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Ultraviolet Irradiation Corrects Vitamin D Deficiency and Suppresses Secondary Hyperparathyroidism in the Elderly

V.G.M. CHEL,[1] M.E. OOMS,[2] C. POPP-SNIJDERS,[3] S. PAVEL,[4] A.A. SCHOTHORST,[4] C.C.E. MEULEMANS,[5] and P. LIPS[2,3]

ABSTRACT

The objective of this study was to compare the effect of ultraviolet radiation (UV) and oral vitamin D_3 on the vitamin D status and parathyroid hormone (PTH) concentration in elderly nursing home patients. The design of the study was a randomized clinical trial. The setting was a psychogeriatric nursing home. Subjects included 45 female psychogeriatric patients with a mean age of 85 years. Exclusion criteria were going outdoors more than once a week and the presence of actinic or cancer skin lesions. Intervention was random allocation of UV-B irradiation at half the minimal erythemal dose of the lower back, three times per week during 12 weeks (UV-B), or oral vitamin D_3 400 IU/day during 12 weeks (VIT-D), or no treatment (CONTR). Main outcome measures were change in fasting serum levels of vitamin D metabolites at 0, 2, 4, 8, and 12 weeks in the treatment groups, compared with the control group. PTH(1–84) was measured at 0 and 12 weeks. Baseline serum 25-hydroxyvitamin D (25(OH)D) was lower than 30 nmol/l in 95% of the participants. It increased to a median value of around 60 nmol/l after 12 weeks both in the UV-B and VIT-D groups, whereas there was no change in the CONTR group. Serum 1,25-dihydroxyvitamin D increased significantly in the UV-B group. Serum calcium increased significantly in both treatment groups. Serum PTH decreased more than 30% in both treatment groups ($p < 0.001$), whereas there was no significant change in the control group. Irradiation with UV-B in the very elderly for a few minutes per day leads to adequate improvement of the vitamin D status. It is as effective as oral vitamin D_3 in increasing serum 25(OH)D and suppressing secondary hyperparathyroidism. (J Bone Miner Res 1998;13:1238–1242)

INTRODUCTION

VITAMIN D DEFICIENCY is common in elderly people and in particular in patients with hip fracture.[1] It causes secondary hyperparathyroidism which leads to cortical bone loss.[2,3] Vitamin D deficiency thus contributes to the pathogenesis of osteoporosis and hip fractures.[4] Vitamin D supplementation in the elderly increases the serum 25-hydroxyvitamin D (25(OH)D) concentration and decreases the serum concentration of parathyroid hormone (PTH).[5] It also decreases wintertime bone loss from the lumbar spine[6] and it may increase bone mineral density of the femoral neck.[7] An annual intramuscular injection of vitamin D has been shown to decrease the incidence of upper limb fractures.[8] Low-dose vitamin D supplementation did not decrease the incidence of hip and other peripheral fractures in The Netherlands,[9] whereas a combination of vitamin D and calcium decreased the number of hip fractures in elderly residents of nursing homes in France.[10]

Elderly people do not often go outside in the sunshine.[1] The amount of ultraviolet (UV) light received by residents of homes for the elderly in The Netherlands has been found to be half that of people with an indoor occupation.[11] In addition, the production of vitamin D in the skin decreases considerably with aging. A study with UV radiation in Boston showed that the production of vitamin D_3 at the age

[1]Psychogeriatric Center Mariënhaven, Warmond, The Netherlands.
[2]Institute for Research in Extramural Medicine, Vrije Universiteit, Amsterdam, The Netherlands.
[3]Department of Endocrinology, Academic Hospital Vrije Universiteit, Amsterdam, The Netherlands.
[4]Department of Dermatology, University Hospital Leiden, Leiden, The Netherlands.
[5]Optical Radiation Consultancy, Eersel, The Netherlands.

of 80 years is around 25% of that at the age of 20 years.[12] Sunshine exposure and consequently vitamin D_3 production is particularly low in immobilized and institutionalized elderly people.[13] Earlier studies have demonstrated that sunlight exposure or UV irradiation could increase serum 25(OH)D in the elderly.[14,15] The present study was undertaken to compare the effects of UV radiation and oral vitamin D supplementation on vitamin D deficiency and secondary hyperparathyroidism in elderly institutionalized people.

SUBJECTS AND METHODS

Subjects were 45 female patients of the nursing home Mariënhaven in Warmond (The Netherlands). All were residents from low and medium care psychogeriatric wards. Exclusion criteria were recent use of vitamin D supplementation and going outdoors more than once per week. The presence of actinic and cancer skin lesions as well as the skin type was checked by a dermatologist. All subjects had skin type 2 or 3. The dietary calcium intake of the subjects was ~1000 mg/day and the vitamin D intake was ~100 IU/day. In The Netherlands, only margarine is fortified with vitamin D_3 (3 IU/g). The diet does not contain vitamin D_2. Written informed consent was obtained from proxies and treatment was discontinued when participants clearly objected or showed signs of discomfort. The protocol was approved by the Ethical Review Board of the Academic Hospital of the Vrije Universiteit.

The participants were randomized in block to receive either ultraviolet B (UV-B) radiation or vitamin D_3 or no treatment. The UV-B radiation was applied at an area of 1000 cm^2 of the lower back, three times a week at half the individual minimal erythemal dose (MED). To optimize comfort, this was done in an adjustable chair. In the back of the chair, an opening of 1000 cm^2 was covered with an acrylate plate. The UV-B source was placed at a distance of 45 cm. The source consisted of three Philips TL12 (20 W) fluorescent tubes (Philips, Roosendaal, The Netherlands), protected by a UV-B transparent acrylate plate. The energy of UV-B at the skin was 17 mW/cm^2. The output was measured with an International Light Radiometer (IL 700) connected to a SEE 400 sensor with a WBS 320 filter (International Light, Inc., Newburyport, MA, U.S.A.). Because only 67% of the measured radiation is in the UV-B range, all readings were multiplied by 0.67 to obtain the UV-B values. MED was determined using the same UV source and UV intensity as used for the treatment. Six areas of 4 cm^2 were irradiated with UV-B doses increasing from 30 up to 140 mJ/cm^2. The areas were subsequently inspected for erythema after 24 h. The irradiations were started following the baseline measurements. The other participants received either 400 IU of vitamin D_3 (Devaron, Duphar, The Netherlands) in 1 tablet daily or no treatment. Fasting blood samples for biochemical measurements were obtained at baseline and after 2, 4, 8, and 12 weeks of treatment. An additional sample was obtained at 16 weeks, i.e., 4 weeks after treatment.

Serum 25(OH)D was measured by radioimmunoassay with an intra-assay coefficient of variation (CV) of 8% (Nichols Diagnostics, San Juan Capistrano, CA, U.S.A.). Serum 1,25-dihydroxyvitamin D ($1,25(OH)_2D$) was measured by radioreceptorassay following column extraction with an intra-assay CV of 7% (Incstar Corp., Stillwater, MN, U.S.A.). Serum PTH was measured by immunoradiometric assay (Medgenix Diagnostics, Fleurus, Belgium) at baseline and at 12 weeks. The intra-assay CV of this technique is 4%. Serum concentrations of sex hormone binding globulin (SHBG) were measured by immunoradiometric assay with an intra-assay CV of 5% (Farmos Diagnostics, Oulunsalo, Finland). For these biochemical parameters, the sera of a single participant were all measured within the same run to increase precision. Serum calcium, phosphate, albumin, and creatinin were measured using standard laboratory procedures. Serum calcium was corrected for serum albumin using the formula: corrected serum calcium (mmol/l) = serum calcium + (40-serum albumin [g/l]) × 0.02.

Statistical analysis was performed using the PC version of the Statistical Package for the Social Sciences (SPSS-PC). The effect of treatment was defined as the difference between the mean changes of the biochemical parameters at week 12 (end of treatment) in either treatment group and the mean change in the control group. This was analyzed using multiple linear regression, checking for normality and constancy of variance of the residuals. The difference between the groups in change of serum 25(OH)D at the various follow-up moments was analyzed using analysis of variance for repeated measurements.

RESULTS

The mean age of the patients was 85 years. Their MED values were in the normal range, varying from 40 to 140 mJ/cm^2. The UV-B irradiations only took 3–7 minutes. No skin erythema or other complications were observed. Patient characteristics and baseline biochemical data are shown in Table 1. Most participants, i.e., 42 out of 45, were vitamin D deficient (serum 25(OH)D $<$ 30 nmol/l) and about 60% were severely vitamin D deficient (serum 25(OH)D $<$ 20 nmol/l). The mean serum PTH was increased in the participants compared with values obtained in young adults (reference value 1.1–6.3 pmol/l). There was no significant correlation between baseline serum PTH and serum 25(OH)D. There was a strong positive correlation between the baseline serum concentrations of 25(OH)D and $1,25(OH)_2D$ ($r = 0.39$, $p < 0.001$). The treatment period of 12 weeks was completed by 11 patients in the UV-B group, 14 in the vitamin D group, and 14 in the control group. In all groups, one patient had died and in the UV-B group three patients had refused further participation.

The course during the study period of serum 25(OH)D in the various treatment groups is shown in Fig. 1. According to analysis of variance for repeated measurements, the increase in both treatment groups was highly significant when compared with the control group (both $p < 0.001$). The increase in serum 25(OH)D after 2 weeks was 11

TABLE 1. CHARACTERISTICS AND BIOCHEMICAL PARAMETERS IN SERUM OF 45 PARTICIPANTS AT BASELINE BY INTERVENTION GROUP

	UV-B (n = *15*)		*Vitamin D* (n = *15*)		*Control* (n = *15*)	
Variable	*Mean*	*SD*	*Mean*	*SD*	*Mean*	*SD*
Age (years)	84.2	7.4	84.4	6.3	85.3	5.2
Calcium (mmol/l)*	2.3	0.08	2.3	0.08	2.4	0.12
Phosphate (mmol/l)	1.02	0.12	1.01	0.14	1.04	0.18
SHBG (nmol/l)†	60.2	16.0	65.6	31.5	66.9	21.6
	Median	Percentiles	Median	Percentiles	Median	Percentiles
25(OH)D (nmol/l)	18	12, 25	23	14, 28	12	8, 18
$1,25(OH)_2D$ (pmol/l)	56	42, 67	68	44, 71	45	34.68
PTH(1–84) (pmol/l)	6.2	4.8, 8.1	5.6	4.4, 7.2	5.1	3.7, 7.9
Creatinine (μmol/l)	80	75, 100	82	70, 92	83	70, 94

*Corrected for serum albumin.
† Serum sex-hormone binding globulin.
For skewed variables, median values, 25th and 75th percentiles are given.

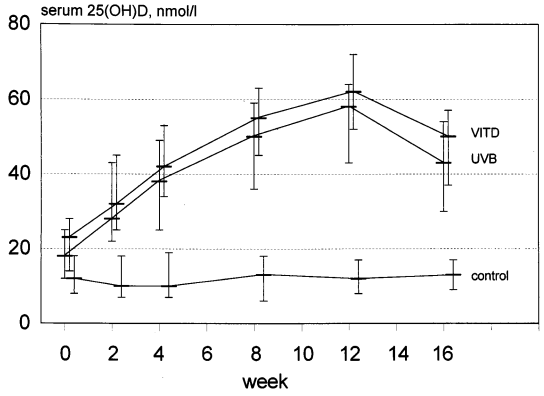

FIG. 1. Serum 25(OH)D (median, 25th– 75th percentile) in elderly women treated during 12 weeks with 400 IU of oral vitamin D (VIT-D, $p < 0.001$) or irradiation of the skin with UV light (UV-B, $p < 0.001$) and in the control group.

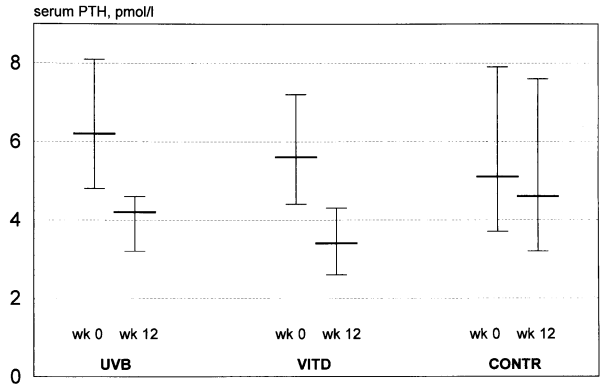

FIG. 2. Serum PTH (median, 25th–75th percentile) in elderly women at baseline (week 0) and after 12 weeks (week 12) of treatment with 400 IU of oral vitamin D (VIT-D, $p = 0.0002$) or irradiation of the skin with UV light (UV-B, $p = 0.0002$) and in the control group.

nmol/l in the UV-B group and 15 nmol/l in the vitamin D group, both significantly different from the 1 nmol/l decrease in the control group ($p < 0.001$). After 12 weeks, the median serum 25(OH)D was 60 nmol/l in both treatment groups ($p < 0.001$). Nonresponders to UV-B or oral treatment were not observed. At week 16, i.e., 4 weeks after discontinuing treatment, serum 25(OH)D had decreased by 16 nmol/l in the UV-B group and 10 nmol/l in the vitamin D group, which was in both groups significantly different from the change in the control group (all $p < 0.001$). In Table 2, the changes in the biochemical parameters due to the interventions are given. Serum $1,25(OH)_2D$ increased significantly in the UV-B group. Serum calcium showed a significant increase in both treatment groups. Serum PTH decreased by 2.2 pmol/l in the UV-B group and 2.1 pmol/l in the vitamin D group ($p < 0.001$), whereas there was little change (−0.1 pmol/l) in the control group (Fig. 2). The effect of treatment on serum PTH was dependent on the serum concentration of SHBG ($p = 0.08$), i.e., serum PTH decreased more when serum SHBG was higher.

DISCUSSION

The results of this study confirm the poor vitamin D status usually observed in institutionalized elderly. Serum 25(OH)D was even lower in these psychogeriatric patients than in institutionalized elderly in The Netherlands, resulting in median serum PTH levels in the upper normal range.[1,13] A negative correlation between serum PTH and serum 25(OH)D was not observed, probably because serum 25(OH)D concentrations were all very low in the patients. The strong positive relation of serum 25(OH)D with serum $1,25(OH)_2D$ suggests that the production of the latter is substrate dependent in these very vitamin D–deficient elderly patients, as has been observed in other studies.[1,16]

Table 2. Mean Change (Δ) from Baseline to the End of the Intervention Period in Biochemical Parameters in Serum by Intervention Group

	UV-B (n = 11)			*Vitamin D (n = 14)*			*Control (n = 14)*	
Variable	Δ	*SD*	p*	Δ	*SD*	p*	Δ	*SD*
$1,25(OH)_2D$ (pmol/l)	11.2	17.1	0.02	−4.0	14.6	0.80	−2.9	10.1
Calcium (mmol/l)†	0.079	0.057	0.01	0.076	0.047	0.01	0.024	0.058
Phosphate (mmol/l)	−0.03	0.14	0.45	0.07	0.18	0.39	0.02	0.14
PTH(1–84) (pmol/l)	−2.2	1.6	0.0002	−2.1	1.1	0.0002	−0.1	1.2
Creatinine (μmol/l)	0.2	10.7	0.95	0.4	11.1	0.90	−0.1	9.6

* *p* value when compared with the control group.
† Corrected for serum albumin.

The treatment with UV-B resulted in a steady, almost linear, increase of serum 25(OH)D, which was very similar to the effects of oral vitamin D_3. It has been observed that the production of vitamin D_3 in the skin following UV-B irradiation at the age of 80 years is around 25% of that at the age of 20 years.[12] The present study shows that the aged skin still has an adequate capacity to produce vitamin D_3 following intense UV-B irradiation of short duration. An earlier study in long-stay geriatric patients showed effects of irradiation during 3 h/day on 4000 cm^2 of skin. In that study, serum 25(OH)D increased 30 nmol/l in 8 weeks.[14] The much smaller skin area and the much shorter irradiation time per session that we needed to obtain similar results may be explained by the fact that we adjusted the individual dose to the sensitivity of the skin as determined by the MED and the intensity was higher.

The decrease of serum PTH was more than 30% in both treatment groups. This is a larger decrease than that observed in our previous vitamin D supplementation study in healthy elderly women, where the decrease of serum PTH was 15%.[7] This is consistent with the greater degree of secondary hyperparathyroidism and more severe vitamin D deficiency observed in these psychogeriatric patients. Moreover, serum $1,25(OH)_2D$ and serum calcium increased, indicating severe deficiency. The effect of treatment on serum PTH was greater when serum SHBG was higher, i.e., when free estrogen levels were lower. In our previous studies, we observed more severe secondary hyperparathyroidism and a greater increase in bone mineral density following vitamin D supplementation when SHBG was high.[7,17] The suppression of PTH secretion may substantially reduce bone turnover and bone loss, although this was not the subject of this study. We conclude that regular exposure of short duration to UV-B can correct vitamin D deficiency and secondary hyperparathyroidism without serious side effects in very elderly nursing home residents. The effects of UV-B are similar to those of oral supplementation with 400 IU of vitamin D_3 per day.

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Address reprint requests to:
Dr. P. Lips
Academic Hospital Vrije Universiteit
Department of Endocrinology
P.O. Box 7057
1007 MB Amsterdam, The Netherlands

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