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ORIGINAL ARTICLE

# Changes in serum 25-hydroxyvitamin D and cholecalciferol after one whole-body exposure in a commercial tanning bed: a randomized study

**Jacob H. Langdahl · Louise Lind Schierbeck · Ulrich Christian Bang · Jens-Erik Beck Jensen**

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**Abstract** We wanted to evaluate the cutaneous synthesis of 25OHD and cholecalciferol after one whole-body exposure to ultraviolet radiation type B (UVB) in a randomized setup. Healthy volunteers were randomized to one whole-body exposure in a commercial tanning bed with UVB emission (UVB/UVA ratio 1.8–2.0%) or an identical placebo tanning bed without UVB. The output in the 280–320 nm range was 450 μW/cm$^2$. Blood samples were analyzed for 25OHD and cholecalciferol at baseline and during 7 days after treatment. We included 20 volunteers, 11 to UVB and 9 to placebo treatment. During the first 6 h, no significant differences in 25OHD between the groups were found. At the end of the study, we found a mean increase of 25OHD in the UVB group of 4.5 nmol/l (SD 7 nmol/l) compared to a decline of −1.2 nmol/l (SD 7 nmol/l) in the placebo group ($p = 0.1$). A linear mixed model yielded an increase of 25OHD in the UVB group of 1.0 nmol/l per 24 h ($p < 0.01$). For cholecalciferol, we found a near significant increase of 1 pmol/l per hour in the UVB group compared to the placebo group during the first 6 h ($p = 0.052$). One tanning bed session had significant, but modest impact on the level of 25OHD during 7 days after exposure to UVB.

**Keywords** Ultraviolet rays · 25-Hydroxyvitamin D · Cholecalciferol · Randomized controlled trial · Ionized calcium · Parathyroid hormone

## Introduction

Vitamin D plays an important role in the maintenance of the bone metabolism [1, 2]. However, in the recent 25 years, it has become clear that a variety of conditions may be related to hypovitaminosis D, including impaired glucose tolerance [3], cancer diseases [4], and schizophrenic disorders [5]. Vitamin D exists in various forms but only 25-hydroxyvitamin D (25OHD) and 1,25-dihydroxyvitamin D have known physiological properties. These metabolites are synthesized from cholecalciferol in the liver and kidney, and the main sources of cholecalciferol are food and cutaneous synthesis. In the skin, 7-dehydrocholesterol metabolizes to pre-vitamin D and then to cholecalciferol when exposed to ultraviolet radiation type B (UVB). From the subcutaneous tissue, it enters the bloodstream and is transported to the liver for further metabolism [6]. The cutaneous photosynthesis of vitamin D metabolites was elucidated mainly by the studies of Holick et al. in the 1970s and 1980s. Experiments on rats demonstrated that UVB induced the conversion of 7-dehydrocholesterol to pre-vitamin D and heat was then required for the formation of cholecalciferol from pre-vitamin D [7]. Further studies on human skin samples showed that increasing age and melanin content would negatively affect the amount of cholecalciferol that was formed in the skin [8, 9]. While age and skin type are unchangeable intrinsic factors, the

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J. H. Langdahl · J.-E. B. Jensen
Faculty of Health Science, University of Copenhagen, Copenhagen, Denmark

L. L. Schierbeck · U. C. Bang (✉) · J.-E. B. Jensen
Department of Endocrinology, Hvidovre Hospital, 541 Kettegård Allé 30, 2650 Hvidovre, Denmark
e-mail: ulrichbangbang@gmail.com

only way to modify the cutaneous synthesis of cholecalciferol is by varying the amount of UVB reaching the skin. There is not, however, a linear relationship between the amount of UVB reaching the skin and cholecalciferol formation because the synthesis of cholecalciferol is limited at around 10–15% of the cutaneous 7-dehydrocholesterol content regardless of continuing UVB exposure. This is due to a photochemical conversion of pre-vitamin D to lumisterol and tachysterol, which has been interpreted as an escape mechanism to prevent intoxication of cholecalciferol after excessive UVB exposure [8]. The two major factors that determine the amount of UV radiation reaching the skin are geography and the meteorological conditions. The latter consist of several dynamic factors: the ozone layer in the stratosphere, cloud cover, and aerosols in the troposphere [10]. These numerous interactions are contained in the UV index that was developed for the general public as a measurement of the UV radiation strength at a given location in a particular day [11].

Hence, only artificial UVB is possible to manage in a standardized way and for that purpose high-intensity UV light from fluorescent tubes is useful. This is used for medical purposes but most widespread in tanning beds [12]. The effect of artificial UVB on vitamin D levels in blood has been investigated in several studies. Initially in 1982 by Adams et al. [13], who reported a dose-dependent rise in cholecalciferol during the first 24 h that was followed by a return to the baseline concentrations. A delayed rise in 25OHD was found after 14 days. They exposed seven participants one time and no control group was included. Later studies examined the effect of several tanning bed sessions and have demonstrated that artificial UVB do increase 25OHD [14, 15].

We wanted to investigate the effect on 25OHD and cholecalciferol during 7 days after a single exposure of UVB in a commercial tanning bed compared to a control group. We speculated if one tanning session was sufficient to increase serum vitamin D as reported in the previous study by Adams et al.

## Materials and methods

### Study population

We recruited 20 healthy Caucasians from the hospital staff in March and April 2010 and the last participants ended the study in the 27th of April 2010. Exclusion criteria were liver and kidney diseases, and pregnancy. The use of vitamin D supplements stopped 7 days before entering the study. All participants gave their written consent and the regional Ethics Committee approved the study, which was registered at Clinicaltrials.gov (NCT01261039). Investigators and participants were blinded throughout the study.

### Treatment

The participants were randomized to receive one full body exposure in either a tanning bed with UV radiation (UVB group) or a placebo tanning bed (placebo group). The two tanning beds were identical (Ergoline Flair 200, JK-Group, Germany) and installed in separate rooms. Each tanning bed was equipped with a total of 27 fluorescence tubes with similar irradiance emission (Electronic Supplementary Material). We installed in the top portion 14 × Ergoline High Power RXL 120W (UVB/UVA ratio 2.0%) and in the bottom portion 13 × Philips CLEO Swift 100W-R (UVB/UVA ratio 1.8%). A transparent filter was installed on the top and bottom screens of the placebo tanning bed (Safety film 2 Mil PS SRC, UV light reduction 98%, Protect Gards Window Films, USA). The UVB emission was verified in both tanning beds with a Solarmeter 6.2 (Solartech, USA). The Solarmeter 6.2 responds mainly to UV rays in the 280–320 nm range and resembles the action spectrum for the production of pre-vitamin D3 being less sensitive for wavelengths longer than 310 nm (Fig. 1) [16]. The UVB output was 450 $\mu W/cm^2$ in the UVB tanning bed and 0 $\mu W$ in the placebo tanning bed. For each participant, we determined the Fitzpatrick skin type, which combines genetic factors and the skin's reaction to sunlight. This scale ranges from I to V. Very sensitive skin with little ability to tan is type I, while less sensitive skin with more ability to tan is types II and III. Skin types IV and V always tan and only rarely experience burns [17]. The manufacturers' recommended session time for a particular skin type was intended for repeated sessions with the intention to obtain tanning of the skin and earlier studies on tanning bed induced vitamin D synthesis did also apply various exposures [14, 15]. For these reasons, and to ensure that our study was not underpowered, we choose an exposure time

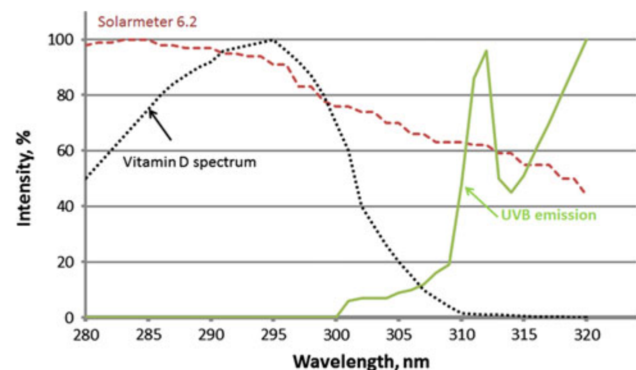


**Fig. 1** Characteristics for the 280–320 nm wavelengths, which is the UVB spectrum. *Green* (*solid*) *line* the emission of the fluorescence tubes has one peak in the UVB spectrum at 312 nm. The major peak is found in the UVA spectrum at 350 nm. *The red* (*dashed*) *line* shows the response of Solarmeter 6.2 that resembles the action spectrum for the production of pre-vitamin D3 (*black dotted line*)

50% longer than the manufacturers' recommended session length. The session length ranged between 10 and 16 min, which corresponded to 375 and 525 J/m$^2$. Hence, each participant received between 3.8 and 5.3 standard erythemal dosis (SED) [18]. Participants were instructed to avoid exposure to natural sun during the study.

### Endpoint

We collected blood samples at baseline, 15 min, 1 h, 2 h, 4 h, 6 h, 1 day, 2 days, 3 days, and 7 days. Cholecalciferol was measured at the Faculty of Agricultural Sciences, Aarhus University with high performance liquid chromatography (Dionex Corporation, USA, CV% 2–4%, detection limit 1.0 ng/l or 2.6 nmol/l). All other samples were analyzed at the Department of Biochemistry, Hvidovre Hospital for 25OHD (Liason®, DiaSorin, Italy, CV% = 6.8–11%, ref. range 50–200 nmol/l), parathyroid hormone (PTH) (Cobas e601, Roche Diagnostics, CV% 3.4%, ref. range 1.1–7.1 pmol/l), $Ca^{2+}$ (Vitros 5.1, Ortho Clinical Studies, CV% 2.3%, ref. range 1.18–1.32 mmol/l), magnesium (Vitros 5.1, CV% 1.6%), and phosphate (Vitros 5.1, CV% 0.6%). To screen the participants for liver and kidney diseases, we measured alanine aminotransferase and creatinine at baseline.

### Statistical analysis

We estimated that a study population of 20 was needed to detect changes in 25OHD of 8 nmol/l with a power of 0.9 in a simple comparison of changes in means at a particular visit. To account for drop-outs, we planned to randomize 22 participants using opaque envelopes in block sizes of 10. We tested all quantitative data for normal distribution using Kolmogorov–Smirnov test and presented data as means (SD) or medians (min–max). We used mixed analysis of repeated endpoints with random intercept to test for differences between the groups. Changes in 25OHD and cholecalciferol during the first 6 h and the whole study period were tested. Two-tailed $p$ values of $<0.05$ were considered significant. All statistical analyses were done with Statistical Analysis Software ver. 9.2 (SAS Institute Inc., Cary, USA).

## Results

Eleven participants were randomized to UVB (group A) and nine were randomized to placebo (group B). Two participants in the UVB group received oral cholecalciferol supplementation prior to the study (3 and 12 µg daily) and five in the placebo group (5, 5, 5, 30, and 30 µg daily) ($p = 0.1$). Baseline characteristics are presented in Table 1 and were comparable for all biochemical measures.

The Fitzpatrick skin type was found to be unevenly distributed between the groups with one participant having type II and 10 participants having type III in the UVB group. In the placebo, seven participants had skin type II and two participants types III and IV, respectively ($\chi^2$ test: $p = 0.045$). Participants with skin type II received one tanning session of 10 min, skin type III received 12 min, and skin type IV received 16 min.

### 25OHD and cholecalciferol

The 25OHD levels of the 20 participants were below 25 nmol/l in two cases, 26–50 nmol/l in nine cases, and were above 50 nmol/l in nine cases (Electronic Supplementary Material). The use of vitamin D supplementation was not related to the mean levels of 25OHD (56 vs. 45 nmol/l, $p = 0.3$). A deviation from the baseline value of 25OHD was found only after 48 h in the UVB group in a

**Table 1** Baseline characteristics of 20 included volunteers

| | UVB ($n = 11$) | Placebo ($n = 9$) | $p$ value |
|---|---|---|---|
| Age (years) | 45 (11) | 38 (11) | 0.2 |
| Body mass index (kg/m$^2$) | 24 (4) | 24 (4) | 0.8 |
| Body surface (m$^2$) | 1.8 (0.1) | 1.9 (0.2) | 0.1 |
| Vitamin D supplementation ($n$) | 2 | 5 | 0.1 |
| Biochemical measures | | | |
| 25-Hydroxyvitamin D (nmol/l) | 46 (17) | 52 (21) | 0.5 |
| Cholecalciferol (nmol/l) | 4.1 (4.0) | 4.3 (6.5) | 0.9 |
| Parathyroid hormone (pmol/l) | 3.6 (1.0) | 4.4 (1.2) | 0.1 |
| Ionized calcium (mmol/l) | 1.2 (0.02) | 1.2 (0.03) | 0.6 |
| Phosphate (mmol/l) | 1.2 (0.2) | 1.1 (0.2) | 0.3 |
| Magnesium (mmol/l) | 0.9 (0.02) | 0.9 (0.05) | 0.7 |

single-sided $t$ test (4.4 nmol/l, $p = 0.02$). During the first 6 h, no statistical differences were found between the groups ($p = 0.1$) (Fig. 2). After 2 days of observation, a plateau was reached in the UVB group and at day 7 of the observation period we found a mean increase of 25OHD of 4.5 nmol/l (7 nmol/l) compared to a decline of −1.2 nmol/l (7 nmol/l) in the placebo group ($p = 0.1$). In a linear mixed model adjusted for baseline levels of 25OHD, we found significant increases in the 25OHD levels in the

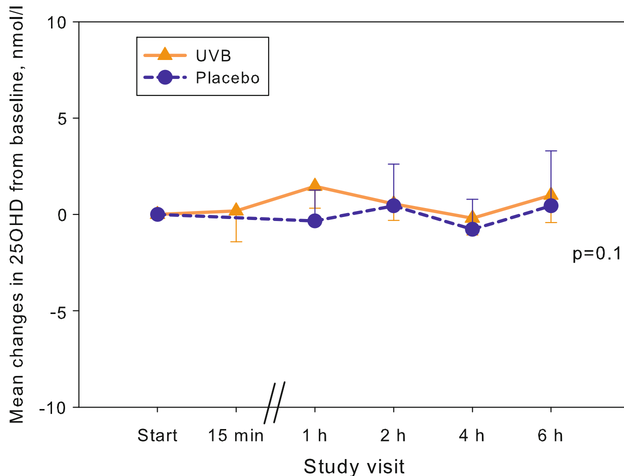


**Fig. 2** Changes in 25-hydroxyvitamin D during the first 6 h after one exposure to UVB or placebo. *Symbols* represent means and *vertical lines* represent standard error. To test for differences between the groups, a mixed analysis model adjusted for baseline level was used ($p = 0.1$)

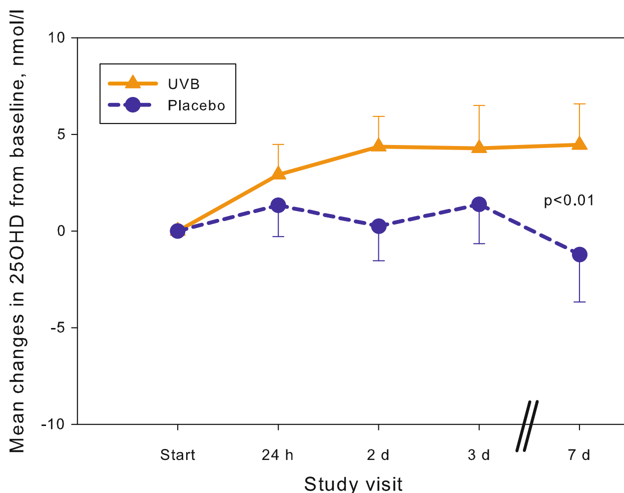


**Fig. 3** Changes in 25-hydroxyvitamin D during the entire study after one exposure to UVB or placebo. *Symbols* represent means and vertical lines represent standard error. To test for differences between the groups, a mixed analysis model adjusted for baseline level was used and an increase of 1 nmol/l (95% CI 0.3–1.8) per day was then found in the UVB group. This differed significantly from the placebo group ($p < 0.01$)

UVB group compared to the placebo group (1.0 nmol/l per 24 h, 95% CI 0.3–1.8, $p < 0.01$) (Fig. 3). Baseline levels of 25OHD were inversely correlated with changes in 25OHD throughout the study ($p = 0.01$).

For cholecalciferol, we found a median increase of 0.1 nmol/l (−10 to 12 nmol/l) in the UVB group and a decline of −0.3 nmol/l (−15 to 25 nmol/l) at day 7. Throughout the first 6 h, an increase of 1 pmol/l per hour occurred in the UVB group, which was nearly significantly different compared to the changes in the placebo group ($p = 0.052$). Throughout the whole study, no differences in linearity between the groups could be demonstrated, though ($p = 0.7$) (Fig. 4). Body surface was not associated with changes in 25OHD or cholecalciferol.

### Other biochemical endpoints

The baseline levels of PTH were inversely associated with levels of 25OHD ($p < 0.01$) and ionized calcium ($p < 0.001$). No significant changes in PTH, ionized calcium, phosphate, or magnesium occurred during the study.

## Discussion

This study showed that one tanning bed session had little but significant effect on the levels of 25OHD but not on cholecalciferol. The study was placebo controlled and blinded in contrast to previous studies on cutaneous vitamin D synthesis using tanning beds [13–15]. The most important confounder in our study was natural sunlight. The weather in Denmark was followed by the Danish Meteorological Institute and for March 2010 the maximal

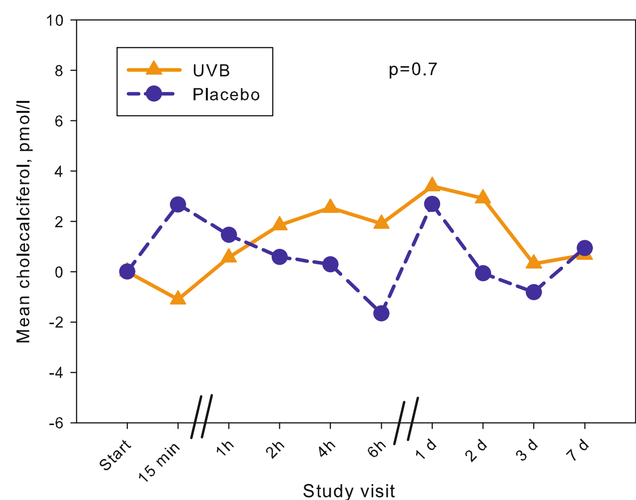


**Fig. 4** Changes in cholecalciferol during the study after one exposure to UVB or placebo. *Symbols* represent means. No differences between the groups during the observations was found ($p = 0.7$). For the first 6 h, an increase of 1.0 nmol/l per hour was found ($p = 0.052$)

UV index registered was 2.2 and the mean UV index was 1.3. Mean temperature for that month was 2.8°C and the highest temperature was 17.7°C. For April, the maximal UV index was 4.0, mean UV index was 2.9, mean temperature 7.0°C, and the highest temperature was 21.4°C. Hence, it cannot be ruled out that some volunteers received UVB beyond what was intended in the protocol, but since no alterations in the 25OHD level occurred in the placebo group, we believe that the participants in general avoided sunlight.

Our outcome differed from earlier studies since only a barely detectable increase in 25OHD and cholecalciferol was found. Adams et al. obtained remarkable dose-dependent increases of cholecalciferol and based on these findings we expected a larger response in our study [13]. Adams et al. used 16 vertically arranged Westinghouse FS40 tubes and measured a UVB output (280–315 nm) of 800 μW per square centimeter. In our study, the UVB output (280–320 nm) was 450 μW per square centimeter, which partly explains the difference between the results. One major reason for the discrepancy is without doubt differences in spectral emission of the sunbed tubes. The emission of the Westinghouse FS40 peaked at 315 nm [19], whereas our fluorescence tanning tubes peaked at both 312 nm (UVB segment) and 350 nm (UVA segment) (Electronic Supplementary Material). In our study, we exposed the participants to 3.8–5.3 SED whereas Adams et al. exposed their volunteers to 1–4 minimal erythema dose (MED) units. The 2 U, SED and MED, are related but only SED is an independent measure (one SED equals 100 $J/m^2$) whereas MED depends on each individual's susceptibility to sunburn. Since none of our participants experienced erythema or burn we estimate that the MED was not reached for any of the participants. Another reason for the discrepancy between our study and the Adams study could be that we applied randomization and blinding together with placebo treatment, which adds to the validity compared to an uncontrolled study. Moreover, we included more participants but statistical tests of repeated measures were nevertheless necessary to establish a significant model. A final explanation for the missing effect on cholecalciferol could be UV-induced degradation of previtamin D as mentioned in the introduction, but that is unlikely since none of the participants received a MED [8].

Unintentionally, we ended up with an uneven distribution of Fitzpatrick skin type between the two groups that resulted in longer tanning sessions in the UVB group. This circumstance does not weaken our results though, as the placebo group did not receive any UVB at all. Increasing length of the tanning session depending on skin type is important as less cutaneous vitamin D synthesis takes place in pigmented skin [20–22].

Previous studies using multiple tanning sessions have reported increased levels of 25OHD, and the tanning bed industry have embraced those findings referring to the beneficial effects of high vitamin D when promoting their product. A reliable dose–response relationship has, however, not been presented to the consumers. With this study, we demonstrated that one session 50% longer than the recommended by the industry is insufficient to induce substantial changes of the 25OHD level. Multiple tanning session are on the other hand not attractive having in mind the carcinogenic properties of UV rays. Moreover, vitamin D tablets are safe and probably cheaper.

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