Contact allergy to Methyldibromoglutaronitrile (MDBGN): ESSCA results from the baseline series, 2009-2012

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Introduction

Preservatives are biocide chemicals added to cosmetics and household, pharmaceutical, and industrial products to prevent the growth of microorganisms that may enter during manufacture or during usage, thereby prolonging the shelf life and the period of use of the products. Although preservatives can be regarded as indispensable agents, many of them have long been recognized as important skin sensitizer and constitute common causes of contact dermatitis. The preservative methyldibromoglutaronitrile (MDBGN) was launched in the 1980s for use in industrial and cosmetic products. During the early 1990s, the prevalence of allergy to MDBGN was relatively low at 0.7%. Following its introduction, sensitivity rates rose to 3.5% in 2000 in the Europe Union (EU), and rose further to 4.5% in 2004-2005. The increasing sensitization to this preservative prompted the European Commission to restrict its use, and MDBGN was first banned from leave-on products in 2003, then, following a recommendation of the Scientific Committee on Consumer Products in 2005, it was also banned in rinse-off products in 2007.

Objectives

To assess the prevalence of contact allergy to MDBGN diagnosed by patch testing following its ban at the EU.

Material and methods

A retrospective analysis was performed on data collected by the European Surveillance System on Contact Allergies (ESSCA) network. The study period was from January 2009 to December 2012 and included 54 departments from 12 European countries. Altogether 59728 consultations involved application of the baseline series. The biocide allergens contained in the European Baseline Series (EBS) were tested in consecutive patients. MDBGN was tested at 0.2%, 0.3% and 0.5% in petrolatum (pet.).

Results

During the study period (2009-2012), 2.5% of the patients reacted positively to MDBGN 0.5% pet., while 2.7% of the patients reacted positively to MDBGN 0.3% and 2.8% to MDBGN 0.2% pet.

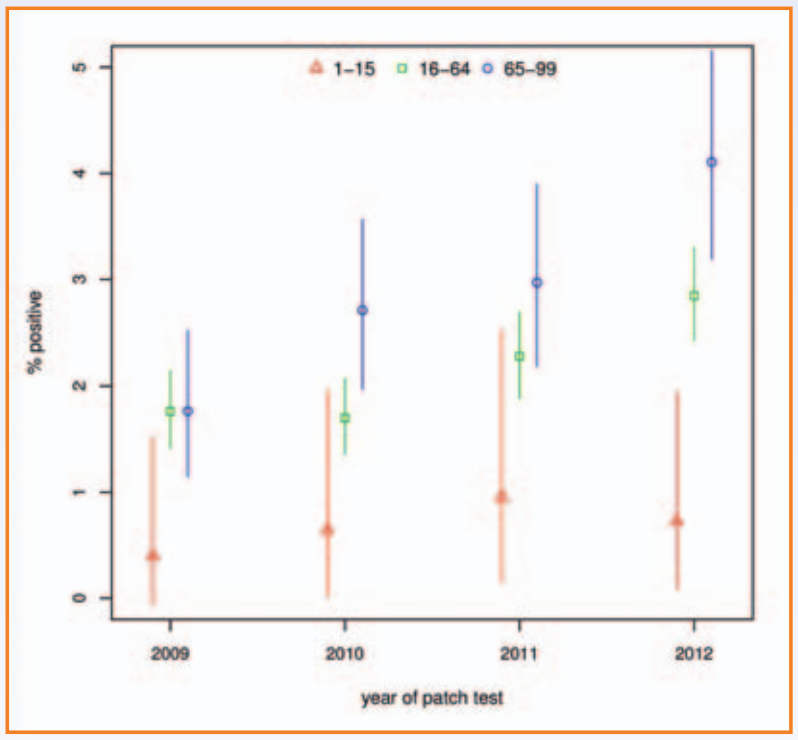
Table 1 shows the MOAHLFA index (Male, Occupational, Atopic dermatitis, Hand eczema, Leg dermatitis, Facial dermatitis, and Age ≥40 years) in all the subjects patch tested and in patients positive to MDBGN, as well as the proportion of individuals tested with the 3 different concentrations, stratified for 3 age groups. Note that the prevalence of positive reactions to MDBGN was higher in the 'old' and 'middle' age groups than in the youngest age group at the 3 different concentrations tested.

Figure 1 shows the time trend regarding MDBGN. It should be noted that 3 different patch test concentrations have been used in the study period, namely, 0.2, 0.3 and 0.5% pet. The usage across the different departments differed significantly between the years ($p<0.001$, χ^2 test), with 0.2% fairly constantly covering 23 (2009) to 27% (2011/12) of all tests, 0.3% decreasing in usage from 60% in 2009 to 47% in 2012, and 0.5% pet. increasing from 16% in 2009 to 26% in 2012. In view of this, the descriptive results in Fig. 1, stratified for age group, with pooled results from all 3 concentrations, should be interpreted with some caution, as they are confounded, to some extent, by the above factor. Statistical analysis, however, does confirm the notion of an upward trend for the two older groups, and a largely stable prevalence for the youngest age group both in a bivariate and an adjusted analysis considering potential confounding by test concentration, sex and country (p<0.001).

Table 1: MOAHLF(A) index in all the subjects patch tested (left column) showing the percentage of them with positive reactions to methyldibromo glutaronitrile (right column), as well as the proportion of patients tested with the 3 different concentrations, stratified for 3 age groups. 'pos. %' indicates the percentage of positive reactions in the subgroup defined by row and column variables. *p*-value: adaptation of Fisher's exact test for heterogeneity of reactivity to MDBGN across the 3 age groups in the strata of the MOAHLF(A) factors (A for age 40+ evidently omitted), e.g., in male patients, in patients with occupational dermatitis, etc.

	Age < 16		Age 16 to 64		Age > 64		
	Tested	pos. %	Tested	pos. %	Tested	pos. %	*p*-value
Number	1931	0.7	42958	2.2	8774	3	< 0.0001
M	772	0.6	14136	2.7	3043	3.2	< 0.0001
O	22	4.5	7213	3.2	122	4.9	0.30
A	915	0.3	10381	1.7	685	3.8	< 0.0001
H	224	0.4	10650	2.1	917	2.1	0.23
L	64	0	1418	3.5	1062	2.2	0.086
F	379	0.3	6369	1.5	1006	2.3	0.020
Conc. 0.2%	228	1.8	10512	2.9	2711	3.7	–
Conc. 0.3%	1280	0.5	22446	1.6	4629	2.6	–
Conc. 0.5%	423	0.7	10000	2.5	1434	3	–

Figure 1: Time trend, in 3 age groups, of contact allergy to methyldibromo glutaronitrile (MDBGN), all test concentrations pooled.



Discussion

Subsequent to the aforementioned regulatory interventions regarding the use of MDBGN, decreasing trends in the prevalence of contact allergy have been reported in Europe. The Danish Contact Dermatitis Group found a decreasing prevalence from 4.6% in 2003 to 2.6% in 2007 and similarly, the Information Network of Departments of Dermatology (IVDK) showed a decrease in the prevalence of sensitization from 4.5% in 2004-2005 to 2.4% in 2008-2009. However, since then, the prevalence of sensitization to this preservative appears to have remained stable, as shown in our data, where the prevalence of contact allergy to MDBGN ranged from 2.5% to 2.8% during the study period (2009-2012). Although most patients nowadays found sensitised to MDBGN might represent 'historical sensitisation', it should be noted that even in the youngest subgroup of patients, which should reflect changes in exposure best, the level of MDBGN sensitization seems not be levelling off. This may suggest that other non-regulated sources are still relevant in terms of eliciting or even sensitizing exposures. These might include a continued occupational exposure, or topical medicaments where MDBGN is not (necessarily) a disclosed ingredient.

Conclusions

Although MDBGN is banned from leave-on and rinse-off products since 2005, the level of awareness is not negligible, suggesting that other sources of exposure are still relevant in terms of eliciting or even sensitizing exposures. Therefore, MDBGN is still an important allergen to include in the EBS, in order to provide further surveillance information.

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