Climatotherapy at the Dead Sea Stimulates Vitamin D₃ Metabolism

Sir,
The Dead Sea is a well-known center for climatotherapy of psoriasis (1). The treatment consists of sunbathing and bathing in the hypersaline Dead Sea, which has an average salinity of 30%. The thick atmosphere layer (1,200 feet below sea level), together with the haze resulting from the extreme evaporation of the sea, results in the outfiltration of shorter wavelength UVB sunburning rays. Therefore, a greater exposure to the longer UVB and UVA rays is allowed (2). The beneficial effect of climatotherapy could involve an impact of ultraviolet light on vitamin D₃ synthesis. Under the influence of ultraviolet light in the range of 290–300 nm, 7-dehydrocholesterol is converted in the epidermis to previtamin D₃, which is isomerized to vitamin D₃ by a temperature process (3). After translocation to the circulation, vitamin D₃ is hydroxylated in the liver into 25-hydroxyvitamin D₃ (25-OH-D₃), and further hydroxylation occurs in the kidney leading to 1,25-(OH)₂-D₃, the active metabolite of vitamin D₃ (4). Also, 1,25(OH)₂-D₃ synthesis may take place in the skin, because cultured keratinocytes have the capacity to convert 25-OH-D₃ into 1,25(OH)₂-D₃ (5). While the circulating levels of 25(OH)-D₃ reflect the amounts of vitamin D taken up from the food and synthesized in the skin, the levels of 1,25(OH)₂-D₃ are tightly regulated by 1-hydroxylase to maintain calcium homeostasis (4). Thus downregulation of 1-hydroxylase is induced by parathyroid hormone (PTH), calcium and 1,25(OH)₂-D₃ itself.

In the present study it is shown that climatotherapy at the Dead Sea is associated with a stimulation of vitamin D₃ metabolism. Because both topical and systemic treatment with vitamin D₃ analogues improves psoriasis (6), the effect on vitamin D₃ metabolism may be important for the anti-psoriatic effect of climatotherapy.

MATERIAL AND METHODS

Patients
It was a prospective, open study of 16 Danish psoriatic patients receiving climatotherapy at the Dead Sea. As controls served 15 psoriatic patients treated in Denmark with tar, a treatment supposed not to affect vitamin D or bone metabolism. The study was approved by the local Ethics Committee.

Every day for 4 weeks the patients lay in the sun for increasing periods of time at the shoreline of the mineral-rich sea. During their stay at the Dead Sea patients received a diet similar to a typical Danish diet, meaning that there was no significant change of the calcium intake.

At the start and at the end of therapy (4 weeks later), the psoriasis area and severity index (PASI) was assessed (7).

Laboratory examinations
Serum concentrations of total calcium (Ca), phosphorus (P), parathyroid hormone (PTH), 25-OH-D₃, 24,25(OH)₂-D₃ and 1,25(OH)₂-D₃ were measured at the start of therapy and 4 weeks later. PTH and vitamin D₃ metabolites were measured by radio-immunoassays.

In 8 of the patients 24-h urine excretion of calcium was also determined before and at the end of therapy.

Statistics
For assessment of statistical significance, Student's t-test for paired data was used. The level of significance was 5%.

DISCUSSION

The presented results show that climatotherapy at the Dead Sea is accompanied by a significant increase in the levels of circulating 25-OH-D₃, 24,25(OH)₂-D₃, while the bioactive form of vitamin D₃, 1,25(OH)₂-D₃, was unchanged. These changes reflect most likely a stimulation of cutaneous vitamin D₃ synthesis. The reason why 1,25(OH)₂-D₃ did not increase was probably a negative feedback regulation exerted by PTH. A PTH decrease results in an inhibition of the hydroxylation of 25(OH)D₃ into 1,25(OH)₂-D₃, while favoring the conversion into 24,25(OH)₂-D₃, synthesis (4). Similar increases of 25(OH)D₃ and 24,25(OH)₂-D₃ levels have been observed after UVB phototherapy (8, 9). Taken together with our results, these studies suggest that phototherapy of psoriasis is associated with a stimulation of cutaneous vitamin D₃ synthesis. In two of these three studies the 1,25(OH)₂-D₃ levels remained unchanged, while a slight increase was found in the third study (8). Although 1,25(OH)₂-D₃ levels were not increased during climatotherapy, there was a significant increase of urinary calcium excretion. This increase of calcium excretion was sufficient to prevent hypercalcemia. Therefore, climatherapy appears to be safe in otherwise healthy patients. In patients with impaired renal function, a reduced capacity to increase urinary calcium excretion may, however, result in hypercalcemia.

While the clinical improvement of psoriasis following sun exposure is well-established, it is not unclear whether stimulation of cutaneous vitamin D₃ synthesis is required for the anti-psoriatic effect of sunlight. It is an argument against this hypothesis that the range of ultraviolet light which induces previtamin D₃ synthesis is very narrow (290–300 nm) (3) and different from the optimal wavelengths (310 nm) for UVB phototherapy (10). If climatotherapy acts partially by stimulating vitamin D₃ synthesis, it might be via hydroxylation of 25-OH-D₃ into 1,25(OH)₂-D₃ locally in epidermal keratinocytes (5). In this context, the influence of daily bathing.

RESULTS
At baseline the mean PASI was 15.2. After climatotherapy the average PASI had decreased by 90%. A complete clearance was achieved in 50% of the patients.

At baseline the levels of the biochemical markers of vitamin D₃ and calcium metabolism were normal. At the end of climatotherapy the levels of 25(OH)D₃ and 24,25(OH)₂-D₃ had increased by 80% and 97%, respectively (Fig. 1). The levels of serum 1,25(OH)₂-D₃ remained unchanged, but there was a significant decrease of serum PTH (28%) (Fig. 1). Serum levels of total Ca and P did not change during therapy (data not shown). In the 8 patients collecting 24-h urine, there was a significant increase of urinary calcium excretion at the end of climatotherapy (from 3.2 to 5.4 mgCa mmol/24 h, p = 0.027). Thus, the mean urinary calcium excretion rose slightly above the normal range.

In controls, i.e. psoriatic patients receiving tar therapy in Denmark, none of the biochemical markers of vitamin D₃ metabolism were changed at the end of therapy (data not shown).
in the Dead Sea should not be neglected. The hypersaline sea water effectively removes scales from the skin lesions and thereby facilitates the penetration of UV-rays into the skin. Therefore, climatotherapy at the Dead Sea may offer advantages, although the UV spectrum may not be ideal for the induction of vitamin D₃ synthesis in the skin.

It is noteworthy that the increase of urinary calcium excretion during climatotherapy is more pronounced than what has been reported during high-dose treatment with topical calcipotriol (11). Despite this finding, climatotherapy should be considered to be safe, because the treatment is only given in short courses.

REFERENCES


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