ORIGINAL ARTICLE

The Effect of Narrowband Ultraviolet B Phototherapy on Vitamin D Status in Psoriasis Patients with Skin Phototype III, IV and V

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Abstract

Background

Narrowband ultraviolet-B (NBUVB) is an effective treatment option for psoriasis. Vitamin D insufficiency is common in psoriasis patients. We assessed the effect of NBUVB on vitamin D levels amongst psoriasis patients with skin phototype III, IV and V.

Methods

Psoriasis patients planned for NBUVB phototherapy were enrolled in a prospective cohort study in Hospital Putrajaya and Hospital Kuala Lumpur from May 2020-December 2020. NBUVB phototherapy was given twice weekly for 12 weeks. Serum 25 (OH)D level was measured at baseline and at week 12.

Results

A total of 21(63.6%) male and 12(36.4%) female patients aged 18-66 years participated. Majority were Fitzpatrick skin phototype (FSP) IV (66.7%) followed by FSP V (21.2%) and FSP III (12.1%). Serum 25(OH)D increased significantly ($p<0.001$) from 52.09±21.43 nmol/L at baseline to 72.80±19.56 nmol/L at week 12 with the most increment seen in skin type V. There was also a significant improvement seen in Body Surface Area (BSA) involvement after 12 weeks of phototherapy ($p<0.001$). There was no correlation seen between BSA at week 12 with serum 25(OH)D and percentage of serum 25(OH) D increment.

Conclusion

NBUVB phototherapy increases the level of serum 25(OH)D in psoriasis patients with darker skin types while simultaneously clearing psoriasis.

Key words: *25-hydroxyvitamin D; Fitzpatrick skin phototype; Psoriasis; Narrowband Ultraviolet-B; Phototherapy*

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Introduction

Psoriasis is an immune-mediated inflammatory skin disease which occurs worldwide and is estimated to affect around 2.0% to 3.0% of the world's population.[1,2] Epidemiological evidence demonstrated variable prevalence of psoriasis amongst different ethnic groups and population.[3] The Malaysian Psoriasis Registry recorded a total of 21,735 psoriasis patients aged ≥18 years

from January 2007 through December 2018.[4]

Narrowband ultraviolet-B (NBUVB) phototherapy is an effective and safe treatment for psoriasis. NBUVB reverses several pathologic alterations in psoriasis which ultimately causes reduction in T-lymphocytes and dendritic cells.[5] Inhibition of maturation, differentiation and migration of dendritic cells are caused by activation of vitamin D. The epidermis plays an important role in vitamin D synthesis but is also a target tissue for activated vitamin D and its analogues. The active form of vitamin D 1,25 dihydroxyvitamin D [1,25(OH)2D] produced by hydroxylation in the liver and kidney suppresses growth and induces differentiation of keratinocytes, thus reducing psoriasis severity. The radiation wavelength of NBUVB (from 311 to 313 nm), lies within the action spectrum responsible for cutaneous vitamin D_3 production.[5] Psoriatic lesions respond well to narrowband ultraviolet B phototherapy.[6] NBUVB positively affects vitamin D status[7,8,9,10] and this could partly account for the beneficial effect of phototherapy in psoriasis.

Skin phototype determines response to UVB radiation, with a greater rate of vitamin D3 synthesis in lighter skin tones as melanin absorbs UVB irradiation.[11] Therefore, people with naturally darker skin are at greater risk of vitamin D deficiency. Increase in serum vitamin D_3 levels as well as improvement in Psoriasis Area and Severity Index (PASI) have been demonstrated after NBUVB therapy.[8,9,10]

Our study was conducted to assess the effect of NBUVB on vitamin D levels amongst psoriasis patients of darker skin types (Fitzpatrick skin phototype III, IV and V), its association with improvement in body surface area (BSA) affected by psoriasis as well as the correlation between cumulative NBUVB dose and the improvement in serum 25(OH)D.

Materials and Methods

An observational cohort study was performed. The study population was psoriasis patients planned for NBUVB phototherapy at the Dermatology Clinics of Hospital Putrajaya and Hospital Kuala Lumpur who fulfilled the inclusion and exclusion criteria during the study period from May 2020 to December 2020. Inclusion criterion was psoriasis patients aged 18 and above with Fitzpatrick skin phototype III, IV or V. Patients with renal or hepatic disease, previous skin malignancy, on vitamin D or calcium supplements were excluded. Psoriasis severity was defined by percentage of BSA affected by psoriasis based on the Malaysian Clinical Practice Guideline for the Management of Psoriasis Vulgaris; mild ≤10%, moderate >10%-30% and severe >30%.[12]

Serum 25(OH)D was measured at baseline prior to NBUVB therapy and after 12 weeks of therapy. NBUVB wasdelivered using either Daavlin 3 Series or MEDLight N-LINEpro cabins. Irradiation protocol was based on the patient's skin type. The irradiation dose started at 0.3J/cm^2andwas increased by 20% on each subsequent visit till just perceptible erythema appeared on uninvolved skin. If symptomatic erythema (burning, pain) developed, phototherapy was stopped till the erythema settled. On restarting therapy, the irradiation dose was decreased by 20%. The dose delivered for each session was documented in a standard form. Phototherapy was given twice weekly on non-consecutive days for 12 weeks. Each phototherapy session was approximately between 10 to 15 minutes. The genitals were shielded and eyes were protected with UV safety glasses. If any patient had a gap in his/her phototherapy session of more than a week, the date for serum 25 (OH)D was postponed appropriately.

Serum 25(OH)D levels were obtained using UniCelDxI 800 Access Immunoassay System which is a chemiluminescent based automated analyser, that accurately and precisely measures 25(OH)D. Levels of 25-OH vitamin D3 were graded as: deficient <25 nmol/L, insufficient 25–74 nmol/L, and normal 75–250 nmol/L.[13]

Sample size estimation was calculated using two population means formulae.[14] Mean

difference in vitamin D levels pre and post NBUVB phototherapy was based on the results of Ryan et al.[9] Serum vitamin D prior to NBUVB therapy was 23±37 nmol/L, the level post treatment increased to 59± 80.0 nmol/L. A minimum sample size of 30 was needed to be able to reject the null hypothesis with probability (power) 0.8 and 10% drop out rate. The Type I error probability in rejecting the null hypothesis is 0.05. Data analysis was performed using IBM SPSS Statistics for Windows Version 22.0.

Comparison of the differences between two sets of normally distributed numerical data was analysed using paired t-test, while the Wilcoxon SignedRank test was used if the data was not normally distributed. Pearson or Spearman rank correlations, where appropriate, were calculated. All probability values are two-sided, and a level of significance of less than 0.05 (*p-value < 0.05*) was considered as statistically significant.

This study was conducted in compliance with ethical principles outlined in the Declaration of Helsinki and Malaysian Good Clinical Practice Guidelines. Data collection was commenced after obtaining Medical Research and Ethics Committee approval (Approval Ref : KKM/NIHSEC/P20-798(12).

Results

A total of 33 subjects were recruited, 30 patients completed 12 weeks of NBUVB phototherapy. Three patients defaulted treatment and follow up due to logistical difficulties caused by the COVID-19 pandemic. There were 12 (36.4%) male patients and 21 (63.6%) female patients with a male to female ratio of 4:7. The patients' mean age was 37.00±12.52, with a range of 18–66 years. The majority of patients were Malay 29 (87.9%) followed by Chinese 3 (9.1%) and Indian 1 (3.0%). There were 4 (12.1%) patients with Fitzpatrick skin phototype (FSP) III, 22(66.7%) with FSP IV, and 7 (21.2%) with FSP V. Duration of disease ranged between 2 and 34 years with a median of 12 years. The mean body surface area (BSA) at baseline was 30.39±22.07%. The majority of patients, 16 (48.5%) had minimal sun exposure having spent less than 1 hour under the sun per week. Milk consumption was notably low with only a median value of 1 cup per week. Table 1 shows the demographic and clinical characteristics of the study population.

Table 1. Demographic and clinical characteristics of the study population (n=33)

Parameters	**n(%)**
Age, (years); mean±SD	37.0±12.5
Age, (range)	18 - 66
Gender	
Male	21 (63.6)
Female	12 (36.4)
Race	
Malay	29 (87.9)
Chinese	3 (9.1)
Indian	1 (3.0)
Fitzpatrick skin phototype	
III	4 (12.1)
IV	22 (66.7)
V	7 (21.2)
Duration of psoriasis, (years)	8.0 (12.0)*
Duration of psoriasis (range)	2-34
Total body surface area (BSA), (%); mean±SD	30.4±22.1
Total BSA (range)	5-80
Psoriasis Severity	
Mild (<10% BSA)	5 (15.2)
Moderate (10-30 BSA)	16 (48.5)
Severe (>30% BSA)	12 (36.4)
Sun exposure, (hours per week)	
< 1 hour	16 (48.5)
1-2 hours	11 (33.3)
> 2 hours	6 (18.2)

**Median (IQR)*

Serum 25(OH)D and psoriasis severity at baseline and after 12 weeks of NBUVB therapy is tabulated in Table 2. At baseline, 2(6.7%) patients were 25(OH)D deficient, 23(76.7%) patients had insufficient levels and 5(16.7%) had normal 25(OH)D levels. The mean 25(OH)D level at baseline was 52.09±21.43 nmol/L. After 12 weeks of NBUVB therapy, 16(53.3%) patients achieved normal 25(OH) D levels whilst 14(46.7%) had insufficient levels. None of the patients were 25(OH)D deficient. There was a statistically significant difference between baseline and week 12 serum 25(OH)D values (52.09±21.43 vs 72.80±19.56,

p=<0.001). Psoriasis severity measured as BSA significantly improved with NBUVB. Median value for baseline BSA was 20 (30%) vs 15 (13%) at week 12 with *p value =<0.001*.

Table 2. Serum 25(OH)D and psoriasis severity at baseline and after 12 weeks of NBUVB therapy (n = 30)

Parameter	Baseline	Week 12	*p* value
Serum 25 (OH)D, mean±SD	52.1±21.4	72.8±19.6	*<0.001*[a]
Deficient (<25nmol/L), n (%)	2 (6.7)	0 (0.0)	*<0.001*[b]
Insufficient (25-74nmol/L), n (%)	23 (76.7)	14 (46.7)	
Normal(75- 250nmol/L), n (%)	5 (16.7)	16 (53.3)	
Psoriasis severity			
Total body surface area, %	20 (30.0)	15 (13.0)	*<0.001*[c]
Mild, n (%)	5 (16.7)	11 (36.7)	*0.002*[b]
Moderate, n (%)	16 (53.3)	17 (56.7)	
Severe, n (%)	9 (30.0)	2 (6.7)	
Fitzpatrick Skin phototype			
III (n =4), median(IQR)	50.9 (25.0)	58.8 (28.3)	*0.144*[c]
IV (n =21), mean±SD	50.5±21.8	72.6±21.8	*<0.001*[a]
V (n =5), mean±SD	56.7±27.7	79.9±8.1	*0.109*[a]

*Data was analysed with [a]Paired t test, [b] Stuart-Maxwell Marginal Homogeneity, [c] Wilcoxon Signed Rank test, *Median (IQR)*

Table 3 presents the effects of Fitzpatrick skin phototype (FSP) on 25(OH)D levels following NBUVB therapy. The results reveal an increase in 25(OH)D levels in all the skin types following phototherapy with the most prominent increase seen in FSP V.

There was no correlation seen between psoriasis severity (week 12 BSA) with week 12 serum 25(OH)D, cumulative NBUVB dose and percentage of 25(OH) D increment. The above data is presented in Table 4.

Table 3. Effect of Fitzpatrick skin phototype on 25(OH)D increment following NBUVB therapy

Fitzpatrick Skin Phototype	% Increment of 25(OH)D Median (IQR)	*p* value
III	23.9 (36.7)	*0.796*[a]
IV	22.9 (101.5)	
V	23.4 (179.3)	

Data analysed with [a]Kruskal-Wallis test

Table 4. Correlations between psoriasis severity (week 12 BSA) with serum 25(OH)D and cumulative NBUVB dose and percentage of 25(OH) D increment

Parameter	*r* value	*p* value
Week 12 serum 25(OH)D	0.221	*0.241*
Cumulative NBUVB dose	0.176	*0.353*
Percentage of 25(OH)D increment	0.290	*0.120*

Data analysed with Spearman's Rho Correlation test

There was also no correlation between cumulative NBUVB dose with serum 25(OH)D and percentage of 24(OH)D increment. (Table 5)

Table 5. Correlations between cumulative NBUVB dose with serum 25(OH)D and percentage of 25(OH)D increment

Parameter	*r* value	*p* value
Week 12 serum 25(OH)D	0.069	*0.717*
Percentage of 25(OH)D increment	-0.102	*0.593*

Data analysed with Spearman's rho test

Spearman's Rho Correlation test was also used to assess the correlation between percentage BSA improvement with percentage of 25(OH) D increment. We found no correlation with *p= 0.585* and r = -0.104.

Adverse events such as dry skin 14(46.7%) and folliculitis 1(3.0%) were reported. These were mild however, and did not require NBUVB dose adjustment or cessation of therapy.

Discussion

Vitamin D status of patients with psoriasis

Vitamin D insufficiency is common in patients with psoriasis and there is a correlation between psoriasis severity with vitamin D deficiency.[15] A meta-analysis demonstrated that circulating 25(OH)D levels are lower in patients with psoriasis, and a small but significant negative correlation exists between 25(OH)D levels and psoriasis severity.[16] Pitukweerakulet al alsofound a significant relationship between low 25(OH)D levels and psoriasis.[17] In agreement to this, the majority (75.8%) of our patients in our

study also had insufficient levels of 25(OH)D. We observed that serum 25(OH)D level in our cohort was lower than that from the northern latitudes.[9] This is likely related to darker skin tones that function as natural sun protection and require at least three to five times longer exposure to make the same amount of vitamin D as a person with fairer skin tone.[18] Another contributing factor could be inadequate sun exposure as the majority of our patients reported less than 1 hour of sun exposure per week.

The effect of NBUVB phototherapy on serum 25(OH)D in psoriasis patients

NBVUB phototherapy is a well-recognized standard treatment for psoriasis. The skin produces around 85% of total vitamin D. The rest is obtained from dietary sources such as fortified foods, eggs and oily fish. Our study confirms the results of several studies showing that NBUVB significantly increases serum 25(OH)D in patients with psoriasis.[9,10,11] NB-UVB and UVA/UVB phototherapy significantly increased 25(OH)D serum level in patients with psoriasis and atopic dermatitis in Western Australia.[19]

Twelve NBUVB exposures within 4 weeks increased serum 25(OH)D concentration significantly more than 20µg of oral cholecalciferol daily.[20] Significantly greater increase in serum 25(OH)D was seen among NBUVB treated individuals compared to those treated with the oral vitamin D3.[21] Our study demonstrated improvement in serum 25(OH)D following NBUVB therapy in psoriasis patients with FSP III, IV or V living in a tropical country.

The effect of skin phototypes on phototherapy induced increment of serum 25(OH)D

There is limited and conflicting information relating to the effect of NBUVB therapy on vitamin D levels in psoriasis patients with darker skin tones, in particular FSP III, IV and V. UV transmission is obstructed by melanin, thus dark skinned individuals are thought to be less capable of vitamin D synthesis compared to fair-skinned subjects. Vitamin D status is also known to differ between geographical latitudes. In our study, the majority of patients with darker skin had vitamin D deficiency. Armas et al reported similarly low levels of 25-OH-D with darker skin.[11] We found an increment in serum 25(OH)D among all FSP (III, IV and V) after 12 weeks of NBUVB therapy, the difference in serum 25(OH)D increment between all FSP was not significant. The mean value of serum 25(OH) D at baseline and after 12 weeks was significant for FSP IV. This could be due to a larger sample size as FSP IV had 21 patients, compared to FSP III (4) and FSP V (5) respectively.

FSP is most likely not a significant predictor of change in vitamin D level as reported by Ryan et al in a cohort where the majority of patients were of FSP III.[9] This was in contrast to Libon *et al* in study comparing serum 25(OH)D levels after a single UVB exposure in fair (FSP II–III) and black skinned (FSP VI) volunteers.[22] The study found that on day 6 post single UVB exposure, serum 25(OH)D levels of fair skinned volunteers increased significantly, but not in black-skinned people suggesting that skin pigmentation negatively influences vitamin D synthesis.

Relationship between cumulative NBUVB dose with improvement in serum 25(OH)D

Ryan et al. found the number of NBUVB exposures was the sole predictor of increase in serum 25(OH)D level.[9] Those with greater number of exposures had a significantly higher serum 25(OH)D level, most likely produced by more prolonged exposure to NBUVB. We found no correlation between cumulative NBUVB dose with improvement in serum 25(OH) D at week 12. The number of phototherapy sessions/ NBUVB exposures rather than the cumulative NBUVB dose may be associated with improvement of serum 25(OH)D. Further research is required to confirm this association.

Relationship between improvement in serum 25(OH)D with reduction in psoriasis severity (body surface area affected by psoriasis)

NBUVB increases serum 25(OH)D levels in inflammatory skin conditions.[8,9,10,17]There is little data on the effect of NBUVB on 25(OH)

D serum levels alongside severity of psoriasis. Our results support previous observations that NBUVB increases 25(OH)D levels in psoriasis patients and decreases the severity of psoriasis. Gupta et al showed significant improvement in Psoriasis Area and Severity Index (PASI) as well as serum 25(OH)D ($p < 0.05$).[10] Ryan et al. also found serum 25(OH)D increased significantly with significant improvement in PASI at the end of NBUVB treatment.[9]As minimal as 2 weeks of NBUVB treatment resulted in significant increase of 25(OH)D3 serum concentration.[23]

We found significant improvement of BSA and increase in serum 25(OH)D levels after the completion of treatment. There was however, no correlation between psoriasis severity at week 12 with serum 25(OH)D or percentage of serum 25(OH)D increment. This is similar to a previous study, whereby the improvement in PASI as well as increase in serum 25(OH)D levels after 12 weeks of NBUVB were significant. However, correlation between PASI and 25(OH)D was weak and was statistically insignificant.[10] Ryan *et al* also found no correlation between change in serum 25(OH)D levels and change in PASI but the change in the PASI correlated with cumulative dose of phototherapy.[9]

Our study had several limitations. There was no control arm for comparison, however baseline and end of therapy were obtained to demonstrate improvement in vitamin D. A few factors influencing 25(OH)D levels such as dietary vitamin D intake and body mass index were not recorded or adjusted during the analysis.[24] Body surface area affected (BSA) was used to represent psoriasis severity, BSA is routinely used in clinical practice however Psoriasis Area and Severity Index (PASI) is the validated gold standard.

Conclusion

NBUVB therapy resulted in a significant rise in 25(OH)D levels amongst psoriasis patients of FSP III, IV and V with significant improvement in psoriasis severity. There was no correlation between cumulative NBUVB dose and improvement in serum 25(OH)D. Vitamin D level is most likely not an important predictor in improvement of psoriasis after NBUVB treatment as there was no correlation between BSA improvement and increment of serum 25(OH)D level.

Conflict of Interest Declaration

The authors have no conflict of interest to declare.

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