

The influence of phototherapy with narrow band UVB on 25-hydroxycholecalciferol serum concentration in psoriasis vulgaris patients

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Post Dermatol Alergol 2011; XXVIII, 2: 97–102

Abstract

Introduction: Narrow band UVB (311-313 nm) is commonly used in the treatment of many skin diseases, including psoriasis vulgaris. Under skin exposure to UVB synthesis of vitamin D occurs.

Aim: The aim of the study was to assess the serum concentration of vitamin D in psoriasis vulgaris as well as the changes in 25-hydroxycholecalciferol (25(OH)D) and parathormone (PTH) serum level under a series of UVB exposures. Additionally, we checked the correlation between the final vitamin D concentration and cumulative NB-UVB dose.

Material and methods: The study group included 47 patients with psoriasis vulgaris in the age range 20-65 years old. The patients were treated with 20 NB-UVB exposures. In each patient, 25(OH)D (RIA – radioimmunoassay) and PTH (immunochemiluminescence assay) serum concentration was checked 3 times: before therapy, and after 10 and 20 exposures.

Results: Baseline vitamin D concentration was 26.5 ng/ml. After the first 10 NB-UVB exposures vitamin D serum concentration statistically increased to the value of 38 ng/ml ($p < 0.001$), and after the next 10 irradiations 25(OH)D level increased (43 ng/ml), although it did not significantly differ compared to the second measurement ($p > 0.05$). A PTH serum concentration did not statistically change during the whole therapy. A positive correlation between the cumulative NB-UVB dose and the final 25(OH)D serum concentration was observed ($p < 0.05$).

Conclusions: Deficiency of vitamin D serum level is observed in psoriatic patients. NB-UVB significantly increases 25(OH)D synthesis dependently on cumulative dose, with no effect on PTH serum level. The lower increase in the vitamin D level in the course of phototherapy testifies to the photoadaptation phenomenon.

Key words: vitamin D, parathormone, narrow band UVB, psoriasis vulgaris, cumulative dose.

Introduction

Vitamin D and its metabolites are 9,10-secosteroids [1]. 1,25-dihydroxycholecalciferol (the active form of vitamin D) plays a key role in the human organism in the maintenance of mineral homeostasis due to its ability to increase the effectiveness of calcium and phosphorane absorption. Analogues of vitamin D are used in dermatological therapy because of their immunomodulating, antiproliferative and prodifferentiating properties [2, 3].

Skin is involved in both synthesis and metabolism of the vitamin [1, 3]. Photochemical reaction under skin exposure to UVB (maximum effectiveness 280-315 nm) results in generation of provitamin D from 7-dehydrocholesterol. Under certain conditions (temperature, time) provitamin D is subsequently isomerized into vitamin D. After binding with proteins, it is transported to the liver where the process of its hydroxylation into 25-hydroxy-vitamin D (calcidiol) – 25(OH)D – occurs [4-6]. Next hydroxylation

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occurs in the kidneys and after these processes an active form of vitamin D, 1,25-dihydroxycholecalciferol (calcitriol; 1,25(OH)₂D) is formed (Fig. 1) [7].

25(OH)D is one of the vitamin D metabolites, which is assessed in standard laboratory tests in order to determine the supply of vitamin D. The serum level of calcidiol is about 1000 times higher than calcitriol, and the half time of 25(OH)D is longer (2-3 weeks) than the half time of 1,25(OH)₂D (4-6 h) [8].

Beside bones, calcitriol has its receptor in various tissues including cells of skin, muscles, the immunological and haematopoietic system and also cells of neoplasms e.g. melanoma. The active form of vitamin D plays an antiproliferative and pro-differentiation role and stimulates cytokine production [1, 9, 10]. Literature data indicate a correlation between vitamin D deficiency and development of neoplasms, autoimmune diseases, diabetes mellitus type II, hypertension, and ischaemic heart disease [11, 12].

Beside production of 7-dehydrocholesterol, skin also participates in direct production of calcitriol using 25- and 1- α -hydroxylases, which occurs in keratinocytes and monocytes. Fibroblasts are able to synthesize just calcidiol, because of lack of these enzymes [13].

Psoriasis is an inflammatory skin disease with excessive proliferation and disorders in differentiation of keratinocytes [14]. The efficiency of vitamin D analogues in therapy of psoriasis, described by Morimoto *et al.* [15], encouraged further investigation into the mechanism of the influence of calcitriol and its analogues, calcipotriol and tacalcitol. These substances are safe in long-term therapy of psoriasis, because they have smaller influence on calcio-phosphoric homeostasis (hypercalcaemia, hypercalciuria) and kidney function (nephrolithiasis) [15-17].

In new types of phototherapy cabins, which are used in therapy of psoriasis, atopic dermatitis, vitiligo or mycosis fungoides [2, 18-22], narrow band UVB (NB-UVB, 311-313 nm) is used [2].

At present the time dosage of UVB which delivers the optimal level of vitamin D has not been defined. Current guidelines of the American Academy of Dermatology and the International Agency for Research on Cancer (IARC) do not recommend exposure of unprotected skin to solar radiation, as a source of vitamin D [23-27]. The definition of vitamin D deficiency has not been precisely made, but a level under 20 ng/ml is usually approved. Because of different data in the literature, it is difficult to determine sufficient and normal vitamin D levels in particular populations. This problem is widely discussed by many authors, and may result from different measurement methods [28].

Regarding the common deficiency of vitamin D and wide use of phototherapy with NB-UVB in treatment of psoriasis, the aim of the study was to assess mean concentration of 25(OH)D in serum of psoriatic patients and the influence of UVB 311 nm irradiation on vitamin D level changes. The correlations between the final concentration of vitamin D and age, sex and cumulative dose of NB-UVB were also assessed.

Material and methods

The study group included 47 Caucasian patients with psoriasis vulgaris (17 females, 30 males) in the age range 20-65 years old (mean 43 years old), with a history of psoriasis from 6 months to 40 years (mean 15 years).

All the patients were treated with a series of 20 irradiations of NB-UVB between October 2008 and February 2009. Only patients with a minimum 6-month gap in phototherapy were included in the study. They were irradiated in a Dermalight – Medisun 2800 PC-AB cabin (Schulze & Böhm GmbH – Brühl, Germany) with TL100W/01 fluorescent lamps (Philips, Eindhoven, Netherlands). The initial dose for all adults was 0.2 J/cm² and was systematically increased daily or every other day (it depended on the individual patient reaction). Mean cumulative dose of UVB 311 radiation was 13.5 J/cm². Before treatment, in all patients intensity of psoriatic lesions was assessed by PASI (Psoriasis Area and Severity Index) [29] and a 7.5 ml sample of blood was taken to measure the concentration of vitamin D and parathormone in serum. These procedures were repeated after the 10th and 20th irradiation of phototherapy.

Before the study volunteers gave written consent. They did not use any oral supplementation or topical agent with vitamin D or its analogue. NB-UVB phototherapy was the only method of psoriasis treatment during the study.

In each patient, 25(OH)D and PTH serum concentration was checked 3 times: before therapy, and after 10 and 20 exposures. Concentration of 25(OH)D was measured by RIA (radioimmunoassay) (BioSource Europe S.A. Nivelles, Belgium) and PTH by immunochemiluminescence assay (IMMULITE Turbointact PTH, Diagnostic Products Corporation, Los Angeles, USA).

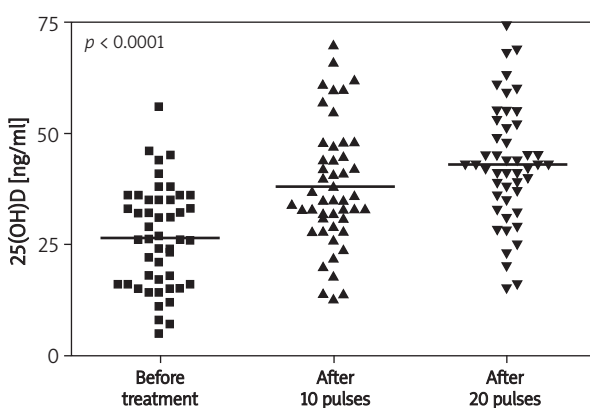


Fig. 1. Changes of 25(OH)D serum concentration during phototherapy

Statistical analysis

Statistical analysis was performed using Tukey's multiple comparison test. The test was statistically significant if $p < 0.05$. The correlation between serum level of 25(OH)D and cumulative dose of UVB 311 nm radiation (J/cm^2) was assessed by Spearman rank correlation.

Results

In the analysed group mean PASI index before phototherapy was 12.7 (range from 3.2 to 32.6) and mean serum concentration of vitamin D 26.5 ng/ml. Sixteen patients had a level of vitamin D under 20 ng/ml, three of them under 10 ng/ml. After a series of 10 NB-UVB pulses concentration of 25(OH)D increased statistically significantly to 38 ng/ml ($p < 0.001$). The next series of 10 NB-UVB pulses also provoked an increase of 25(OH)D level to 43 ng/ml, but it was not statistically significant compared to the second measurement ($p > 0.05$). The increase in 25(OH)D concentration after 20 irradiations of phototherapy was significantly higher than before therapy (43 ng/ml vs. 26.5 ng/ml, $p < 0.001$). When the level of vitamin D in the third measurement was analysed, it was revealed that only two patients had a level under 20 ng/ml (15 ng/ml and 16 ng/ml). The highest value after 20 irradiations increased to 75 ng/ml, when the initial concentration was 22 ng/ml (Tab. 1, Fig. 1).

Concentration of parathormone (PTH) during phototherapy did not change statistically significantly ($p > 0.05$). Mean level of PTH was 35.5 ng/l (Tab. 2, Fig. 2). A statistically significant positive correlation ($r = 0.345$, $p = 0.017$) between cumulative dose of UVB radiation (mean 13.5 J/cm^2) and final concentration of 25(OH)D in serum (mean 43 ng/ml) was observed (Fig. 3).

In the group of patients under 50 years old the mean initial level of vitamin D did not differ statistically significantly from the group of patients over 50 years old (27.6 ng/ml vs. 31 ng/ml, $p > 0.05$). Despite the increase of mean level of vitamin D after 10 and 20 irradiations,

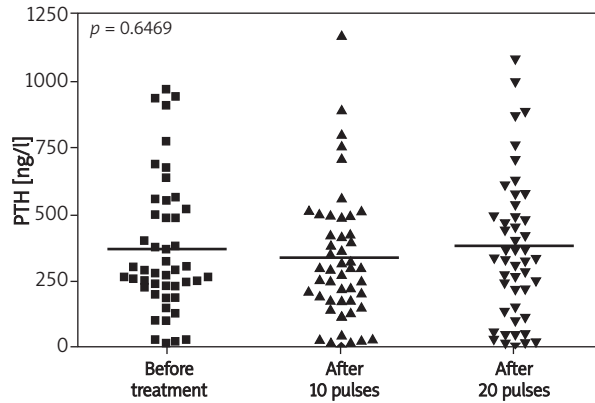


Fig. 2. Changes of PTH serum concentration during phototherapy

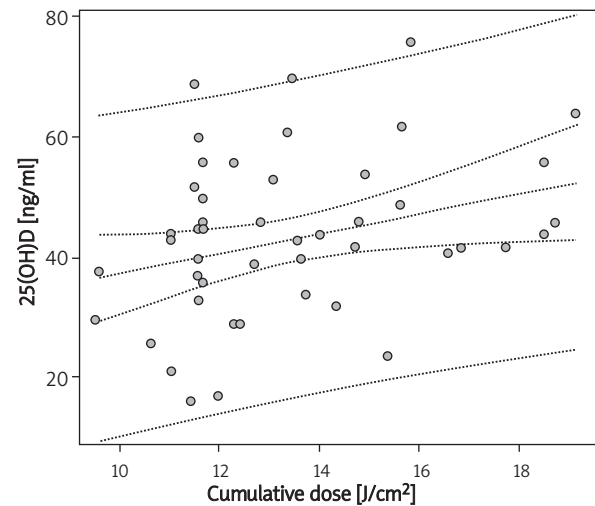


Fig. 3. Correlation between 25(OH)D level and cumulative dose of UVB 311 nm radiation

Tab. 1. Mean differences in 25(OH)D concentration during therapy

Tukey multiple comparison test	Mean differences	95% CI	Value of p
Before therapy vs. after 10 pulses	-11.54	-17.81 to -5.279	< 0.001
Before therapy vs. after 20 pulses	-16.5	-22.80 to -10.21	< 0.001
After 10 pulses vs. after 20 pulses	-4.961	-11.26 to 1.337	> 0.05

Tab. 2. Mean differences in PTH concentration during therapy

Tukey multiple comparison test	Mean differences	95% CI	Value of p
Before therapy vs. after 10 pulses	35.15	-91.05 to 161.3	> 0.05
Before therapy vs. after 20 pulses	-12.88	-139.1 to 113.3	> 0.05
After 10 pulses vs. after 20 pulses	-48.02	-174.2 to 78.17	> 0.05

Tab. 3. Changes of 25(OH)D serum concentration depending on clinical features

Feature		Mean serum concentration of 25(OH)D [ng/ml]		
		Before therapy UVB 311 nm	After 10 pulses UVB	After 20 pulses UVB
Age	> 50 years old (n = 22)	27.6	41.4	46.1
	≤ 50 years old (n = 25)	31	38.2	40
Sex	Males (n = 30)	25.6	39.3	45.5
	Females (n = 17)	28.7	35.8	38.6
PASI index before UVB 311 nm therapy	> 10 (n = 26)	24.9	36.3	44.6
	≤ 10 (n = 21)	26	34.9	43

there were also no statistically significant differences between both groups (Tab. 3. $p > 0.05$ for all comparisons). In female patients mean initial concentration of 25(OH)D was 28.7 ng/ml, and in males 25.6 ng/ml. There were no statistically significant differences between these values. During phototherapy a relevant increase in mean level of 25(OH)D was observed and was significantly higher in males than females (45.5 ng/ml vs. 38.6 ng/ml after 20 irradiations, $p < 0.05$). In the analysed group there was no correlation between PASI index and mean initial concentration of vitamin D and its increase during phototherapy ($p > 0.05$ for all comparisons). Mean concentrations of 25(OH)D in serum before, and after 10 and 20 irradiations of UVB in correlation with sex, age and PASI index are presented in Tab. 3.

Discussion

In many recent publications the problem of vitamin D influence on development of constitutional disease, proper supplementation of vitamin D and the problem of establishing general ranges for 25(OH)D in particular populations is discussed. The Polish scientist Jędrzej Sniadecki made the first observations about the influence of solar radiation on vitamin D level. He noticed increased risk of rickets in a group of children with poor solar exposure living in industrialised areas [30]. Although there is a belief that sunscreens cause vitamin D deficiency, guidelines of the American Academy of Dermatology and the International Agency for Research on Cancer (IARC) do not recommend exposure to ultraviolet radiation as a method of vitamin D supplementation [23, 24]. Recent data from the literature confirm this, because exposure of 35% of skin at noon in summer for 13 min at the latitude of Great Britain is sufficient for production of adequate amounts of vitamin D by the human body [31]. According to the literature data, there is no evidence that UVB 311 nm could be a supplementation method of vitamin D insufficiency. This results from the characteristics of UVB radiation, its capacity for DNA damage with subsequent production of photoproducts, mutations and increasing

expression of cyclooxygenase 2. These processes initiate photocarcinogenesis and occur even after exposure to non-erythematous doses of UVB [32-34].

In 2010 Vähävihi *et al.* published a study [18] describing the influence of NB-UVB therapy on vitamin D serum concentration changes in a group of 56 healthy female volunteers during winter. The authors postulated that UVB 311 nm phototherapy can be beneficial for patients with vitamin D deficiency. This suggestion needs to be checked in patients from the risk group [6, 18]. It might seem that in some cases, e.g. in autumn and winter months, in postmenopausal women, therapy with artificial sources of UV radiation could be a method of vitamin D supplementation, but initiation of photocarcinogenesis by UV radiation tends to exclude this form of treatment.

In this study mean concentration of 25-hydroxycholecalciferol in serum of patients was lower than recommended by a group of experts led by Lorenc *et al.* – range 30-80 ng/ml [35]. Thirty-four percent of patients have vitamin D deficiency with a level lower than 20 ng/ml.

This study revealed that the increase in vitamin D level between the 2nd and 3rd measurement was significantly lower than after the first 10 irradiations of NB-UVB. This observation can testify to the photoadaptation phenomenon, which may be a result of the body's response to production of toxic doses of 25(OH)D and inactive forms of vitamin D such as tachysterol or lumisterol [36]. These data show that overproduction of vitamin D caused by NB-UVB is dissimilar, because inactive forms are produced. This hypothesis can be confirmed by the fact that the highest value of 25(OH)D concentration in the group study was 75 ng/ml. It was lower than the level accepted as a border of toxic concentration (150 ng/ml), which can lead to hypercalcaemia, hypercalciuria and dysfunction of internal organs [37]. A similar phenomenon of vitamin D degeneration is observed during skin irradiation with solar lamps, where the proportion of UVB to UVA was 0.04 [38].

After treatment with NB-UVB only 4.3% of patients showed deficiency of vitamin D compared to 34% before treatment. This indicates that phototherapy with this spe-

cific ultraviolet band is an important factor of vitamin D production and can improve patients' clinical condition [7, 39]. A study which compares the effectiveness of UVB phototherapy with oral supplementation with calcitriol proves this hypothesis. The authors' observations showed that both methods are efficient in treatment of psoriasis. The effectiveness of combined treatment did not differ in comparison to single therapy [40].

No correlation between changes in concentration of vitamin D and parathormone was found. This indicates that the increase of vitamin D level was in the normal range, feedback reaction of mineral homeostasis was not activated and the concentration of parathormone did not secondarily decrease. Our observations differ from data obtained by Osmancevic *et al.* [7]. They reported an increase of PTH serum level during phototherapy with broad band UVB (9290-315 nm). This may result from the fact that their study group consisted of 24 postmenopausal women with deregulation of calcium-phosphorus homeostasis and concentration of parathormone over the normal range recommended by Szczeklik *et al.* (10-60 ng/l) [41].

On the basis of these results we conclude that patients with psoriasis vulgaris have deficiency of vitamin D. NB-UVB significantly increases 25(OH)D synthesis dependently on cumulative dose, with no effect on PTH serum level. The lower increase in the vitamin D level in the course of phototherapy testifies to the photoadaptation phenomenon.

Therapy with narrow band UVB significantly increases 25(OH)D synthesis in all patients, especially in the initial part of treatment, and increases serum vitamin D concentration to an optimal value. In case of excessive exposure to UVB B 311 nm radiation, some internal mechanism deactivates the active form of vitamin D. This mechanism defends against overproduction of vitamin D toxic metabolites. UVB therapy could be considered as one method of vitamin D supplementation, especially in the winter period. However, because of side effects of ultraviolet radiation, this statement should be further investigated in long-term studies on photocarcinogenesis.

Acknowledgments

The paper was funded by Medical University of Lodz Research Project no. 503-11-52-1 and Polish Scientific Committee no. NN402253336.

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