

Effect of Psoriasis Heliotherapy on Epidermal Urocanic Acid Isomer Concentrations

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A noninvasive Finn Chamber sampling method and HPLC analysis were used to determine epidermal urocanic acid (UCA) concentrations of psoriasis patients during 4 weeks of heliotherapy on the Spanish Canary Islands and a follow-up period of 8 weeks.

During heliotherapy the epidermal *cis*-UCA concentration increased from a mean initial value of 0.2 nmol/cm² to a mean final value of 2.9 nmol/cm². The total UCA concentration decreased during the first week of heliotherapy from an initial value of 5.5 nmol/cm² to a nadir of 2.0 nmol/cm². Thereafter, a steady increase was recorded in the total UCA level, with a maximum of 10.2 nmol/cm² in week 2 of the post-treatment follow-up period.

Suberythemal sun exposures caused near-maximal UCA isomerization, and during heliotherapy the *cis* isomer constituted 63.7–74.3% of the total UCA concentration. Clinical response of psoriasis to heliotherapy, however, seemed to be independent of UCA isomer levels. *Key word: Ultraviolet radiation.*

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Heliotherapy, i.e. sunbathing at southern resorts, is a popular treatment alternative for psoriasis patients living in northern countries, but only a few controlled studies on its efficacy have been published (1–2). The mode of action, concerning the therapeutic effect of heliotherapy and UV radiation in psoriatic skin, is not known exactly.

The epidermis of humans and other mammals contains the deamination product of histidine, *trans*-urocanic acid [3-(1*H*-imidazol-4-yl)propenoic acid; UCA] (3). UV radiation causes isomerization of *trans*-UCA to the *cis* isomer in vivo (4). We have recently described a simple, noninvasive epicutaneous chamber sampling method to determine the epidermal UCA isomer concentrations (5).

Using chamber samples, the epidermal UCA isomer concentrations of psoriasis patients were studied during four weeks of heliotherapy and a subsequent follow-up period of eight weeks. The results were analysed in relation to the dose of solar UV radiation received and the therapeutic effect of heliotherapy.

PATIENTS AND METHODS

Patients

Thirty psoriasis patients participated in the heliotherapy trial. Three patients were excluded from analysis because of recent exposure to either UVB treatment or a UVA solarium. Of the remaining 27 patients, eighteen also took part in the post-heliotherapy follow-up.

Ten patients had predominantly guttate, and seventeen the vulgaris type of psoriasis. The mean age of the patients was 38 years (range, 20 to 60 years).

Heliotherapy

The four-week heliotherapy course was carried out from October 27th to November 26th, 1989, in the Spanish Canary Islands. Two sunlight exposure schedules were used, for easily burned and for other skin types. The daily UV exposure time increased in the course of the first week from an initial 0.5–1 hour to a maintenance level of 4–6 hours. The personal cumulative erythemal units (EU) of each patient were calculated using personal daily sunbathing hour recordings; hourly readings of the solar irradiance were recorded using a Robertson-Berger Sunburning Unit meter (Solar Light CO. Philadelphia, Pennsylvania) (6).

UCA sampling

The noninvasive Finn Chamber sampling technique (5) was used to obtain samples for the HPLC analysis of the UCA isomers. Samples were taken in triplicate, on uninvolved skin of the upper back or mid-back, changing the sampling site on subsequent occasions. The samples were stored at +5°C in the dark for a maximum of two weeks, transported under refrigeration to Finland, and thereafter deep frozen. For UCA isomer measurement, the samples were thawed and subjected to HPLC as described elsewhere (7). The mean of each triplicate sample was used for the calculations.

The UCA samples were taken from all patients on the day before departure from Finland and then weekly during the four-week therapy period in the Canaries. In addition, samples were collected from nine of the patients every other day during the first week of treatment, taking samples from five of the patients on odd-numbered days and from four of the patients on even-numbered days. During the follow-up, samples were taken one, two, three, five and eight weeks after the treatment period, in a number of patients (Table I). A total of 235 triplicate samples were obtained. Three out of the 235 samples (1.3%) were technically unsuccessful and were eliminated from the analysis.

Scoring of psoriasis

The improvement of psoriasis during the treatment was followed using a psoriasis severity index (PSI) on a scale of 0–60. The equation is described in detail in another report (8). For the index, the scaling, thickness and extent of the psoriasis plaques were recorded separately for the head, body, arms and legs. The improvement of psoriasis was regarded as excellent when the index decreased by more than 90% and as fair or good when it decreased by less than 90% but more than 60%.

Statistics

The statistical significance of changes in the UCA isomer concentrations was calculated using the sign test and the Wilcoxon signed rank test. In the comparison of UV doses, the Mann-Whitney test was used.

RESULTS

The mean epidermal *cis*-UCA isomer concentration was 0.2 ± 0.2 nmol/cm² at start. A steady, statistically highly significant increase was detected during the heliotherapy weeks ($p < 0.0001$): In week 1 the mean *cis*-UCA was 1.4 ± 0.9

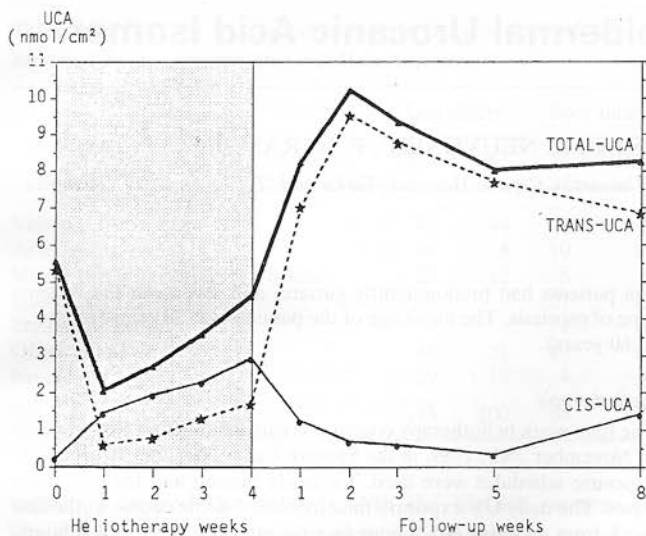


Fig. 1. Epidermal urocanic acid (UCA) concentrations during the 4-week heliotherapy and the 8-week follow-up.

nmol/cm², and in week 4, at the end of heliotherapy, it was 2.9 ± 1.4 nmol/cm² (Fig. 1).

The mean total UCA decreased from 5.6 ± 2.8 nmol/cm² to 2.1 ± 1.5 nmol/cm² during the first week of treatment. This change was statistically highly significant ($p < 0.0001$). Total UCA began to increase again during heliotherapy weeks 2 to 4. At the end of the heliotherapy course, a level of 4.6 ± 2.2 nmol/cm², i.e. almost the pretreatment value, was reached. The mean total UCA concentration continued to increase during the follow-up period, reaching the peak level of 10.2 ± 10.3 nmol/cm² in follow-up week 2. Thereafter, a declining total UCA concentration was recorded.

The mean percentage of the epidermal *cis*-UCA was $4.4 \pm 3.5\%$ at the onset of the study. Even the first exposure to sunlight induced isomerization of *trans*-UCA, giving a mean *cis*-UCA value of $61.3 \pm 9.7\%$. Further exposures increased the mean percentage of the *cis* isomer only slightly (Table I). The change compared with the initial value was statistically highly significant ($p < 0.0001$). The peak individual values were over 80% in 8 of the 27 patients, and the highest individual value recorded was 87.4%. During the first follow-up week the mean *cis*-UCA per cent declined to $16.0 \pm 6.4\%$ (Table I), but this was still statistically highly significantly above the pre-treatment level, ($p < 0.001$). From week 5 to 8 of the follow-up period, the total (Fig. 1) and relative (Table I)

values for *cis*-UCA increased highly significantly ($p < 0.001$). This was a general phenomenon throughout the patient group.

The median alleviation of psoriasis during heliotherapy was 96% (range, 92 to 100%) in the excellent and 74% (range, 65 to 86%) in the fair or good improvement patient groups calculated from PSI. The Mann-Whitney-test showed no statistical difference in the UV doses or the percentages of the *cis*-UCA isomers, between the two improvement groups (Table II).

DISCUSSION

Some studies (9, 10) on the effect of UV radiation on UCA isomerization have been published earlier, but our study is the first, where UCA isomers and improvement of psoriasis have been studied in parallel, during heliotherapy.

The low, initial *cis*-UCA proportion (4.4%) is in agreement with our earlier results for human skin (7). Norval et al. (9) found an epidermal *cis*-UCA ratio of 4.7% in nonirradiated mouse epidermis, with an increase to 31.1% immediately after a single dose of UVB irradiation. In a previous study, we found a *cis*-UCA ratio of 55% after a single erythemogenic exposure of human skin to UVB radiation from a phototherapy treatment cabin (7). In our present study, the very first 0.5–1 h of sun exposure, corresponding to approximately 0.5–1 erythema units (11), induced a mean epidermal *cis*-UCA value of 61.3% (Table I). On the other hand, even after prolonged (up to 6 hours per day) sun exposure, conversion of epidermal UCA to the *cis* isomer only exceptionally exceeded 80% of the total UCA concentration, and the single maximal *cis*-UCA value was 87.4%. Previous investigators have reported maximal *cis*-UCA percentages of up to 74% and 35–40% after in vitro UV irradiation of urocanic acid (12, 13), and up to 40–50% and 50–60% after in vivo irradiation of skin (10, 12). The fact that the absolute amount of *cis*-UCA steadily increased during the heliotherapy period is explained from the end of week 1 by an overall increase in the amount of epidermal total UCA (Fig. 1).

We were surprised by the very significant decrease in the epidermal total UCA concentration during the first days of heliotherapy. This decrease could be due, at least partly, to an increased washout by sweating, or to augmented systemic absorption of UCA due to increased cutaneous blood flow. However, from the end of week 1 the total UCA concentration steadily increased, almost restoring the original UCA level by the end of week 4, and greatly surpassing the original value by the end of the second follow-up week after helioth-

Table I. Urocanic acid *cis* isomer concentration (%) during heliotherapy and follow-up periods

	Heliotherapy							Follow-up								
	Days			Weeks				Weeks					Weeks			
	0	1	2	3	4	5	6	1	2	3	4	1	2	3	5	8
%	4.4	61.3	72.3	65.3	69.5	73.8	68.6	72.1	74.3	63.7	63.0	16.0	7.6	7.0	5.0	17.3
SD	3.5	9.7	6.1	6.7	3.7	7.3	7.7	8.1	6.0	4.0	6.2	6.4	2.7	3.2	2.6	4.1
N	27	5	4	5	4	5	4	27	27	27	27	18	7	17	15	16

Table II. *Cis* isomerization of UCA and cumulative UV doses compared with alleviation of psoriasis during a four-week heliotherapy

Therapeutic response	Improvement of Psoriasis (%)			UV-dose (EU)		CIS-UCA (%)			
	n	Median	Range	Mean	SD	Initial		Final	
						Mean	SD	Mean	SD
Excellent	19	96	92-100	102	11	3.9	3.5	63.8	2.4
Fair/good	8	74	65-86	102	14	5.6	3.5	61.2	11.1

erapy (Fig. 1). This may result from accelerated synthesis of epidermal UCA, possibly by induction of the UCA-forming enzyme, histidase (14). In 1977, Pratzel et al. (15) described a doubling of epidermal total UCA in healthy human subjects in a series of 8 exposures from Hanau light equipment. It would have been useful to measure non UV exposed areas as an internal control of UCA levels, but in this study the patients sunbathed undressedly. Further experiments will be needed to delineate more closely the details of the inducing effects of UV on epidermal UCA synthesis, including such factors as wavelength dependency and maximal obtainable concentration.

Our study did not directly address possible biological effects of the variations in epidermal concentrations of total UCA or of its isomers. Much attention has lately been paid to the role of *cis*-UCA in, for instance, immunomodulation (16). The remarkable effect of heliotherapy on epidermal UCA isomer concentrations described in our present study could be relevant for understanding the antipsoriatic effect. We were, however, not able to find any difference in the mean *cis* isomerization level between the patients with excellent improvement and those with a less complete improvement in their psoriasis.

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