

Skin susceptibility of atopic individuals

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The relevance of the irritant skin reaction of individuals with an atopic history (atopic dermatitis, rhinoconjunctivitis or atopic asthma) to sodium lauryl sulfate (SLS), a widely used irritant, is still controversial. The aim of this study was to evaluate transepidermal water loss (TEWL) as an indicator of stratum corneum integrity, before and after SLS patch testing, in various groups of atopic individuals with and without atopic dermatitis. 95 volunteers were divided into 4 groups: (1) individuals with active atopic dermatitis; (2) individuals with a history of atopic dermatitis but without active skin lesions; (3) individuals with rhinoconjunctivitis or atopic asthma without any symptoms at the time of testing; (4) healthy individuals serving as controls. The volunteers were patch-tested at the unaffected volar side of the forearm with aqueous SLS 0.5% for 48 h. TEWL was measured before application and after removal of the patch. Individuals with active atopic dermatitis showed a significantly higher TEWL value after SLS and a tendency to a higher basal TEWL as compared to the 3 other groups. There were no significant differences in TEWL between individuals who were classified as atopic but without active dermatitis, individuals with rhinoconjunctivitis or atopic asthma and healthy controls, either at the basal or at the post-SLS measurement. Enhanced skin susceptibility is only present in individuals with active dermatitis. The skin susceptibility of atopic individuals might therefore be increased as soon as the skin becomes eczematous, suggesting a reduced epidermal integrity probably caused by the endogenous atopy and/or respiratory allergens. When interpreting the atopy score in relation to skin susceptibility, the actual condition of the skin should hence be taken into consideration.

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Chronic irritant contact dermatitis of the hands is one of the most frequent skin diseases (1–4). It is likely that patients with an atopic history, particularly atopic dermatitis, suffer more frequently from irritant hand dermatitis than non-atopics (3, 5). This may be best explained by an impaired skin barrier function in atopic patients. This view is supported by studies showing higher transepidermal water loss TEWL values following irritant exposure in patients with active atopic hand eczema (6–9). It has also been demonstrated that a significantly greater response to sodium lauryl sulfate (SLS) (6–8, 10), as well as a tendency to increased skin susceptibility, is related to the degree of severity of the dermatitis (11). By contrast, there have been conflicting observations concerning the skin susceptibility of individuals with a history of atopic dermatitis but without any active lesions (2, 12).

Results of studies on the skin susceptibility of patients with respiratory atopy (RA), in the form of rhinitis or atopic asthma, without a history of atopic dermatitis are likewise contradictory. While some authors have found increased reactivity to

SLS in patients with RA as compared to healthy controls (6), other authors have not (13, 14).

It is known that the season in which skin susceptibility is tested influences test outcomes. In healthy volunteers, increased skin susceptibility has been observed more in winter (15, 16). Tupker et al. (17) showed that particularly patients with AD showed reduced barrier function and skin hydration in winter.

The aim of this study was to ascertain the skin susceptibility of individuals with active and inactive atopic dermatitis, and in patients with a respiratory atopy, as compared to healthy controls. The study was performed on unaffected skin areas during winter. The patients had no rhinitic symptoms.

Patients and Methods

Study population

95 volunteers (52 women, 43 men), aged 14 to 60 years, participated in this study. They were recruited from the out-patient and in-patient clinics

of the Department of Dermatology, University of Marburg. Informed consent was obtained from all participants, and the study was approved by the ethical committee of the University of Marburg.

The volunteers were divided into 4 groups.

(i) Atopic dermatitis with active dermatitis (AAD, 23 patients): atopic dermatitis was diagnosed by typical clinical manifestations (e.g., flexural eczema), a family atopic history, personal atopic history (without respiratory allergies) and signs of atopy (e.g., Hertoghe sign, dirty neck sign, xerosis, wool intolerance, white dermographism). These factors were used to calculate the score of atopy, as proposed by Diepgen et al. (18, 19). Using this score, it was possible to define an atopic constitution without taking the current skin condition into account. The volunteers were defined as having AD when the atopic score was higher than 10 and acute eczema was present.

(ii) Inactive atopic dermatitis (IAD, 21 patients): these volunteers were defined similarly to the 1st group, but they had to have been free from active eczematous lesions at the time of testing and for the past 2 years.

(iii) Respiratory atopy (RA, 25 patients): individuals with a typical history of rhinoconjunctivitis or atopic asthma *and* showing at least 1 positive prick test to a relevant aeroallergen. Volunteers with both AAD and RA were excluded, as well as individuals with coincidental IAD and RA.

(iv) Healthy controls (26 volunteers) without any history of atopy.

Test procedure

Volunteers were patch tested with 60 μ l aqueous SLS 0.5% (SLS Sigma, 99% purity) in large Finn Chambers® (inner diameter 1.2 cm, Epitest Ltd., Hyrlä, Finland) for 48h on clinically unaffected skin on the flexor side of the forearm. TEWL was measured before (basal) and 1 h after removal of the patch with the TEWAMETER TM210 (Courage & Khazaka, Cologne), because TEWL after SLS patch tests seems to reach a stable plateau preferably 1 h after patch removal (20). Test evaluation was performed by 2 trained persons according to the guidelines of sodium lauryl sulfate exposure tests of the Standardization Group of the European Society of Contact Dermatitis (21). The volunteers had rested for at least $\frac{1}{2}$ h at a room temperature between 20–22°C, with relative humidity between 35–62%. The tests were done within a period of 20 weeks during fall and winter 1997/98.

Statistical methods

Data were calculated with SPSS for Windows. After calculation with the Kolmogorov-Smirnov-test, the TEWL values were shown as medium $\pm$ standard deviation. Differences in TEWL between the groups were calculated using ANOVA variance analysis with the subsequent Duncan test.

Results

Baseline TEWL values

Individuals with AAD showed a higher baseline TEWL as compared to all other groups, but the differences were not statistically significant. Moreover, a tendency to slightly higher values in the control group, as compared to IAD and RA groups, was observed (Table 1).

Postexposure TEWL values

The differences in TEWL values between basal and post-SLS tests were significant in all 3 patient groups. Significantly higher postexposure TEWL values were found in the AAD group as compared to healthy volunteers. No significant differences could be obtained between the groups of IAD, RA and healthy individuals, either in post-SLS values or Δ TEWL. A tendency to slightly higher values in the IAD group was found when compared to the control group (Table 1).

Discussion

Patients with an atopic constitution suffer rather frequently from hand dermatitis (3–5). These findings, however, do not necessarily mean that there is a genuinely increased skin susceptibility in patients with an atopic constitution. Unfortunately, it is still unclear which kind of atopic patients have an increased skin susceptibility.

We investigated 3 groups of individuals with an atopic constitution: (i) patients with active atopic dermatitis (AAD); (ii) patients with inactive atopic dermatitis (IAD); (iii) patients with a history of respiratory atopy (RA).

Most previous studies found increased basal TEWL values in individuals with IAD (10–12, 22). However, our results indicate that IAD did not influence the basal TEWL. This may fit with the findings that the basal TEWL does not correlate with Diepgen's atopy score (23). The difference between our and previous results may be explained by the fact that our tested individuals had not had any active AD for the past 2 years, so their AD may have been 'burned out' for years. Besides, these results stress the importance of clear-cut defi-

Table 1. Basal, post-SLS and Δ (post-basal) values of TEWL

	Active atopic dermatitis (AAD)	Inactive atopic dermatitis (IAD)	Respiratory allergy (RA)	Controls
basal-TEWL	8.6 $\pm$ 3.6	7.1 $\pm$ 2.1	7.2 $\pm$ 1.2	8.3 $\pm$ 3.3
post-SLS-TEWL	25.4 $\pm$ 9.1*	19.6 $\pm$ 8.6	17.4 $\pm$ 7.2	17.9 $\pm$ 8.2
Δ -values	16.8 $\pm$ 9.0*	12.5 $\pm$ 8.9	10.2 $\pm$ 7.2	9.6 $\pm$ 7.7

TEWL: transepidermal water loss (g/m² h). Mean $\pm$ standard error; *significant difference to the control group ($p \leq 0.05$).

nitions of atopy, when comparing different studies. Individuals with AAD showed a slightly increased basal TEWL reflecting a subclinical disturbance of the epidermal barrier. This supports other studies, which have found (statistically significant) increased basal TEWL values in patients with AAD (24, 25). Clearly, the severity of dermatitis is of importance in investigating skin susceptibility (11). Hence, for a comparison between different studies on atopic patients, the use of a clinical score system, e.g. SCORAD, would be helpful.

However, regarding increased skin susceptibility, a history of previous chronic irritant dermatitis is definitely of importance, as the basal TEWL of these individuals is significantly higher as compared to healthy controls (26).

Concerning TEWL after SLS testing, recent studies did not show any significant differences in skin susceptibility between patients with IAD and healthy controls (12, 22). Even a study of Basketter et al., with ranges of concentrations and exposure times, showed virtually no differences between atopic persons (without differentiation of the severity of their dermatitis) and healthy controls (27). However, most previous studies (where mainly volunteers with AAD were investigated) resulted in dissimilar findings (6, 7, 10, 28). These discrepancies could probably be explained by varying definitions of atopy or atopic dermatitis. Concerning the definition of an atopic constitution, numerous conditions have been demanded. Mostly, lesions of atopic dermatitis must be visible (11, 29), though sometimes a history of affected skin only or a history of respiratory allergy is sufficient as a criterion (10, 30). Even the 2 widely used lists of criteria of atopy (or atopic dermatitis), proposed by Hanifin & Rajka (31) and by Diepgen et al. (18, 19), differ from each other.

In this study, the definition of Diepgen was employed, and only patients with AAD showed increased skin susceptibility to the detergent SLS. Individuals with IAD, who did not show any eczematous lesions but belonged to the group of atopics, did not show an increased skin susceptibility (12, 22). There is clearly a difference in skin susceptibility between individuals without signs of dermatitis (IAD), and individuals with active atopic dermatitis (AD).

For the investigation of skin susceptibility, the atopy score according to the definition of Diepgen might not be sufficient: volunteers with an atopic constitution can be differentiated by the activity of their dermatitis in a group with increased skin susceptibility to SLS (AAD) and a group without increased skin susceptibility to SLS (IAD). Individuals with AAD may have a disturbed epidermal barrier, even in clinically unaffected areas. This skin is more susceptible to irritants like SLS, leading to a faster induction of hand dermatitis in atopic individuals. For further investigations, a clear distinction between these 2 groups is hence required. The limitation of the atopy score was recently emphasized by Gehring et al. (32) as well.

The influence of respiratory allergies on the skin susceptibility of atopic individuals has likewise been controversial. Enhanced susceptibility to irritants has been found by some authors (10, 33), but there are also opposite findings (14). Our study suggested that patients with RA did not show abnormal skin irritability. The reason for the discrepancies between our and earlier studies could be a defined seasonal time of testing. We performed the study in winter, and none of the volunteers had features of rhinoconjunctivitis. So the burden of the skin with aeroallergens was relatively low. This seems to be important, because it has been shown that the epidermal barrier is disrupted by aeroallergens during atopy patch testing (34). Perhaps the skin of atopic patients becomes more susceptible to irritants when it is simultaneously exposed to clinically relevant aeroallergens. Indeed, Nassif et al. (6) demonstrated an increased skin susceptibility in patients with RA suffering from rhinoconjunctivitis at the time of testing.

The influence of the season on the skin susceptibility may, however, be very complex. Apart from RA, Tupker et al. (17) showed an increased skin susceptibility in atopic patients in the winter season, suggesting an influence of dry air in winter. We consider, in addition, that skin susceptibility in patients with RA may also be influenced by the degree of the aeroallergen burden. Thus, pollen allergy may provide additional factors responsible for susceptible skin in spring and summer. On the other hand, patients with allergy to indoor allergens (e.g., mite dust) may have such soreness over the whole year.

Furthermore, Tupker et al. (11) demonstrated that the intensity of the skin response to irritants and bioactive agents is correlated to the disease severity. Hypothetically, the skin susceptibility of individuals with IAD and RA is not primarily increased, but the susceptibility to irritants and to allergens will increase as soon as the skin becomes eczematous and somewhat impaired. This could in turn be induced by the endogenous activity of atopy or by relevant aeroallergens resulting in a reduced epidermal barrier.

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