Climatotherapy at the Dead Sea Stimulates Vitamin D_3 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 D_3 synthesis. Under the influence of ultraviolet light in the range of 290–300 nm, 7-dehydrocholesterol is converted in the epidermis to previtamin D_3, which is isomerized to vitamin D_3 by a temperature process (3). After translocation to the circulation, vitamin D_3 is hydroxylated in the liver into 25-hydroxyvitamin D_3 (25-OH-D_3), and further hydroxylation occurs in the kidney leading to 1,25$(OH)_2$ D_3, the active metabolite of vitamin D_3 (4). Also, 1,25$(OH)_2$ D_3 synthesis may take place in the skin, because cultured keratinocytes have the capacity to convert 25-OH-D_3 into 1,25$(OH)_2$ D_3 (5). While the circulating levels of 25(OH)-D_3 reflect the amounts of vitamin D taken up from the food and synthesized in the skin, the levels of 1,25$(OH)_2$ D_3 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$(OH)_2$ D_3 itself.

In the present study it is shown that climatotherapy at the Dead Sea is associated with a stimulation of vitamin D_3 metabolism. Because both topical and systemic treatment with vitamin D_3 analogues improves psoriasis (6), the effect on vitamin D_3 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 solarium and took baths in 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-D_3, 24,25$(OH)_2$ D_3 and 1,25$(OH)_2$ D_3 were measured at the start of therapy and 4 weeks later. PTH and vitamin D_3 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%.

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 D_3 and calcium metabolism were normal. At the end of climatotherapy the levels of 25-(OH)-D_3 and 24,25$(OH)_2$ D_3 had increased by 80% and 97%, respectively (Fig. 1). The levels of serum 1,25$(OH)_2$ D_3 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 uCa 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 D_3 metabolism were changed at the end of therapy (data not shown).

DISCUSSION

The presented results show that climatotherapy at the Dead Sea is accompanied by a significant increase in the levels of circulating 25-OH-D_3 and 24,25$(OH)_2$ D_3, while the bioactive form of vitamin D_3, 1,25$(OH)_2$ D_3, was unchanged. These changes reflect most likely a stimulation of cutaneous vitamin D_3 synthesis. The reason why 1,25$(OH)_2$ D_3 did not increase was probably a negative feed-back regulation exerted by PTH. A PTH decrease results in an inhibition of the hydroxylation of 25$(OH)D_3$ into 1,25$(OH)_2$ D_3, while favouring the conversion into 24,25$(OH)_2$ D_3 synthesis (4). Similar increases of 25$(OH)D_3$ and 24,25$(OH)_2$ D_3 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 D_3 synthesis. In two of these three studies the 1,25$(OH)_2$ D_3 levels remained unchanged, while a slight increase was found in the third study (8). Although 1,25$(OH)_2$ D_3 levels were not increased during climatotherapy, there was a significant increase of urinary calcium excretion. This increase of calcium excretion was sufficient to prevent hypercalcaemia. Therefore, climatotherapy 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 hypercalcaemia.

While the clinical improvement of psoriasis following sun exposure is well-established, it is not clear whether stimulation of cutaneous vitamin D_3 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 D_3 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 D_3 synthesis, it might be via hydroxylation of 25-OH-D_3 into 1,25$(OH)_2$ D_3 locally in epidermal keratinocytes (5). In this context, the influence of daily bathing

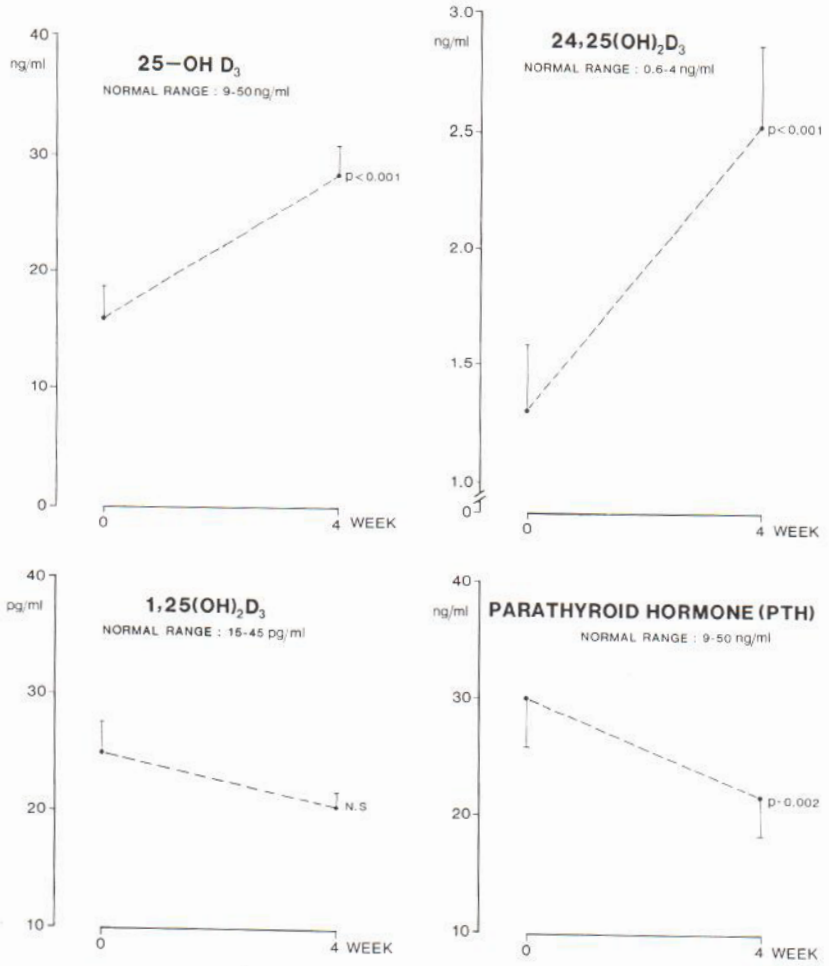

Fig. 1. Serum levels of 25-OH-D_3, 1,25$(OH)_2$ D_3 and PTH before and at the end of climatotherapy. Values are mean $\pm$ SEM ($n=16$).

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 D_3 synthesis in the skin.

It is noteworthy that the increase of urinary calcium excrection 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.

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