

Allergic contact dermatitis from methyldibromo glutaronitrile – clinical cases from 2003

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Of the 766 patients with eczematous skin disease patch tested in 2003 at the Department of Dermatology, University Clinic Gentofte, 38 (4.9%) showed a positive reaction to methyldibromo glutaronitrile (MDBGN), and in an additional 2 patients, a doubtful positive patch test reaction was found to be of relevance. Among these, 27 had hand eczema, with a relevant exposure predominantly from wash-off products, either liquid soaps or shampoos, in 24 patients. Following identification of the allergen by patch testing and subsequent avoidance of products containing MDBGN, the hand eczema either improved or cleared in 19 patients. Chemical analysis showed 11 p.p.m. to 473 p.p.m. MDBGN in products used by the patients. Based on the present clinical study and accumulated evidence in the literature, it is concluded that MDBGN is not suitable for use in any type of cosmetic product.

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Methyldibromo glutaronitrile (MDBGN) is recognized as a significant cosmetic contact allergen. In 1998–2000, the level of MDBGN allergy in dermatological clinics in Europe exceeded the level of allergy to all other preservatives, with a frequency of 3.5% in 2000 (1). These data stimulated a change in the 7th amendment of the EU Cosmetic Directive, to be implemented during 2005. In future, MDBGN will be banned from use in leave-on products, while it is still permitted for use in wash-off products at a maximum concentration of 1000 p.p.m. These changes have been known for the last 2 years and have probably already led to reformulation of a number of cosmetic products. Notwithstanding the regulatory focus on this preservative, the frequency of new cases of contact allergy to MDBGN has continued to rise in our area and is now about 5% of consecutively patch-tested patients (2). This ongoing epidemic prompted us to analyse our new clinical cases of MDBGN allergy from 2003, with respect to type of product exposure and chemical analysis of products brought in by the patients.

Materials and Methods

766 patients with eczematous skin disease were patch tested in 2003 at the Department of

Dermatology, Gentofte Hospital, University of Copenhagen, with the European standard series supplemented with cosmetic allergens including MDBGN 0.3% petrolatum (Hermal, Reinbeck, Germany). Finn Chambers[®] (Epitest OY, Helsinki, Finland) on Scanpor[®] tape (Norgesplaster A/S, Oslo, Norway) were used for occlusion. The test materials were placed on the upper back and left there for 2 days, and reactions were read at days 3, 4 and 7. Patch tests were scored according to ICDRG guidelines (3).

A thorough clinical assessment was made, including inspection of the cosmetic products used by the patients. When possible, the products used by the patients were obtained and subjected to chemical analysis by a high-performance liquid chromatography method employing reductive electrochemical detection (4). The detection limit for MDBGN was 5 p.p.m.

Results

A total of 38 patients (4.9%) gave a positive patch test (+ to +++) to MDBGN in 2003, and an additional 2 patients with a doubtful patch test were included in this study, as they had relevant exposure. 24 patients were females and 16 were males. Hand eczema was present in 27 of 40

(68%) patients. The frequency of hand eczema for the whole group of patch-tested patients was 33%. In 9 cases, a more diffuse dermatitis was seen, and in 2 cases, severe genital dermatitis was caused by vaginal examination gel.

Based on either product labelling or chemical product analysis, MDBGN allergy was found to be relevant in 24 of the 27 cases with hand eczema. The product exposure and results of chemical analysis are presented in Tables 1 and 2, respectively. The predominant exposure was from wash-off products, either liquid soaps or shampoos (Table 2).

The hand eczema either improved or cleared in 19 of the 27 (70%) patients within 6 months following identification of the contact allergen MDBGN by patch testing and subsequent avoidance of MDBGN-containing products, while the hand eczema was unchanged in 5 and the outcome unknown in 3 patients.

In the 9 cases with widespread dermatitis but without hand eczema, shampoos seemed to be the predominant exposure. After patch testing, the dermatitis either cleared or greatly improved in all 9 within 2 months.

Wash-off products preserved with MDBGN in the concentration range from 11 p.p.m. to 473 p.p.m. were involved with respect to both hand and widespread dermatitis (Table 2). Most of the patients, when we analysed their products, cleared within weeks to months independently of the MDBGN concentration in the product. The products were predominantly local Scandinavian brands.

Table 1. Types of exposure in the 24 cases of relevant contact allergy to methyldibromo glutaronitrile in the 27 patients with hand dermatitis

	Liquid soaps	Shampoos	Cream/lotion	Others
Hand involvement	11	7	9	2

Some patients were exposed to more than 1 product.

Table 2. Methyldibromo glutaronitrile (MDBGN) content (p.p.m.) in products used by patients with contact allergy to MDBGN and clinical outcome after patch testing

Liquid soaps		Shampoos		Cream/lotions		Vaginal examination gel	
Concentration	Outcome*	Concentration	Outcome*	Concentration	Outcome*	Concentration	Outcome*
11	Improved	32	Improved	138	Unchanged	157/170	Clear
19	Clear	44	Clear	148	Clear	311	Clear
22	Clear	103	Clear	398	Clear		
66	Clear	473	Clear				
174	Clear						

*Clinical outcome after patch testing and avoidance of products with MDBGN.

Discussion

Methyldibromo glutaronitrile was the 3rd most frequent contact allergen in our clinic in 2003, exceeded only by fragrance and nickel. Data from the National Allergy Centre concerning cases reported from dermatologists in private office practice in Denmark also gave a frequency of 5.0% for MDBGN allergy (2).

As approximately 25 000 new patients are patch tested yearly in Denmark, the total number of new cases of MDBGN in 2003 can be estimated to exceed 1200.

This number includes only the most severe cases with contact dermatitis typically lasting for months, with severe symptoms and, in the case of hand involvement, sick leave. The MDBGN cases are of significant clinical importance because of their high degree of hand involvement, 68% compared to the average of 33% in all patch-tested patients. Uncovering the source of the allergy, the dermatitis both on the hands and also more widespread cleared or significantly improved after a recovery phase of up to 6 months (Tables 1 and 2).

Chemical analysis of patients' products showed contents of MDBGN ranging from 11 p.p.m. to 473 p.p.m. The finding of rather low levels in some cases may be due to the use of MDBGN as part of the raw materials, binding of MDBGN to ingredients in the product, making it insoluble for analysis, or degradation in the products.

Originally, MDBGN was permitted for use in all cosmetic products at a maximum concentration of 1000 p.p.m. Based on clinical and experimental data, it was realized that the risk assessment had failed (5) or at least not been followed. Because of the high frequency of contact allergy, its use has now been restricted to wash-off products only but with an unchanged permitted concentration of 1000 p.p.m. (7th amendment EU Cosmetic Directive). Recent experimental studies have addressed this decision. Jensen et al. (6) exposed 19 MDBGN-sensitive individuals to experimental wash-off

products containing 1000 p.p.m. MDBGN in a controlled blinded study. Clear elicitation of contact allergy was observed in about 1/3 of cases to this experimental wash-off product. The effect of single versus repeated exposures has shown that the eliciting capacity of a single application of 400 p.p.m. MDBGN a day is comparable with the application of 100 p.p.m. 4 times a day (7).

The present study has shown that wash-off products (liquid soaps or shampoos used repeatedly daily) are involved in first-time contact dermatitis from MDBGN either on hand or widespread dermatitis.

Clinical data can never be perfect as compared with experimental human and animal studies. But, clinical data represent the endpoint outcome of human exposure to chemicals. Based on the present clinical study and accumulated evidence in the literature, it is concluded that MDBGN is not suitable for use in any type of cosmetic product.

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