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Patch Testing with Markers of Fragrance Contact Allergy

Do Clinical Tests Correspond to Patients' Self-reported Problems?

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The aim of the present study was to investigate the relationship between patients' own recognition of skin problems using consumer products and the results of patch testing with markers of fragrance sensitization. Eight hundred and eighty-four consecutive eczema patients, 18–69 years of age, filled in a questionnaire prior to patch testing with the European standard series. The questionnaire contained questions about skin symptoms from the use of scented and unscented products as well as skin reactions from contact with spices, flowers and citrus fruits that could indicate fragrance sensitivity. A highly significant association was found between reporting a history of visible skin symptoms from using scented products and a positive patch test to the fragrance mix, whereas no such relationship could be established to the Peru balsam in univariate or multivariate analysis. Our results suggest that the role of Peru balsam in detecting relevant fragrance contact allergy is limited, while most fragrance mix-positive patients are aware that the use of scented products may cause skin problems. ***Key words: questionnaire; cosmetic allergens; multivariate analysis.***

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The fragrance mix was introduced for patch testing in the late 1970s (1). Bonnevie began routine patch testing with Peru balsam in 1939 to detect sensitization to topical preparations containing Peru balsam (2). Since then it has been used as a screening agent for perfume allergy (3, 4). A high prevalence of patch test reactions to the fragrance mix and/or Peru balsam has been reported in many studies of eczema patients. In a recent German multicentre study of 9,835 patients, 15.3% were positive to the fragrance mix and 8.3% to Peru balsam (5). The aims of the present study were to investigate the frequency of self-reported adverse reactions to scented products among consecutive eczema patients and to describe the relationship of this personal awareness to diagnostic patch testing.

MATERIAL AND METHODS

Study population

Prior to patch testing, 925 consecutive eczema patients, aged 18 to 69 years, were invited to participate in the study. It took place in a 4-month period at two hospital departments of dermatology and two private clinics from the 3 main parts of Denmark: Seeland, Funen and Jutland. Nine hundred (97.3%) of the invited patients accepted to participate. It is estimated that about 20,000 diagnostic patch tests are performed per year in Denmark; thus the sample in this study comprised 10–15% of all patients tested in the study period. Approval from the regional ethics committees was obtained as well as written informed consent from each participant.

Patch test materials

The European standard patch test series from Hermal was used in 3 centres and the True test panels 1 and 2 (Pharmacia) in 1 centre (Odense). Peru balsam and the fragrance mix were included in both series as markers of fragrance sensitization. Peru balsam was tested as 25% in pet. (Hermal) or 800 μg/cm^2 (True test). The fragrance mix consisted of 8 fragrance materials: cinnamic aldehyde, cinnamic alcohol, α-amyl cinnamic aldehyde, eugenol, isoeugenol, geraniol, hydroxycitronellal and oak moss each 1% in pet. together with the emulsifier sorbitan sesquioleate 5% (Hermal). In the True test the perfume mix had an identical composition of fragrance materials and was tested in 450 μg/cm^2 .

Questionnaire

A self-administered questionnaire was used to obtain information about patient characteristics and adverse reactions experienced by patients in conjunction with the use of scented products. Three questions dealt with visible skin reactions to scented products (Table I: question 3 abc). They pertained to rash associated with the use of scented products, and whether the patients believed scented products had caused or aggravated their eczema. A question about subjective skin symptoms or asthma/rhinitis related to scented products was also included (Table I: question 4). Rash from contact with flowers, spices or citrus fruits was included as a possible indicator of fragrance sensitivity (Table I: questions 5–7). A question about rash from unscented products was used as a control. A pilot test of the questionnaire was performed by personal interview of 20 eczema patients, and it was further tested by 10 dermatological nurses and 10 eczema patients. The questionnaire was given to the 900 patients prior to patch testing and collected again before the patch test was read.

Patch testing

The patches were applied to the upper back and left for 2D. Readings were taken D2/D3 and in most cases also D5/7. A positive reaction and thus the presence of contact allergy was defined as at least erythema and infiltration as required by the ICDRG (6). In case several readings were taken, the maximum reaction was recorded and used in the analysis.

Data handling, definitions and statistics

Two different outcomes were studied. In the first analysis, fragrance sensitivity was studied as outcome defined either as a positive patch test response to the fragrance mix or to Peru balsam (Tables I and II). The relationship between these markers of fragrance allergy and patient characteristics (sex, age, atopy) as well as possible indicators of fragrance sensitivity in the patients' history were studied.

In the second analysis, the reporting of skin symptoms to either scented or unscented consumer products was studied as outcome. An analysis was made of the possible influence of atopy and sensitization to potential cosmetic allergens from the standard series (Table III).

A crude analysis of the association between the outcome and the separate variables was carried out by means of the chi-square test or – if appropriate – Fisher's test (Tables I and III).

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(OR : 2.02), young age (OR: 1.34), childhood dermatitis with a flexural distribution (OR : 1.86), sensitivity to fragrance mix (OR: 2.38) and methylchloroisothiazolinone/methylisothiazolinone (MCI/MI) (OR : 2.8) were significantly associated with skin symptoms to scented products (Table III). Contact allergy to the preservatives MCI/MI and parabens showed the strongest association with rash from unscented products (OR: 3.65 and 7.26, respectively). There was no correlation between sensitivity to the fragrance mix or Peru balsam and rash from unscented products (Table III).

DISCUSSION

In this study 11.5% of eczema patients had a positive patch test response to either the fragrance mix or Peru balsam. We found a highly significant association between a history of visible skin symptoms from using scented products and a positive reaction to the fragrance mix, whereas no such relationship could be established to Peru balsam (Table II). The three questions concerning the occurrence of rash, cause and/or aggravation of skin disease from scented products were mutually related but also supplemented each other in detecting cases with a positive history. A simultaneous application of all three questions was used to improve the ability to identify cases with a positive history of fragrance sensitivity. Furthermore the questions indicated different stages in the progression of skin disease from an initial rash to persistent skin symptoms and subsequent aggravation by specific exposures. Previous studies have shown that a history of perfume dermatitis and fragrance mix sensitivity tend to coincide (7, 8). We found that a history of adverse skin reactions to perfumed products was significantly associated with fragrance mix sensitivity at all stages of developing skin disease, as indicated by the three questions (Table II). In addition, the influence of possible confounders such as atopy, sex and age was taken into account in the multivariate analysis.

Peru balsam is a complex mixture of resinous compounds and an essential oil. It is included in the European standard patch test series as an indicator of fragrance allergy. However, in this study we were unable to demonstrate a significant relationship between any of the questions on adverse skin reactions to scented products and Peru balsam sensitivity (Table II). Previously, Peru balsam was found to be of limited value in detecting sensitivity to a range of essential oils (9) and frequently sold fine fragrances (10). The composition of perfumes is subject to changes in fashion. Peru balsam itself has been banned from consumer products by The International Fragrance Association since 1974. Peru balsam contains fragrance materials and undoubtedly indicates fragrance sensitivity in some cases (4, 11, 12). However, the value of testing with Peru balsam in addition to the fragrance mix seems to be limited in the detection of relevant perfume contact allergy.

Questions on rash from contact with spices, plants or citrus fruits were included (Table I). Spices may contain some of the same allergens present in the fragrance mix or Peru balsam (13) and concomitant reactions are seen (14). The same applies to compositae allergy and reactions to the fragrance mix/Peru balsam (15). In this study neither problems with spices nor problems with plants indicated allergy to fragrance mix or Peru balsam. Hjorth showed that hand dermatitis from contact with orange peel was associated with reactions to Peru balsam (3). We found that the chance of being allergic to Peru balsam was 4 times higher in the group of subjects with previous rash from citrus fruits than in subjects without rash. This finding is interesting, considering that Peru balsam is primarily regarded as an indicator of fragrance sensitivity and that in the present study Peru balsam-positive subjects had no more recognized problem with using scented products than Peru balsam-negative subjects.

About half of the patient population stated that they had a history of rash caused by a scented product, and about 10% had a rash from an unscented product (Table III). The great majority of individuals in an American study were able to correctly interpret their adverse reactions to cosmetic products (16). Rash may be caused by consumer products for several different reasons other than fragrance materials, such as contact allergy to preservatives, dyes, emulsifiers or lipids. Irritant effects of cosmetics and cleaning agents are also well recognized. The sensitivity of the questions on adverse skin reaction to perfumed products in relation to fragrance mix sensitization was 76.9%, and the specificity was 52.4%. Similar questions have been used in other studies concerning adverse reactions to cosmetics and only in a minority of cases has contact allergy been verified (17, 19). The inclusion in our study of adverse reactions to cleansing agents may have affected the specificity of the questions, as many irritant reactions may have been reported. Undetected cases of perfume contact allergy may also be expected in the study population (10).

The European standard patch test series includes 9 allergens, which may be present in consumer products. The possible role of these 9 allergens in relation to a current or previous history of a rash caused by consumer products was studied in the second analysis (Table III). Sensitization to the fragrance mix and the preservative MCI/MI proved to have the strongest association with reporting skin symptoms from scented products ($p=0.0007$ and $p=0.04$, respectively). In comparison, sensitization to the preservatives MCI/MI and parabens was significantly related to reporting rash from unscented products ($p=0.01$ and 0.04, respectively), while fragrance sensitivity had no importance in this regard. In a study of an unselected Danish population sample, 3.7% were found to be sensitive to one or more of the above-mentioned 9 standard allergens, which may be found in cosmetic products. The fragrance mix and Peru balsam most frequently gave rise to positive patch test results, followed by preservatives (17). In an American study of patients with cosmetic dermatitis, fragrances and fragrance ingredients were responsible for the largest number of reactions (18). This is in accordance with the results of a Dutch study (19). The fact that we found similar results and that the reporting of a rash from unscented products was related to sensitivity to preservatives and not to fragrances indicates that the patients are generally able to identify specific products responsible for adverse skin reactions.

A question about flexural dermatitis in childhood was incorporated into the questionnaire. Even though the diagnosis of atopic dermatitis is complex, flexural dermatitis in childhood is a key feature and we had to rely on the memory of the patients in the current study. 13.9% of the eczema patients stated that they had flexural dermatitis in childhood (Table I). Most studies find a lower rate of contact sensitization in patients with atopic dermatitis (20). In our study, fragrance sensitization was no more common among those with a history of childhood flexural dermatitis than among those without such a history (Tables I and II). de Groot investigated a

sample of the general population and clients of beauticians (19). It was concluded that atopic individuals may have a greater risk of developing skin irritation from cosmetics. In the current study flexural dermatitis in childhood was found to be significantly related to reporting skin symptoms caused by both scented and unscented products (Table III).

Unlike most investigations on contact allergy, this study included information on the patients' own experiences and thereby provides a further development of methods used to evaluate allergic contact dermatitis from consumer products. We found a statistically significant agreement between the patients' own recognition of problems in the past and the results of patch testing with the fragrance mix. In addition, the current understanding that fragrance sensitization plays an important role in the spectrum of contact allergy to consumer products was substantiated. While a good correlation between patients' history of reactions to scented products and positive patch tests to the fragrance mix was found, no such relationship could be established for Peru balsam, indicating a limited role of Peru balsam in detecting relevant fragrance allergy.

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