	$<.001^a$
Median serum calcium level (25th–75th quartiles), mg/dL	9.73 (9.50–9.98)	9.74 (9.40–10.28)	.483 ^a
Mean (SD) serum phosphorus level, mg/dL	3.56 (0.49)	3.57 (0.51)	.917 ^b
Median ALP level (25th–75th quartiles), U/L	200.50 (168.00–245.50)	156.00 (79.25–209.00)	.001 ^a
Median PTH level (25th–75th quartiles), pg/mL	47.26 (33.77–53.66)	34.81 (28.04–54.23)	.019 ^a

Abbreviations: PASI, psoriasis area and severity index; 25(OH)D, 25-hydroxyvitamin D; ALP, alkaline phosphatase; PTH, parathyroid hormone.

^aWilcoxon t test.

^bPaired t test.

Table 2.

Narrowband UVB Treatment Doses (n=32)

	Mean (SD)	Minimum	Maximum
Treatment sessions, n	30.09 (7.53)	16	56
MED, mJ/cm ²	611.88 (240.14)	245	1080
Maximum dose, mJ/cm ²	2090.09 (341.78)	820	2537

Abbreviation: MED, minimal erythema dose.

a statistically significant increase in serum 25(OH)D levels following NB-UVB treatment in patients with moderate to severe chronic plaque psoriasis ($P < .001$). This result supports other studies reporting that NB-UVB treatment in psoriasis patients increases serum 25(OH)D levels.¹³⁻¹⁸

The main factor in the effective UVB level for vitamin D synthesis is the angle at which solar radiation reaches the earth, which is affected by the longitude, latitude, and time of day.¹⁹ For this reason, we planned to perform our study at a single center. Patients who stayed in open areas for more than 2 hours per day during the summer months (May through September) were excluded from the study to decrease the effect of seasonal changes on vitamin D levels. We evaluated the seasonal variation of vitamin D levels and found no relationship between seasonal changes and serum 25(OH)D levels. Therefore, the potential effect of seasonal changes on the vitamin D levels of study participants was excluded from the study.

The response to UV radiation changes according to age and Fitzpatrick skin type because 7-dehydrocholesterol levels decrease with age and melanin prevents the access of UVB photons to 7-dehydrocholesterol.²⁰ The basal serum 25(OH)D levels were deficient in 81.63% of participants and inadequate in 18.37%. In this study, we also observed that the basal serum 25(OH)D levels were significantly lower in patients with Fitzpatrick skin type II than in Fitzpatrick skin type I ($P = .039$). The mean (SD) serum 25(OH)D level at baseline was 14.14 (6.70) ng/mL and posttreatment was

46.42 (15.51) ng/mL in the 32 patients who completed the study. Serum 25(OH)D levels showed a statistically significant increase after NB-UVB treatment ($P < .001$). The increased serum 25(OH)D levels after NB-UVB phototherapy were not associated with Fitzpatrick skin type, which was consistent with the results of Osancevic et al.¹⁷ The adjusted NB-UVB doses according to the different skin types might be responsible for this result in our study.

Participant age did not have a significant effect on serum 25(OH)D levels, similar to other studies in the literature.^{13,17} We believe that artificial UVB radiation at high doses can compensate for the 7-dehydrocholesterol that decreases in the skin with aging.

We observed no significant change in the serum calcium and phosphorus levels with NB-UVB treatment in our study. None of the participants had a metabolic disorder related to increased 25(OH)D levels. The serum ALP and PTH levels decreased significantly following treatment ($P = .001$ and $P = .019$, respectively), which may have been secondary to increased serum 25(OH)D levels.

Posttreatment serum 25(OH)D levels were compared with the number of NB-UVB phototherapy sessions and maximum dose values. The posttreatment serum 25(OH)D levels were found to be related to the number of sessions received, but this value was not correlated with the maximum dose received. The MED and maximum dose were determined according to the Fitzpatrick skin type of the participants. Therefore, increased serum 25(OH)D levels with an increased number of sessions was an expected result. Our observation is in accordance with the finding described by Ryan et al.¹⁴ On the other hand, an in vitro study conducted by Olds et al.²¹ reported that the relationship between UV light and cholecalciferol synthesis was not linear.

We found that increased serum 25(OH)D levels after treatment were not correlated with the decrease in PASI score, similar to studies by Romani et al.¹⁸ and Ryan et al.¹⁴ These results suggest that the clinical improvement following NB-UVB treatment is independent of the increased serum 25(OH)D levels in psoriasis patients.

Conclusion

In conclusion, we found that the serum 25(OH)D levels that increase as a result of NB-UVB therapy for the treatment of chronic plaque psoriasis has no statistically significant relationship with the age, Fitzpatrick skin type, baseline PASI score, changes in PASI, or maximum dose, while a positive relationship is present between the serum 25(OH)D levels and the number of sessions of NB-UVB.

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