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Is methylisothiazolinone contact allergy a risk factor for polysensitization?

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Methylisothiazolinone (MI) is a preservative with a high allergenic potential that has been present in cosmetics, without methylchloroisothiazolinone (MCI), since the early 2000s, causing the current MI contact allergy 'epidemic' (1). The recommended concentrations in cosmetics have been recently revised by the Scientific Committee on Consumer Safety (2). Polysensitization can be defined as the presence of contact allergy to three or more unrelated allergens. The susceptibility to development of multiple contact allergies has been studied, and a genetic background has been suggested in those individuals who do not have high-risk exposures. The main goal of this study was to determine whether polysensitization is more frequent in patients with MI contact allergy, and its associated factors. Seven allergens have previously shown statistically significant positive associations with polysensitization (although these allergens are known for their weak positive reactions, and, in some cases, may be considered to be irritants), and five have shown negative associations (Table 1) (3).

Material/Methods and Results

A total of 1705 patients were consecutively patch tested in 2010–2013 with the European baseline

series, including MCI/MI 100 ppm and MI 500 and 2000 ppm (all aq.). Patch testing was performed with Finn Chambers® (8 mm; Epitest Ltd, Oy, Finland) on Scanpor® tape (Norgesplaster A/S, Alpharma, Vennesla, Norway). The patch test was placed on the upper back for 2 days, and read on D2, D3/D4, and D7, according to ICDRG guidelines.

Forty-six patients (2.7%) reacted to MI, 45 to both concentrations, one only to 2000 ppm, and 33 (1.9%) reacted to MCI/MI with no simultaneous reaction to MI. These two groups of patients, along with a sample of 100 randomly selected individuals with other contact allergies from the same period, were included in the study. The results are shown in Tables 1 and 2.

During the study period, 165 patients (9.6%) presented with polysensitization. Pearson exploratory chi-square testing yielded significant differences ($p < 0.05$) between groups regarding the proportion of polysensitized patients, the presence of concomitant reactions to allergens that are negatively associated with polysensitization, the products involved, and the relevance of the contact allergy (Table 1). However, after Bonferroni adjustment for multiple comparisons, only differences in polysensitization (on comparison of MI-allergic and MCI/MI-allergic with non-MI/MCI-sensitized patients) and the products involved (on comparison of MI-allergic with non-MI/MCI-sensitized and MCI/MI-allergic patients) remained significant.

Discussion

In the light of these results, polysensitization may be considered to be an important factor among MI-allergic patients, who show significant differences in the contact

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Table 1. Sample characteristics and the relevant statistical findings. Polysensitisation: contact allergy to 3 or more unrelated allergens

Variable	A	B	C	p-value*
Age in years [mean (SD)]*	47.0 (19.3)	39.5 (21.0)	48.6 (18.3)	
Female (%)	69.6	66.7	77.0	
Number of sensitizations including MI and MC/MI, resp.	1: 26.1%	1: 33.3%	1: 39.0%	
	2: 15.2%	2: 18.2%	2: 40.0%	
	3: 19.5%	3: 12.1%	3: 8.0%	
	>=4: 39.2%	>=4: 36.4%	>=4: 13.0%	
Polysensitized patients, no. (%)	27(58.7%)	16 (48.5)	21(21%)	A-C: p < 0.001 B-C: p = 0.002
Concomitant reaction to allergens positively associated with polysensitization ^a , no. (%)	13 (28.3)	12 (36.4)	34 (34.0)	p > 0.05
Concomitant reaction to allergens negatively associated with polysensitization ^b , no. (%)	15 (32.6)	16 (48.5)	55 (55.0)	A-C: p = 0.01 B-C: p = 0.002
Products involved	Cosmetics: 80.4% Cleansing: 19.6%	Cosmetics: 42.4% Cleansing: 9.1% Textile: 9.1% Other: 15.2% Unknown: 24.2%	Cosmetics: 24.0% Cleansing: 2.0% Textile: 16.0% Other: 43.0% Unknown: 15.0%	A-C: p < 0.001 A-B: p = 0.002 B-C: p = 0.04
Final diagnosis	ACD: 40 (87.0%) CA: 4 (8.7%) Other: 2 (4.3%)	ACD: 32 (97.0%) Other: 1 (3.0%)	ACD: 88 (88.0%) CA: 9 (9.0%) Other: 3 (3.0%)	
Relevance	Current: 89.1% Past: 2.2% Unknown: 8.7%	Current: 72.7% Past: 6.1% Unknown: 21.2%	No: 2.0% Current: 64.0% Past: 16.0% Unknown: 18.0%	A-C: p = 0.01 B-C: p = 0.16
Male, no. (%)	14 (30.4)	11 (33.3)	23 (23.0)	p > 0.05
Occupational, no. (%)	2 (4.3)	3 (9.1)	12 (12.0)	
Atopic dermatitis, no. (%)	12 (26.1)	7 (21.2)	19 (19.0)	
Hand, no. (%)	16 (34.8)	11 (33.3)	32 (32.0)	
Leg, no. (%)	6 (13.0)	4 (12.1)	11 (11.0)	
Face, no. (%)	14 (30.4)	6 (18.2)	20 (20.0)	
Age >40 years, no. (%)	26 (56.5)	17 (51.5)	69 (69.0)	

ACD, allergic contact dermatitis; CA, contact allergy; SD, standard deviation.

Group A: methylisothiazolinone (MI)-sensitized (n = 46: 11 only MI-sensitized; 35 MI-sensitized and methylchlorisothiazolinone (MCI)/MI-sensitized). Group B: MCI/MI-sensitized, and no MI positivity (n = 33). Group C: neither MI-sensitized nor MCI/MI-sensitized (n = 100).

^aAllergens positively associated with polysensitization: parabens mix, isopropylaminodiphenylamine, sesquiterpene lactone mix, cobalt chloride, wool alcohols, potassium dichromate, and *Myroxylon perei*.^bAllergens negatively associated with polysensitization: neomycin sulfate, *p*-phenylenediamine, epoxy resin, nickel sulfate, and primin.*Significant *p*-values after Bonferroni adjustment are in bold.**Table 2.** Analysis based only on polysensitized patients

Variable	A (n = 27)	B (n = 16)	C (n = 21)	p-value
Products involved	Cosmetics: 88.9% Cleansing: 11.1%	Cosmetics: 46.7% Textile: 6.7% Other: 26.7% Unknown: 20.0%	Cosmetics: 52.4% Cleansing: 0% Textile: 14.3% Other: 28.6% Unknown: 4.8%	A-C: p = 0.01 A-B: p = 0.02 B-C: p > 0.05
Final diagnosis	ACD: 27 (100%)	ACD: 15 (100%)	ACD: 20 (95.2%) CA: 1 (4.8%)	
Relevance	Current: 88.9% Past: 0% Unknown: 11.1%	Current: 73.3% Past: 6.7% Unknown: 20.0%	Current: 76.2% Past: 14.3% Unknown: 9.5%	p > 0.05
Male, no. (%)	8 (29.6)	4 (25.0)	4 (19.0)	p > 0.05
Occupational, no. (%)	2 (7.4)	3 (18.8)	1 (4.8)	
Atopic dermatitis, no. (%)	8 (29.6)	2 (12.5)	6 (28.6)	
Hand, no. (%)	8 (29.6)	6 (37.5)	4 (19.0)	
Leg, no. (%)	5 (18.5)	0 (0)	3 (14.3)	
Face, no. (%)	7 (25.9)	5 (31.3)	6 (28.6)	
Age >40 years, no. (%)	14 (51.9)	7 (43.8)	13 (61.9)	

ACD, allergic contact dermatitis; CA, contact allergy.

allergy sources: cosmetics are the most frequent products involved in MI allergy. This might explain why polysensitization among these patients predominantly involves allergens such as fragrances, preservatives, and especially formaldehyde and its releasers. Interestingly,

MI-allergic patients are less frequently sensitized to allergens negatively associated with polysensitization.

This study emphasizes the importance of MI as a relevant contact allergen, and its potential role as an individual allergen associated with polysensitization.

References

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