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Biophysical Characteristics of Healthy Skin and Nonlesional Skin in Atopic Dermatitis: Short-Term Effects of Ultraviolet A and B Irradiation

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Key Words

Skin surface · Viscoelasticity · Profilometry · Cutometry · Atopic eczema · Photodamage

Abstract

The present study was designed to evaluate basic differences in surface structure and viscoelastic properties of nonatopic versus atopic skin and facultative acute changes following ultraviolet irradiation. Therefore, biophysical measurements by means of profilometry and cutometry were carried out on sun-protected unaffected gluteal skin areas in both groups before and 24 h after single UVA and UVB irradiations. The results indicate that the clinically unaffected skin of patients with atopic eczema differs from normal skin in terms of increased roughness parameters, but not concerning depth of furrows or viscoelastic properties (viscosity and biological elasticity, cutometrically calculated). Single UVA irradiation with 50 J/cm^2 induced neither measurable changes in the skin's surface structure nor in its viscoelastic properties in both groups after 24 h. However, irradiation with a single erythemogenic dose of 1 MED UVB was followed by a short-term significant increase in the depths of furrows and decrease in biological elasticity in normal and atopic skin, accompanied by an increase in viscosity in normal skin.

Introduction

Though atopic eczema, being a common chronic skin disorder, is dealt with in many clinical and experimental studies, only very little has been reported on the quantitative topographical differences between clinically unaffected atopic skin and normal skin [1, 2]. Evaluations and quantifications of the viscoelastic properties of atopic versus normal skin are furthermore generally lacking. Whereas

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well-known dysfunction of the epidermal barrier and neurovegetative imbalance in atopic skin can account only partly for its increased nonspecific irritability, further information concerning surface structure and biomechanical properties would provide more insight into specific characteristics and possible additional dysfunctions in atopic skin. In this context we were particularly interested in studying the biomechanical properties of normal and atopic skin with regard to potential differences. Therefore, we combined the profilometry method to quantify skin surface structures and the cutometry method to quantify dynamic viscoelastic properties.

As biomechanical properties, especially the viscoelastic parts of the skin, are significant basic parameters in terms of damaging UV effects, and with regard to the importance of phototherapeutic measures, particularly in atopic eczema, we investigated to what extent single irradiation with UVA or UVB might affect these biomechanical parameters and whether atopic skin might behave differently.

Subjects and Methods

A total of 20 persons receiving an established standardized UV skin test participated in the study after having given informed consent. They were subjected to an established standardized UV skin test in order to evaluate skin sensitivity to UV either before phototherapy (patients with atopic dermatitis) or in the common diagnostic course concerning polymorphous light eruption. Because of these clinical indications for UV treatment, medical ethics committee support was not necessary.

The group included 10 nonatopics (5 men, 5 women) and 10 patients (4 men, 6 women) suffering from atopic eczema according to the criteria of Hanifin and Rajka [3]. All belonged to UV skin types II or III corresponding to the criteria of Fitzpatrick [4]. None of them had taken medication during the previous 3 months. Both groups were matched for age, the average age being 31.9 ± 9.1 years. Each person received a single dose of 50 J/cm^2 UVA and of 1 minimal erythema dose (MED) UVB (range 0.03–0.05 J/cm^2 individually) in two separate 15-mm circular areas of clinically unaffected healthy looking skin on the right gluteal site. The UVA dosage was defined as mentioned above and not by the individual MED because experience shows that it is difficult and sometimes not possible to produce significant erythema with clearly defined borders by clinical doses of UVA irradiation, and changes in skin kinetics and metabolism after UVA are not necessarily accompanied by noticeable cutaneous erythema [5]. Thus, the applied dose of UVA corresponded in 8 cases (5 nonatopics, 3 atopics) to an individual 1- to 1.2-fold MED, and in 12 cases (5 nonatopics, 7 atopics) no significant erythema was noted.

The Multitester Saalmann (Saalmann, Herford, Germany) served as the radiation source (UVB spectrum: wavelength range 285–350 nm, maximum emission about 315 nm; UVA spectrum: 320–400 nm, maximum emission 350–390 nm).

After marking the gluteal test field, 1 skin replica for profilometric measurements and 3 cutometric measurements were carried out before and 24 h after irradiation. Obtaining the replicas, their orientation was kept constant in one defined direction. As measurements after irradiation were taken separately from a subdivided UVA and UVB test area, altogether 3 profilometric and 9 cutometric measurements were performed on each patient.

Skin Replica and Profilometry

Negative casts of the gluteal skin surface were obtained using monomeric silicone material of low viscosity (Silasoft N, Detax, Karlsruhe, Germany), which polymerizes within some minutes at body temperature when mixed with the accompanying catalyzer. Slide frames (Quickpoint N, Loersch, Germany) served as templates here.

Profilometric measurements of the replicas were carried out using the Hommeltester T 2000 (Hommelwerke, Schwenningen, Germany) equipped with a TKC 300 pickup. Control of the Hommeltester and data collection were performed by means of an AT computer (Software T 2000 Controller). The measurement technology has already been described in detail elsewhere and may be referred to in this context [6, 7]. Each replica was scanned 10 times in parallel traces (length of trace 10 mm, space 1 mm) perpendicularly to the major furrows as standard position. The calculated parameters of roughness and waviness (defined by German Industrial Standards and International Standards) of each replica reflect the mean value of these 10 scans. Various parameters were determined, for final evaluation the following parameters were

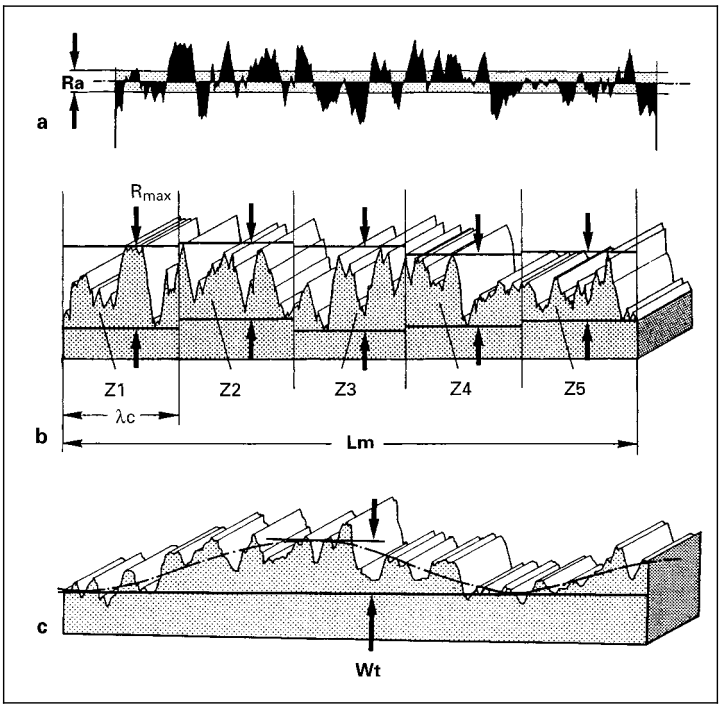

Fig. 1. Profilometric parameters. **a** Ra = Mean arithmetic roughness value. **b** Rz = Mean depth of roughness, i.e. arithmetic mean of the depths of roughness (distance between upper and lower arrow) of five consecutive equally spaced profile sections (Z1–Z5); R_{max} = maximum depth of roughness; Lm = overall length of measurement; λc = length of measurement of each section. **c** Wt = Waviness, i.e. height of maximum peak to valley tangents within the profile.

regarded as being representative: Ra (DIN 4768, DIN 4762, ISO 4287/1) = mean arithmetic roughness value (fig. 1a); Rz (DIN 4768) = mean depth of roughness (fig. 1b); Wt = waviness (fig. 1c).

The roughness parameters Ra and Rz are independent of the waviness parameter Wt. Ra predominately represents the roughness of the surface structure, Rz also reflects roughness, minor furrows and anatomically preformed lines [8]. Wt, on the other hand, indicates deeper furrows and changes in cutaneous turgor, and is regarded as an expression of the skin's wave structure and tension [9].

Cutometry

The measure principle is based on a suction method in the course of which the skin surface is drawn into the opening of a special probe by means of a defined vacuum, thus allowing an optical registration of the skin's invasion depth into the probe without friction. Probe and main unit are linked to and controlled by an AT computer (Software CT). The measurements were carried out using the skin elasticity meter Cutometer SEM 474 (Courage and Khaza, Cologne, Germany) which is based on the suction method described briefly above and earlier in detail [10]. In this context the time/strain mode was used with a 5-second application of a 500-mbar load perpendicular to the skin, followed by a 3-second relaxation time. Because of the small test area of about 3 mm^2, influences on skin elongation contributable from the dermosubdermal junction were negligible [10, 11].

The skin deformation was plotted as a function of time. The deformation curve (fig. 2) is composed of a fast deformation reflecting a purely elastic part, followed by a viscoelastic and finally purely viscous part. The same differentiation in the sequence of elastic, viscoelastic and viscous parts is noted in the retraction phase of the tissue. According to the nomenclature proposed by Agache et al. [12], the parameters calculated were immediate distension (Ue), delayed distension (Uv), immediate retraction (Ur) and final distension (Uf). All of these parameters are a function of skin thickness and thus cannot simply be compared between subjects, but certain biologically important rations of these parameters have been reported to be independent of skin thickness [11, 12]. These include: Uv/Ue = ratio between delayed and immediate distension indicating the viscous component of the mechani-

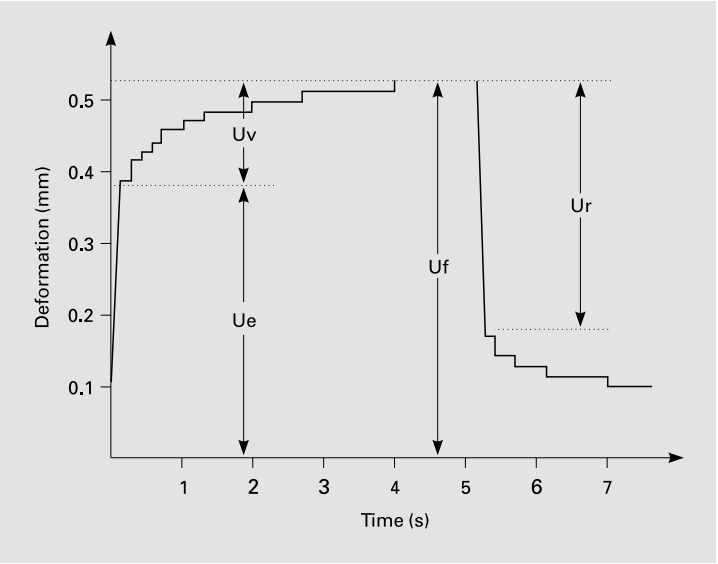

Fig. 2. Cutometric deformation curve of normal skin. Ue = Immediate distension; Uv = delayed distension; Ur = immediate retraction; Uf = maximum distension; Uv/Ue = viscosity; Ur/Uf = elasticity.

cal skin deformation; Ur/Uf = ratio between immediate retraction and total distension representing the skin's ability to return to its initial position after deformation, i.e. biological elasticity.

Statistics

Discrete characteristics are expressed by the arithmetic mean value and its standard deviation. Differences between the 2 groups were tested for their statistical significance by applying Student's t test for unpaired data. The normal distribution of data was evaluated by the Kolmogorof-Smirnof test. Baseline values before treatment were compared to values after irradiation using Wilcoxon's signed rank test for paired data. A p value of ≤ 0.05 was considered statistically significant.

Results

Profilometry

The calculated mean value and standard deviation of each parameter before and after UVA and UVB irradiation are displayed in table 1. The differences in basic parameters of roughness Ra 0 and Rz 0 (Ra and Rz before irradiation) between normal and noneczematous atopic skin reached statistical significance ($p = 0.04$ for Ra 0; $p = 0.03$ for Rz 0) indicating increased roughness in atopic versus normal skin. As the skin test areas were macroscopically inconspicuous in both groups, these findings did not correspond to dry skin or lichenification. Though tending towards higher values in patients with atopic eczema, the parameter of waviness Wt 0 (Wt before irradiation) did not reveal statistically relevant differences between the 2 groups ($p > 0.05$). 24 h after UVA irradiation neither roughness nor waviness parameters had changed significantly in both groups ($p > 0.05$). UVB irradiation as well did not alter roughness parameters remarkably ($p > 0.05$), whereas the depth of furrows expressed by Wt was significantly increased in nonatopic ($p = 0.01$) as well as in atopic skin ($p = 0.009$) 24 h after UVB irradiation.

Cutometry

The mean value and standard deviation of each parameter before and after radiation

Table 1. Mean roughness and waviness parameters of normal skin and unaffected atopic skin before and 24 h after UVA or UVB irradiation

	Nonatopic persons (n = 10)	Atopic persons (n = 10)	Difference
Surface roughness Ra, µm			
Before UV: Ra 0	18.5 ± 2.3	21.4 ± 3.6	p = 0.04
After UVA: Ra A	18.2 ± 2.8[a]	21.3 ± 3.7[a]	
After UVB: Ra B	17.8 ± 2.3[a]	20.5 ± 3.8[a]	
Roughness and minor furrows Rz, µm			
Before UV: Rz 0	94.7 ± 11.8	112.0 ± 19.3	p = 0.03
After UVA: Rz A	93.3 ± 12.7[a]	111.9 ± 20.0[a]	
After UVB: Rz B	94.0 ± 11.6[a]	109.4 ± 20.6[a]	
Major furrows – 'waviness' Wt, µm			
Before UV: Wt 0	114.7 ± 24.5	139.0 ± 32.5	n.s.
After UVA: Wt A	113.0 ± 24.9[a]	152.2 ± 47.8[a]	
After UVB: Wt B	148.7 ± 44.9[b]	180.1 ± 39.7[c]	

Difference: [a] Not significant; [b] p = 0.01; [c] p = 0.009.

Table 2. Mean viscosity and biological elasticity of normal skin and unaffected atopic skin before and 24 h after UVA or UVB irradiation

	Nonatopic persons (n = 10)	Atopic persons (n = 19)	Difference
Viscosity, Uv/Ue			
Before UV: Uv/Ue 0	0.37 ± 0.06	0.32 ± 0.08	n.s.
After UVA: Uv/Ue A	0.40 ± 0.07[a]	0.34 ± 0.09[a]	
After UVB: Uv/Ue B	0.52 ± 0.12[b]	0.38 ± 0.16[a]	
Elasticity, Ur/Uf			
Before UV: Ur/Uf 0	0.69 ± 0.08	0.68 ± 0.10	n.s.
After UVA: Ur/Uf A	0.70 ± 0.09[a]	0.62 ± 0.13[a]	
After UVB: Ur/Uf B	0.48 ± 0.15[c]	0.50 ± 0.11[d]	

Difference: [a] Not significant; [b] p = 0.03; [c] p = 0.0001; [d] p = 0.005.

treatment are shown in table 2. There were no significant differences in basic ratios Uv/Ue 0 and Ur/Uf 0 (Uv/Ue and Ur/Uf before irradiation) between the 2 groups.

UVA irradiation did not particularly alter these findings. However, 24 h after irradiation, UVB induced an increase in Uv/Ue (viscosity) which proved to be significant in normal skin (p = 0.03) but not statistically significant (p > 0.05), yet existing in atopic skin. Ur/Uf (elasticity) was significantly decreased in normal (p < 0.0001) and atopic skin (p = 0.005) 24 h after UVB irradiation.

Discussion

According to our observations normal skin and clinically bland atopic skin basically differ in terms of roughness, but not significantly concerning depth of furrows or viscoelastic properties. Our observation of significantly increased roughness parameters Ra and Rz in clinically bland atopic skin in contrast to non-atopic skin is in agreement with former examinations by means of scanning electron microscopy which demonstrated that normal skin shows a regular system of furrows in contrast to the topography of noneczematous atopic skin exhibiting a more irregular coarse pattern [1, 2]. Taking into consideration that minor furrows are restricted to an epidermal level whereas major furrows reach up to the dermal surface, the profilometrically quantified increased roughness of unaffected atopic skin may constitute the morphological correlate of the well-known upper epidermal changes of noneczematous atopic skin such as hyper(para)keratosis, defects in stratum corneum lipid composition and 'clumping' of corneocytes [13].

The profilometric parameter Wt representing deeper furrows did not differ significantly between normal and atopic skin though it tended slightly towards increased values in the latter. These results probably show that pathological changes in the area of the basal layer and dermis play a minor role in noneczematous atopic skin.

Concerning the viscoelastic parameters viscosity and elasticity in atopic versus non-atopic skin, we could not show significant differences in the baseline values. Cutometric parameters are predominantly determined by the dermal collagenous and elastic fiber network, embedded in a viscous matrix, with only very little contribution from the epidermis. The viscous component of the mechanical properties of the skin (Uv/Ue) results from the quality of the dermal intercellular matrix, consisting mainly of glycosaminoglycans and water [11], and the collagenous fibers [14]. The biological elasticity (Ur/Uf) reflecting the skin's ability to return into its initial position after deformation by means of elastic retraction [11, 14] is specially correlated with the function of the elastic fiber network [10]. Our cutometric results emphasize the minor role of dermal changes in noneczematous atopic skin.

Single erythemogenic UVB irradiation resulted in an increase in the depth of furrows in both groups, but not in remarkable changes concerning roughness. Furthermore, there was a significant change in viscoelastic properties of the skin 24 h after irradiation, e.g. a decrease in cutaneous elasticity in normal skin as well as in unaffected atopic skin and an increase in viscosity in normal skin (also existing but not statistically significant in the atopic group).

The increased uniaxial accentuation of depth of major furrows was already realized macroscopically. These findings are not explainable by epidermal UVB effects such as intraepidermal edema or acanthohyperkeratosis [15, 16], as intraepidermal edema is expected to reduce waviness and acanthohyperkeratosis is not fully developed but just starting 24 h after irradiation [16]. The results may be explained for example by early microedemas in dermal papillae, which induce pronunciation of the physiological skin relief, thus increased depth of furrows resulting more indirectly. Leveque and Corcuff [6, 17] drew similar conclusions though under different conditions from ours, as they demonstrated comparable substantial alterations in skin relief after UV irradiation by means of image analysis. Taking into consideration that the cutaneous relief also depends on the organization of collagenous bundles and elastic fibers in the upper dermis [6], it is possible

that, by analogy to results in chronically sun-damaged skin [9], the increase in the depth of furrows after UVB irradiation already indicates injury to the dermal fiber network. Thus, single erythemogenic UVB irradiation seems to induce short-term physicomechanical changes in junctional and upper dermal structures rather than in upper epidermal structures, due to the early cytokine-mediated dermal reactions [18] such as vasodilatation, edema, perivascular infiltration [19] and alterations in the collagen metabolism of the fibroblasts [20].

Correspondingly our cutometric results demonstrated a significant decrease in the biological elasticity in atopic and nonatopic skin 24 h after UVB irradiation. Berardesca and Maibach [21] also speculated that short-term UVB irradiation reduces skin elasticity, as did de Rigal and Leveque [22], who nevertheless attributed it to increased thickening of the epidermis. The decreased elasticity suggests acute damage to the elastic fibers, as it is observed more pronouncedly after repeated UVB exposures [15]. The observed increase in viscosity after UVB irradiation can be interpreted as an expression of altered dermal matrix equilibrium caused by dermal edema, alteration of collagenous fibers or an increase in dermal inflammatory infiltrate [15].

Single UVA irradiation with 50 J/cm^2 had no significant effect on the investigated parameters in both groups in the present study.

The lack of changes in our profilometrically calculated roughness and waviness parameters after single UVA irradiation may be explained by the comparably minor influence of UVA on the epidermis. This is in contrast to some clinical experiments in which epidermal hyperplasia and thickening of stratum corneum could be provoked, though mostly repeated UVA irradiations or single doses of at least 72 J/cm^2 were necessary [15].

Though cutometrically measured dermal viscoelastic properties remained unchanged 24 h after one single dose of 50 J/cm^2 UVA, it is well known that UVA is capable of inducing inflammatory and tissue-damaging dermal reactions via direct or indirect mechanisms [15, 16, 23]. Thus, assuming that even single UVA irradiation with 50 J/cm^2 is probably able to induce changes on molecular and histological levels, these changes seem to be too small to influence the actual structural, functional and mechanical properties of the skin.

Conclusion

According to our findings unaffected atopic skin, despite an altered dispersed surface structure, exhibits the same viscoelastic properties as healthy skin and has no higher susceptibility to acute photodamage. The observed short-term UVB-induced changes (increase in depth of furrows, decrease in elasticity, increase in viscosity) in both groups give rise to the crucial question as to how far these alterations are still reversible, therefore long-term dose-response studies on UV-induced biomechanical skin changes, also including higher UVA doses, are to follow.

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