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PUVA-treated Psoriatic Skin as a Model for Cutaneous Wrinkling Assessed by Skin Replicas

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Psoriatic patients may offer a useful model for PUVA-induced skin wrinkling. This study deals with the changes induced by PUVA therapy on the cutaneous microrelief of psoriatic patients assessed by surface replicas. A non-exposed body area (buttocks) was considered. The microrelief was evaluated by means of replicas analysed by an automatic image analyser. Three groups of patients were considered: 1) 10 psoriatic patients who had been undergoing PUVA treatment for the first time and who had received a total PUVA dose of 200±20 J/cm²; 2) 16 psoriatic patients in long-term PUVA treatment (>1000 J/cm²); 3) 13 psoriatic controls whose buttocks had never been affected by psoriasis nor exposed to sunlight or PUVA. The results showed that the number and the entity of the cutaneous crests and furrows had been increased by PUVA therapy. In particular the skin pattern analysis showed significant statistical differences between the second and the third group, while no changes were evident between the first and third group (ANOVA and Tukey test for multiple comparisons). In conclusion, our findings indicate that long-term PUVA therapy causes marked changes in the cutaneous microrelief, that this phenomenon can be measured non-invasively and that the changes observed are dependent on the PUVA-dose energies received. ***Key words: microrelief; skin replicas; psoriasis; PUVA therapy.***

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INTRODUCTION

PUVA therapy, which is characterized by the association of psoralens and exposure to UVA radiation (365 nm), is an effective and well-tolerated therapy for psoriasis (1). This treatment does not always produce lasting remissions and therefore long-term, repetitive treatments are required. One of the adverse effects of prolonged use of PUVA is described in the form of premature cutaneous ageing resembling photoageing (2–5). In particular, one of the clinical stigmata of prolonged PUVA therapy is the alteration of the cutaneous microrelief (6).

The aim of this work was to assess, non-invasively, changes in skin microtopography caused by short and long-term PUVA therapy, in psoriatic patients, using the buttocks, a skin area not usually exposed to sunlight.

MATERIALS AND METHODS

Three groups of patients were considered:

Group 1: 10 psoriatic patients (male, average age 40 years) who were undergoing PUVA treatment for the first time and had received a total PUVA dose of 200±20 J/cm².

Group 2: 16 psoriatic patients (male, average age 45 years) who had been undergoing PUVA therapy for 5 years and had received a total PUVA dose of 1000 J/cm².

Group 3: 13 control psoriatic patients matched for age and sex who had never been treated with photochemotherapy.

The measurements were carried out on the right buttock, a skin area never exposed to sunlight. Furthermore, no psoriatic plaques were present at the site of the measurement. The study was carried out using negative replicas of the skin surface (7, 8). These replicas consist of a rubber monomer of "Siflo Flexico" silicone which, when mixed with some drops of a catalyst, is applied to the surface to be tested. A Hewlett Packard adhesive disc is placed on the skin surface, as a support for the resin. As the skin surface pattern is anisotropic in most body areas it is advisable to make a mark on the replica indicating the direction of the body, e.g. a notch or a tag. The Hewlett Packard disc is supplied with a tag indicating the direction of the measurement: in our case the tag was pointed in the direction of the head.

All the replicas were assessed using a computerized image analyser, Philips NMS 8280 Software videographics MSX-DOS. The replica was placed under a macro-Philips 12 NC videocamera and laterally illuminated by a halogen lamp (50 Watts) at an angle of 26° and placed opposite to the video scan direction. The replica was always placed under the videocamera with the tag parallel to the light and the primary furrows vertical to the monitor that they appeared on. The data were processed using a Philips NMS 8280 computer with a software program evaluating the intensity of the greys in relation to the length of the shadows projected by the crests; the computer gives an average reading,

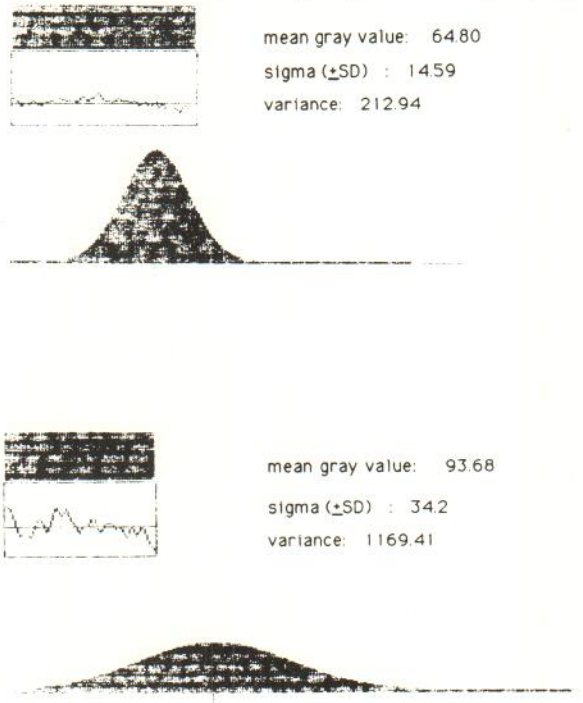

Fig. 1. Graphic elaboration of the image analysis made by the software program. The graph represents the analysis of the skin replica; the horizontal line expresses the mean grey level *M*; the crests and furrows correspond to the standard deviation of the mean grey level (sigma). *A*) Elaboration relating to a control's skin replica. *B*) Elaboration relating to a patient's skin replica (PUVA dose > 1000 J/cm²).

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M, which represents the mean grey level. Furthermore, the software program also calculates sigma σ, corresponding to the standard deviation of the mean grey level line (Fig. 1). The data collected were analysed using standard statistical methods (ANOVA and Tukey test for multiple comparisons).

RESULTS

No significant differences between Group 1 (PUVA dose 200±20 J/cm^2) and Group 3 (control group) were found as regards either the *M* level or the sigma σ level. On the other hand the comparison of measurements between Group 2 (PUVA dose ≥1000 J/cm^2) and Group 3 (control group) revealed significant differences as regards both mean grey level *M* and sigma σ level (± SD) (Table 1). ANOVA analysis is significant at a level of $P = 0.001$ for mean grey levels and at $P = 0.03$ for sigma levels respectively. ($P = 0.05$ Tukey test for multiple comparisons).

Table I. *Mean grey M and sigma σ levels (±SD) in psoriatic patients during photochemotherapy and controls*

	Mean grey level *M* (±SD)	Sigma σ (±SD)
Control	87.5±5.2*	15.0±3.6°
180 J	92.2±4.3	17.7±5.5
1000 J	95.9±6.2*	21.2±77°

ANOVA analysis is significant at a level of $p = 0.001$ for mean grey *M* levels and at $p = 0.03$ for sigma σ levels respectively. Controls and patients treated with doses higher than 1000 J/cm^2 are significantly different (*°, $p = 0.05$ Tukey test for multiple comparisons).

DISCUSSION

Wrinkles are the most commonplace of all the signs of cutaneous aging (9). Structural changes in the skin occurring with ageing and after sun-exposure alter the skin's surface clinical appearance. The cutaneous microrelief reflects the condition of the epidermis and the dermis, their thickness, the presence of papillae and the amount of elastic and collagen tissue; it reflects the anisotropy of the epidermis and the dermis (10, 11).

Many studies have demonstrated that changes in each of these structures alter the cutaneous microrelief, as shown in intrinsic ageing and photoageing (8, 12, 13, 14).

PUVA therapy offers a useful model when studying the effects of UVA irradiation on the skin in a controlled manner. This treatment, using long-wave ultraviolet light plus psoralens, causes wrinkling, teleangectases and changes in the skin markings (5, 6, 15). Many studies have described numerous changes in PUVA patients' skin histologically, histochemically and ultrastructurally (16).

In our work we studied the changes in cutaneous microrelief of PUVA-treated patients using a non-invasive method. (7, 8).

Several conclusions may be drawn from the data produced in this study:

1) PUVA therapy does not induce changes in the surface skin pattern at doses of 200±20 J/cm^2 (average value considered: 180 J/cm^2);

2) significant differences in the surface patterns are seen after cumulative doses of PUVA of 1000 J/cm^2 or more. These changes are significant both for the *M* values, that is for the number of wrinkles present (which had increased) and for the sigma σ level which increases with the increase in the depth of the wrinkles:

3) in practice, prolonged photochemotherapy causes changes to the skin surface: not only does the depth of the wrinkles increase, but new crests and depressions are formed, as can be seen from the morphometric analysis. There is, therefore, a huge increase in skin surface which is difficult to interpret as anything else but an attempt by the skin to deaden and dispel the energy of the photonic impact, spreading it out over a greater surface area;

4) the importance of the damage is also dose-related and proportional to the amount of energy received even though in this study the difference between 200 and 1000 J/cm^2 is too great to establish the critical PUVA level which is required to cause significant surface changes. Studies are being carried out by us to identify this critical point.

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