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CLINICAL REPORT

Do Atopics Tolerate Alcohol-based Hand Rubs? A Prospective, Controlled, Randomized Double-blind Clinical Trial

Günter KAMPF[1,2], Walter WIGGER-ALBERTI[3] and Klaus-Peter WILHELM[3]
[1]Bode Chemie GmbH & Co., Scientific Affairs, [2]Institut für Hygiene und Umweltmedizin, Ernst-Moritz-Arndt Universität, Greifswald, and [3]proDERM, Schenefeld, Germany

Alcohol-based hand rubs are used frequently in healthcare settings, but their tolerance among atopic subjects is unknown. The dermal tolerance to five alcohol-based hand rubs was assessed among atopic and non-atopic subjects in a repetitive occlusive patch test. In total, 54 subjects were analysed. One half of the subjects were atopic (modified Erlanger atopy score ≥ 8), the other half were non-atopic. Treatments were controlled with water and 2% sodium dodecyl sulphate (SDS). Treatment sites were assessed by visual inspection (tolerability score 0-4). Skin redness was determined with a chromameter. The overall mean tolerability to all five hand rubs was lower than or identical to the negative control (0.02±0.07) and significantly different from the SDS control (0.19±0.39). Skin redness was in the same range as for the negative control (0.15±0.8) which was significantly lower than the SDS control (1.35±1.6). A comparison of the atopic and non-atopic subjects revealed no significant difference. In conclusion, we found that tolerance to the five alcohol-based hand rubs was good among atopic and non-atopic subjects. ***Key words: dermal tolerance; atopic; alcohol-based hand rub; repetitive occlusive patch test.***

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PD Dr Günter Kampf, Bode Chemie GmbH & Co., Scientific Affairs, Melanchthonstr. 27, D-22525 Hamburg, Germany. E-mail: guenter.kampf@bode-chemie.de

Occupational contact dermatitis (OCD) is a frequent finding among healthcare workers (1). In a study of 1301 hospital employees, 21.2% were found to have dermatitis on the hands and/or forearms (2). In another survey 69% of healthcare workers in three paediatric intensive care units described having skin problems on their hands (3). The most common type of hand dermatitis among healthcare workers is irritant contact dermatitis (4). It can be caused by frequent hand washing (5) or various disinfectant agents, for example chlorhexidine (2). One risk factor for OCD is the presence of an atopic predisposition (6, 7). Among ICU healthcare workers, 32.8% were reported to be atopic (8). Various studies have described the risk associated with the presence of atopy and the development of hand dermatitis. A study among 2452 newly employed hospital workers showed that the diagnosis of an atopic dermatitis increases the risk for developing hand eczema by three times in both wet and dry work (9). In addition, the severity of hand eczema was higher among subjects with atopic dermatitis (9). The atopic constitution has also been described as predisposing for the development of permanent or periodic hand dermatitis in healthcare workers (10, 11). Finally, it has been described that persons with atopic dermatitis have a considerable risk of developing hand eczema when exposed to occupational agents that are a burden to the skin (12). Overall, atopic healthcare workers are an accepted risk group for developing OCD.

Dermal tolerance to preparations for hand disinfection is crucial in order to maintain a high rate of compliance in hand hygiene (13). Antiseptic soaps have been described to cause significant damage to the skin (14). Well-formulated alcohol-based hand rubs, however, are in general well tolerated by subjects with healthy skin (13, 15–17). Although alcohols have so far not been reported to be the causative agents for contact dermatitis (4, 18–20) their dermal tolerance has never been studied among atopic subjects. We therefore investigated the dermal tolerance to five different alcohol-based hand rubs among atopic and non-atopic subjects.

METHODS

Study design

A mono-centric, prospective, double-blind, controlled (positive and negative control), randomized, clinical trial was performed. It was a repetitive semi-occlusive patch test. The study was conducted in accordance with the ethical principles that have their origins in the current version of the Declaration of Helsinki (52nd WMA General Assembly, Edinburgh, Scotland, October 2000). The ethics committee of the medical chamber Schleswig-Holstein granted approval for the study (12.02.2003 and 26.02.2003).

Study preparations

The following alcohol-based hand rubs were used: Sterillium, based on 45% 2-propanol, 30% 1-propanol and 0.2% mecetronium etilsulfate; Sterillium pure, based on 45% 2-propanol, 30% 1-propanol and 0.2% mecetronium etilsulfate; Sterillium Gel, based on 85% ethanol; Sterillium Virugard, based on 95% ethanol; and Amphisept E, based on 80% ethanol. The experiments were controlled with de-mineralized water (negative control) and 2% sodium dodecyl sulphate (SDS; positive control). All hand rubs were manufactured by Bode Chemie GmbH & Co.,

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Hamburg, Germany. The hand rubs and the controls were randomly assigned a letter (blinding of the test formulations).

Selection of study population

A total of 55 subjects were recruited. Half of the volunteers should have an atopic predisposition with a modified (without IgE results and Phadiatop) Erlanger atopy score ≥ 8 (21).

Inclusion criteria were**:** Caucasian men or women of skin type I–IV according to Fitzpatrick (22); between 18 and 65 years of age; signed written informed consent; had a negative urine pregnancy test (female panellists of child-bearing potential); and signed written confirmation to use safe contraception (female panellists of child-bearing potential).

Exclusion criteria were**:** pregnant or during lactation; had active skin diseases, moles, etc.; had severe illness on account; had psychiatric conditions that might limit the participation; took drugs interfering with the immune system (e.g. antiphlogistics, corticosteroids, immunosuppressants or antihistamines); had topical therapy in the test region in the last 2 weeks; had recent intensive ultraviolet-light exposure (less than 2 weeks); had a known allergy to the ingredients of the test products; had a history of drug or alcohol addiction in the past 3 years; had an infectious disease (e.g. AIDS or hepatitis); were insulin-dependent diabetic; or were known to have poor compliance.

Repetitive semi-occlusive patch test

Test areas were marked on both forearms. 150 µl of the coded test material (product or controls) were applied on days 1, 2 and 3 to one of the marked test areas according to the randomization list. The test material was left under semi-occlusive conditions for 3×23 h (Trumed patches, Trumed Technologies Inc., Burnsville, USA).

Assessment of tolerability

All evaluations were carried out by the same investigator. In order to avoid bias, the grading assessments were done before the chromameter measurements. Visual assessment was performed before the application on day 1, before each application on days 2, 3 and 4 (15 min to 2 h after patch removal), as well as 48±2 h (day 5) and 72±4 h (day 6) after the last product application. The scale used is shown in Table I. In case of a score ≥ 2 on days 2 and 3, no further product was applied. Skin tolerability was expressed as the mean tolerability score over days 4, 5 and 6.

Assessment of skin redness

Skin reactions were quantified objectively using reflection measurements with a tri-stimulus chromameter (CR 300, Minolta, Langenhagen, Germany). Measurements were made on the designated treatment areas in triplicate before the product application on day 1 (baseline) and during the final visit on day 6. The mean of the three values was calculated by the instrument and entered in the data sheet. The difference in parameter a* (a* correlates with the visual assessment of redness) between the respective test points and baseline were taken for analysis.

Table I. *Tolerability scale by visual assessment*

Score	Description of skin reaction
0	No apparent cutaneous involvement
0.5	Faint, diffuse erythema (greater than 0, but less than 1)
1	Definite, moderate to severe erythema but skin intact, without papules
2	Severe erythema (possibly moderate oedema) may have a few papules, deep fissures, or other defects of skin surface
3	Very severe erythema, generalized papules or vesicles, and/or other defects of the skin surface extending beyond test site
4	Very severe erythema with oedema extending beyond test site and vesicles or eschar formations

Statistics

For statistical analysis of tolerability data, the mean tolerability score after visual assessment and baseline-adjusted chromameter a* measurements were used. Calculations were performed for the whole panel as well as for the subgroups of atopic and non-atopic panellists separately. Data is presented descriptively as mean±standard deviation. Primary analysis consisted of the calculation of the upper limits of one-sided 97.5% confidence intervals (CI) according to standard methods for each product under investigation.

Additionally, non-overlapping two-sided 95% CI served as indicators of statistically significant differences between products and between subgroups.

RESULTS

One of 55 subjects was excluded due to the systemic use of an antihistamine preparation during the study. Among the remaining 54 subjects, 45 were women and 9 men. The mean age was 45.0 ± 13.5 years.

Skin type classification and atopy score

Most volunteers were of skin type III (46.3%), followed by skin type II (31.5%), IV (18.5%) and I (3.7%).

The modified Erlanger atopy score was used to categorize the volunteers into atopics (score ≥ 8 points) and non-atopics (score < 8 points). The mean atopy score among 26 atopics was 12.1±3.1 (range 8–19.5) and 2.1±2.2 among 28 non-atopics (range 0–7.5). Among the atopics, incorporated various anamnestic and clinical criteria of atopy, such as history of eczema or hay fever were present.

Visual assessment

The overall mean tolerability with the five hand rubs was between 0.01±0.03 (Sterillium Gel) and 0.02±0.1 (Sterillium Virugard), which is lower or identical to the mean tolerability of the negative control (0.02±0.07). The positive control with 2% SDS revealed a significantly higher value (0.19±0.39). For all test products the upper limit of the 97.5% CI for the mean tolerability score proved to be well below 1, indicating no to mild skin irritation and therefore good to very good tolerability.

A comparison of the atopic and non-atopic subjects revealed an equal or slightly better tolerance among the atopic subjects with all hand rubs (Table II). Indications of statistically significant differences were found neither between any pair of hand rubs among all 54 volunteers

Table II. *Mean±SD tolerability and difference in skin redness for five different alcohol-based hand rubs among atopic (n=26) and non-atopic subjects (n=28), controlled with demineralized water and 2% sodium dodecyl sulphate (SDS)*

Type of hand rub	Tolerability			Difference in skin redness		
	Atopic subjects	Non-atopic subjects	All subjects (n = 54)	Atopic subjects	Non-atopic subjects	All subjects (n = 54)
Demineralized water (negative control)	0.01 ± 0.03	0.04 ± 0.08	0.02 ± 0.07	0.31 ± 0.7	0.00 ± 0.8	0.15 ± 0.8
2% SDS (positive control)	0.15 ± 0.37	0.22 ± 0.41	0.19 ± 0.39	1.12 ± 1.8	1.56 ± 1.5	1.35 ± 1.6
Sterillium	0.01 ± 0.03	0.01 ± 0.04	0.01 ± 0.04	0.03 ± 0.9	0.16 ± 0.9	0.10 ± 0.9
Sterillium pure	0.01 ± 0.03	0.02 ± 0.07	0.01 ± 0.05	0.38 ± 1.0	0.18 ± 1.1	0.28 ± 1.0
Sterillium Gel	0.00 ± 0.00	0.01 ± 0.04	0.01 ± 0.03	-0.03 ± 0.9	0.05 ± 1.1	0.01 ± 1.0
Sterillium Virugard	0.01 ± 0.05	0.04 ± 0.13	0.02 ± 0.10	0.16 ± 1.2	0.32 ± 1.0	0.24 ± 1.1
Amphisept E	0.01 ± 0.03	0.02 ± 0.07	0.01 ± 0.05	0.02 ± 0.9	0.02 ± 0.8	0.02 ± 0.9

nor between atopic and non-atopic subjects for any of the products.

Determination of skin redness

The overall effect on skin redness (difference between day 6 after 3 treatments and baseline) with the five hand rubs was between 0.01±1.0 (Sterillium Gel) and 0.28±1.0 (Sterillium pure), which is in the same range as negative control (0.15±0.8). The positive control with 2% SDS revealed a significantly higher degree of skin redness (1.35±1.6). A comparison of the atopic and non-atopic subjects revealed an equal or slightly better tolerance with 4 of 5 hand rubs, and a slightly worse tolerance with 1 hand rub among the atopic subjects (Table II). Indications of statistically significant differences were found neither between any pair of hand rubs among all 54 volunteers nor between atopic and non-atopic subjects for any of the products.

Adverse events

Three adverse events were observed: two cases of mild headache and one case of common cold. All three cases recovered without complications. None of them was considered to be related to the study preparations.

DISCUSSION

Healthcare workers have a significantly higher incidence of OCD than most other occupational groups and ICD accounts for the vast majority of occupational dermatoses (23). Agents in the hospital, such as soaps, solvents and cleansers (4) or chlorhexidine (2), have been shown to have a negative impact on atopic healthcare workers' skin. Wet work in particular seems to enhance hand dermatitis among atopic subjects (9). However, the question as to whether atopics show a pronounced reaction to irritants still is under debate (24–26). It was found that a considerable number of subjects with a personal history of atopic dermatitis managed to work in risk occupations without developing hand eczema (27) and recently it was demonstrated that among metal workers the presence of atopy did not bear a significant risk for hand eczema (28). Though individuals with atopy seem to run a higher risk of OCD (12), a distinction must be made between mucosal atopy (asthma and hay fever) and atopic skin diathesis regarding the risk of developing OCD (29). This is especially true for the relevance of irritant skin reaction of individuals to SDS in experimental patch tests. Individuals who were classified as atopic but without active dermatitis did not show an enhanced skin susceptibility to SDS compared with atopic individuals with rhinoconjunctivitis or atopic asthma and even healthy controls (30). Only individuals with active atopic dermatitis demonstrated significantly stronger irritant reactions to SDS. For disinfectants, the level of pre-existent skin irritation is the pertinent factor in product-related skin susceptibility to irritation (18). That is why the presence of an atopic predisposition alone should not have a negative impact on overall dermal tolerance to well-formulated alcohol-based hand rubs. The key factors seem to be removal of the surface lipid layer or production of cellular damage (4). The surface lipid layer is not removed by an alcohol-based hand rub. In addition, most hand rubs contain emollients to provide additional protection for the skin (15–17). This may be why alcohol-based hand rubs were found to be well tolerated in our study population.

The positive control SDS 2% itself induced in this test model only low, but significant, skin irritation that is explained by the semi-occlusive patch test design that was chosen since the test products contain different concentrations of alcohol and since it is known that alcohol can cause irritant reactions when applied occlusively. Additionally, the semi-occlusive application of the test products was chosen in order to reflect the actual clinical usage of disinfectants.

We were able to show that five commercially available alcohol-based hand rubs were well tolerated by atopic subjects in a repetitive semi-occlusive patch test. Skin reactions and skin redness were in the same range as the negative control among atopics and non-atopics.

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