

The impact of ultraviolet therapy on stratum corneum ceramides and barrier function

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Summary

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The ceramide profile as well as the barrier function is known to be deteriorated in atopic eczema and psoriasis, and ultraviolet (UV) light is known to improve the barrier function. The impact of UV light on ceramides, however, is not clarified. The aim of this study was to examine the effect of UV therapy in dermatological patients on ceramides and skin barrier function. We found that UV light treatment does not change the ratio of important stratum corneum lipids, but we confirm earlier findings of decreased susceptibility to irritants after UV- therapy.

The barrier of the skin is located in the stratum corneum (SC), which mainly consists of proteins and lipids. The SC lipids are dominated by ceramides, cholesterol and free fatty acids, and, especially, the ceramides are believed to be of importance for the barrier function of the skin (1). Both people with atopic dermatitis (AD) and psoriasis have an altered ceramide profile as compared with healthy controls, both groups having lower levels of ceramide 1 and 3 as compared with healthy controls (1, 2).

The use of ultraviolet (UV) light for treatment of various skin diseases is widespread, and people with AD and psoriasis are both groups that are known to benefit from UV therapy. Yet the mechanism of action is not known. It has been speculated that UVA induces T-lymphocyte apoptosis, and that UVB reduces the level of skin surface bacteria. Additionally, *in vitro* studies point to increased ceramide syntheses after UV irradiation (3). And as people with AD have an altered lipid profile compared with healthy controls (1), an increased synthesis might explain the beneficial effect seen in the clinical setting. One group has found that UV light leads to an increased amount of SC lipids including most ceramide subgroups (4). However, this result is given as the amount of SC lipids per square centimetre, and may therefore be biased by the increased thickness of SC after UV therapy (5) rather than an increase in the concentration.

The aim of the present study was to compare levels of ceramide subgroups independent of the amount of SC, before starting UV therapy as compared with after UV therapy, as well as to correlate this result with changes in barrier measurements.

Materials and methods

Eighteen patients were enrolled in the study after informed consent. All patients were enrolled on a consecutive basis from people starting full-body UV therapy at a dermatologic outpatient clinic. The study was approved by the local ethical committee (SJ-7-13986-3).

Fourteen patients (median age 60) received UVB therapy, one received UVA and three received psoralen and UVA. Six were treated for psoriasis, five were treated for atopic eczema, four were treated for pruritus, two were treated for nummular eczema and one was treated for vitiligo.

All patients had a cyanoacrylate SC sample taken for lipid analysis from the mid-volar forearm from normal-appearing skin. The sample was taken before starting treatment, after nine treatments and after 18 treatments, respectively. This was followed by extraction and lipid analysis by high-performance thin-layer chromatography. From the opposite volar forearm, all patients had a 24-h 1% sodium lauryl sulphate (SLS) irritation

Table 1. Results

	Before treatment	After 9 treatments	After 18 treatments
Cer 1 (EOS)	15.0 (10.8–16.2)	13.8 (11.6–17.2)	14.5 (13.5–18.3)
Cer 2 + 9 (EOP + NS)	19.4 (16.2–20.5)	20.7 (18.5–23.2)	19.2 (15.7–22.2)
Cer 3 (NP)	19.0 (15.9–20.7)	17.5 (14.3–20.4)	17.1 (13.3–18.2)
Cer 4 (EOH)	7.3 (6.5–8.9)	6.6 (5.9–9.1)	7.5 (5.9–10.3)
Cer 5 + 8 (AS + AH)	18.4 (16.1–21.2)	18.4 (15.7–20.4)	18.1 (17.3–20.2)
Ceramide 6 (NH)	10.2 (8.2–11.0)*	9.6 (8.6–9.9)	8.5 (7.4–9.9)*
Ceramide 7 (AP)	11.7 (10.8–13.8)	11.4 (10.6–13.6)	11.8 (10.7–12.5)
Ceramide/cholesterol ratio	1.9 (1.6–2.3)	2.0 (1.5–2.1)	2.1 (1.7–2.8)
Delta TEWL (g/m ² /h)	21.3 (14.0–27.7)*	Not performed	9.5 (7.9–16.1)*
Delta erythema	2.9 (2.0–3.5)	Not performed	2.5 (1.0–4.6)

* $P < 0.05$.

Percentage distribution of ceramides (Cer) and ceramide/cholesterol ratio in relation to ultraviolet treatment.

Ceramide levels are presented in percentages and 1st and 3rd quartiles are written in brackets. Note that ceramide/cholesterol is not a percentage, but illustrates a ratio.

Delta trans-epidermal water loss (TEWL): [TEWL after sodium lauryl sulphate (SLS) irritation] minus (TEWL at an unaffected area).

Delta erythema: (erythema after SLS irritation) minus (erythema at an unaffected area).

EOS, ester-linked w_hydroxyl acid sphingosine; EOP, ester-linked w_hydroxyl acid phytosphingosine; NS, nonhydroxy fatty acid sphingosine; NP, nonhydroxy fatty acid phytosphingosine; EOH, ester-linked w_hydroxyl acid 6-hydrosphingosine; AS, a-hydroxy fatty acid sphingosine; AH, a-hydroxy fatty acid 6-hydrosphingosine; NH, nonhydroxy fatty acid 6-hydrosphingosine; AP, a-hydroxy fatty acid phytosphingosine.

patch test performed using large Finn[®] chambers (SmartPractice, Phoenix, AZ, USA), evaluated by trans-epidermal water loss (TEWL; g/m²/h; Dermalab[®], Cortex technology, Hadsund, Denmark) and erythema (Minolta Chroma Meter CR-300, Minolta Camea Co., Osaka, Japan). This was done before starting the treatment and after 18 treatments. TEWL and erythema measurements were performed on both the SLS irritated area and at an unaffected area, and delta values were calculated for further analysis. All participants were asked to expose their volar forearms to the UV light during the therapy.

Throughout the manuscript, the simple nomenclature for ceramides '1–9' is used, but to avoid any misunderstandings, the nomenclature proposed by Motta is added in Table 1 (2).

Statistics

Nonparametric statistics were applied. The Friedman's test was used as an omnibus test for differences between ceramides and ceramide/cholesterol ratio for differences between the three time points. If any significance was found, the Wilcoxon test was used for pairwise comparison. The Wilcoxon test was used for differences between delta values of barrier measurements. $P < 0.05$ was chosen as the level of significance. We did not correct for multiple testing, and our analysis should accordingly be considered explorative.

Results (Table 1)

Ceramide subgroups and ceramide/cholesterol ratio were compared for differences before treatment and after nine and 18 treatments of UV light. Statistically significant differences were found between the three time points for ceramide 6 ($P = 0.017$). No other subgroup of ceramide or the ceramide/cholesterol ratio was found. For pairwise comparison, ceramide 6 was

statistically lower after 18 treatments as compared with before treatment ($P = 0.002$).

As for the barrier measurements, we found statistically significant differences between the delta TEWL values, with significantly higher delta TEWL before treatment as compared with after treatment ($P = 0.034$). For delta erythema, we found no statistically significant differences from before treatment as compared with after 18 treatments (Table 1).

Discussion

We find a decrease in ceramide 6, as well as a decrease in skin barrier susceptibility to SLS as measured by TEWL, in relation to UV therapy.

Only two human studies have investigated the effect of UV light on SC lipids, both studies performed in experimental settings on healthy volunteers (4, 5). This present study is the first to investigate SC lipids on patients in a clinical setting.

One study with three weekly UV radiations found a total increase of all SC lipids (4). However, a known outcome of UV exposure is an increase in the thickness of SC (5), and because the results of the study are presented per square centimetre, it is difficult to distinguish the increase in SC lipids from an increased amount of SC due to increased SC thickness (4). Nonetheless, even though the relative amount of the SC lipids may not have increased, a total increase because of a thicker SC is also an important information and probably beneficial for the barrier function. The same group performed a study in a similar setup and, in addition to the SC lipids, they examined the response to irritation after UV light, and found that UV light had a protective effect against SLS (5).

In conclusion, in previous SC lipid research performed on humans together with the research performed in vitro on

keratinocytes (3), the data are not uniform, yet most studies point to a possible increase in the lipids.

Our finding of statistically significant differences for ceramide 6 was not expected. Particularly because ceramide 6 has not been a ceramide, known to differ between groups of, for instance, people with AD (1). We tend to be skeptical toward the analysis of this finding because of the historical insignificance of ceramide 6, and hence, it may be a result of multiple testing. More interesting is the finding that none of the other ceramide subgroups or the ceramide/cholesterol ratio changed. For the barrier measurements, our finding that the reaction to SLS irritation is decreased after UV therapy is in agreement with the knowledge of the increased thickness of SC following UV irradiation (5). The erythema measurements are supportive of this, however not statistically significant (Table 1). These observations are in agreement with earlier findings (5). Yet, the reason does not seem to be a change in lipid profile.

In conclusion, we do not find convincing differences in ceramide or ceramide/cholesterol ratio in relation to UV therapy. We do, however, confirm the protective effect of UV light against SLS

irritation as evaluated by TEWL. Apart from a changed lipid profile, this study points to other explanatory mechanisms behind the positive effect of UV light.

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