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INVESTIGATIVE REPORT

Response to Thermal Stimuli in Skin Pretreated with Sodium Lauryl Sulfate

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Skin irritation is mostly a multifactorial process. Competitive effects of different chemical irritants are well known. This study investigates the influence of a thermal stimulus on skin pre-irritated with sodium lauryl sulfate (SLS). Seventy-seven volunteers were patch-tested with SLS 0.25% and 0.5% for 48 h. Water served as control. Skin reaction was evaluated by measurement of transepidermal water loss, skin blood flow and skin color. After measurement, a thermal stimulus was applied on the test area. The increase in skin blood flow was measured. There was a significant correlation between the degree of irritation and the increase in skin blood flow after thermal stimulus. Pre-irritated skin reacted to thermal stimulus with a shorter and sharper increase in skin blood flow. This increase was dependent on the SLS concentration. Hence, the thermally stimulated blood flow may be a model of non-chemical irritation and seems to be a relevant co-factor in the pathogenesis of irritant dermatitis. *Key words: bioengineering methods; epidermal barrier; irritant contact dermatitis; Laser Doppler flowmetry; skin color; transepidermal water loss.*

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The development of irritant contact dermatitis depends on endogenous and exogenous factors (1, 2). There is usually more than one exogenous factor involved. Recently, it has become apparent that the concurrent effect of irritants on the skin is a serious problem, because it produces cumulative damage on the skin barrier (3, 4). Besides chemical irritants, factors like climatic changes, pressure or friction can alter the epidermal barrier and other epidermal and dermal functions. The aim of this study was to determine the effect of a thermal stimulus on skin when pre-irritated by sodium lauryl sulfate (SLS).

MATERIALS AND METHODS

Study population

Seventy-seven volunteers (43 women and 34 men, 18–60 years) participated in this study. They were recruited from the outpatient and inpatient clinic of the Department of Dermatology, University Hospital of Marburg. Atopic patients (according to the definition of Diepgen et al. (5)) were excluded. All individuals were free from skin abnormalities at the test areas. Informed consent was obtained and the study was approved by the ethics committee of the hospital.

Measurements

Physiological skin parameters were obtained by measurement of the transepidermal water loss (TEWL) with an evaporimeter (TEWAMETER TM210. Courage & Khazaka, Cologne, Germany), by measurement of skin color with a Chromameter (CR-300. Minolta, Japan) and by measurement of the skin blood flow with a Laser Doppler Flowmeter (PF 5020. Perimed, Sweden).

The TEWL measurement is the best way to evaluate the water permeability barrier of the skin (6–8). The measurement was performed by two trained persons in accordance with the guidelines for TEWL measurement of the Standardization Group of the European Society of Contact Dermatitis (7).

The Chromameter measures the skin color in a three-dimensional scale, where L* expresses the luminance (brightness), b* expresses the color spectrum from blue to yellow, and a* expresses the color spectrum from green to red (9). For skin evaluation, the a* value is considered to be the appropriate parameter. Each TEWL and Chromameter value of one patient is the mean of three single measurements.

For the Laser Doppler Flowmeter, the temperature probe PF 5020 (fixed by the special adhesive tape of the probe) was used. Initially, measurement of the basal blood flow was performed, with the temperature probe being applied to the test site at a temperature of 22–25°C. Subsequently, the temperature of the probe was raised to 40°C. Skin blood flow increased and reached a plateau higher than the basal blood flow at 22–25°C. Values obtained were the amount of thermal-stimulated blood flow (TSBF), the period of time from starting the temperature stimulus until reaching a stable plateau of TSBF (TSBF time) and the slope of the raising blood flow curve (BF slope).

Test procedure

Volunteers were patch-tested with fresh aqueous SLS 0.25% and 0.5% (SLS Sigma, 99% purity). Water served as control; 60 µl was applied in Large Finn Chambers® (inner diameter 12 mm, Epitest Ltd., Hyrlä, Finnland). Patches were applied for 48 h on clinically unaffected skin in the middle of the flexor side of one forearm. Each measurement was performed before patch application and 24 h after patch removal. Before measurement, the volunteers had rested for at least half an hour at a room temperature of between 20°C and 22°C, with a relative humidity varying between 32% and 45%.

Statistical methods

Data were calculated with SPSS for Windows. Calculation of distribution was performed by use of the Kolmogorov-Smirnov test. Correlation between the different values obtained was analyzed by means of Pearson's correlations coefficient. The differences within a measured parameter (e.g. difference between TEWL before and after SLS testing) were calculated by use of the Wilcoxon test.

RESULTS

The Kolmogorov-Smirnovtest did not show a normal distribution of the values obtained. The values (median ± 25%) are given in Tables I and II. The increase in TEWL and Laser Doppler (LD) values was significant after SLS patch testing, and for the LD values even after water application.

There was a significant correlation between all measured

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Table I. *Median values of bioengineering measurements before thermal stimulation. After application of water or sodium lauryl sulfate delta-values to the basal values were calculated*

	TEWL		a*		LD	
Basal	6.7	5.0[a]	9.1	7.6[a]	5.6	4.5[a]
		9.5[b]		10.8[b]		7.9[b]
After water	0.4	−1.2[a]	0.4	−0.7[a]	1.4	−0.8[a]
		1.3[b]		1.9[b]		3.5[b]
After SLS 0.25%	12.3	7.7[a]	1.8	0.5[a]	11.9	4.9[a]
		18.3[b]		3.3[b]		22.8[b]
After SLS 0.5%	21.5	14.8[a]	3.6	1.6[a]	24.0	11.0[a]
		30.7[b]		5.4[b]		50.1[b]

[a]25% percentile. [b]75% percentile.
a* = a-value of chromametry.
LD = Laser Doppler Flowmetry values (arbitrary units).
*Significant correlation to SLS concentration, $p<0.01$.

Table II. *Median values of bioengineering measurements after thermal stimulation*

	LD-TSBF		TSBF time		BF slope	
Basal	59.1	36.6[a]	2.7	2.2[a]	19.3	11.8[a]
		80.0[b]		3.0[b]		32.4[b]
After water	14.8	−10.9[a]	−0.1	−0.5[a]	4.5	−8.6[a]
		39.3[b]		0.3[b]		15.6[b]
After SLS 0.25%	19.7[#]	−11.7[a]	−0.8[#]	−1.4[a]	11.8[#]	−2.9[a]
		56.1[b]		−0.3[b]		30.6[b]
After SLS 0.5%	57.7[#]	15.1[a]	−1.1[#]	−1.5[a]	25.9[#]	7.5[a]
		103.5[b]		−0.4[b]		49.0[b]

LD-TSBF = Stable Laser Doppler values during temperature stimulation (temperature stimulated blood flow).
TSFB-time = Time until LD values under temperature stimulation becomes stable.
BF slope = Slope of the LD curve under temperature stimulation before reaching stable values.
*Significant correlation to TEWL measurement (after patch testing but without temperature stimulation), $p<0.05$.
[#]Significant difference to basal values (temperature stimulation of normal skin without patch testing before), $p<0.05$.
[a]25% percentile. [b]75% percentile.

biophysical skin parameters and the SLS concentration (0%, 0.25% and 0.5%). The higher the SLS concentration, the higher the values of TEWL, chromameter-a* and LD. After thermal stimulation the SLS-irritated skin reacts (depending on SLS concentration) with an abrupt increase in blood flow (Fig. 1). The time period until reaching a steady state of blood flow is shortened, and hence the slope of the curve rises (Fig. 1). The differences in TSBF values between basal areas (no patch test) and SLS-patch areas were significant ($p<0.05$), as well as the difference between the TSBF values of both SLS concentrations.

There was a significant correlation between TSBF values and all other measured values (TEWL, a* and LD) after SLS testing.

DISCUSSION

Non-chemical irritation may cause irritant dermatitis. The intolerance of sensitive or atopic skin to wool or synthetic clothes is a typical example of non-chemical irritation (5, 10). A cumulative effect of several disparate irritants has often been described, and recently Wigger-Alberti et al. demonstrated an additive effect of different chemical irritants on the skin barrier (4). The concurrent effect of chemical and non-chemical irritation is less well investigated, although it is common. The effect of an irritant may depend on its temperature. It has been shown that irritants tested at a low temperature produce only slight barrier damage, while testing at a higher temperature increases the barrier damage (11–14). Furthermore, Ohlenschlaeger et al. showed that the extent of erythema and electrical capacitance depends on the temperature at which the detergent is tested (11). Previous studies have focused on the effect of different temperatures of the tested detergent solution. Our study first investigated the effect of the applied detergent and subsequently performed temperature stimulus on that pre-irritated skin.

We investigated the effect of a thermal stimulus on the skin blood flow of untreated and SLS-irritated skin. There was a significant correlation between all measured biophysical values and the SLS concentration. This phenomenon is known for TEWL, skin blood flow and skin color (6, 8). Moreover, we found a correlation between TSBF and SLS concentration. Raising SLS concentrations increased impairment of the skin barrier and the skin blood flow. The thermal stimulus provoked a stronger and faster increase in blood flow of pre-irritated skin. The correlation between TEWL and TSBF confirmed the effect of thermal stimulation on skin irritation. In irritated skin with barrier impairment (raised TEWL), the effect of temperature on the skin blood flow is even more pronounced. The skin blood flow was markedly increased by a thermal stimulus, which could be seen at the shortened period until a steady state of TSBF was reached.

A thermal stimulus raises the blood flow. This is a physiological process of an axon reflex coordinated by the temperature regulating system (15, 16). When the skin is irritated by SLS, an inflammatory process is initialized. The inflammation may alter the temperature-regulating system, resulting in a pronounced sensitivity (17) with a raised TSBF. Even when there is only slight inflammation and no clinically visible skin changes are apparent, a thermal stimulus may lead to an increase in TSBF. This phenomenon can also be seen after water application, which is a weak irritant (18). While TEWL did not significantly increase, the blood flow after thermal stimulus increased markedly, indicating that an increased TSBF is a phenomenon also observable in mildly irritated skin. This phenomenon may explain early inflammatory signs on irritated hands due to work in hot environments (e.g. kitchen, furnace, etc.).

As any inflammatory process is followed by increased blood flow, a high surrounding temperature (e.g. the air, chemicals contacting the skin) may additionally increase the inflammation. This pronounced inflammation can lead to stronger irritative skin changes which, in turn, further impair the skin barrier. Hence, when evaluating the irritant potential of substances, the temperature during and after exposure must be taken into account.

Taken together, the level of blood flow increase after thermal stimulation correlates with the intensity of pre-irritation (evaluated by measurement of TEWL, LD and skin color). A thermal stimulus to pre-irritated skin aggravates the inflammatory signs. The thermally stimulated blood flow may be a

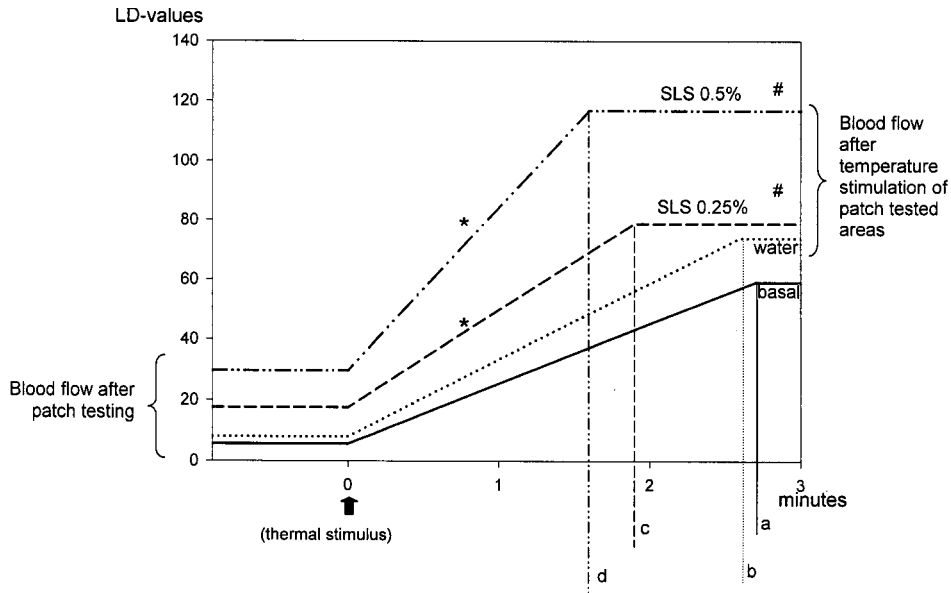

Fig. 1. Schematic kinetics of cutaneous blood flow during thermal stimulus (temperature rise to 40°C at time point 0, respectively) after different pretreatments (patch test with 0.5% and 0.25% SLS, and water), or no pretreatment (basal).

*Significant difference between the slope of SLS tested areas and the non-pretreated areas; $p<0.05$.
#Significant difference between the blood flow after temperature stimulation (TSBF) of SLS tested areas and the non-pretreated areas, $p<0.05$.
a, b, c, d = Time until LD values under temperature stimulation become stable after various types of pretreatment.

model of non-chemical irritation and seems to be a relevant co-factor in the development of irritant dermatitis.

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