

The diagnostic value of patch tests with two fragrance mix I preparations for detection of clinically relevant perfume allergy

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Sensitization to fragrances is common, with an estimated prevalence of approximately 1.6–3.7% (1–3). Since the late 1970s, fragrance mix I (FM I) has been used as a screening tool for fragrance contact allergy (4). Studies suggest that it detects 70–80% of patients who are allergic to fragrances (5). The aim of this study was to evaluate two different FM I test preparations for their ability to detect perfume contact allergy in consecutively tested eczema patients.

Patients and Methods and Results

All patients with suspected allergic contact dermatitis patch tested in the period May 2000 to September 2002 were included in the study. Prior to patch testing, the patients were placed into one of four groups by a nurse, according to their recollection of adverse reactions to perfumes or perfumed products:

- (1) Certain: has reacted with an itching dermatitis to at least one denominated fine perfume or aftershave, and has reacted to other perfumed products;
- (2) Probable: has reacted to one or more perfumed products (e.g. deodorant), but a certain perfume has not been identified as the cause of a clinical reaction;
- (3) Possible: has reacted to various cosmetic products with and without perfume; materials other than

fragrance constituents may be the cause of the reaction; and

- (4) None: has never reacted to a perfumed material.

In order to compare the diagnostic value of the fragrance mixes in this study, a gold standard for the diagnosis of fragrance contact allergy was defined on the basis of the questionnaire responses as a certain history of adverse reaction to fragrances. Thus, patients with a probable or possible history were excluded from further analysis.

The patients were patch-tested with two FM I perfumes: FM I 450 µg/cm² (TRUE Test®; MEKOS Laboratories A/S, Hillerød, Denmark), and FM I 8% pet. (Trolab®; Almirall Hermal, Reinbek, Germany). Finn Chambers® on Scanpor® tape were used for the pet.-based preparations. Patch tests were performed according to International Contact Dermatitis Research Group guidelines, and read on D3 and D5–7. Reactions from + to +++ were regarded as positive, and included in further analyses. At the last reading, the patch test result and relevance were assessed by a dermatologist.

Results

A total of 989 patients were patch tested. Of these, 40 were excluded from further analysis because of incomplete questionnaires or patch testing with only one of the preparations, giving a final study population of 949 patients (63% females and 37% males). A certain history of contact dermatitis caused by a specified perfumed product was found in 70 patients (7.4%), 92 (9.7%) had a probable history of adverse reactions to perfumes, 122 (12.9%) had a possible history of adverse reactions to perfumes, and 665 (70.1%) had no history of adverse reactions to perfumes.

A positive reaction to FMI TRUE Test® was found in 43 patients (4.5%), and a positive reaction to FM I Trolab®

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was found in 80 patients (8.4%). In total, 89 patient (9.4%) reacted to one or both of the perfume markers, and 34 reacted to both. The results, along with statistical calculation of sensitivity, specificity, and positive and negative predictive values, are shown in Table 1.

Discussion

It is well known that FM I is inadequate for screening for fragrance sensitivity, and reports have suggested that it may fail to diagnose as many as 33% of patients who are sensitive to fragrances (2). A self-assessed history of possible perfume allergy by the patient prior to testing is deliberately selected here as the gold standard for the diagnosis of fragrance allergy. Based on this premise, the statistical calculations are a tool with which to assess and compare the diagnostic values of the two fragrance mix preparations, FM I Trolab® and FM I TRUE Test®. Patch testing with FM I Trolab® has the highest sensitivity, and testing with FM I TRUE Test® has a slightly higher specificity and a higher positive predictive value (PPV). Consequently, when screening for a fragrance contact allergy, it is advantageous to test with both FM I preparations. However, the low sensitivity rates for both FM I preparations found in this study strongly support the use of additional fragrance allergens.

It is also important to note that the 7.4% prevalence of 'certain' perfume allergy (measured with a patient-assessed 'certain' history) in this study is a result of patch testing in a group of patients with suspected allergic contact dermatitis. If the FM I patch test is applied to large cohorts of the normal population, the PPV decreases dramatically, because of the relative increase in false-positive test results caused by the lower prevalence of perfume allergy in the general population (6).

To underline the diagnostic insufficiency of FM I, several trials have shown that the more fragrance allergens tested, the more positive reactions can be observed (7–9). Even with the improvement of the recent implementation of FM II in the European baseline series, the sensitivity of the screening tests are still undoubtedly far from 100% (10). The ever-changing and evolving composition of perfumes and fragranced products in general highlights the importance of researching and detecting new allergens (1). Also, additional diagnostic testing, such as patch testing with patients' own products, use testing, and repeated open application testing, is essential in patients suspected of having fragrance sensitivity, in order to close a potential diagnostic gap (11).

Table 1. Distribution of results for patch testing with FM I TRUE Test® and FM I Trolab® in the study population after exclusion of patients with a probable or possible history; results of calculations of sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and *p*-values

	History			Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	<i>p</i> -value
	Certain	No	Total					
FM I Trolab®								
Positive reaction	27	28	55	38.6% (35.1–42.1%)	96% (94.6–97.4%)	49% (45.4–52.6%)	94% (92.3–95.7%)	<i>p</i> -value < 0.001
Negative reaction	43	637	680					
Total	70	665	735					
FM I TRUE Test®								
Positive reaction	20	12	32	28.6% (25.5–31.7%)	98% (96.9–99%)	63% (59.5–66.5%)	93% (91.1–94.8%)	<i>p</i> -value < 0.001
Negative reaction	50	653	703					
Total	70	665	735					

References

- 1 Uter W, Geier J, Frosch P, Schnuch A. Contact allergy to fragrances: current patch test results (2005–2008) from the Information Network of Departments of Dermatology. *Contact Dermatitis* 2010; **63**: 254–261.
- 2 Nardelli A, Carbonez A, Ottoy W, Drieghe J, Goossens A. Frequency of and trends in fragrance allergy over a 15-year period. *Contact Dermatitis* 2008; **58**: 134–141.
- 3 Thyssen J P, Carlsen B C, Menné T, Johansen J D. Trends of contact allergy to fragrance mix I and Myroxylon pereirae among Danish eczema patients tested between 1985 and 2007. *Contact Dermatitis* 2008; **59**: 238–244.
- 4 Storrs F J. Fragrance. *Dermatitis* 2007; **18**: 3–7.
- 5 Van Oosten E J, Schuttelaar M L A, Coenraads P J. Clinical relevance of positive patch test reactions to the 26 EU-labelled fragrances. *Contact Dermatitis* 2009; **61**: 217–223.
- 6 Vecchio T J. Predictive value of a single diagnostic test in unselected populations. *N Engl J Med* 1966; **274**: 1171–1173.
- 7 Trattner A, David M. Patch testing with fine fragrances: comparison with fragrance mix, balsam of Peru and a fragrance series. *Contact Dermatitis* 2004; **49**: 287–289.
- 8 Johansen J D, Rastogi S C, Menné T. Contact allergy to popular perfumes; assessed by patch test, use test and chemical analysis. *Br J Dermatol* 1996; **135**: 419–422.
- 9 Frosch P J, Johansen J D, Menné T et al. Further important sensitizers in patients sensitive to fragrances. II. Reactivity to essential oils. *Contact Dermatitis* 2002; **47**: 279–287.
- 10 Uter W, Geier J, Schnuch A, Frosch P J. Patch test results with patients' own perfumes, deodorants and shaving lotions: results of the IVDK 1998–2002. *J Eur Acad Dermatol Venereol* 2007; **21**: 374–379.
- 11 Johansen J D. Fragrance contact allergy. A clinical review. *Am J Clin Dermatol* 2003; **4**: 789–798.