

Effects of narrowband ultraviolet B exposure on serum 25-hydroxyvitamin D concentrations A pilot study

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Abstract

It is known that ultraviolet B exposure increases serum 25-hydroxyvitamin D(25(OH)D) concentrations. However, little is known about the influence of narrowband ultraviolet B exposure from a light-emitting diode (NBUVB-LED) on serum 25(OH)D levels. Thus, the purpose of this study was to investigate the effect of NBUVB-LED exposure on serum 25(OH)D concentrations.

Two healthy adults were enrolled in this pilot study. Their skin was exposed to ultraviolet B light (60 mJ/cm²) 3 times a week for 4 weeks in the first intervention and every day for 4 weeks in the second intervention. Serum levels of 25(OH)D were measured every 2 weeks.

Serum 25(OH)D levels were decreased in both subjects at the end of the first intervention $(32.1 \rightarrow 21.4 \text{ ng/mL}, 33.9 \rightarrow 21.4 \text{ ng/mL}, mL, respectively)$, whereas serum 25(OH)D levels were increased in the 2 weeks of the second intervention (29.5 and 28.0 ng/mL, respectively). At the end of the second intervention, the 25(OH)D concentrations were 19.0 and 20.4 ng/mL, respectively.

NBUVB-LED exposure might increase serum 25(OH)D concentrations. Future studies should expand the number of participants and adjust for confounding factors.

Abbreviations: NBUVB-LED = narrowband ultraviolet B exposure from a light-emitting diode, PTH = parathyroid hormone, UVB = ultraviolet B, 25(OH)D = 25-hydroxyvitamin D.

Keywords: 25-hydroxyvitamin D, light-emitting diode, narrowband ultraviolet B, vitamin D, ultraviolet B

1. Introduction

Vitamin D deficiency is a global issue and a recent health concern of Koreans.^[1] Vitamin D not only affects bones and muscles but also affects chronic conditions, such as type 2 diabetes mellitus, hypertension, autoimmune diseases, infectious diseases, and various types of cancer.^[2–4] It is mainly acquired by dermal synthesis in response to ultraviolet B (UVB) sun radiation. The dietary sources of vitamin D are limited.^[5]

In summer in Korea (36°N), about 30 minutes of exposure to the forearms and face at least 3 times a week during midday is considered to be sufficient for maintaining serum vitamin D concentrations.^[6] However, drastic changes in modern environments, including indoor lifestyles and the novel SARS-CoV-2 outbreak, have made vitamin D deficiencies one of the most prevalent health problems.^[7] Other atmospheric conditions, such as ozone and suspended particles, can also decrease UVB radiation.^[8] In this situation, vitamin D supplementation is recommended to maintain adequate serum 25-hydroxyvitamin D (25(OH)D) concentrations. However, daily supplementation is not easy for some populations. Young healthy people, old people, and patients who have medical conditions, such as bowel disease, fat malabsorption, and obesity, are at risk of vitamin D

Conflict of interests: Seoul Viosys Co., Ltd. (Ansan, Korea) provided narrowband ultraviolet B light-emitting diodes. The authors have no conflicts of interest.

All data generated or analyzed during this study are included in this published article.

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UVB from the sun or artificial lights can stimulate the photosynthesis of vitamin D in human skin.^[13,14] This wavelength range is the only part of the ultraviolet radiation spectrum that produces vitamin D.^[15] Previous studies showed that serum 25(OH)D concentrations were significantly increased in healthy subjects with UVB exposure.^[16,17] Therefore, artificial UVB exposure might be an additional method to increase serum 25(OH)D levels.

In clinical practice, UVB exposure is considered an easy and cost-effective means of increasing 25(OH)D levels. The action spectrum for the conversion of 7-dehydrocholesterol to 25(OH) D is thought to be within the specific UVB wavelengths of 290–315 nm.^[18] Compared to broad-band ultraviolet light, a narrowband ultraviolet lamp is therapeutically more efficient and better tolerated. It avoids harmful and unnecessary UVB radiation wavelengths while supplying 25(OH)D.^[19] However, little is known about the efficiency of narrowband UVB exposure from a light-emitting diode (NBUVB-LED) (295nm) to increase serum 25(OH)D levels. Thus, the purpose of this pilot study was to assess the effect of NBUVB-LED exposure on serum 25(OH) D concentrations.

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2. Methods

2.1. Study subjects and design

This pilot study was conducted from April 2021 to September 2021. Two healthy young adults 20-60 years old with a body mass index of $<25 \text{ kg/m}^2$ were enrolled. The exclusion criteria were a prior diagnosis of osteoporosis (T-score < -2.5), chronic alcoholic liver disease, alcoholism, primary parathyroid disease, or metabolic bone disease; serum aspartate aminotransferase or alanine aminotransferase >120 mg/dL; serum creatinine >2.0 mg/dl; thyroid-stimulating hormone >10 µIU/mL or TSH < 0.15 µIU/mL; subjects who were taking medications such as antihypertensives, diabetes medications, steroids, diuretics, and vitamin D supplements within 3 months; a medical history of malignancy (including skin cancer); subjects who had any kind of dermatitis; subjects who had photo-allergies; and subjects whose skin color was too bright or dark. Two healthy men without medical history voluntarily participated in this study after providing written informed consent. After enrollment, the subjects were requested to visit the outpatient department every 2 weeks for a routine check for adverse events, as well as 25(OH)D measurements. This study was approved by the Institutional Review Board of Ajou University Hospital (AJIRB-MED-INT-20-590).

2.2. Intervention

The intervention schedule is summarized in Figure 1. During the 2 months of the intervention, the subjects were requested to remove their shirts and sit in front of an NBUVB-LED while wearing protective goggles to prevent eye damage. The subjects were kept 30–50 cm from the light source panel, which was adjusted with a height controller to their upper body (Fig. 2). The exposed area included the face, the anterior aspects of both upper extremities, chest, and upper abdomen. They had about 30% skin exposure calculated from an adaptation of "the rule of nines," representing adult body surface area.^[20]

The subjects received 60 mJ/cm² of UVB (a peak wavelength of 295 nm) light for 10 minutes in each treatment. Artificial ultraviolet light was provided by an NBUVB-LED from Seoul Viosys Co., Ltd. (Ansan, Republic of Korea). The lamp was controlled by a timer that turned off the light after 10 minutes. The dose was much lower than that used for ultraviolet light therapy for some kinds of dermatitis, which usually ranges from 300 to 500 mJ/cm², and might cause erythema or rashes. Therefore, we

assumed that the radiation dose would not be harmful to the skin. The participants were instructed not to use sunscreen when getting narrow-band UVB exposure. The dose was maintained throughout the study for each subject. During the 2 months of the intervention, the participants were exposed 3 times a week for 4 weeks in the first session and 7 times (every day) a week for 4 weeks in the second session. There was a washout period of 2 weeks between the 2 sessions. Serum 25(OH)D levels were measured every 2 weeks. Anthropometrical measurements and assessments of serum parathyroid hormone (PTH), ionized calcium, and phosphorus were conducted at visits 1, 3, 4, and 6. Two weeks after visit 6, phone calls were made to check whether any adverse events occurred. We also educated them to eat foods during the study as they usually had.

2.3. Body proportion measurements and laboratory assessments

Body proportion measurements, including body weight, muscle mass, fat mass, and fat % mass, were performed with a bio-impedance analysis device (InBody770, Biospace, Seoul, Korea). Blood samples for biochemical measurements were obtained from each subject. Serum concentrations of 25(OH) D, PTH, ionized calcium, and phosphorus were assessed. Serum 25(OH)D was assessed at every visit. Parathyroid hormone, serum calcium, and phosphorus were assessed at visits 1, 3, 4, and 6. The primary outcomes were differences in the serum levels of 25(OH)D in each subject at baseline, visit 3, and visit 6. Blood samples were collected year-round after an 8-hour fast. They were immediately processed, refrigerated, and transported in cold storage to the central testing institute (NeoDin Medical Institute, Seoul, South Korea), where they were analyzed within 24 hours. Serum 25(OH)D was measured with a radioimmunoassay kit (25(OH)D¹²⁵I RIA Kit; DiaSorin Inc., Stillwater, MN) using a gamma-counter (1470 Wizard; PerkinElmer, Turku, Finland). The inter-assay coefficients of variation were 13% and 10% at 31 nmol/L and 47 nmol/L, respectively, while the intraassay coefficients of variation were 5.1% and 4.9% at 30 nmol/L and 54 nmol/L, respectively. Serum 25(OH)D was measured in the same institute that conducted quality control assessments every other week throughout the analysis period to minimize analytical variation. Serum parathyroid hormone was analyzed using a chemiluminescence assay (DiaSorin). Ionized calcium was measured in whole blood with an ABL700 blood gas analyzer (Radiometer a/s, Denmark) using an E733 ion-selective

Socio-demographic questionnaire								
	1st intervention period		riod Washout period		2 nd intervention period			
eeks -4	0	2	4		• 6	8	10	1
Visit 0	Visit 1	Visit 2	Visit 3		Visit 4	Visit 5	Visit 6	Visit
Physical examination								
	-							
Physical examination Anthropometric measurement	1	•					1	
Physical examination Anthropometric measurement Complete blood count, routine chemistry, and lipid profile		•	1		÷	•	÷	
Physical examination Anthropometric measurement Complete blood count, routine chemistry, and lipid profile Serum 25-hydroxyvitamin D		2	Į.		1	:		
Physical examination Anthropometric measurement Complete blood count, routine chemistry, and lipid profile Serum 25-hydroxyvitamin D Serum parathyroid hormone		:	ļ			:		
Physical examination Anthropometric measurement Complete blood count, routine chemistry, and lipid profile Serum 25-hydroxyvitamin D Serum parathyroid hormone Serum calcium(ionized), phosphorus		:				•		







Figure 2. Photograph of actual NBUVB-LED radiation. During NBUVB-LED exposure, the subjects were requested to remove their shirts while wearing eye-protective goggles.

electrode. The intraseries coefficient of variation was 0.66% at 1.6 mmol/L and the inter-series coefficient of variation was 1.24% at 1.6 mmol/L.

2.4. Statistical analysis

Descriptive statistics were used to present the data, mean, and standard deviation before and after the interventions in each subject. No formal statistical comparison testing was done.

3. Results

The baseline characteristics of the 2 subjects are presented in Table 1. The blood pressure of subject B was high. We assumed that it might be a white-coat effect since he had never had high blood pressure before. The baseline serum 25(OH)D levels were 32.1 and 33.9 ng/mL (80.3 and 84.8 nmol/L), respectively. Serum PTH levels were different between the 2 subjects (8.0 pg/mL and 27.0 pg/mL). Other baseline variables, such as liver enzymes, cholesterol, uric acid, calcium, and phosphate, were within the reference values.

Table 2 shows changes in the anthropometric and biological markers of the 2 subjects. During the second intervention, subject A gained 3.4kg of weight and 2.7kg of muscle mass with decreases in body fat mass and visceral adipose tissue. The weight gain might have been due to sustained resistance exercise. Otherwise, there were no significant changes between the visits.

Table 1

Baseline characteristics of subjects.

	Subject A Visit 1	Subject B Visit 1
Age (yr)	25	25
Height (cm)	172.6	185.1
Weight (kg)	70.9	83.4
Body mass index (kg/m ²)	23.8	24.3
Muscle mass (kg)	34.2	40.6
Body fat mass (kg)	10.8	12.8
Body fat percentage	15.2	15.4
Visceral fat mass (cm ²)	40.7	54.1
Systolic blood pressure (mm Hg)	124	153
Diastolic blood pressure (mm Hg)	75	97
Smoker	No	Yes
Pack-year	-	2.25
Alcohol consumption	No	No
Co-morbidities	No	No
25-hydroxyvitamin D3 (ng/mL)	32.1	33.9
Parathyroid hormone	8.0	27.0
White Blood cell (10 ³ /µL)	4.8	7.9
Hemoglobin (g/dL)	15.9	15.3
AST (mg/dL)	17	23
ALT (mg/dL)	15	23
ALP (mg/dL)	77	83
Total protein (mg/dL)	7.5	7.7
Albumin (mg/dL)	5.1	4.8
Total cholesterol (mg/dL)	152	219
Triglyceride (mg/dL)	95	94
HDL-Cholesterol (mg/dL)	57	60
LDL-Cholesterol(mg/dL)	76	140
Fasting glucose (mg/dL)	85	98
BUN (mg/dL)	13.0	18.6
Creatinine (mg/dL)	1.06	1.03
Uric acid (mg/dL)	5.3	5.2
Calcium (mg/dL)	9.8	9.8
Phosphorus (mg/dL)	3.2	3.1

 $\label{eq:asymptotic} AST = aspartate aminotransferase, ALT = alanine aminotransferase, ALP = alkaline phosphatase, \\ HDL = high-density lipoprotein, LDL = low-density lipoprotein, BUN = blood urea nitrogen.$

Table 2		
Changes o	f anthropometric and biologic markers in subjects.	

	Changes of anthropometric markers			
	Subject A: visit 1 \rightarrow visit 6	Subject B: visit 1 \rightarrow visit 6		
Weight (kg)	$70.9 \rightarrow 74.3$	83.4 → 83.9		
Body mass index (kg/m ²)	$23.8 \rightarrow 24.9$	$24.3 \rightarrow 24.5$		
Muscle mass (kg)	$34.2 \rightarrow 36.9$	$40.6 \rightarrow 40.6$		
Body fat mass (kg)	$10.8 \rightarrow 11.0$	$12.8 \rightarrow 12.4$		
Body fat percentage	$15.2 \rightarrow 14.8$	$15.4 \rightarrow 15.4$		
Visceral fat mass (cm ²)	$40.7 \rightarrow 32.7$	$54.1 \rightarrow 48.2$		

	Changes of biologic markers				
	Subject A: V1 \rightarrow V3 \rightarrow V6	Subject B: $V1 \rightarrow V3 \rightarrow V6$			
White Blood cell (103/µL)	$4.8 \rightarrow 5.1 \rightarrow 5.3$	$7.9 \rightarrow 6.5 \rightarrow 7.4$			
Hemoglobin (g/dL)	$15.9 \rightarrow 15.9 \rightarrow 15.5$	$15.3 \rightarrow 15.7 \rightarrow 15.2$			
AST (mg/dL)	$17 \rightarrow 32 \rightarrow 20$	$23 \rightarrow 40 \rightarrow 29$			
ALT (mg/dL)	$15 \rightarrow 23 \rightarrow 18$	$23 \rightarrow 26 \rightarrow 24$			
ALP (mg/dL)	$77 \rightarrow 76 \rightarrow 65$	$83 \rightarrow 84 \rightarrow 80$			
Total protein (mg/dL)	$7.5 \rightarrow 7.3 \rightarrow 7.4$	$7.7 \rightarrow 7.2 \rightarrow 7.4$			
Albumin (mg/dL)	$5.1 \rightarrow 4.9 \rightarrow 4.8$	$4.8 \rightarrow 4.5 \rightarrow 4.7$			
Total cholesterol (mg/dL)	$152 \rightarrow 155 \rightarrow 145$	$219 \rightarrow 209 \rightarrow 205$			
Triglyceride (mg/dL)	$95 \rightarrow 88 \rightarrow 50$	$94 \rightarrow 167 \rightarrow 85$			
HDL-Cholesterol (mg/dL)	$57 \rightarrow 58 \rightarrow 56$	$60 \rightarrow 47 \rightarrow 49$			
LDL-Cholesterol (mg/dL)	$76 \rightarrow 79 \rightarrow 79$	$140 \rightarrow 129 \rightarrow 139$			
Fasting glucose (mg/dL)	$85 \rightarrow 87 \rightarrow 89$	$98 \rightarrow 82 \rightarrow 93$			
BUN (mg/dL)	$13.0 \rightarrow 14.4 \rightarrow 14.3$	$18.6 \rightarrow 14.3 \rightarrow 15.0$			
Creatinine (mg/dL)	$1.06 \rightarrow 1.05 \rightarrow 1.02$	$1.03 \rightarrow 1.13 \rightarrow 1.08$			
Uric acid (mg/dL)	$5.3 \rightarrow 4.8 \rightarrow 4.3$	$5.2 \rightarrow 5.0 \rightarrow 5.4$			
Calcium (mg/dL)	$9.8 \rightarrow 10.1 \rightarrow 9.6$	$9.8 \rightarrow 9.3 \rightarrow 9.8$			
Phosphorus (mg/dL)	$3.2 \rightarrow 4.3 \rightarrow 3.3$	$3.1 \rightarrow 2.7 \rightarrow 3.6$			

AST = aspartate aminotransferase; ALT = alanine aminotransferase; ALP = alkaline phosphatase;BUN = blood urea nitrogen; HDL = high-density lipoprotein; LDL = low-density lipoprotein; V1 = visit 1; V3 = visit 3; V6 = visit 6.

Table 3 summarizes the effects of radiating NBUVB-LED on 25(OH)D and PTH levels. Contrary to our expectation, the serum 25(OH)D levels of the subjects were decreased at the end of the first session, showing the same value of 21.4 ng/mL in both subjects. After the 2-week wash-out period, the serum 25(OH)D concentrations in subjects A and B were 26.5 and 25.5 ng/mL, respectively. After 2 weeks of daily exposure in the second session, the serum 25(OH)D levels in each subject showed subtle increases to 29.5 ng/mL and 28.0 ng/mL, respectively. However, subject A reported a tingling sensation on his skin at visit 6. We suspected that light exposure might have caused such a side effect as this symptom had never happened before. Thus, we recommended reducing the frequency of exposure in subject A to 3 times per week. The serum 25(OH) D levels of subject A were decreased after visit 7. The tingling symptom of subject A was improved. Except for this symptom, no other adverse effects were detected in this study. Finally, the last serum 25(OH)D concentrations were 19.0 ng/mL in subject A and 20.4 ng/mL in subject B.

4. Discussion

The results of this preliminary study can be summarized as follows. In healthy men, daily NBUVB-LED exposure to 30% of the body surface for 10 minutes tended to increase serum 25(OH)D concentrations, whereas 10 minutes of exposure 3 times a week did not. Most of the NBUVB-LED effects seemed to be associated with the frequency of exposure since increases in serum 25(OH) D concentrations occurred at the end of the first 2 weeks of the second intervention but returned to basal levels after reducing the frequency of exposure in subject A. This decline might have been due to decreased NBUVB-LED exposure since there was no significant increase in body fat mass.

The decreases in serum 25(OH)D concentrations at the end of the first and second intervention periods were unexpected. A previous study^[21] reported a similar phenomenon. Although phototherapy increases 25(OH)D levels, some patients did not show a significant increase. A few others even showed decreases in 25(OH)D concentrations. The reasons for such decreases are not yet fully understood. Several factors might contribute to this phenomenon. First, despite unknown mechanisms, 25(OH)D may act as negative feedback for 25-hydroxylase in the liver, which prompts the hydroxylation of vitamin D3 to 25(OH) D. The conversion of 25(OH)D to the 1,25-dihydroxyvitamin D metabolite could explain part of the decrease in 25(OH)D. Second, the subjects conducted the interventions themselves. The absence of a supervisor may have decreased compliance and introduced errors. Third, the decrease might have been caused by the severe acute respiratory syndrome coronavirus 2 pandemic since people spent less time outdoors with less sun exposure, consequently reducing the production of 25(OH)D. Fourth, sinusoidal changes in 25(OH)D concentrations related to the season may have affected the results.

It is difficult to obtain enough vitamin D from the diet even if foods fortified with vitamin D are consumed.^[22] Therefore, adequate sunlight exposure is necessary to improve the vitamin D status. Godar et al^[23] investigated indoor-working adult Americans to calculate how much vitamin D3 they produced. They reported that certain adults with skin type II (22–59 years old) met their minimum vitamin D3 needs only during the summer with sun exposure over more than 30% of the body surface. Considering that skin type III is the predominant skin type in Korea,^[24] we presume that most indoor-working Korean adults do not produce sufficient amounts of vitamin D from sunlight exposure. Therefore, it is necessary to find an additional way to produce vitamin D.

Data regarding the efficiency of NBUVB-LED for producing 25(OH)D in healthy adults are lacking, although recent investigations have examined the possible role of NBUVB-LED exposure in increasing serum 25(OH)D levels. Vähävihu et al^[25] showed that 2 standard erythema doses of NBUVB exposure for 7 consecutive days improved vitamin balance in winter in healthy women with skin type II-III.^[26] Cicarma et al^[21] found

Table 3

		1 st intervention				2 nd intervention		
		Visit 1	Visit 2	Visit 3		Visit 4	Visit 5	Visit 6
Subject A	25(OH)D (ng/mL)	32.1	22.8	21.4	Wash-out for 2 weeks	26.5	29.5	19.0
	PTH (pg/mL)	8.0		7.0		5.0		28.0
Subject B	25(OH)D (ng/mL)	33.9	24.1	21.4		25.5	28.0	20.4
,	PTH (pg/mL)	27.0		38.0		9.0		46.0
Exposures	/	10	minutes, 3 times/v	veek		10 minut	es, 7 times/week	

NBUVB-LED = narrowband ultraviolet B from a light-emitting diode, 25(OH)D = 25-hydroxyvitamin D, PTH = parathyroid hormone.

that low-dose NBUVB treatment significantly increased vitamin D status. Karppinen et al^[27] showed that a suberythemal dose of NBUVB exposure to healthy subjects every second week over the winter months could maintain postsummer 25(OH)D concentrations. Based on these findings, we speculate that UVB therapy might influence the concentrations of 25(OH)D. Our study indicated that daily NBUVB-LED exposure could increase serum 25(OH)D concentrations, while exposure every other day was insufficient in affecting 25(OH)D levels. Whether this represents a true biological change, the effect of other factors, or simply increases in the mean is unknown. Thus, our results may partly support previous data and suggest that a larger study is needed.

This study had several limitations. First, the sample size was fairly small for valid statistical analysis to detect changes in 25(OH)D concentrations. In addition, 8 weeks were not long enough for the treatment response to reach a steady state. Second, NBUVB-LED exposure was conducted solely by education without any supervision by health personnel. Third, this study did not address UVB responses in obese participants. We already know that body fat decreases 25(OH)D in human skin. Thus, we would expect a lower 25(OH)D response to a given amount of UVB exposure in obese participants. However, confounding factors such as body fat mass were not well controlled. Fourth, there was no control with which to compare serum 25(OH)D levels. Fifth, the food intake of the subjects has not been fully assessed, which might affect serum 25(OH)D concentrations. However, we educated them to eat foods during the study as they usually had. Nevertheless, to the best of our knowledge, this was the first study to evaluate serum 25(OH) D concentrations using NBUVB-LED in Korea. A larger sample size is needed to examine the effect of NBUVB-LED on changes in serum 25(OH)D concentrations.

In conclusion, this pilot study indicated that NBUVB-LED exposure may increase serum 25(OH)D concentrations. Future studies should expand the number of participants and adjust for confounding factors. In addition, the safety of NBUVB-LED exposure should be assessed.

Author contributions

All authors contributed to the data collection, interpretation, drafting, and editing of the manuscript.

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