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INVESTIGATIVE REPORT

Effect of Moisturizers on Skin Susceptibility to Irritants

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Moisturizers are used for the treatment of dry and irritated skin. The benefit of moisturizers when used on *normal* skin has recently been challenged, since an earlier study indicated that the increased hydration that follows long-term use of moisturizers on normal skin may facilitate penetration of irritants. The aim of the present study was to evaluate *short-term* use of 2 different moisturizers used on normal skin: cream A (high lipid content) and B (moderate/low lipid content). Nineteen healthy volunteers applied the moisturizers on the upper arm/forearm 3 times daily for 5 days, while the other upper arm/forearm served as symmetrical control. The day after moisturizer treatment was stopped the skin was challenged with a patch test of sodium lauryl sulphate. Skin reactions were evaluated by bioengineering measuring methods and clinical scoring. Skin response to sodium lauryl sulphate was increased on moisturizer-treated arms compared to controls for one of the moisturizer (cream A), while this was not statistically significant for the other moisturizer (cream B). Data confirm previous indications that some moisturizers when used on normal skin may increase skin susceptibility to irritants. *Key words: bioengineering measuring methods; skin susceptibility; sodium lauryl sulphate; TEWL.*

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Wet work employees use moisturizers for prevention and treatment of irritant skin changes due to wet work tasks. The positive effect of moisturizers used on irritated human skin is well documented (1, 2). However, moisturizers are also commonly used on normal skin for cosmetic reasons or to alleviate subjectively dry skin. Not much attention has been given to moisturizers used on normal skin (3–6). A previous study by our group indicated that long-term use of moisturizer on normal skin may increase skin susceptibility to sodium lauryl sulphate (SLS) (7). When the skin is hydrated following use of moisturizers it may become more permeable to hazardous substances. The present study was undertaken to determine the effect of short-term use of moisturizers on normal skin. Two moisturizers commonly used in Denmark were chosen for the study, one with a high lipid content and one with a low. The study was performed without any commercial interests.

MATERIAL AND METHODS

Participants

Nineteen healthy Caucasian volunteers (15 females, 4 males; mean age 42.2 years, range 24–58) were included in the study. They had no history or clinical signs of atopic dermatitis or contact dermatitis. Written informed consent was obtained from all volunteers and the study was approved by the local ethics committee.

Moisturizers

Two moisturizers widely used in Denmark (cream A and B) were chosen for this study.

Cream A (high lipid content): Locobase® (Yamanouchi Pharma) contains paraffinum molle album, aqua, paraffinum liquidum, sodium citrate, citric acid, methylparaben, cetomacrogol 1000 and cetearyl alcohol, lipid content: 70%. This moisturizer was used in another study on the influence of long-term daily use of moisturizers on normal skin (7) and has been used by our group as a model moisturizer in other studies (8, 9).
Cream B (moderate/low lipid content): Decubal (Dumex-Alpharma) contains aqua, isopropyl myristate, glycerin, sorbitan stearate, lanolin, dimethicone, cetyl alcohol, polysorbate 60, sorbic acid, lipid content: 38%. This moisturizer was used in another study on moisturizer efficacy testing (9).

The participants were not allowed to use any other moisturizer on the arms 7 days prior to entering the study or during the study period. Each participant was given a supply of the 2 moisturizers (about 20 g of each moisturizer) and a checklist for daily recording of the treatment.

Sodium lauryl sulphate

A patch test (extra large Finn Chambers, diameter 18 mm, Epitest, Helsinki, Finland) with 210 μl of an aqueous 0.25% SLS solution on a filter disc (> 99% purity, Sigma Chemical Co., St. Louis, USA) was applied on each upper arm/forearm to elicit an irritant skin reaction. The patches were placed symmetrically on each upper arm/forearm using a ruler to ensure precise positions of each patch. SLS is widely used in experimental studies on contact dermatitis as a model irritant (10).

Study design

The study period was 12 days. On day 1, baseline measurements were taken and afterwards the volunteers were randomized to have either left or right upper arm/forearm treated with 2 different moisturizers, respectively, 3 times daily for the following 5 days (days 1–5). The other upper arm/forearm served as a symmetrical control. The randomization code was blinded to the investigator. Selection of a period of 5 days of moisturizer treatment was chosen because a pilot study indicated that a plateau hydration level was reached after 3–5 days of treatment for both moisturizers. Each moisturizer was tested in half of the volunteers on the forearm and in the other half on the upper arm. On day 6 (the day after the moisturizer treatment was stopped) measurements were taken and the skin was challenged with SLS patches for 24 h. The participants were instructed to shower in the morning before measurements on day 6 to ensure no residual cream was left on the skin. They removed the SLS patches themselves on day 7 and rinsed the test area with luke-warm water. Evaluation of the irritant skin response was performed on days 8 and 12. The following bio-engineering measuring methods were used:

Transepidermal water loss (TEWL) is an indicator of the integrity of the skin barrier function and was measured with an Eviporimeter (Servo Med, Stockholm, Sweden). Measurements were taken in accordance with the Guidelines for TEWL measurements established by the ESCD (11).
Electrical capacitance as an indicator of the hydration level of the skin was measured with a Corneometer®CM820 (GMBH, Köln, Germany)

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(12). Measurements were taken on days 1 and 6, but not on days 8 and 12, since the instrument was used for determination of the hydration level only and not for measurement of the irritant response.
Laser Doppler flowmetry is an indicator of the inflammation level of the skin. A laser Doppler blood flow monitor MBF3 (Moor Instruments, England) was used according to the Guidelines (13).
Skin colour was evaluated with a Minolta Chroma Meter CR-300. The colour is expressed in a 3-dimensional coordinate system (L*a*b*). Redness of the skin is measured on the a* colour coordinate, which is an indicator of the presence of haemoglobin reflecting the inflammation level of the skin (14).
Clinical scoring of erythema on the patch test sites was registered on days 8 and 12 in accordance with the following scale: 0 = no reaction, 0.5 = very weak spotty erythema, 1 = slight erythema, 2 = moderate erythema, 3 = intense erythema.
Recordings of measurements: 2 recordings for evaporimetry and 3 recordings of laser Doppler flowmetry, corneometry and skin colour on each test site were performed, and the mean value was used for statistical calculations. On days 8 and 12, measurements were taken only on SLS-irritated skin. The study was carried out in the month of March–April. Room temperature was kept at 20–23°C and ambient humidity was 32–48%.

Statistics

To compare moisturizer-treated arms with untreated symmetrical controls, paired non-parametric statistics was used: the Wilcoxon signed-rank test for continuous data (bio-engineering measuring methods) and the Marginal Homogeneity test was used for ordinal data (clinical scoring). All calculations were done using SPSS 10.0 for Windows. A significance level of $p < 0.05$ was chosen.

RESULTS

Data on baseline values (day 1) and after 5 days of moisturizer treatment (day 6) are given in Table I. The hydration level was significantly increased on moisturizer-treated arms on day 6 compared to untreated symmetrical controls for both cream A and B. No statistically significant difference between cream A and B on day 6 was found with respect to influence on hydration level (Δ electrical capacitance = moisturizer-treated arms – untreated arms) ($p = 0.31$). The following results are from days 8 and 12 (after SLS challenge):

Cream A. On day 8 significantly higher TEWL, a* values and clinical scores were found on moisturizer-treated arms compared to untreated symmetrical controls (Table I). The difference in TEWL (ΔTEWL) between the treated and untreated arms for each participant can be seen in Fig. 1. For laser Doppler flowmetry there was no statistically significant difference between moisturizer-treated arms and control arms (Table I). On day 12 significantly higher TEWL and a* values were found on moisturizer-treated arms compared to untreated arms, but no significant differences were found for laser Doppler flowmetry and clinical scoring (Table I).
Cream B. No significant differences were found between moisturizer-treated and untreated controls after SLS challenge on days 8 and 12 (Table I); a trend toward increased values on the moisturizer-treated arms was observed on day 8, however.

DISCUSSION

The present data show that when normal skin is treated with a lipid-rich moisturizer (cream A) for 5 days before challenge with SLS, the moisturizer-treated skin has a more intense irritant reaction to SLS compared to untreated skin. This may

Table I. *Results given (medians and 25/75 percentiles) for Cream A and B (days 1–12)*

	Day 1		Day 6		Day 8		Day 12	
	Control arm	Treated arm	Control arm	Treated arm	Control arm	Treated arm	Control arm	Treated arm
Cream A								
TEWL ($g/m^2/h$)	7.2 (6.2–8.0)	6.6 (5.6–7.5)	6.3 (5.3–7.1)	6.5 (5.2–7.4)	24.2 (13.9–30.3)	$26.8^{\#\#\#}$ (20.1–43.3)	12.3 8.7–14.8)	$14.5^{\#}$ (10.8–15.6)
Electrical capacitance	66 (63–69)	66 (64–71)	67 (64–70)	$78^{\#\#\#}$ (73–81)	–	–	–	–
Laser Doppler	23 (21–25)	22 (17–25)	22 (19–30)	23 (17–27)	91 (65–131)	97 (57–149)	35 (26–53)	33 (27–45)
Colorimetry (a*)	7.9 (6.6–8.7)	7.5 (6.4–9.0)	6.8 (6.1–8.0)	7.0 (6.0–7.9)	10.9 (10.1–13.3)	$12.1^{\#}$ (10.5–14.2)	8.8 (7.8–10.0)	$9.7^{\#\#}$ (8.8–11.2)
Clinical scoring	–	–	–	–	0.8 (0.5–1.0)	$1.3^{\#\#}$ (0.8–1.5)	0.5 (0.5–1.0)	0.6 (0.5–1.4)
Cream B								
TEWL ($g/m^2/h$)	7.3 (6.3–7.7)	7.1 (6.0–7.9)	6.7 (5.5–7.4)	7.3 (5.1–8.3)	25.5 (15.8–33.8)	26.5 (17.3–34.7)	13.6 (12.0–15.0)	12.8 (10.0–15.4)
Electrical capacitance	66 (61–71)	67 (62–70)	67 (58–69)	$80^{\#\#\#}$ (76–85)	–	–	–	–
Laser Doppler	21 (17–23)	21 (19–24)	22 (17–28)	21 (18–27)	97 (40–126)	80 (57–124)	33 (27–48)	30 (23–41)
Colorimetry (a*)	7.3 (6.5–8.6)	7.2 (6.6–8.6)	6.8 (6.3–7.9)	6.9 (5.7–7.5)	12.0 (10.2–13.9)	12.6 (10.5–14.0)	10.4 (8.1–11.0)	10.0 (8.2–11.1)
Clinical scoring	–	–	–	–	1.0 (0.5–1.3)	1.0 (0.8–1.5)	0.8 (0.5–1.2)	0.8 (0.5–1.3)

$^{\#}p < 0.05$, $^{\#\#}p < 0.01$, $^{\#\#\#}p < 0.001$ compared to control arm.

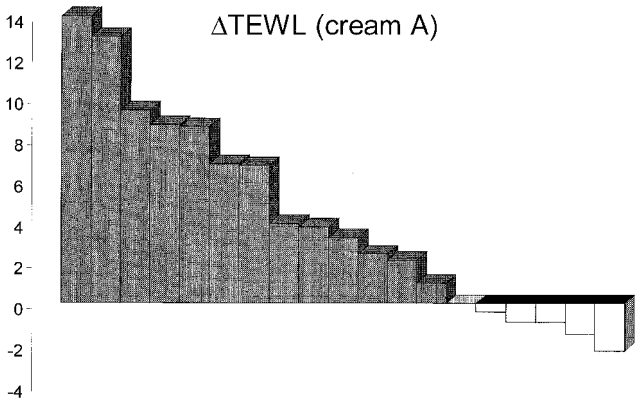

Fig. 1. Cream A. Differences between TEWL values (ΔTEWL g/m^{2}h) on moisturizer-treated and untreated arms on SLS-irritated area on day 8. Each dark column represents a person with higher TEWL on the moisturizer-treated arm. Each white column represents a person with higher TEWL on the untreated arm ($n = 19$).

be due to an increased penetration of the hydrophilic substance. The result was confirmed by bio-engineering measuring methods (TEWL and colorimetry) as well as by clinical scoring. This means that both the barrier function and the inflammation level were more affected by SLS in moisturizer-treated skin compared to untreated skin, supporting results from a previous study on long-term use of moisturizer (7). However, in the present study, observations were confirmed by different non-invasive measuring methods as well as by clinical scoring, whereas in the previous study evaluation was only by measurements of TEWL (7). TEWL has been reported to be the most suitable method for evaluation of SLS-induced skin damage (15, 16) and colorimetry (a* measurements) has been shown to correlate well with clinical scoring (17). The less lipid-rich moisturizer (cream B) tested in the present study did not have the same influence on skin susceptibility. This difference between cream A and B with respect to influence on skin susceptibility is most likely due to differences in lipid content but may also reflect influence by other ingredients in the moisturizer; for example, emulsifiers, humectants or preservatives. More studies are needed to investigate this. Application of moisturizers on normal skin causes an increased hydration state of stratum corneum, which lasts for days. This has been shown in experimental studies (7, 18) and in a field study (19). A lipid-rich moisturizer is more occlusive than a less lipid-rich moisturizer, which may influence the hydration state of stratum corneum. Theoretically, the hydration level of stratum corneum may affect the permeation properties of the skin. However, only a few studies have evaluated the effect of moisturizers used on normal skin with respect to barrier properties and susceptibility to irritants. Under average environmental conditions the stratum corneum contains between 10% and 20% of water, but daily use of moisturizers may artificially increase this percentage. When stratum corneum is hydrated beyond normal level the barrier properties are progressively reduced; a principle used in occlusive therapy and known from treatment of intertriginous body sites (20, 21). This aspect deserves further consideration, since it may have implications for wet work employees who are encouraged to use moisturizers and at the same time are exposed to water and detergents.

Other studies have indicated a protective effect of long-term moisturizer treatment of normal skin. Lodén found a decreased skin response to SLS compared to untreated skin after treatment for 20 days with 2 urea-containing moisturizers, while 2 moisturizers not containing urea did not influence skin susceptibility to SLS (18). Treatment with the urea-containing moisturizers (for 20 days) did not increase skin hydration level as measured by the electrical capacitance, whereas treatment with moisturizers without urea resulted in a significantly increased hydration level. These results therefore also indicate that the hydration level may have an impact on skin susceptibility. In another study by Lodén and co-workers in patients with atopic dermatitis, SLS challenge was also made after 20 days of treatment with a urea-containing moisturizer (24). A significantly lower skin response on the arm pretreated with moisturizer was found. Atopics have a general defective skin barrier also in skin that is clinically normal, and the moisturizer may possibly have treated subclinical dermatitis, thereby normalizing a defective skin barrier before the SLS challenge. Data from this study are therefore not directly comparable to data from the present study.

Several studies have shown that moisturizers used as barrier creams provide a protecting film on the skin, thereby limiting penetration of potential damaging substances (8, 22, 23). In the present study, effort was made to ensure that no residual cream was left on the skin before challenge with SLS. The present study did not therefore test the capability of the moisturizers as barrier creams.

The present findings indicate that treatment with moisturizers does not necessarily protect the skin, but may instead lead to increased susceptibility to irritants. This further complicates the debate about the use of moisturizers, barrier creams and after-work emollients. Experimental evidence from previous studies has shown that some moisturizers when used immediately before exposure to soap and water will prevent skin irritation. We also have experimental evidence and clinical experience that moisturizers improve irritant skin reactions and speed up the regeneration of irritant reactions, indicating a positive effect of after-work emollients. Our findings now indicate that unlimited and undocumented use of moisturizers on normal skin may have some side effects.

Work-place recommendations for the use of moisturizers (barrier creams/after-work emollients) should be carefully considered with respect to skin exposure. Further research, independent of commercial interests and including field studies, is necessary.

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