Heliotherapy improves vitamin D balance and atopic dermatitis

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Summary

Background Vitamin D insufficiency during winter is common in the Nordic countries. Heliotherapy (HT) may heal atopic dermatitis (AD) but its effect on vitamin D balance has not been examined.

Objectives To study the effect of HT on serum calcidiol (25-hydroxyvitamin D) concentration and on healing of AD.

Methods Twenty-three adult patients with AD received a 2-week course of HT in the Canary Islands in either January or March 2005. Daily solar ultraviolet (UV) radiation was measured and personal UV exposure calculated as standard erythema doses (SED). Blood samples were taken during HT and during a 1–2 month follow-up. Serum calcidiol concentration was measured by radio-immunoassay. Healing of AD was examined by SCORAD index.

Results Before HT 17 (74%) AD patients had vitamin D insufficiency (calcidiol < 50 nmol L\(^{-1}\)) and four patients high (> 80 nmol L\(^{-1}\)) serum calcidiol values. The median personal UV dose during the 2-week HT course was 60 SED in the January group and 109 SED in the March group. Serum calcidiol concentration increased significantly in both groups, by 13 ± 4 and 24 ± 0 nmol L\(^{-1}\), respectively, and after HT only four (17%) patients had vitamin D insufficiency. SCORAD improved from 34 to 9 in the January HT group and from 30 to 9 in the March group.

Conclusions A 2-week course of HT significantly improved vitamin D balance by increasing serum calcidiol concentration, and caused a marked healing of AD. These parallel positive responses should be taken into account when the benefits of HT are considered.

Vitamin D made in the skin after exposure to sunlight or ingested in the diet is essential for human health. Keratinocytes have the capacity for ultraviolet (UV) B-induced photochemical conversion of 7-dehydrocholesterol to vitamin D.\(^1\) Thereafter, vitamin D is hydroxylated to form calcidiol (25-hydroxyvitamin D), which is the major circulating form of vitamin D and the best indicator of vitamin D status.\(^2\) A second hydroxylation is needed to form calcitriol (1α,25-di-hydroxyvitamin D), the active and hormone-like metabolite of vitamin D. Calcitriol is not only crucial in calcium metabolism and bone health, but also has a wide variety of other biological functions, such as regulation of cell growth, including keratinocyte growth, and modulation of the immune system.\(^3–5\) The capacity to regulate keratinocyte growth is used in dermatology when treating psoriasis with calcipotriol, a vitamin D derivative, or with calcitriol.\(^6\)

UVB phototherapy is effective in reducing symptoms of psoriasis and of atopic dermatitis (AD).\(^7,8\) Heliotherapy (HT) in winter in the Canary Islands is an alternative chosen by many patients from Nordic countries because HT treatment results have been good both in psoriasis and in AD.\(^9,10\)
Northern people.\textsuperscript{11,12} At present, a large number of Finnish and Norwegian people is known to suffer from seasonal vitamin D insufficiency or even deficiency.\textsuperscript{13–16} In the present study we examined whether a 2-week course of HT in the Canary Islands in winter improves vitamin D balance and simultaneously heals AD.

**Materials and methods**

**Patients and heliotherapy protocol**

Twenty-five patients (20 women, five men; mean ± SD age 36 ± 12 years, range 21–57) with AD living in various parts of Finland (60–70°N) were included in the study. Inclusion criteria were skin types II or III according to Fitzpatrick,\textsuperscript{17} and no phototherapy, solarium, sun holidays or vitamin D supplementation during the preceding 2 months. The ethics committee of Päijät-Häme Central Hospital approved the study protocol and all patients gave their informed consent to participate. At the beginning two women withdrew from the study for personal reasons. The severity of AD was scored by SCORAD index\textsuperscript{18} at the beginning and at the end of HT.

HT was undertaken in Puerto Rico, Gran Canaria, Spain (30°N) in winter 2005. The first group of 11 patients (nine women, two men) received HT from 24 January to 4 February and the second group of 12 patients (nine women, three men) from 12 March to 26 March. On the first day the sun-bathing time was 15 min for patients with skin type II or severe AD (eight patients) and 30 min for the rest. Patients sunbathed while lying on both sides of the body, without sunscreens. The time was increased daily by 15 min until a maximum duration of 2 h in the sun was reached. Thereafter, clothes and sunscreen with sun protection factor (SPF) 15 or higher were used to protect the skin from the sun.

**Personal ultraviolet exposure and solar ultraviolet radiation measurements**

The patients recorded each day in a diary the exact times of sunbathing, hours spent outdoors and use of clothes and sunscreens. The data were recorded in 10-min intervals and stored in a computer.

The solar UV radiation was measured continuously with a Robertson Berger type broadband UV meter (Solar Light Model 501 UV-meter s/n 4845; Solar Light Co. Inc., Glenside, PA, U.S.A.) which also gives the results in 10-min intervals. The UV meter is calibrated annually at the Radiation and Nuclear Safety Authority, Helsinki, Finland. The calibration uncertainty (2\sigma) of the broadband UV meter is 8% and the calibration is traceable to the National Institute of Standards and Technology (Gaithersburg, MD, U.S.A.). The UV meter was placed on a high roof near the place the patients were sunbathing. The UV doses are given as biologically weighted standard erythema doses (SED). One SED is equivalent to 10 mJ cm\(^{-2}\) CIE erythema-weighted irradiance.\textsuperscript{19} The personal UV exposure was calculated from the UV meter and diary data. The protective effect of clothes was calculated using coverage factors based on the rule of nines (e.g. 0·44 for trousers, 0·22 for shorts, 0·42 for a pullover, 0·30 for a T-shirt, 0·28 for a woman’s swimsuit, 0·10 for a man’s swimming trunks or for a bikini). The protective factor of sunscreens (SPF > 15) applied after sunbathing was divided by four\textsuperscript{20} and one application was assumed to give UV protection for 3 h.

**Calcidiol measurements**

The dietary intake of vitamin D was determined by a semi-quantitative food frequency questionnaire\textsuperscript{21} completed 1 month before and 1 month after HT. Blood samples were taken 1 day before HT and in the evenings of days 1, 2, 6 and 13. Follow-up samples were taken 1 month and 2 months (January group only) after HT. The samples were protected from light, centrifuged, and serum was frozen (–20 °C) and transported to Finland.

Serum calcidiol concentration was measured in duplicate by radioimmunoassay (Immunodiagnostic Systems, Boldon, U.K.). At calcidiol levels of 26·5, 58·4 and 151 nmol L\(^{-1}\), the intra-assay variation was 5·3%, 5·0% and 6·1%, respectively. At calcidiol levels of 19·6, 56·7 and 136 nmol L\(^{-1}\), the interassay variation was 8·2%, 8·1% and 7·3%, respectively. A calcidiol concentration below 50 nmol L\(^{-1}\) was regarded as vitamin D insufficiency and below 25 nmol L\(^{-1}\) as deficiency.\textsuperscript{22}

**Statistical methods**

Because of the non-normal distributions of the variables involved, the data are described as medians and lower and upper quartiles unless otherwise specified, and nonparametric methods were used. The significance of the changes in serum calcidiol concentrations and in SCORAD was analysed by Wilcoxon signed rank test. For the correlations between the personal UV dose received and changes in serum calcidiol concentrations as well as changes in SCORAD, Spearman’s rho was used. The analyses were accomplished by SPSS for Windows, version 11.5 (SPSS, Chicago, IL, U.S.A.).

**Results**

**Calcidiol concentration before heliotherapy**

Before HT 17 patients with AD (74%) had mild or moderate vitamin D insufficiency, showing serum calcidiol concentrations < 50 nmol L\(^{-1}\). The lowest value was 27·4 nmol L\(^{-1}\). In four patients, three of whom had received UV phototherapy 2–3 months earlier, the calcidiol concentration exceeded 80 nmol L\(^{-1}\), and their results were assessed separately. Before HT the median dietary vitamin D intake of the 23 patients was 4·7 μg daily (range 1·3–10·8) and it was the same 1 month after HT; there were no statistically significant differences between the January and the March group. The intake of

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vitamin D before HT was not associated with the initial calcidiol concentrations in the January group \( (r = 0.28) \), while there was a moderate correlation in the March group \( (r = 0.50) \).

**Effect of heliotherapy on calcidiol concentration**

In the January group \( (n = 8) \) the median personal UV dose received during the 2-week course of HT was 60 SED (Table 1). In the March group \( (n = 11) \) the UV dose was almost double this value, at 109 SED, although the duration of sunbathing was equal in both groups. Also the median increase in serum calcidiol concentration was almost double in the March group compared with the January group, at \( 24.0 \text{ nmol L}^{-1} \) and \( 13.4 \text{ nmol L}^{-1} \), respectively. The increase was statistically significant in both groups \( (P < 0.001, P = 0.008, \text{Table 1}) \). Already at day 6 the increase in calcidiol concentration was almost significant in both the January and the March groups, at \( 4.8 \text{ nmol L}^{-1} \) \( (P = 0.055) \) and \( 13.3 \text{ nmol L}^{-1} \) \( (P = 0.067) \), respectively (Fig. 1). Two days of sunbathing in January and 1 day in March induced a small drop in the calcidiol concentration, but the decrease was statistically nonsignificant in both groups. Similarly, in the four patients with initial calcidiol concentrations > 80 nmol L\(^{-1}\) the concentration decreased on the first 2 days while thereafter it increased markedly in two of them (Fig. 2). There was no correlation between the initial calcidiol concentration and its increase either in the January group \( (r = -0.24) \) or in the March group \( (r = 0.16) \). Four patients (21%) were still vitamin D insufficient at the end of HT, showing serum calcidiol concentrations < 50 nmol L\(^{-1}\). After HT the calcidiol concentration slightly decreased in the January group, while in the March group it continued to increase further (Fig. 1); both changes were statistically nonsignificant.

**Effect of heliotherapy on atopic dermatitis**

At the onset of HT the median SCORAD was 34 (range 15–41) in the January group and 30 (range 6–57) in the March

<table>
<thead>
<tr>
<th>Patient group</th>
<th>Personal UV dose (SED), median (IQR)</th>
<th>Median calcidiol (nmol L(^{-1}))</th>
<th>Change in calcidiol (nmol L(^{-1})), median (IQR)</th>
<th>SCORAD, median (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>At start</td>
<td>At end</td>
<td>P-value</td>
<td>At start</td>
</tr>
<tr>
<td>January (n = 8)</td>
<td>60.2 (48.0–75.1)</td>
<td>42.9</td>
<td>56.4</td>
<td>13.4 (8.5–18.5)</td>
</tr>
<tr>
<td>March (n = 11)</td>
<td>109.3 (84.7–150.7)</td>
<td>42.4</td>
<td>62.3</td>
<td>24.0 (12.0–39.5)</td>
</tr>
</tbody>
</table>

SED, standard erythema doses; IQR, interquartile range.

Fig 1. Calcidiol concentrations during and after a 2-week course of heliotherapy (HT) in patients with atopic dermatitis in January \( (n = 8) \) and March \( (n = 11) \).
group and at the end of HT it was 9 in both groups (Table 1). Accordingly, the net improvement of AD in the SCORAD was 74% \((P = 0.008)\) in the January group and 57% \((P = 0.002)\) in the March group. The initial SCORAD of the four patients with high calcidiol concentrations ranged from 22 to 48, and their scores also decreased markedly, ranging from 0 to 7 at the end of HT.

**Personal ultraviolet dose, calcidiol concentration and SCORAD**

In the March HT group, the personal UV dose received and the increase in serum calcidiol concentration showed a positive correlation \((r = 0.63, \text{Fig. 3a})\) during the 2-week course of HT. No such correlation was found in the January group \((r = 0.07)\) although in both groups a UV exposure of 10 SED was equivalent to a median increase of 2.2 nmol L\(^{-1}\) in serum calcidiol. In the March group, but not in the January group, there was also a positive correlation between the personal UV dose and the improvement of the AD assessed using SCORAD \((r = 0.67, \text{Fig. 3b})\). Similarly, there was a positive correlation between the increase of calcidiol concentration and improvement of SCORAD in the March \((r = 0.50)\) but not in the January group \((r = -0.48)\).

**Discussion**

Solar UV exposure is crucial for vitamin D synthesis and as much as 90% of all requisite vitamin D has to be formed in the skin. Calcitriol, the active form of vitamin D produced in the liver and kidney, but also in other tissues such as the skin or prostate, is considered to be an autocrine or paracrine hormone, which regulates various cellular functions including cell growth. Due to this, vitamin D insufficiency seems to have much more extensive consequences than previously thought, ranging from well-known bone disease to prostate and other cancers and even to autoimmune diseases. Knowledge of this has led to the on-going debate on the balance between the positive (vitamin D) and the negative (skin cancer) effects of sunlight. In summer at latitude 42\(^\circ\)N in Boston (MA, U.S.A.), 5–10 min of solar exposure three times a week on the hands, arms and face is sufficient to maintain vitamin D balance, but in winter very little, if any, vitamin D is produced in the skin. In line with this, many people living in Northern Europe, like in Finland and Norway, and possibly also in other northern European countries, have been found to have mild to moderate seasonal vitamin D insufficiency.

In the present study 17 of 23 (74%) patients with AD showed vitamin D insufficiency, i.e. their serum calcidiol concentration was < 50 nmol L\(^{-1}\) at the onset of the study. The 2-week course of HT in the Canary Islands proved to have a significant effect on serum calcidiol concentration which increased to an optimal level in 13 of 17 (76%) patients. The median increase was 13 nmol L\(^{-1}\) in the January group and
24 nmol L\(^{-1}\) in the March group. Interestingly, a 2-week HT course had a similar increasing effect on serum calcidiol concentration as fortifying milk products and margarine with vitamin D. This nationwide dietary intervention occurred in Finland in 2003 and in young men it increased the serum calcidiol concentration by a mean of 17 nmol L\(^{-1}\).\(^{16}\)

In the first 2 days of HT serum calcidiol concentration seemed to decrease a little (Fig. 1). This tendency was more apparent in the four patients with high initial calcidiol concentrations. Perhaps UV exposure is capable of destroying vitamin D in the skin, or alternatively of producing inert isomers when the vitamin D status is well saturated.\(^{25}\) It has also been shown that when calcidiol concentration exceeds 100 nmol L\(^{-1}\) the synthesis of 24-hydroxylase increases which leads to inactivation of calcidiol.\(^{26}\) An important finding was also that in the January group, after HT, the increased calcidiol concentration persisted at nearly the same level for the next 2 months. In the March group the calcidiol concentration continued to increase after HT. It is not known whether this could be due to outdoor exposure to sun in April or due to some other factors.

The improvement of AD was significant during the 2-week course of HT. This is in agreement with an earlier study.\(^{10}\) The median decrease in SCORAD was 70%, i.e. about the same as that achieved with UVB phototherapy.\(^{7,27}\) In the March group the personal UV dose received was double compared with the January group. The reason is mainly due to the difference in the zenith angle of the sun but the weather also was unfavourably cloudy in January. This might explain why in the March, but not in the January HT group, there was a clear correlation between the personal UV dose received and the improvement of SCORAD. Despite the lack of this correlation the patients healed well in the January group, implying that also factors other than UV dose alone seem to have an impact on improvement of AD during HT.

The present study was performed in the Canary Islands where a Finnish patient association has organized HT courses for many years. During HT specially educated nurses guide patients how to sunbathe according to an individual plan made by a dermatologist. Despite this, the personal cumulative UVB doses showed large variation because of different personal behaviour after the programmed sunbathing time. This indicates that it is much more difficult to standardize HT than the UVB treatments given in outpatient clinics at home. No major sunburns occurred during the present courses but the possible long-term effects of HT should be considered. A retrospective, nationwide cohort study of Danish patients with psoriasis who had received climatotherapy at the Dead Sea during 1972–93 showed an increased risk for basal cell and squamous cell carcinomas.\(^{28}\) In contrast, a controlled cross-sectional study of 460 patients with psoriasis from the same treatment place did not find any increase in nonmelanoma skin cancers but it documented significantly more actinic damage in the patients with psoriasis than in controls.\(^{29}\) We are not aware of any similar skin cancer studies in HT-treated patients with AD. Such studies are, however, warranted even though epidemiological or long-term follow-up studies of hospitalized patients with AD have not shown any evidence for increased nonmelanoma or other cancer risks.\(^{10,31}\)

A recent study in mice showed that calcitriol is able, via signalling in keratinocytes, to induce an AD-like syndrome.\(^{32}\) Whether this mechanism could somehow be implicated in the pathogenesis of AD should be examined, although it seems unlikely in humans. AD is known to be exacerbated in adults and also in children during winter,\(^{33}\) when serum calcidiol concentration is at its lowest. Moreover, in the present study the March HT group showed a positive and the January group a negative correlation between the increase in calcidiol concentration and healing of AD. The question whether UV-induced calcidiol synthesis could have any influence on the healing of AD remains to be elucidated in further studies.

In conclusion, the present study showed that a 2-week course of HT is capable of significantly correcting serum calcidiol insufficiency and AD simultaneously. The positive effect of HT on vitamin D balance should be taken into account when considering the benefits and risks of HT for patients with AD.

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