Accepted Date: 25-Dec-2009
Article Type: Original Article

Narrow-band UVB course improves vitamin D balance in women in winter

Short title: Narrow-band UVB and vitamin D

Key words: calcidiol, vitamin D, UVB radiation, skin

K.VÄHÄVIHU,*† ‡ L.YLIANTTILA,§ H.KAUTIAINEN,0 H.VILJAKAINEN,¶ C.LAMBERG-ALLARDT,¶ T.HASAN,‡ P.TUOHIMAA,** T.REUNALA,‡ †† E.SNELLMAN*‡‡

**Department of Dermatology, Päijät-Häme Central Hospital, Lahti, Finland*

†Department of Dermatology, Kanta-Häme Central Hospital, Hämeenlinna, Finland

‡Department of Dermatology, Tampere University Hospital, P.O. Box 2000, FIN-33531, Tampere, Finland

§Radiation and Nuclear Safety Authority, Non Ionizing Radiation Laboratory, Helsinki, Finland

0ORTON Foundation, Helsinki, Finland

¶Department of Applied Chemistry and Microbiology, University of Helsinki, Helsinki, Finland

***Department of Anatomy, Medical School, University of Tampere, Tampere, Finland*

††Department of Dermatology, Medical School, University of Tampere, Tampere, Finland

‡‡ Ministry of Social Affairs and Health, Helsinki, Finland

Corresponding author: Dr. Katja Vähävihu, MD,

Department of Dermatology, Tampere University Hospital, P.O. Box 2000, FIN-33531, Tampere, Finland, e-mail katja.vahavihu@uta.fi

Summary

Background: Vitamin D insufficiency is common in winter in the Nordic countries.

Objectives: To examine whether a short course of narrow-band ultraviolet B (NB-UVB) improves vitamin D balance.

Patients/Methods: Fifty-six healthy, Caucasian women (mean age 41 years) volunteered and 53 completed the study. NB-UVB exposures were given on seven consecutive days either on the whole body (n = 19), on the head and arms (n = 9) or on the abdomen (n = 14). Similarly seven solar simulator exposures were given on the face and arms (n = 11). The cumulative UVB dose was 13 standard erythema units (SED) in all regimens. Serum calcidiol (25-hydroxyvitamin D) concentration was measured by radioimmunoassay before and after the NB-UVB exposures. Follow-up samples were taken from the whole body NB-UVB group at two months.

Results: At onset forty-one women (77 %) suffered from vitamin D insufficiency (calcidiol < 50 nmol L^{-1}) and six (11 %) from vitamin D deficiency (calcidiol < 25 nmol L^{-1}). Calcidiol concentration increased significantly, by a mean of 11.4 nmol L^{-1} when NB-UVB was given on the whole body, by 11.0 nmol L^{-1} when given on the head and arms and by 4.0 nmol L^{-1} when given on the abdomen. Solar simulator exposures given on the face and arms increased calcidiol by 3.8 nmol L^{-1}. After two months serum calcidiol was still higher than initially in the group who received NB-UVB exposures on the whole body.

Conclusion: NB-UVB exposures given on seven consecutive days on different skin areas of healthy women significantly improved serum calcidiol concentration. A short low-dose NB-UVB course can improve vitamin D balance in winter.

Introduction

An adequate vitamin D supply is crucial for health of bones and it is hypothesised to be important in the prevention of certain cancers and autoimmune diseases.[1-3] Solar UV exposure is the major source of vitamin D and as much as 90 % of all requisite vitamin D has to be formed in the skin .[4, 5] The desirable circulating concentration of calcidiol (25-hydroxyvitamin D), which is the best indicator of vitamin D status,[1] is still under debate, but a concentration of 50 – 80 nmol L^{-1} is considered to be optimal for the skeleton.[6] At present vitamin D insufficiency or deficiency is common worldwide.[7] In the Nordic countries and Britain this condition frequently affects people especially in winter when vitamin D synthesis induced by sun is zero.[8-11] In Finland fortification of milk and margarine with vitamin D has only partially improved vitamin D balance.[12] Recently, we found that 74 % of patients with atopic dermatitis had vitamin D insufficiency in winter, i.e. their serum calcidiol was below 50 nmol L^{-1}.[13] A two-week heliotherapy course in the Canary Islands healed atopic dermatitis and at the same time significantly improved serum calcidiol concentration.[13] Artificial UVB irradiation is also able to induce vitamin D synthesis. Broadband UVB exposures have earlier shown to increase serum calcidiol in healthy subjects and in postmenopausal women with psoriasis.[14, 15]

Narrow-band ultraviolet B (NB-UVB) cabins equipped with TL01 tubes are now widely used in the treatment of psoriasis, atopic dermatitis and various other inflammatory skin diseases.[16, 17] The output of NB-UVB is predominantly within wavelengths 311-313 nm, i.e. near the optimal

wavelength, 297 nm, for vitamin D synthesis.[4] In the present study we examined whether a short course of NB-UVB would improve vitamin D balance in winter in healthy women. To study the response of various skin sites, NB-UVB exposures were given either on the whole body, on the head and arms or on the abdomen. For comparison, one group received exposures with a solar simulator on the face and arms.

Materials and methods

Subjects

Fifty-six healthy, white, female healthcare workers (nurses or doctors) or students (mean age 41 years, range 21-61 years, table 1) with skin type II - III[18] volunteered in the study. The study was performed in the Central Hospitals of Päijät-Häme and Kanta-Häme (location 67N° and 34 or 25°E) in winters (December – March) 2004 - 2006. The ethics committees of the hospitals approved the study protocol and all subjects gave an informed consent to participate. Inclusion criteria were no phototherapy, solarium, sun holidays or vitamin D supplementation during the two preceding months. Three women withdrew from the study, one for personal reasons and two due to mild erythema after one or two NB-UVB exposures and they were excluded from the study.

Narrow-band UVB and solar simulator exposures

NB-UVB or solar simulator exposures were given on seven consecutive days. The UVB dose was 1 SED (standard erythema dose) on the first day and thereafter 2 SED on each of the following six days. The daily dose was below one minimal erythemal dose (MED), since 2 SED corresponds 1/3 - 1 MED in Caucasian people depending on their skin phototype.[19] One SED is equivalent to 10 mJ cm^{-2} CIE-erythema weighted irradiance.[20]

Group I (n = 19) received NB-UVB exposures on the whole body with a round Waldmann UV 7001 cabin equipped with twenty TL01 tubes located 30 cm apart from the subject (table 1). Group II (n = 9) received NB-UVB exposures on the head and arms, i.e. the T-shirt free area, with a similar Waldmann UV 7001 cabin equipped with forty TL01 tubes. The third group (n = 14) received NB-UVB on the abdomen with a Waldmann UV 801KL panel equipped with four TL01 tubes. The exposed area was 25 cm x 40 cm and the distance from the tubes 20 cm. The fourth group (n = 11) received solar simulator exposures by a Philips HB411 panel equipped with a broad band UVB lamp (HPA 400) on the face and arms. The subjects were sitting in front of the panel and holding their forearms and upper arms beside their face. The distance from the panel was 30 cm. The non-exposed skin areas were carefully protected from radiation using a thick, white T-shirt and trousers containing 65 % polyamide and 35 % cotton. The penetration of UVB rays through this clothing measured by a spectroradiometer (Ocean Optics S2000) was negligible, 0.15 %.

The spectral irradiances of the lamps measured with an Ocean Optics S2000 single-monochromator spectroradiometer are shown in Fig. 1. The spectroradiometer was placed into the round cabin to the same distance, 30 cm, from the tubes than the skin is when the exposed subject is standing in the cabin. The height of the measurement point was 110 cm. Similarly, the spectroradiometer was placed in front of the flat irradiators to the same distance of the tubes than the exposed skin is. The exact time to receive a dose of 2 SED was determined in all regimens. When the stray light and other systematic errors are corrected, the estimated measurement uncertainty (2σ) is 14 %[21] and the measurements are traceable to National Institute of Standards and Technology, USA.

Calcidiol measurements

Blood samples for serum calcidiol measurements were taken before the first NB-UVB or solar simulator exposure and thereafter 24 hours after the first, third and seventh exposure. In addition fourteen subjects from group I gave follow-up samples at two week intervals up to two months.

The serum samples were protected from light, centrifuged and then stored at -20° C. Calcidiol concentration was analysed in duplicates by using radioimmunoassay (Immunodiagnostic Systems, Boldon, UK) as in our previous study.[13] A calcidiol concentration below 50 nmol L^{-1} was regarded as vitamin D insufficiency and below 25 nmol L^{-1} as deficiency.[6]

The dietary intake of vitamin D was determined by a semi-quantitative food frequency questionnaire[22] before and one month after the study.

Statistical methods

The changes in serum calcidiol concentration in the four study groups were analysed by using permutation test. The changes in serum calcidiol concentration between the study groups were analysed by a bootstrap type analysis of covariance (ANCOVA) with the baseline values as covariables. The 95 per cent confidence intervals (95% CI) were obtained by bias-corrected and accelerated bootstrapping (5000 replications), because of the skewed distribution of the variables.

Results

Serum calcidiol and dietary intake of vitamin D at onset of the study

At onset of the study the mean dietary intake of vitamin D was 6.6 μg d^{-1} (range 0.2 – 18.5 μg d^{-1}, Table 1) and the mean serum calcidiol concentration was 39.1 nmol L^{-1} (range from 16.4 to 81.6 nmol L^{-1}, Table 2). Forty-one subjects (77 %) suffered from vitamin D insufficiency (calcidiol < 50 nmol L^{-1}) and six (11 %) from vitamin D deficiency (calcidiol < 25 nmol L^{-1}). The serum calcidiol concentration correlated positively with the dietary intake of vitamin D ($r = 0.30$, $P = 0.011$).

Effect of narrow-band UVB or solar simulator exposures on serum calcidiol

Seven NB-UVB or solar simulator exposures caused a statistically significant increase in serum calcidiol concentration in all four study groups (Table 2, Fig. 2). Exposing the whole body to NB-UVB caused the highest increase, 11.4 nmol L^{-1}. Nearly the same, 11.0 nmol L^{-1}, was seen when NB-UVB was given only on the head and arms. Already after three NB-UVB exposures the increase of serum calcidiol was significant in both of these groups, i.e. 7.3 nmol L^{-1} and 6.8 nmol L^{-1}. Seven NB-UVB exposures given on the abdomen increased serum calcidiol by 4.0 nmol L^{-1}. Seven solar simulator exposures given on the face and arms caused an increase of 3.8 nmol L^{-1} (Table 2, Fig. 2). The increase in serum calcidiol in the four groups was not due to changes in dietary intake of vitamin D since it remained the same one month after the NB-UVB course than before it (P = 0.66).

Fourteen women in the group receiving NB-UVB on the whole body were followed up to two months. The highest mean serum calcidiol (65.2 nmol L^{-1}) was seen two weeks after the NB-UVB course (Fig. 3). Thereafter, serum calcidiol slowly decreased but still, two months after the NB-UVB course, it was markedly higher (56.1 nmol L^{-1}) than at onset of the study (48.0 nmol L^{-1}). At onset seven, at the end four and two weeks after the NB-UVB exposures only one of the fourteen women were insufficient with vitamin D.

Discussion

In the present study we showed that a seven-day course of NB-UVB significantly increased serum calcidiol concentration, i.e. markedly improved vitamin D balance in healthy, Finnish women in winter. The increase in serum calcidiol was 11.4 nmol L^{-1} when NB-UVB was given on the whole body and 11.0 nmol L^{-1} when given on the head and arms only. We are not aware of similar studies

with NB-UVB in healthy subjects. Recently, Czarnecki[23] treated seven patients with psoriasis with eighteen NB-UVB exposures and in agreement with the present results found markedly increased serum calcidiol in all patients. Similarly, a mean of over 20 broadband UVB exposures both in postmenopausal women with psoriasis and other psoriatic patients have shown a significant increase in serum calcidiol.[15, 24] In the light of our present study with healthy subjects and the one of Armas et al.[14] it is, however, apparent that also psoriatic patients could obtain a significant increase in serum calcidiol with a markedly lower number of exposures than twenty. When comparing to sun exposure, it is of interest, that in the present study the increase in serum calcidiol after seven NB-UVB exposures was about the same than that achieved by patients with atopic dermatitis during a two-week heliotherapy course in winter in Canary Islands.[13]

In the present study the response in serum calcidiol was almost the same whether NB-UVB was given on the whole body or only on the head and arms. This was surprising, since the latter consists of only one fourth of the total body area. Both groups received NB-UVB with a Waldmann 7001 cabin, and the cumulative UVB dose was the same, i.e. 13 SED. One explanation could be that the skin areas most often exposed to the sun, i.e. the face and arms, might have a more rapidly activated and effective system for vitamin D synthesis than other skin areas. The exposed groups were, however, rather small and different both in size and in initial serum calcidiol concentration. Due to this the result should be confirmed in a further study. Also direct comparisons of calcidiol responses after exposure of the abdomen with NB-UVB or solar simulator exposure of the face and arms should be avoided, because the exposures in these regimens were given with a panel of lamps and not in a round cabin as in the two other regimens. However, it is attempting to estimate that the exposed abdominal area was 6 – 10 % and the T-shirt free area 20 – 25 % of the total body area. If, after all, comparing the results of these groups, it would mean that the abdominal skin is nearly as effective in producing vitamin D as the skin of head and arms is. There arises a question whether there is a certain saturation point in the capacity to hydroxylate vitamin D to calcidiol. The

important result is, however, that all the four regimens with a cumulative dose of 13 SED significantly increased serum calcidiol.

After the NB-UVB course given on the whole body, serum calcidiol concentration was followed up in fourteen women up to two months. Interestingly, serum calcidiol continued to increase and it was at its highest two weeks after the last NB-UVB exposure. The study was performed in the middle of winter, so sun exposure could not affect this result. Unfortunately – for practical reasons – the other groups were not followed up. Apparently, despite of the minimal UVB doses, the UVB exposures caused reversible photoisomerization of both previtamin D_3 and vitamin D_3 to biologically inert sterols, which afterwards were mobilised and further converted to calcidiol.[25, 26] This self regulating system inhibits overdosing of vitamin D by UVB. One month after the NB-UVB course serum calcidiol had decreased somewhat but at two months it was still markedly higher than initially. A similar long-lasting increase in serum calcidiol was also seen in our previous heliotherapy study.[13]

Vitamin D insufficiency or deficiency is common in winter in healthy adults in the Nordic countries and in Britain.[8-11, 13] In agreement with this, as many as 88 % of the women in the present study had serum calcidiol below 50 nmol L^{-1} before the NB-UVB exposures. The women were doctors, nurses and other health-care workers who obviously have better knowledge than people in average about healthy food and need for vitamin D in winter. Their dietary vitamin D intake was somewhat lower than the recommended intake, 7.5 μg d^{-1},[27] indicating that even after fortification of milk and margarine people do not get enough vitamin D from food in winter in Finland.[12] Similarly, in Britain, the prevalence of hypovitaminosis D was recently found to be alarmingly high during winter and spring in a cohort of 45-year-old adults and the authors recommended actions both at population level and in risk groups.[11] Vitamin D supplements, such as cod liver oil and multivitamin products, are used to improve vitamin D balance. To obtain recently recommended calcidiol concentrations of over 75 nmol L^{-1} a dietary intake of vitamin D for 17-20 micrograms

daily is required .[28, 29] Thus the current dietary recommendation is too low. The present study shows that a short course of NB-UVB is one possible way to improve vitamin D balance in women and presumably also in men in winter. Seven suberythemal NB-UVB exposures rapidly increased serum calcidiol and the response was long-lasting, i.e. it persisted partly up to two months. The time to receive 2 SED of NB-UVB in a Waldmann 7001 cabin is short, below one minute. Theoretically, tens of subjects could be handled during a day with one NB-UVB cabin for the treatment or prophylaxis of vitamin D insufficiency. To find out the optimal NB-UVB protocol to improve vitamin D insufficiency or deficiency warrants clearly a further study. Different NB-UVB doses and schedules, e.g. daily compared to one to three times a week, should be investigated to find out which dosage gives the maximum response in serum calcidiol. A study comparing NB-UVB course to oral vitamin D substitution would also be of importance.

The safety aspect of NB-UVB includes the risk for skin cancer.[30] Several authors consider NB-UVB less risky than broad-band UVB.[16] In agreement with this, a recent British study of nearly 4000 patients found no significant association between NB-UVB treatment and squamous or basal cell carcinoma, or malignant melanoma.[30] In regard to cancer risk, it is also noteworthy that the treatment of psoriasis or atopic dermatitis with NB-UVB usually needs at least 20 exposures with a cumulative dose of 80 - 100 SED. These doses are markedly higher than the 13 SED used in the present study, suggesting that vitamin D balance can be improved with a short NB-UVB course unlikely to importantly increase skin cancer risks. Moreover, the dose of 2 SED, which is usually below one minimal erythemal dose (MED),[19] was well tolerated and only two women got mild erythema in the present study.

To conclude, the present study shows that a short course of NB-UVB is an effective way to improve vitamin D balance in healthy women in winter. To find the optimal NB-UVB schedule and to show whether NB-UVB course is effective also in the risk groups such as postmenopausal women and old people having risk for fractures warrants further studies.

Acknowledgments

This study was supported by National Graduate School of Clinical Investigation and by Medical Research Funds of Tampere University Hospital and Central Hospitals of Päijät-Häme and Kanta-Häme.

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Figure legends

Figure 1. Spectral irradiances of the narrow-band UVB (NB-UVB) equipment (UVB 311; Waldmann UV 7001 cabin or 801KL panel with TL01 tubes) and solar simulator (Philips HB411) used in the study. The optimal wavelength for vitamin D synthesis in the skin is 297 nm.

Figure 2. Change in serum calcidiol concentration after seven NB-UVB or solar simulator exposures. NB-UVB exposures were given either on the whole-body (group I, n = 19), on the head and arms (group II, n = 9) or on the abdomen (group III, n = 14) and solar simulator exposures on the face and arms (group IV, n = 11). Mean values are marked with dots and 95% confidence intervals by bars.

Figure 3. Serum calcidiol concentration at onset and up-to two months after seven NB-UVB exposures on the whole body in fourteen women. Mean values are marked with dots and 95%

confidence intervals by bars. The highest calcidiol concentration was measured at week 3, i.e. two weeks after the NB-UVB course.

Table 1. Characteristics of the study groups receiving narrow-band UVB (NB-UVB) or solar simulator exposures on seven consecutive days.

	Group I NB-UVB Whole body	**Group II** NB-UVB Head and arms	**Group III** NB-UVB Abdomen	**Group IV** Solar simulator Face and arms
Number of women	19	9	14	11
Age; years, mean (range)	42 (21 – 57)	44 (22 - 58)	35 (21 – 58)	47 (28 – 61)
Skin phototype[1] II / III	9 / 10	3 / 6	11 / 3	6 / 5
Dietary vitamin D intake at onset; μg d^{-1}, mean ± SD	5.9 ± 3.3	7.2 ± 5.5	7.7 ± 3.5	6.4 ± 2.8

[1]according to Fitzpatrick[18]

Table 2. Serum calcidiol response to seven NB-UVB or solar simulator exposures. The cumulative UVB dose was 13 standard erythema doses in all four groups.

Group	**Mean serum calcidiol nmol/L^{-1}**			P-value ‡
	At onset Mean (Range)	**After seven exposures Mean (Range)**	**Change in serum Mean (95% CI†)**	
I. NB-UVB whole body *n* = 19	44.3 (24.5 – 81.6)	55.8 (34.5 – 85.4)	11.4 (8.9 to 14.1)	<0.001
II. NB-UVB head and arms *n* = 9	37.8 (21.8 – 71.4)	48.8 (32.0- 92.9)	11.0 (6.2 to 16.7)	0.0046
III. NB-UVB abdomen *n* = 14	35.1 (16.4 – 49.1)	39.2 (23.6 – 55.6)	4.0 (1.4 to 6.3)	0.011
IV. Solar simulator face and arms *n* = 11	38.1 (22.7 – 58.2)	41.9 (27.2 – 59.1)	3.8 (0.8 to 7.6)	0.038

† CIs for the means were obtained by bias-corrected and accelerated bootstrapping (5000 replications)

‡ Permutation test