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Contact allergy to methyldibromoglutaronitrile and certain other preservatives

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Key words: allergic contact dermatitis; preservatives; cosmetics; paints; Euxyl K 400; methyldibromoglutaronitrile; dibromodicyanobutane; patch testing technique; imidazolidinyl urea; Germall 115. © Munksgaard, 1996.

Euxyl K 400 appeared to be a good substitute as a preservative for Kathon CG (Euxyl K 100) (1, 2). Euxyl K 400 is antimycotic and anti-bacterial and consists of a mixture of phenoxyethanol and methyldibromoglutaronitrile, in a ratio of 4:1 (3, 4). It was introduced to the European market in 1985 (5, 6). Contact allergy to methyldibromoglutaronitrile (dibromodicyanobutane) was first described in 1983 (7). Euxyl K 400 has been used as a preservative in latex paints and emulsions, adhesives, colouring agents and agents used in metal working since 1982, but its use in The Netherlands as a preservative in cosmetics and moist toilet paper is more recent (1988) (3).

Patients and Methods

At the Department of Dermatology of the Academic Hospital Rotterdam-Dijkzigt, patch tests were conducted in 1307 patients suspected of having allergic contact dermatitis, between 1 January 1993 and 31 May 1995. All patients ($n=1307$) (group 1) were patch tested with a standard series, including the preservatives Kathon CG, formaldehyde, quaternium 15 and the parabens mix. In addition, 1019 patients (group 2) of group 1 were also tested with the preservatives Euxyl K 400 (0.5% pet.) (Trolab), methyldibromoglutaronitrile (0.1% pet.), phenoxyethanol (1% pet.) and imidazolidinyl urea (2% pet.). Tests were scored according to accepted guidelines (8) and were read after 2 and 3 days.

Results and Discussion

A summary of the positive reactions to preservatives observed in both groups is presented in Table 1. In group 2 ($n=1019$), positive reactions to Euxyl K 400 (0.5% pet.) were observed in 24 patients, indicating a frequency in this group of 2.4%. In this study, all 24 patients positive to Euxyl K 400 were also positive to methyldibromoglutaronitrile; in none of the patients al-

lergic to Euxyl K 400 was the test to phenoxyethanol positive.

In a previous study in The Netherlands in 1991, 1142 patients suspected of contact allergy were tested with methyldibromoglutaronitrile 0.05% pet. (3). A frequency of 0.5% was observed in that study (3), considerably lower than that observed in the present study. 0.5% Euxyl K 400 corresponds to 0.1% methyldibromoglutaronitrile. Therefore, the difference in the frequency may be because the test concentration of methyldibromoglutaronitrile (0.05%) used in the earlier study (3) was half that (0.1%) used in the present study. Another possible explanation may be that Euxyl K 400 is a slow sensitizer, so that there may be an increase in the prevalence with increasing length of time (9, 10).

Higher frequencies (0.6%–2%) than 0.5% for methyldibromoglutaronitrile sensitization were previously reported in certain Italian studies (6, 11, 12). In these studies, however, the diluent for Euxyl K 400 (ethanol, water/ether or propylene glycol) was different from that in our study, and the test concentrations used were also higher (0.2–2.5%). Test concentrations of methyldibromoglutaronitrile of 0.1%, as used for current commercial test allergens, may be too low to avoid false-negative results, which may result in too low %s for the frequency of sensitization to this allergen.

Because, in most of our patients, contact with Euxyl K 400-containing products (in particular cosmetics) correlated with exacerbation of their eczema, clinical relevance for the positive tests was suspected, but in the vast majority of these patients, further testing (use test) could not be established. It is of interest that 2 patients, both men, had exacerbations of their hand eczema after using methyldibromoglutaronitrile-containing latex paint.

In group 1 ($n=1307$), positive reactions to other preservatives, particularly Kathon CG, were observed (Table 1). A frequency of sensitization to parabens of 0.2% has been reported (13). This is in agreement with the data in our study (Table 1). We observed in group 2

Table 1. Positive reactions to preservatives in the standard series (group 1) and the supplementary series (Euxyl K 400 and imidazolidinyl urea) (group 2)

		No. pos. reactions	% in this study	% in the literature
Routine standard series (group 1, n=1307)				
parabens mix	15% pet.	3	0.2	0.2 (13)
quaternium 15	1% pet.	7	0.5	0.2 (15)
formaldehyde	1% aq.	20	1.5	2.0 (13)
Kathon CG	100 ppm aq.	29	2.2	1.4 (13)
Supplementary series (group 2, n=1019)				
imidazolidinyl urea	2% pet.	14	1.4	0.5 (14)
Euxyl K 400	0.5% pet.	24	2.4	0.5 (3)
methyldibromoglutaronitrile	0.1% pet.	24	2.4	
phenoxyethanol	1% pet.	0	0	

a frequency for imidazolidinyl urea of 1.4%. It is of interest that some hypo-allergenic cosmetics (Sporex® products, used in The Netherlands and Belgium) contain imidazolidinyl urea (Germall 115). We observed positive reactions to imidazolidinyl urea in 3 patients who all had used Sporex® products.

Euxyl K 400, and in particular methyldibromoglutaronitrile, may be regarded nowadays as an important allergen in cosmetics, but the preservative may also play a sensitizing rôle in non-cosmetic products. The data of the present study indicate that Euxyl 400 shows an increasing trend as a contact allergen in the population generally suspected of contact allergy.

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