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A Dose-response Study of Irritant Reactions to Sodium Lauryl Sulphate in Patients with Seborrhoeic Dermatitis and Atopic Eczema

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The susceptibility of the skin of patients with seborrhoeic dermatitis to surfactant irritation was investigated and compared to that of a group of normal subjects and patients with a history of atopic eczema. Responses to six concentrations of sodium lauryl sulphate (SLS), applied to forearm skin, were assessed clinically and measured by laser Doppler flowmetry. Analysis of dose-response curves showed statistically significant increased susceptibility to SLS-induced irritation in patients with seborrhoeic dermatitis and atopic eczema compared with normal subjects. Increased susceptibility to chemical irritation may be important in the pathogenesis of seborrhoeic dermatitis.

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An increased susceptibility of the skin to the effects of physical and chemical injury is said to occur in patients with seborrhoeic dermatitis (1–3), and it has been postulated that this contributes to exacerbation and persistence of the disease (4) and a high incidence of "contact" dermatitis (5). There is, however, little experimental data concerning irritant responses in patients with this disorder (6–8). Although it has been established that the yeast *Pityrosporum ovale* is the cause of seborrhoeic dermatitis (9), the pathogenic mechanism is not known. Irritant responses may be important, however, as enzymes from the yeast can liberate fatty acids (10) which may produce a local irritant effect. The purpose of the present study was to establish whether patients with seborrhoeic dermatitis have an increased reactivity to chemical irritation compared with normal subjects and patients with atopic eczema, a disorder which is considered to be associated with an enhanced sensitivity to irritation (11). Objective measurements of the inflammatory response were made, allowing study of the dose-response relationship for chemical irritation in individual patients.

PATIENTS AND METHODS

Patients

Three groups of patients were studied.

Seborrhoeic dermatitis. Thirteen patients (7 males, age range 20 to 37 years, mean 29 years) with seborrhoeic dermatitis of the face. No patient had a history of previous atopic eczema.

Atopic eczema. Thirteen patients (7 males, age range 16 to 35 years, mean 24 years) with a history of mild to moderate eczema mainly localized to the antecubital or popliteal fossae within the previous 8 years and the presence of positive prick tests to common inhaled allergens. Apart from 2 patients, with a localized patch of eczema on the antecubital or popliteal fossae, patients were clear of all eczema at the time of testing.

Control subjects. Seventeen subjects, (8 males, age range 16 to 35 years, mean 27 years) were recruited from a group of new patients attending the skin department with localized skin tumours, or hospital employees who volunteered to participate in the study. None had a history of atopic eczema or inflammatory skin disease.

Exposure to irritants

Aliquots of 15 µl of six concentrations (4%, 2%, 1%, 0.5%, 0.25%, 0.125%) of SLS (99% purity BDH), and distilled water as a control, were placed on filter paper discs, inserted into 8 mm Finn chambers and secured onto the volar surface of the non-dominant forearm. These covered an area of 15 cm^2, the position kept constant with the two lowest contrations of irritant positioned approximately 10 cm distal to the radial styloid process. Patches were removed after 48 h and responses measured after a further 24 h.

Assessment of response

At 72 h (i.e. 24 h after the test doses were removed) the lowest concentration of SLS to produce an erythematous response was recorded and triplicate measurements of blood flux were made at each site using a laser Doppler flowmeter (Periflux-Pf2, Perimed, Sweden). The output from the flowmeter was relayed to a chart recorder and measured for a period of at least 30 seconds at each site after a steady state had been achieved. The mean deflection during this time on the chart recorder was estimated visually (12).

Analysis of results

For each patient the mean increase in blood flux over that recorded for the control site was plotted against the logarithm of the concentration of SLS. A logit function was fitted to these data using an iterative least squares technique (13). The maximum slope of this function was calculated, and also the dose required to result in an increase in blood flux over a background level of 0.125 volts ($D_{0.125}$). An increase in blood flux of 0.125 volts approximately corresponded to "just detectable erythema" (clinical score of +1). Differences in slope and $D_{0.125}$ values for the three groups were analysed using one way analysis of variance and the *t*-test. The Kruskal-Wallis test was used to analyse the significance of any observed differences in visually assessed responses between groups.

RESULTS

Of the 43 patients studied, one, a male from the control group (number 17) showed no reaction to any dose of SLS. For purposes of statistical analysis the smallest dose of SLS to produce a visible response and $D_{0.125}$ in this subject was taken as 4%.

Visual assessment

The smallest dose to produce erythema was significantly different between groups ($p = 0.019$, Kruskal-Wallis test) (Table

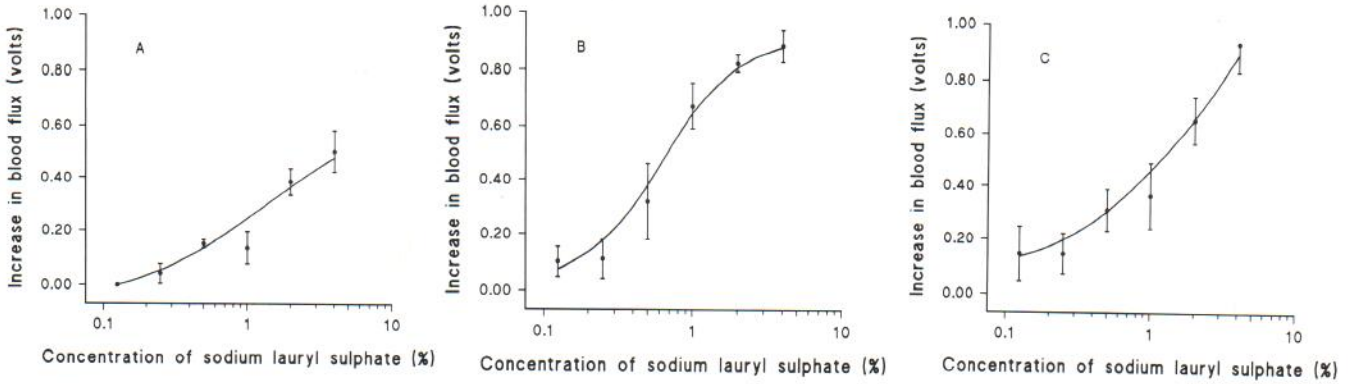

Fig. 1. Representative dose-response curves for (A) normal control subject, (B) seborrhoeic dermatitis patient and (C) atopic eczema patient. The mean (SD) increase in blood flux over background levels is plotted against log concentration of SLS. The solid line drawn through the data points is the logit function obtained by the iterative least squares technique.

I). Irritant reactions occurred at a significantly lower dose in patients with a history of atopic eczema compared to normal subjects ($p = 0.006$). Patients with seborrhoeic dermatitis also reacted at a lower dose compared to normal subjects but this difference was not statistically significant ($p = 0.13$).

Blood flux response

Fig. 1 shows representative dose-response curves in 3 patients. Analysis of variance showed a significant difference in $D_{0.125}$ between the three groups ($p = 0.016$), with mean $D_{0.125}$ for patients with atopic eczema significantly lower than normal subjects ($p < 0.01$, *t*-test), (Table I). The mean $D_{0.125}$ for patients with seborrhoeic dermatitis was also significantly lower than normal subjects ($p = 0.05$). Analysis of variance showed no significant difference in slope of response for the three groups.

The mean $D_{0.125}$ was significantly lower in female patients compared to male patients in the atopic eczema ($p < 0.05$) and control groups ($p < 0.05$).

DISCUSSION

We have shown that patients with seborrhoeic dermatitis and atopic eczema have an increased irritant reactivity to SLS compared with normal control subjects. Objective measurement allowed detection of a significant difference in irritant response between the patients with seborrhoeic dermatitis and the control group that was not apparent using conventional visual grading.

Although quantitative techniques to measure skin reactivity to irritants are now used widely, the response to one or two concentrations of irritant is usually assessed, rather than to a range of doses. Construction of a full dose-response curve for individual patients should yield more information than study

Table I. *Visual threshold, $D_{0.125}$ and the slope values for the three groups of patients*
NR = no response

Patient number	Normal subjects			Atopic eczema			Seborrhoeic dermatitis		
	Visual threshold (% SLS)	$D_{0.125}$ (% SLS)	Slope (relative units)	Visual threshold (% SLS)	$D_{0.125}$ (% SLS)	Slope (relative units)	Visual threshold (% SLS)	$D_{0.125}$ (% SLS)	Slope (relative units)
1	F 0.125	0.04	381	F 0.125	0.07	149	M 0.125	0.18	177
2	F 0.125	0.53	235	F 0.125	0.14	160	F 0.125	0.13	182
3	F 0.25	0.34	329	M 0.125	0.23	174	F 0.125	0.05	109
4	F 0.25	0.21	170	F 0.125	0.35	87	M 0.125	0.19	176
5	M 0.25	0.37	226	M 0.125	0.58	96	F 0.25	0.54	204
6	M 0.25	1.22	255	M 0.125	0.06	106	M 0.25	0.10	104
7	M 0.5	0.63	187	F 0.125	0.03	115	F 0.25	0.20	174
8	F 0.5	0.31	247	M 0.25	0.25	140	M 0.5	0.71	222
9	F 0.5	0.56	102	M 0.25	0.57	159	F 0.5	0.55	75
10	F 0.5	1.74	94	M 0.25	0.54	244	M 1.0	1.16	165
11	F 1.0	0.90	339	F 0.25	0.13	250	F 1.0	1.28	263
12	M 2.0	1.84	364	F 0.5	0.50	183	M 1.0	0.51	101
13	M 2.0	1.81	49	M 1.0	0.82	478	M 2.0	0.80	163
14	M 2.0	0.89	128						
15	F 2.0	0.60	70						
16	M 2.0	1.34	578						
17	M 4	4	NR						
	0.5 (median)	1.02 (mean)	235 (mean)	0.125 (median)	0.33 (mean)	180 (mean)	0.25 (median)	0.49 (mean)	163 (mean)

of a single point. Laser Doppler flowmetry, as used in the present study, has been shown to detect a clear relationship between the applied dose of SLS, the recorded blood flux values and the corresponding clinical scores (14, 15). The groups were compared by calculating for each patient the dose of SLS required to produce an increase in blood flux of 0.125 volts, an objective measurement of response that corresponds approximately to just detectable erythema (clinical grade +1). The fact that the $D_{0.125}$ and not the slope of the dose-response curves differed significantly between the three groups of patients suggests a difference in susceptibility to SLS but a common mechanism for the irritant response.

Atopic skin is considered to be vulnerable to dermatitis because of its diminished threshold for irritation (11). Although there has been lack of agreement in earlier studies concerning general irritant reactivity (16), our results are in keeping with previous reports of an increased sensitivity to detergents (17, 18).

Although irritant contact dermatitis is commoner in females than in males, studies of experimentally induced irritation with surfactants have yielded conflicting results. Goh & Chia (19) reported an increased sensitivity in female compared with male patients while Björnberg (20) and Lammintausta et al. (21) recorded no statistically significant sex differences to patch tests with SLS. Although an overall increased sensitivity to irritation was seen in females compared to males in the present study, this difference was not significant in patients with seborrhoeic dermatitis.

Although patients with seborrhoeic dermatitis have been considered to have an increased sensitivity to irritation, to date there is little experimental evidence to support this view and no quantitative studies examining irritant reactivity have been performed. Although in the present study there was no significant difference in visually assessed response to SLS between patients with seborrhoeic dermatitis and normal controls, the change in blood flux was significantly greater, demonstrating the value of objective measurement of response.

The factors that determine this increased sensitivity to irritation in patients with seborrhoeic dermatitis are not clear. The contribution of an abnormal barrier function, which is an important determining factor in surfactant irritation (22), is not known; however dry skin, which may be associated with an increased susceptibility to irritation (18), was not obvious clinically in the patients with seborrhoeic dermatitis that we studied. As surfactants are among the commonest irritants implicated in hand eczema (23), an increased incidence of irritant contact eczema in patients with seborrhoeic dermatitis might be expected. It has been suggested that patients with seborrhoeic dermatitis are bad "industrial risks" and have an increased incidence of contact eczema (1, 5). Although Hug (6) found varying degrees of seborrhoeic dermatitis in 76% of patients with irritant dermatitis compared to 24% of patients with otherwise normal skin, a recent study of patients with seborrhoeic dermatitis failed to show any significant increase in hand eczema compared to controls (NC Cowley, unpublished observations).

Whether the increased sensitivity to SLS reflects a general tendency to irritation in seborrhoeic dermatitis is not clear. Björnberg (24) has shown that it is not possible to predict the strength of reaction to one irritant by knowing the strength of reaction to another irritant. However, the possibility of an inherent susceptibility to irritation in these patients may be of importance in the pathogenesis of the disease. *Pityrosporum ovale,* the causative organism in seborrhoeic dermatitis (9), possesses lipolytic ennzymes and has been shown to play a part in the breakdown of lipids on the skin when the number of C. acnes bacilli is low (10), as is the case in dandruff and seborrhoeic dermatitis (25). Fatty acids are irritant when applied to the skin (26), and the possibility that patients with seborrhoeic dermatitis may be more sensitive to these effects compared to unaffected individuals requires investigation.

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