

The MOAHLFA index of irritant sodium lauryl sulfate reactions: first results of a multicentre study on routine sodium lauryl sulfate patch testing

WOLFGANG UTER¹, JOHANNES GEIER², DETLEF BECKER³, JOCHEN BRASCH⁴ AND HARALD LÖFFLER⁵ FOR THE GERMAN CONTACT DERMATITIS RESEARCH GROUP (DKG) AND THE INFORMATION NETWORK OF DEPARTMENTS OF DERMATOLOGY (IVDK)*

¹Department of Medical Informatics, Biometry and Epidemiology, University of Erlangen-Nürnberg, D-91054 Erlangen, ²Centre of the Information Network of Departments of Dermatology, Institute at the University of Göttingen, D-37075 Göttingen, ³Department of Dermatology, University of Mainz, D-55101 Mainz, ⁴Department of Dermatology, University of Kiel, D-24105 Kiel, and ⁵Department of Dermatology, Philipp-University, D-35033 Marburg, Germany

In a multicentre study of the German Contact Dermatitis Research Group, sodium lauryl sulfate (SLS) 0.25% and 0.5% aq. has been added to routine allergen patch tests to assess its properties as a convenient diagnostic indicator of individual susceptibility to irritation at the time of patch testing. Previous studies indicated that irritant SLS reactivity may be related to individual factors such as age and sex. As these factors are, in turn, among the important predictors of contact allergy to many allergens, e.g. summarized in the 'MOAHLFA index', the impact of the MOAHLFA factors on irritant SLS patch test reactivity, and thus a potential for confounding, was assessed in the 5971 participating patients. As a result of 2 logistic regression analyses with an irritant reaction to 0.25% and 0.5% SLS, respectively, as outcome, male sex was identified as a relatively weak but significant risk factor (OR 1.38), while age 40 years or older was an even weaker risk factor (OR 1.22 and 1.15, respectively). Upon detailed analysis, no clear age gradient could, however, be identified. 1-day exposure time almost halved the odds of an irritant SLS reaction. In conclusion, this type of SLS patch test can be regarded as robust, indicating individual irritability relatively independent from the individual factors analysed here.

Key words: individual susceptibility; irritant reaction; patch testing; sodium lauryl sulfate.
© Blackwell Munksgaard, 2004.

Accepted for publication 17 September 2004

Routine patch testing with the irritant sodium lauryl sulfate (SLS), supplemental to diagnostic

patch testing with allergens, has recently been advocated as an aid to the interpretation of certain erythematous, possibly infiltrated allergen patch test reactions as presumably irritant (in case of an irritant reaction to SLS) or probably allergic (if no reaction to SLS was observed), at the time of patch test reading, in addition to the well-introduced post hoc validation processes such as ROAT, threshold testing, etc. (1) A distinct impact of ambient meteorological conditions on SLS reactivity has already been identified (2), supported by bioengineering results (3). However, the question remains whether SLS reactivity might also be related to the well-known individual determinants of the spectrum of allergens, in terms of exposure or susceptibility surrogates, namely, the components of the MOAHLFA index (Table 1) (4).

*The following IVDK centres contributed data (in alphabetical order): Augsburg (A. Ludwig), Berlin Charité (T. Zuberbier, M. Worm), Dortmund (P. J. Frosch, C. Pirker, R. Herbst), Essen (U. Hillen), Freudenberg (Ch. Szliska), Graz (W. Aberer, B. Kränke), Halle (G. Gaber, D. Lübke), Hamburg (M. Kiehn, R. Weißbecher), Heidelberg (U. Jappe, M. Hartmann), Kiel (J. Brasch), Krefeld (M. Lilie, A. Wallerand, S. Wassilew), Lübeck (J. Grabbe), Mainz (D. Becker), Marburg (I. Effendy, H. Löffler), München Schwabing (M. Agathos), Nürnberg (I. Müller), Osnabrück (S. M. John, H. J. Schwanitz, N. Schürer), Rostock (H. Heise), Ulm (P. Gottlöber, G. Staib, H. Pillekamp, R. Hinrichs).

Table 1. Comparative demographic characteristics of patients with irritant reaction to SLS (0.25% and 0.5%, respectively), tested July 2001 to June 2003, supplemented with results of a logistic regression analysis; additionally adjusted for the final diagnosis irritant contact dermatitis

			0.25% SLS positive (n = 1345)		0.5% SLS positive (n = 2114)	
		Tested (n = 5971)(%)	%	OR (95% CI)	%	OR (95% CI)
Male	M	38.0	44.0	1.38 (1.21–1.56)*	42.8	1.38 (1.24–1.55)*
Occupational dermatitis	O	14.5	17.2	1.16 (0.95–1.41)	15.7	1.03 (0.86–1.23)
Atopic dermatitis	A	17.2	18.1	1.06 (0.91–1.25)	17.8	1.05 (0.91–1.22)
Site: hand†	H	28.0	30.8	0.88 (0.61–1.30)	29.2	0.89 (0.63–1.25)
Site: leg†	L	11.6	11.8	0.85 (0.57–1.27)	11.4	0.84 (0.59–1.20)
Site: face†	F	13.8	13.9	0.86 (0.59–1.28)	13.5	0.86 (0.61–1.22)
Age 40+	A	66.3	68.1	1.22 (1.06–1.40)*	67.3	1.15 (1.02–1.30)*
Duration of patch test exposure (1 day versus 2 days)		22.1	14.2	0.52 (0.44–0.62)*	16.3	0.58 (0.50–0.66)*

*Significant ($P < 0.05$).

†Additional sites contained in model to allow full coding: arm, feet, head (excluding face) or neck, trunk with axillae, ano-genital (as reference), other and missing site.

In the case of such an association, some confounding of the relationship between irritation to SLS and allergen reactivity would be expected, i.e. consideration of age, sex, etc., when interpreting allergen patch test reactions in the light of the SLS reaction would be mandatory. Hence, an adjusted, multifactorial analysis addressing the independent impact of these patient characteristics on irritant SLS patch test reactions was performed.

Methods

Between July 2001 and June 2003, 5971 patients were patch tested with SLS 0.25% and 0.5% SLS in water (aq.) routinely, in addition to diagnostic allergen patch testing, by members of the German Contact Dermatitis Research Group (DKG). In 17 departments (5145 patients), small Finn Chambers® (Epitest, Tuusula, Finland) were used as carrier for the allergens and the SLS (20 µl). In the remaining 2 departments, Haye's test chambers (Haye's Service BV, Rotterdam, The Netherlands) were used (826 patients). Allergen preparations were purchased from Hermal, Reinbek, Germany. An aqueous stock solution of SLS (Sigma Chemicals, Steinheim, Germany, 99% purity) was prepared at the Department of Dermatology, Philipp University of Marburg. Dilutions for patch testing were prepared and sent out to the participating centres at 6-month intervals. Application time was 48 hr in 4652 patients (conducted by 14 centres) and 24 hr in 1319 patients (conducted by 5 centres), and application site was the upper back. Patch tests were read at least after 48 hr (D2) and 72 hr

(D3). Test reactions to allergens were documented following the ICDRG recommendations and DKG guidelines (5), and skin reactions to SLS were evaluated according to the proposal of the Standardization Group of the European Society of Contact Dermatitis (6), which was slightly modified (7). 3723 reacted to neither concentration, 134 only to 0.25%, 903 only to 0.5% and 1211 to both concentrations at D3 (72 hr after start of exposure), using a scoring system presented in (1). Exposure time was 24 hr in 22.1% of patients and 48 hr in the remainder. Detailed results of the study of the DKG are being published elsewhere (7). The association between irritant reaction to SLS (any degree) and the MOAHLFA factors and the duration of patch test exposure, respectively, was quantified by the mutually adjusted odds ratios (ORs), accompanied by profile likelihood-based CIs, derived from logistic regression analysis (SAS, version 8.2, SAS Institute, Cary, NC, USA). In the logistic regression model, we adjusted for irritant contact dermatitis as final diagnosis to account for a potential confounding effect of this diagnosis on, for example, the effect estimate of occupational causation.

Results

The association between SLS reactivity and the factors analysed is mostly weak and non-significant (Table 1), with 3 exceptions: the risk of an irritant reaction to SLS is significantly increased in males and in older patients, respectively, and significantly decreased in those patients exposed

for only 1 day. Interestingly, the 2 concentrations do not differ much in these respects, although irritant reactions to 0.5% SLS were much more common than to 0.25%. It can be seen that, for most factors, the crude proportions show a greater departure from the average for those positive to 0.25% than for those reacting to 0.5%.

Discussion

Our study addresses a particular, clinically relevant aspect of the routine use of SLS patch testing together with diagnostic allergen patch testing, which has been evaluated by a large study of the DKG under real-life conditions, i.e. including several centres, multiple observers and both 24- and 48-hr exposure time (7). While these somewhat diverse conditions will introduce some random variation, the massive impact of exposure time is very clearly conceivable from our analysis: the odds of an irritant SLS reaction about double with doubled exposure time (Table 1, last row), in accordance with previous findings (8). However, the focus of this paper is an analysis of the association between SLS reaction and the factors of the MOAHLFA index, and not a consideration of the methodological variation and other, more general aspects of supplemental SLS patch testing (7); our assessment has been adjusted for the potentially confounding effect of exposure time by means of multifactorial analysis.

Irritability to SLS, which has been found to be related to irritability to certain allergens, seems to be an individual property only weakly associated with most known determinants of the spectrum of allergens (MOAHLFA factors). In other words, as a measure of current individual susceptibility to irritation at the time of patch testing, the irritant SLS patch test reaction appears to be quite independent of these factors and thus uniformly useful in different contact dermatitis patients.

One exception regarding this robustness is male sex, which is in contradiction to early results of Lammintausta et al. (9, 10), but in line with more recent experimental observations (11) and epidemiological results in hairdressing apprentices (12). In contrast, the seemingly increased risk of an irritant reaction to occlusively applied SLS in patients age 40 years or older (using our very crude dichotomous categorization) does contradict the study using short-term irritation already quoted (11) and other evidence (13, 14). Analysing our data using a finer age categorization (10 years intervals), significant heterogeneity was observed only regarding 0.25% SLS ($P=0.027$, likelihood ratio χ^2 test), albeit without significant

age gradient (Cochran-Armitage trend test, data not shown). Hence, a clear association between age and SLS reactivity, with the mode of application chosen here, could not be demonstrated.

Further analyses of SLS patch test results will surely increase our understanding of the relationship between individual factors, environmental conditions, SLS reactivity and allergen reactivity, including possible intra-individual fluctuation of SLS patch test results that we were unable to address. For the time being, as a practical consequence, the huge impact of patch test exposure duration must be considered when relating irritant SLS patch test reactions to allergen reactivity. The MOAHLFA factors seem to be less important, possibly with the exception of sex, according to these first results, which should be critically re-evaluated in future studies.

References

1. Geier J, Uter W, Pirker C, Frosch P J. Patch testing with the irritant sodium lauryl sulfate (SLS) is useful in interpreting weak reactions to contact allergens as allergic or irritant. *Contact Dermatitis* 2003; 48: 99–107.
2. Uter W, Hegewald J, Pfahlberg A, Pirker C, Frosch P J, Gefeller O. The association between ambient air conditions (temperature and absolute humidity), irritant sodium lauryl sulfate patch test reactions and patch test reactivity to standard allergens. *Contact Dermatitis* 2003; 49: 97–102.
3. Löffler H, Happle R. Influence of climatic conditions on the irritant patch test with sodium lauryl sulfate. *Acta Derm Venereol* 2003; 83: 338–341.
4. Schnuch A, Geier J, Uter W et al. National rates and regional differences in sensitization to allergens of the standard series. Population adjusted frequencies of sensitization (PAFS) in 40,000 patients from a multicenter study (IVDK). *Contact Dermatitis* 1997; 37: 200–209.
5. Schnuch A, Aberer W, Agathos M, Brasch J, Frosch P J, Fuchs T, Richter G. Leitlinien der Deutschen Dermatologischen Gesellschaft (DDG) zur Durchführung des Epikutantests mit Kontaktallergenen. *Hautarzt* 2001; 52: 864–866.
6. Tupker R A, Willis C, Berardesca E, Lee C H, Fartasch M, Agner T, Serup J. Guidelines on sodium lauryl sulfate (SLS) exposure tests. A report from the Standardization Group of the European Society of Contact Dermatitis. *Contact Dermatitis* 1997; 37: 53–69.
7. Löffler H, Becker D, Brasch J, Geier J. Simultaneous sodium lauryl sulfate testing improves the diagnostic validity of allergic patch tests. Results from a prospective multicentre study of the German Contact Dermatitis Research Group (Deutsche Kontaktallergie-Gruppe, DKG). *Br J Dermatol* (accepted for publication).
8. Aramaki J, Löffler C, Kawana S, Effendy I, Happle R, Löffler H. Irritant patch testing with sodium lauryl sulfate: interrelation between concentration and exposure time. *Br J Dermatol* 2001; 145: 704–708.
9. Lammintausta K, Maibach H I, Wilson D. Irritant reactivity in males and females. *Contact Dermatitis* 1987; 17: 276–280.
10. Goh C L, Chia S E. Skin irritability to sodium lauryl sulfate – as measured by skin water vapour loss – by sex and race. *Clin Exp Dermatol* 1988; 13: 16–19.
11. Robinson M K. Population differences in acute skin irritation responses. Race, sex, age, sensitive skin and repeat subject comparisons. *Contact Dermatitis* 2002; 46: 86–93.

12. Uter W, Pfahlberg A, Gefeller O, Schwanitz H J. Hand dermatitis in a prospectively-followed cohort of hairdressing apprentices: final results of the POSH study. Prevention of occupational skin disease in hairdressers. *Contact Dermatitis* 1999; 41: 280–286.
13. Coenraads P J, Bleumink E, Nater J P. Susceptibility to primary irritants: age dependence and relation to contact allergic reactions. *Contact Dermatitis* 1975; 1: 377–381.
14. Cua A B, Wilhelm K P, Maibach H I. Cutaneous sodium lauryl sulfate irritation potential: age and regional variability. *Br J Dermatol* 1990; 123: 607–613.

Address:

Wolfgang Uter, MD
Department of Medical Informatics, Biometry and
Epidemiology
Friedrich Alexander-Universität Erlangen-Nürnberg
Waldstr. 6
91054 Erlangen
Germany
Tel: +49 9131 8522720
Fax: +49 9131 8522721
e-mail: wolfgang.uter@rzmail.uni-erlangen.de