

An evaluation of the relationship between 'atopic skin' and skin irritability in metalworker trainees

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Skin hyperirritability to irritants as well as atopy are considered to be predisposing factors for contact dermatitis. The aim of the study was to evaluate whether these predictive factors are independent or whether they are so closely related that one could possibly replace the other. 205 metalworker trainees underwent skin examination for skin atopy, including standardized questionnaire, clinical examination of the skin and a series of skin irritability tests. These tests included measurements of transepidermal water loss (TEWL) before and after irritation with 3 different irritants: sodium lauryl sulfate (SLS), dimethylsulfoxide (DMSO) and sodium hydroxide (NaOH). The results of the linear regression analysis demonstrate that skin atopy is not associated with increased skin irritability, as assessed by the irritability testing methods presented.

Key words: skin irritancy; irritant contact dermatitis; transepidermal water loss; sodium lauryl sulfate; dimethylsulfoxide; sodium hydroxide; atopy score. © Munksgaard, 1997.

Accepted for publication 21 January 1997

Skin hyperirritability and atopy are considered to be predisposing factors for contact dermatitis. A better understanding of these factors and their independence may therefore help to predict contact dermatitis more precisely in the future (1-8).

Tests for skin irritability induce experimental irritant contact dermatitis (ICD) and assess skin reactivity to chemical stimuli either clinically or by bioengineering methods, such as measurement of transepidermal water loss (TEWL). One method of inducing experimental, TEWL-controlled ICD is patch testing with sodium lauryl sulfate (SLS) (9, 10). Other methods are the modification of the alkali resistance test (10) and the dimethylsulfoxide (DMSO) test (11). The relationship between atopy and skin irritability has so far been investigated by comparing patients with atopic eczema to normal controls or to patients with other types of skin disease (5, 6). Patients with atopic eczema were found to react more severely to SLS than healthy controls, as assessed by TEWL measurements (9, 11). However, besides atopic eczema, other criteria of skin atopy have to be considered. Such criteria were evaluated recently by Diepgen & Fartasch (1). As a result, they proposed a score that sums up a series of atopic features (Table 1), indicating the probability of skin atopy. The aim of the study presented was to investigate the relationship between

skin atopy as proposed by Diepgen et al. (1, 2) and skin irritability, as assessed by the series of skin irritability tests mentioned above.

Patients and Methods

Study population

205 male metalworker trainees, from 15 to 20 years of age, from 19 different companies in eastern Switzerland, participated in the study. Within 18 weeks of the start of their training, they underwent dermatological examination, composed of standardized history, clinical evaluation of the skin and tests for irritability of the skin. Information on the atopic history of the family, personal atopic history and signs of atopy (e.g., Hertoghe sign, xerosis, wool intolerance) were used to calculate a score of skin atopy as proposed by Diepgen et al. (1, 12). Irritancy exposure of the job was assessed according to a method proposed by Hinnen & Elsner (13).

Applications

Induction of irritation by SLS. On the medial 1/3 of the flexor side of the forearm, 50 µl of 0.5% aqueous solution (w/v) of sodium lauryl sulfate (SLS, high purity, Sigma, St. Louis, MO) in Finn

Chambers (inner diameter 1.2 cm, Epitest Ltd., Hyrlä, Finland) were applied for 23 h. A control site (application of a 0.9% aqueous solution of NaCl (w/v, also in Finn Chambers) was chosen on the same forearm, close to the SLS application site.

DMSO test. 50 µl of 90% and 95% dimethylsulfoxide (90%,95%: aq. solution, v/v) were pipetted at exactly defined sites on the medial 1/3 of the forearm and left there for 5 min by means of plastic blocks. To obtain reliable measurements of TEWL, the application area (21–32 mm) was chosen to be greater than that proposed by Frosch (11).

Modified alkali resistance test. 0.1 ml 0.2 mol/l NaOH (aqueous solution, w/v) were applied to the skin on the medial 1/3 of the forearm for 5 min, at the same time as the DMSO test, by means of plastic blocks (21 to 32 mm) (14).

Measurements

Transepidermal water loss (TEWL). TEWL was measured with an evaporimeter (Tewameter, Courage & Khazaka, Cologne, Germany). TEWL measurements were performed before applications of the test substances and afterwards, following the recommendations for measurements of TEWL of Pinnagoda et al. (8). Before measurements, subjects had rested for the least 15 min. For irritation induced by SLS, TEWL measurements after the challenge phase were made 1 h after removal of the challenge patch test. TEWL measurements following the application of NaOH or DMSO were performed 5 to 10 min after the irritants had carefully been wiped off. As TEWL rises with increasing skin temperature (15), we also measured the skin temperature and converted the TEWL measured to a standard temperature of 30°C. The effect of the challenge tests on TEWL was expressed by calculating delta (Δ)-TEWL values (TEWL_{after irritation}-TEWL_{before irritation}).

Experiments were performed within a period of 16 weeks in the fall of 1994. Room temperature varied between 21–24°C, relative humidity between 33–60%.

Statistics

Data were analyzed by means of a statistical package (SPSS for the Macintosh, SPSS, Chicago, IL) on an Apple Macintosh computer. A multivariate regression analysis was performed to evaluate the relation between skin irritability and atopy score, as well as the single components of the score. 4 regression models were created, choosing Δ -TEWL after irritation by NaOH, DMSO90%,

DMSO95% or SLS as dependent variable. Confounding factors, like exposure to metalworking fluids (MWF), skin care/protection and domestic irritancy exposure, were also included in the models.

Results

Information on atopic history was collected from all 205 participants and all were examined for clinical signs of skin atopy. According to atopy score, 6% of the participants had skin atopy (≥ 10 points) and in 16% skin atopy was likely (7–9 points) (Table 1). Results of skin irritancy testing are given in Table 2. Results of DMSO 90% and DMSO 95%

Table 1. Atopic history and atopy signs in 205 metalworker trainees

	No (%)	Yes (%)	No answer (%)	
Basic features				
Family history of atopy:				
eczema	86	13	1	
rhinitis/asthma allerg.	74	26	0	
Personal atopy history:				
flexural eczema	94	5	1	
rhinitis/conjunctivitis allerg.	78	22	0	
asthma allerg.	90	10	0	
facial erythema	95	2	3	
itch when sweating	87	12	1	
intolerance to wool	67	30	3	
metal sensitivity	96	3	1	
light sensitivity	89	10	1	
food intolerance	95	5	0	
Minor features:		uncertain (%)		
xerosis	94	5	1	
ear rhagade	95	1	4	
dyshidrosis	98	2	0	
pityriasis alba	98	2	0	
pulpitis sicca	94	5	0	
nipple eczema	100	0	0	
perlèche	65	35	0	
white dermographism	97	3	0	
acrocyanosis	95	5	0	
Atopic stigmata	no (%)	not sure (%)	sure (%)	strong (%)
hyperlinear palms	66	1	30	3
Herthoge's sign	98	0	2	0
dirty neck	98	0	2	0
keratosis pilaris	77	0	15	8
Dennie- Morgan fold	65	2	28	5
infraorbital fold	74	2	19	5
AD of scalp	97	1	2	0
	0-6 points (%)	7-9 points (%)	more than 10 points (%)	
Total	78	16	6	

0–6 points: atopy unlikely, 7–9 points: possible atopy, >10 points: high probability of atopy

Table 2. TEWL before and after irritation (r^2 : coefficient of determination; *: $p < 0.05$; **: $p < 0.001$)

	TEWL			Correlation TEWL _{before} - TEWL _{after} r^2
	mean	SD	median	
DMSO, 90% ($n=205$)				
before	9.8	3.6	10.0	
after	12.2	3.4	12.3	
Δ -TEWL	2.4		2.3	0.682**
DMSO, 95% ($n=205$)				
before	9.8	3.6	10.0	
after	13.2	3.8	13.2	
Δ -TEWL	3.4		3.2	0.627**
NaOH, 0.2 mol/l ($n=205$)				
before	9.8	3.6	10.0	
after	19.9	6.6	19.4	
Δ -TEWL	10.1		9.4	0.420**
SLS, 0.5% ($n=186$)				
before	11.4	10.2	10.7	
after	16.4	5.9	15.8	
Δ -TEWL	5.0		5.1	0.156*
NaCl, 0.9% ($n=186$)				
before	11.4	10.2	10.7	
after	11.7	3.9	11.5	
Δ -TEWL	0.3		0.1	0.231*

Table 3. Relationship between atopy score and TEWL increase of irritation ($n=196$)

Dependent variable: Δ -TEWL after irritation	Coefficient of determination (r^2)	p
irritation by NaOH	0.028	0.241
irritation by DMSO 90%	0.054	0.029*
irritation by DMSO 95%	0.065	0.012*
irritation by SLS	0.034	0.196

*Significant at the level of 0.05.

testing did significantly correlate, though the other tests did not, probably indicating that the 3 tests investigated are not equivalent for determining the individual susceptibility to chemical irritants (16).

Table 3 presents the results of multivariate regression analysis evaluating the relationship between atopy score and skin irritability. Taking into account important confounding factors like MWF exposure and skin care, insignificant or only weak correlations were found between the 2 parameters. The relationship between single atopic features and skin irritability was analysed by means of a model that included all atopic features (Table 1) separately. Most of these features were not correlated at

all with the results of the different tests of skin irritability, some showed very weak correlation with part of the tests (xerosis, keratosis pilaris, history of asthma and light sensitivity) (data not presented in Table 3).

Discussion

Atopic dermatitis is considered to be related to increased irritability of the skin. Van der Valk & De Jong (17) and Agner (18, 19) found enhanced skin reactivity to SLS in patients with current atopic dermatitis compared to controls (17–19). Frosch (11) described an increased irritability to DMSO in patients with chronic atopic dermatitis compared to healthy controls (11). Moreover, Tupker et al. (20) reported an increased susceptibility to irritants in 20 patients with healed atopic dermatitis.

Considering these reports, the results of our study are somewhat surprising, since linear regression analysis demonstrated that skin atopy was not associated with increased irritability, as assessed by the irritant testing presented. However, the population in our study differs significantly from those of the above-mentioned authors, all our subjects being young and healthy. Applying the criteria for skin atopy defined according to Diepgen et al. (1, 2), only in a proportion of them was atopic skin detected.

We conclude that the relationship between skin atopy in healthy subjects and skin irritability differs significantly from that between atopic dermatitis and irritability of the skin. Skin atopy and skin irritability seem to be independent factors. This finding indicates that information on atopy as well as on skin irritability has to be collected in order to include all risk factors for hand eczema.

Acknowledgements

The present study is part of the ongoing Prospective Metal Workers' Eczema Study (PROMETES) performed in cooperation between the Department of Dermatology and of Social and Preventive Medicine, University of Zürich. We acknowledge support by the Swiss Accidents Insurance (SNAI) and by the Swiss National Foundation.

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