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INVESTIGATIVE REPORT

Tandem Application of Sodium Lauryl Sulfate and n-Propanol Does Not Lead to Enhancement of Cumulative Skin Irritation

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Irritant contact dermatitis has a broad spectrum of clinical features and is a leading cause of occupational disease worldwide. It has been shown previously that a combination of chemically different irritants may cause an additive effect compared to single application of these substances. In this study, tandem application of sodium lauryl sulfate and n-propanol was investigated in 20 human volunteers using non-invasive bioengineering methods, such as measurement of transepidermal water loss and chromametry. N-propanol did not enhance cumulative skin irritation when used with sodium lauryl sulfate, as has been reported for toluene. As n-propanol is the active ingredient in many disinfectants, this is of particular interest regarding occupational skin irritation in health care workers. ***Key words: bioengineering; chromametry; irritant contact dermatitis; occupational diseases; transepidermal water loss (TEWL).***

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Irritant contact dermatitis (ICD) is the leading cause of occupational contact dermatitis, the most frequent occupational contact dermatitis in many countries. Topical application of detergents, acids, alkaline substances and organic solvents to the skin can alter the cutaneous permeability barrier (1). It has been shown previously that the mechanism of skin impairment is dependent on the type of irritant (2–4).

Previous studies have concentrated on the effects of single irritant exposure (5, 6), in particular sodium lauryl sulfate (SLS), which has been studied as a model irritant (2, 3, 7–9). It has been demonstrated that tandem application of different agents may modify the cutaneous response compared to single application (4, 10, 11), thus leading to an additive effect of the irritants.

Using non-invasive bioengineering methods, this study aims to quantify the effects of repetitively applied SLS or n-propanol (Prop) compared to combined application of both substances. Especially health care workers with a high frequency of ICD are exposed to both substances, since SLS may be present in hand wash products and n-propanol is a standard disinfectant (12) according to the German Society for Hygiene and Microbiology (DGHM).

MATERIAL AND METHODS

Study population

We studied 20 healthy non-preselected Caucasian volunteers (10 women and 10 men; aged 21–34 years; median 23.3 years) with no skin disease. The study was approved by the local ethics committee and informed consent was obtained from all participants. Subjects were instructed not to apply detergents, moisturizers or emollients directly on the test area during the investigation period of 5 days.

Procedure

Four adjacent skin areas of clinically normal skin were premarked as test fields on a medial volar forearm of each subject. Placement of test fields was otherwise random. Irritants were applied for 30 min under occlusion (Finn Chambers, 12 mm diameter, filling volume 0.05 ml; Epitest Ltd., Hyrlä, Finland). Thus, 0.5% aqueous SLS solution (Sigma, St. Louis, MO, USA), according to Schnetz et al. (13), and 60% aqueous n-propanol (Prop), according to the common concentration of the substance in widely used disinfectants, were tested. After a 3-h interval, a second exposure was performed with one of the irritants to induce a repetitive effect of irritation. In total, four treatment options were investigated following the scheme SLS/SLS, Prop/Prop and SLS/Prop and a plain control field. Experimental irritation was performed constantly for 4 days with a 24-h interval.

The same procedure but including pretreatment with petrolatum was performed on the other forearm of each volunteer to assess the protective effect of petrolatum as a basic agent in most skin care products.

Measurements and instrumentation

Visual scoring, transepidermal water loss (TEWL) and skin colour reflectance measurement were used to assess skin irritation. Visual scoring and bioengineering measurements were performed by the same observer before treatment on days 1–4 and on day 5. Measurement conditions of the laboratory were standardized as regards air-condition, room temperature 20–22°C and relative humidity 34–46%.

The visual test readings were scored in accordance with a conventional scale (14) based on three fundamental types of skin lesion: erythema, scaling and fissuring (erythema: 1+ slight redness (spotty or diffuse), 2+ moderate and uniform redness, 3+ intense redness, 4+ fiery red with erythema; scaling (sight and touch): 1+ fine, 2+ moderate, 3+ severe with large flakes; fissures: 1+ fine cracks, 2+ single or multiple broader fissures, 3+ wide cracks with hemorrhage or exudation). Treatment exposure was stopped if a cumulative score of 5 was reached and overall values obtained at discontinuance were used for final data analysis.

TEWL is a highly sensitive parameter for obtaining information on the integrity of the stratum corneum barrier and is based on vapour pressure gradient calculation (15). Measurement was carried out with an evaporation meter (Tewameter TM 210, Courage & Khazaka, Cologne, Germany) in accordance with the Guidelines of the Standardization Group of the European Society of Contact Dermatitis (16).

Intensity of erythema was assessed with a Minolta Chromameter (CR-200. Minolta, Osaka, Japan) in accordance with published recommendations (17). The instrument measures colour reflectance and computes the chromatic dimensions of colour by means of the L* a* b* 3-dimensional colorimetric system. To quantify erythema, the a* value is of specific interest measuring the red-green distinction (18). This non-invasive, bioengineering technology provides essential information on the cutaneous response to irritants applied to the skin (19).

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Statistics

Statistical analysis was conducted with SPSS for windows (Version 10.0; SPSS, Chicago, ILL, USA). Data of the visual score were presented regarding the median and quartiles. ΔTEWL (difference between baseline TEWL and TEWL after overall irritation) and Δa* (difference between baseline a* and a* after overall irritation) were evaluated and presented as mean±SEM.

Differences between means were checked for significance using the Wilcoxon test for the erythema score, comparison of ΔTEWL and skin colour. The chosen level of significance was $p \leq 0.05$ adjusted according to Bonferroni.

RESULTS

The visual score data are given in Fig. 1A as box plots; results of ΔTEWL and Δa* are presented in Fig. 1B and 1C as mean±SEM. The cumulative application of SLS 0.5% on normal skin induced a marked irritant skin reaction. The longer the cumulative irritation time the more intense the skin reaction presented according to the clinical score, the TEWL values (ΔTEWL) as well as the a+ values (Δa*). There was a significant difference between the baseline values and the final values after irritation. On day 5, repetitive application of SLS induced significantly stronger skin reactions than those caused in other test fields – except for the data evaluated by chromametry in the area treated with SLS/Prop. Regarding the repetitive skin irritation of n-propanol, a mild increase in the visual score started at day 4 and in total this test area was irritated least.

Tandem application of SLS and n-propanol resulted in a moderate increase in the visual score, ΔTEWL and Δa*. On day 5, these measured values were significantly lower than after repetitive single application of SLS according to the visual score and ΔTEWL, but significantly higher than after repetitive single application of n-propanol referring to the ΔTEWL. Regarding ΔTEWL on day 5, skin irritation was significantly reduced by pretreatment with petrolatum (Fig. 2).

DISCUSSION

Chronic ICD is a major clinical problem. Frequently caused by repetitive contact with a variety of irritants in a particular work setting, it may completely disable the worker to the point s/he cannot continue in his/her occupation (20). As indicated in recent studies, contact with different irritants in the daily life situation puts immense stress on the natural cutaneous balance. Not much is known about the mechanism of irritant dermatitis produced by repeated or combined exposure to clinical or subclinical doses of irritants. However, differences between tandem application and single agent exposure have been demonstrated. Ale et al. reported synergistic effects of SLS and retinoic acid on the epidermal barrier (10). Moreover, the applied substances may affect each other, either by aggravating or reducing irritant effects (11). Thus, application interval, sequence, dose and type of agent are considered to be important modulating aspects in regard to the skin reaction (10, 11, 19, 21, 22).

As reported recently, repetitive irritation with SLS induces a significantly higher increase in TEWL than with toluene (23). Nevertheless, tandem application of both irritants does not lead to a mitigated effect. On the contrary, we demonstrated an even more than additive effect of skin irritation after tandem application of SLS and toluene independently

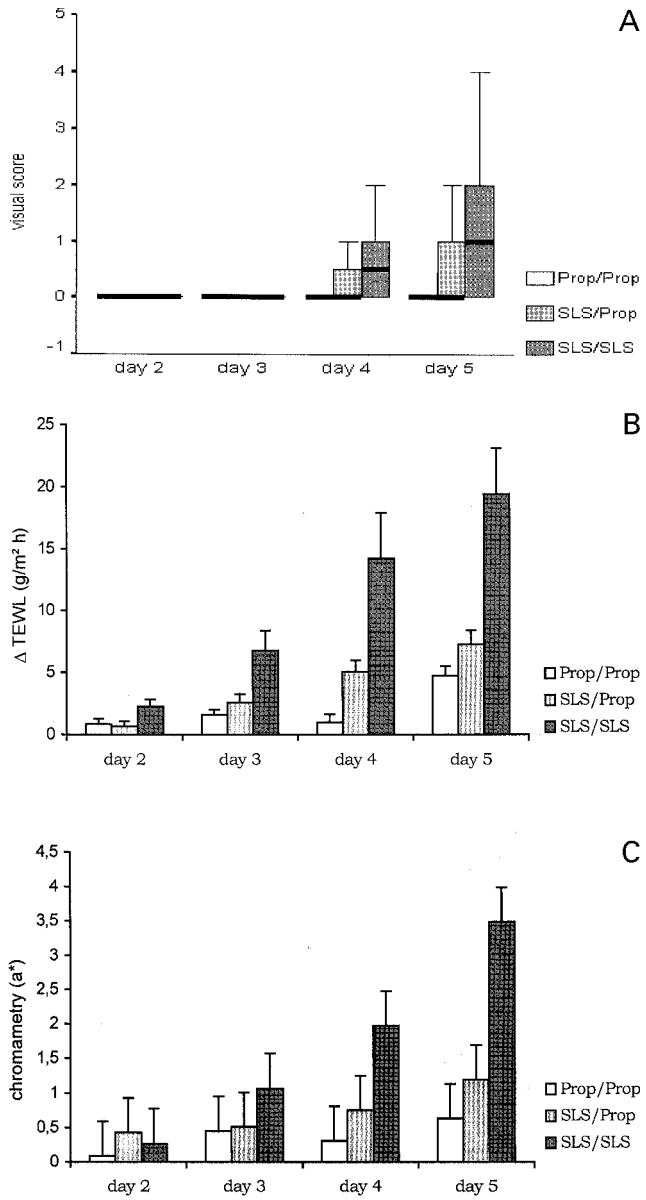

Fig. 1A–C. Box plots (mean±SEM) of visual score, ΔTEWL and Erythema Δa* after sequential application of Prop/Prop, SLS/Prop and SLS/SLS for 5 days ($n=20$). Regarding the visual score, differences between Prop/Prop and SLS/SLS, SLS/Prop and SLS/SLS and, regarding the ΔTEWL differences between Prop/Prop and SLS/SLS, SLS/Prop and SLS/SLS, Prop/Prop and SLS/Prop, regarding the Erythema Δa* differences between Prop/Prop and SLS/SLS were statistically significant ($p<0.05$). (SLS=sodium lauryl sulfate. Prop=n-propanol).

from the application turn (21). In this regard, interaction of other combinations relevant in the work place is of great concern.

Our findings in 20 participants who underwent single and tandem application of SLS and n-propanol do not support the concern of a more than additive effect in this combination. They do not even assume a plain additive effect. Therefore people exposed to SLS and additionally n-propanol, e.g. in a hospital setting, are probably not at increased risk of acquiring ICD. Short-term exposure to different irritants under experimental conditions, however, does not reflect the daily life

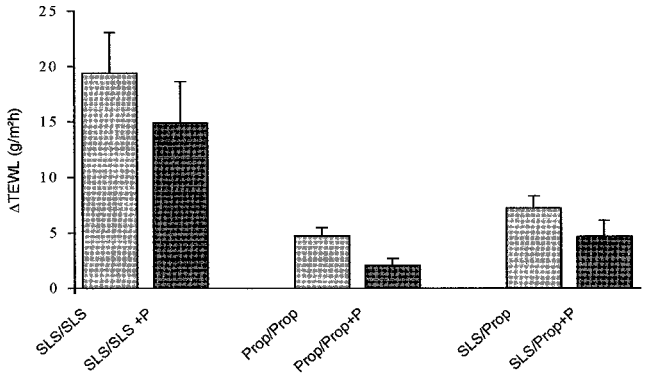

Fig. 2. Comparison of ΔTEWL (mean±SEM; $n=20$) with and without application of petrolatum before sequential application of SLS/SLS, Prop/Prop and SLS/Prop for 5 days. The differences with and without petrolatum in analog test areas were statistically significant ($p<0.05$). (SLS=sodium lauryl sulfate. Prop=n-propanol, P=petrolatum).

situation. Longer periods of exposure to n-propanol might increase sensitivity to SLS or the synergistic effect.

This finding confirms how difficult it is to predict the interactive effect of even well-known single agents, and since the action mechanism of even single irritants is poorly understood, the effects of interaction between different agents are even more complex. However, this suggests that interactive profiles of widely used agents that may lead to ICD should be thoroughly investigated.

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