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CLINICAL REPORT

Are Adverse Skin Reactions to Cosmetics Underestimated in the Clinical Assessment of Contact Dermatitis? A Prospective Study among 1075 Patients Attending Swedish Patch Test Clinics

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It is known that cosmetics and skin care products can cause adverse skin reactions. However, the frequency of adverse reactions reported to the Medical Product Agency (MPA) in Sweden is low. The purpose of the present study was to evaluate the occurrence of adverse skin reactions to cosmetics among patients referred for standard patch testing owing to suspected contact dermatitis in general, most frequently hand eczema. Consecutive patients at four patch test clinics in Sweden were invited to participate; 1075 were included. Of these, 47.3% (54.2% women and 30.8% men) reported current or previous adverse skin reactions to cosmetics and skin care products. This group showed significantly more positive patch test reactions, a higher prevalence of atopic dermatitis and the dermatitis was more frequently located in the face and neck region. Our results show that patients referred for standard patch testing have – or have had – a large proportion of self-reported adverse reactions to cosmetics or skin care products. We conclude that among patients with suspected contact dermatitis, adverse reactions to cosmetics can be a more important aetiological and/or complicating factor than is commonly acknowledged and that the reporting of such reactions to the MPA probably can be improved. ***Key words: contact dermatitis; patch testing; cosmetics and skin care products; adverse reactions; contact allergy.***

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Contact dermatitis and contact allergy are common problems in the general population (1–3). In developed countries the use of cosmetics and skin care products has increased. In Sweden, the total sales increased by more than 143% from 1986 to 2001 (Table I). During recent decades we have become aware that cosmetics and skin care products (products and ingredients) can cause both allergic and irritant contact dermatitis (4–7). In a recent population-based study it was found that 51.4% of the women and 38.2% of the men considered themselves to have sensitive skin and of these 57% and 31.4%, respectively, had experienced side effects from using cosmetics or skin care products (8).

In an attempt to exercise control of cosmetics and skin care products and provide greater safety for Swedish consumers, a control system was introduced in 1989 at the Medical Products Agency (MPA) (9). This includes a voluntary adverse reaction reporting procedure for cosmetics and skin care products (10).

Compared with the expected number of adverse reactions to cosmetics in the Swedish general population (5), very few side effects have been reported to the MPA (9). Most reports concern cases with positive patch tests to the suspected products, thus excluding the probably most common group of consumers – those who experience irritant reactions. In order to gain more knowledge about adverse reactions to cosmetics, the MPA has initiated studies on the use, adverse effects and contact allergy elicited by these products. In a previous study (5), 1077 young people were asked to fill in a questionnaire about their use and adverse effects of cosmetics and skin care products during the preceding 5 years. Of these, 18% of the women and 6% of the men reported that they had experienced such adverse effects. They were interviewed personally and

Table I. *Total sale of cosmetics and skin care products in Sweden**

Year	Sales in 10^9 SEK
1986	3.7
1991	4.8
1999	>8.0
2000	>8.7
2001	>9.0

*The Swedish Cosmetic, Toiletry and Detergent Association, Hygiene and skin care products in Sweden (personal communication).

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offered patch testing with the TRUE Test™ standard panel (5).

The present study was performed to determine (i) the occurrence of adverse skin reactions to cosmetics among patients referred for standard patch testing and (ii) the prevalence of contact allergy among these patients. Consecutive patients referred for standard patch testing at four Swedish dermatology clinics were invited and interviewed concerning their use and possible adverse effects of cosmetics. The standard test panel and a new panel comprising 12 cosmetic allergens was used to establish whether complementary addition of test substances would be relevant.

MATERIALS AND METHODS

Patients

The study was performed over a period of 15 months, starting in September. Four Swedish patch test clinics participated: University Hospital, Uppsala; Karolinska Hospital, Stockholm; Sahlgrenska University Hospital, Gothenburg and Ryhov Hospital, Jönköping. A total of 1075 patients accepted and were included. The study was approved by the medical ethics committee, Uppsala University.

Questionnaires and clinical information

The patients filled in a self-administered questionnaire concerning their use of cosmetics and skin care products and reported suspected current or previous adverse reactions to such products (5). At the time of patch testing, the responsible dermatologist completed the questionnaire, inserting information about the location of the dermatitis and any history of atopy. At the time of patch testing, 61.1% of those reporting adverse reactions to cosmetics had active dermatitis compared to 66.4% among the others. Furthermore, 26.3% and 22.1%, respectively, had dermatitis during the preceding 3 months. The most frequently reported locations of dermatitis were hands (50%), face (25%), arms (16%), around the eyes (10%) and trunk (10%).

Patch testing

The Finn chamber™ technique (11) was used except in Uppsala, where the TRUE-test™ was employed (12) supplemented with Finn chambers. The patients were patch-tested with the Swedish standard series and an additional test series consisting of 12 substances related to cosmetic and skin care products (Table II). In Gothenburg and Uppsala, thiomersal was included in the standard series ($n=741$). Two new fragrance mixes (TF1 and TF2) were included. Perfume mix I (TF1) contained anethole 3%, anisyl alcohol 3%, benzaldehyde 3%, benzyl alcohol 1%, benzyl benzoate 1% and benzyl salicylate 1% in petrolatum, while Perfume mix II (TF2) consisted of coumarin 1%, dihydrocoumarin 1%, lilial 1%, majantol 1% and sanalol-α 1% in petrolatum (13).

The patch tests were applied to the upper back for 48 h, read at 72 h and most tests (85.8%) were also evaluated a second time, on days 5–7 according to the international rules. Reactions 1+, 2+ and 3+ were regarded as positive. Irritant (IR) or doubtful (?) reactions were combined as IR for statistical analysis.

Statistical analysis

A software package, Statistica 5.5™ from Statsoft, Tulsa, USA, was used for the analysis. To compare different patient groups, χ^2 analysis was applied and correlations were evaluated with the Spearman rank correlation test. ANOVA was used to test the age distribution between different patient groups. A p value <0.05 was considered significant.

RESULTS

Of 1075 patients included in the study, 509 (47.3%) reported present or previous adverse reactions to cosmetics or skin care products (AR group), while 308 (28.7%) reported no such reactions (NoAR group). A third group, 21.6% ($n=232$), did not know (DnK group) and 26 persons (2.4%) did not answer this question (NA group). Significant differences were found in age distribution between the four groups, showing a shift towards older persons in the AR group. There were significantly more females ($n=760$) than males ($n=315$) participating. A significant difference

Table II. *Results of patch testing with the additional series*

Test substance	Females	Males	Total	IR/doubtful
2-Bromo-2-nitropropane-1,3-diol 0.25 % in petrolatum	1.2	0.6	1.0	0.1
DMDM-hydantoin 2% in water	1.3*	0.0	0.9	0.7
Imidazolidinurea	1.2	1.0	1.1	0.4
Perfume mix I (TF1)	0.3	0.0	0.2	0.1
Perfume mix II (TF2)	1.2	1.0	1.1	0.6
Butyl methoxydibenzoylmethane 2% in petrolatum	0.0	0.0	0.0	0.1
4-Methylbenzylidenecamphor 2% in petrolatum	0.1	0.0	0.1	0.0
Benzophenone-3 2% in petrolatum	0.0	0.3	0.1	0.2
Octyl methoxycinnamate 2% in petrolatum	0.0	0.0	0.0	0.4
Cocamidopropylbetaine 1% in water	2.4	3.8	2.8	6.5
Propyl gallate 1% in petrolatum	0.8	0.6	0.7	0.1
Melaleuca alternifolia (tea-tree oil) 5% in alcohol	3.0	1.9	2.7	3.1

The percentage of positive reactions (+, ++, +++) is given; INCI names are given except for the Perfume mixes. Statistical comparison of females vs males is also given. *$P<0.05$; $n=1075$. INCI, International Nomenclature of Cosmetic Ingredients; DMDM-hydantoin, 1,3-dimethylol-5,5-dimethyl hydantoin; IR, irritant reaction.

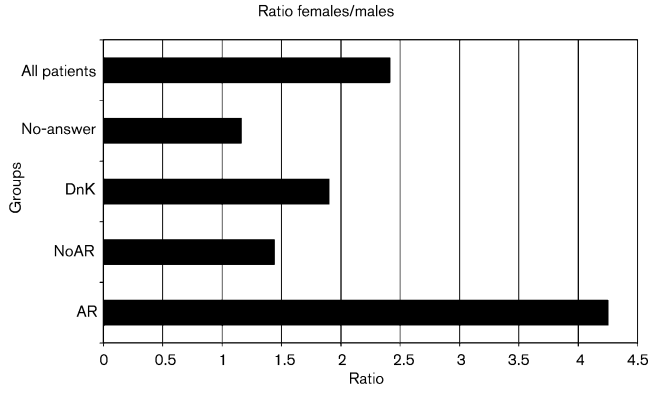

Fig. 1. Ratios between the number of females and males in the different groups of patients. AR, adverse reactions; NoAR, no adverse reactions; DnK, do not know.

was observed in the male/female ratio between the groups (AR, NoAR, DnK, NA) with 54.2% of the females (412 persons) in the AR group compared with 30.8% of the men (97 persons) (Fig. 1).

Patients with present or previous atopic dermatitis reported significantly more adverse reactions (37.3% vs 23.8%). Those in the AR group had dermatitis in the face and neck region significantly more often than those in the NoAR group. There were no differences regarding other body locations.

The reported daily use of cosmetics and skin care products for the whole study population ($n=1075$) is presented in Table III. The products reported to be suspected of causing skin problems are listed in Table IV. Reported adverse skin symptoms are given in Fig. 2.

In the patch test evaluation, 561 persons had positive tests (57% of AR, 48% and 47% of NoAR and DnK groups, respectively). There were significantly more positive patch tests in the AR group and among females. The test results for the additional test series are given in Table II. Twenty-five of all tested persons (2.3%) reacted only to allergens in the additional cosmetic series (11 AR, 9 NoAR, 5 DnK). Regarding individual test substances, there was no significant difference between the groups in the patch test results, except for the preservative DMDM-hydantoin, which elicited a higher frequency of positive reactions in the AR group.

When testing with the additional test series, we obtained positive test reactions for all but one test substance and very low frequencies for the sunscreen components (Table II). Of those with positive tests to

Table IV. *Products reported to be causing adverse skin reactions; percentage of persons reporting adverse skin reactions to cosmetics and toiletries ($n=509$: 412 females, 97 males)*

Product group	Females	Males	Total
Eye make-up	47.4	0.0	38.4
Soaps	32.4	31.3	32.2
Deodorants	26.8	46.9	30.6
Moisturizers and cleansers	32.0	12.5	28.3
Hair care products (e.g. shampoos/balsams)	22.4	21.9	22.3
Perfumes/aftershave	20.0	26.0	21.1
Facial foundations	20.0	2.1	16.6
Sunscreens	11.7	3.1	10.1
Lipstick	7.6	0.0	6.1
Hair dyes	5.9	2.1	5.1
Intimate hygiene products	4.9	0.0	4.0
Hair permanents	4.6	0.0	3.8
Hair removal products	3.4	1.0	3.0
Shaving products	1.2	9.4	2.8
Nail varnish	2.9	1.0	2.6
Toothpaste	2.2	0.0	1.8

Table III. *Reported daily use of different products*

Product group	Females	Males	Total	AR group
Toothpaste	97	96	97	98
Soaps	92	93	92	92
Deodorants*	81	61	75	80
Moisturizers and cleansers*	78	45	69	74
Eye make-up (mascara, eyeliner, etc.)*	57	<1.0	41	50
Hair care products (e.g. shampoos, balsams)	39	53	43	41
Perfumes, aftershaves	40	32	38	40
Lip make-up (lipsticks, lipgloss, lipsalve)*	41	<1.0	29	34
Facial foundations (powders, rouge, etc.)*	30	0	21	27
Shaving products	1	24	8	6
Nail varnish*	6	<1.0	5	6
Personal hygiene products*	6	<1.0	5	16
Hair dyes*	1	<1.0	<1.0	1
Depilatories*	<1.0	<1.0	<1.0	<1.0
Hair permanent wave solutions	1	<1.0	<1.0	<1.0

Percentages for the whole group ($n=1075$) and the AR group ($n=509$) are given. A significant variation between the different groups of patients (AR, NoAR, DnK, others) in the use of some products was found (*) with the highest reported use in the AR group (χ^2 test, $P<0.05$). AR, adverse reactions; NoAR, no adverse reactions; DnK, do not know.

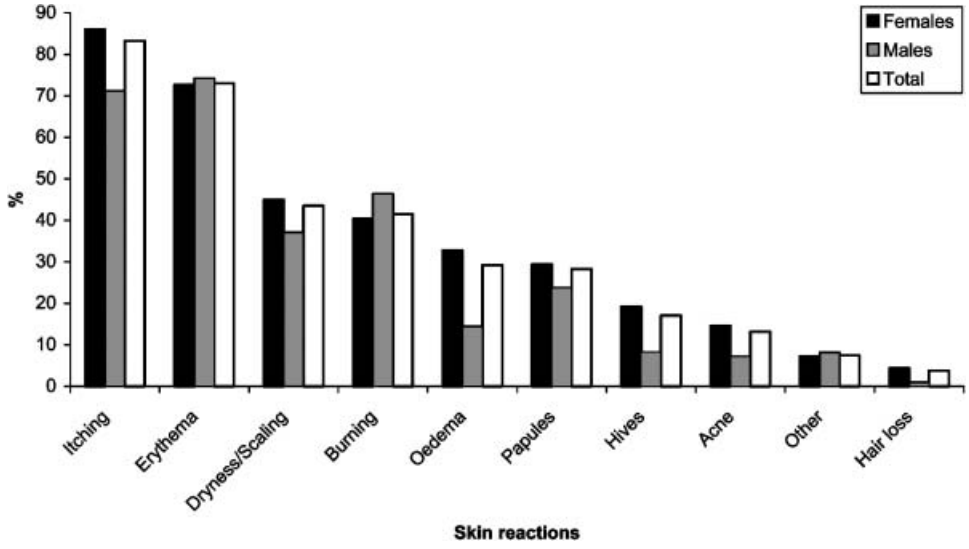

Fig. 2. Reported adverse reactions: percentage of number of persons with reported reactions ($n = 509$).

Quaternium 15, 28% also reacted to formaldehyde. The corresponding figures were diazolidinylurea for 55%, imidazolidinurea 66%, DMDM-hydantoin 40%. We also found a few positive reactions to the two new fragrance mixes. Patch testing with tea-tree oil and cocamidopropyl-betaine elicited a high frequency of positive test reactions, but also frequent irritation (Table II). There was no correlation between positive reactions to colophony and tea-tree oil.

DISCUSSION

The present study demonstrates that patients referred for standard patch testing have – or have had – a large proportion of self-reported adverse reactions to cosmetics or skin care products. Adverse reactions were significantly associated with sex (females), atopic dermatitis, increased number of positive patch tests, and dermatitis on face and neck, thus confirming previous reports (5, 14, 15). There were also differences in the reported use of cosmetics and skin care products. Although we cannot exclude a bias in the willingness of patients at the patch test clinics to participate in the study, our results do indicate that adverse reactions to cosmetics and skin care products can be an important aetiological and/or complicating factor in cases of suspected contact dermatitis.

Patch testing did not reveal any major differences between the patient groups, except for DMDM-hydantoin. However, among those reporting adverse reactions we found significantly more positive test reactions. This can in part be explained by the higher age and the preponderance of women in this group, as contact dermatitis and contact allergy are more common among women, and are more common with increasing age (1, 3, 16). In this context it is important to note that men also have high frequencies of positive patch tests to fragrances and that the gender difference noted is not dependent on these substances. It was interesting to see that by adding 12 substances related to cosmetic and skin care products, we could identify 25 persons not reacting to the standard series, yet only 44% of these had reported adverse reactions. Formaldehyde releasers are not completely covered by testing with formaldehyde in the standard series (17–19). Our findings are in agreement with this. The tested sunscreen components elicited very few positive reactions. When testing with sunscreens, a photo patch test should always be performed in addition to standard patch tests (20). In the present study we did not perform further testing with the components of the two new fragrance mixes used. Several of the components of these mixes were also recognized as important allergens (21). Obligatory labelling of these ingredients has been proposed within the EU. Of the two new fragrance mixes added, the TF2 mix elicited 1.1% positive reactions. This mix contains some of the fragrances under discussion for inclusion as new substances in the standard series (22).

We found that atopy was more common in the AR group. It has been reported that the function of the skin barrier is defective in atopic dermatitis, increasing the risk of developing contact dermatitis of the irritant type (23–26). Atopy itself is not considered to be associated with an increased predisposition to develop contact allergy. However, it has been suggested that the combination of a defective barrier and a frequent application of skin care products and pharmaceuticals intended for skin treatment could increase the risk of developing contact allergy to such products.

The reported use of cosmetics and skin care products differed between the patient groups. The AR patient group reported a higher daily usage compared with all participants (Table III). This indicates that an increased use of cosmetics carries increased risk for adverse effects.

It has been shown that contact sensitivity to cosmetic-related allergens is increasing (2, 14, 27, 28).

Application of products or substances to the skin surface can elicit both irritant and allergic reactions. It is also conceivable that persons with known risk factors for contact dermatitis (i.e. known atopic dermatitis and established contact allergies) are more likely to experience adverse reactions to cosmetics and skin care products. However, the frequency of reported side effects of cosmetics in Sweden is low.

In conclusion, patients referred for standard patch testing because of eczema report a high incidence of adverse effects to cosmetics or skin care products (or their components). This suggests that adverse reactions to such products can constitute a more serious aetiological and/or complicating factor for a current dermatitis than is commonly recognized. It is therefore important to include exposure to such products in the patient's case history and to discuss this aspect in the preventive information given to eczema patients. The results also indicate that there is a need for an improved system regarding the reporting of adverse effects to the MPA.

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