

Contact sensitivity to preservatives in Turkey

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This study was designed to evaluate the frequency of contact sensitivity to 14 common preservatives among patients with contact dermatitis in Turkey. From 2000 to 2004, 308 patients with the diagnosis of contact dermatitis were patch tested in the Department of Dermatology, Ankara University School of Medicine. All patients were patch tested with European standard series. In addition to the four preservatives included in the standard series, patients were also tested with DMDM hydantoin, imidazolidinyl urea, bromonitropropane diol, diazolidinyl urea, thimerosal, propylene glycol, chlorocresol, chloroxylonol, methylidibromoglutaronitrile/phenoxyethanol (MDBGN/PE) and benzalkonium chloride. Out of the 308 patients suspected of having contact dermatitis, 23 patients were found to have positive reactions to one or more preservatives. Preservatives that were the most frequent cause of positive reactions were thimerosal (1.6%), benzalkonium chloride (1.6%), formaldehyde (1.3%) and MDBGN/PE (0.9%). In our study, 65% of the positive reactions were caused by allergens not present in the standard series, such as thimerosal, benzalkonium chloride and MDBGN/PE. Although thimerosal caused a high rate of contact sensitivity, it may not be considered as an important allergen, because clinical relevance could not be found in any of the patients.

Key words: benzalkonium chloride; contact sensitivity; formaldehyde; methylidibromoglutaronitrile; patch test; preservatives; thimerosal; Turkey. © Blackwell Munksgaard, 2005.

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Cosmetics are the causative agents in 5%–10% of all patients suspected of having contact dermatitis (1). Fragrances are the leading cosmetic allergens in both the United States and Europe. Preservatives, which are added to cosmetics to inhibit the growth of microorganisms, are the second most frequent cause of contact sensitivity to cosmetics (2). This study was designed to evaluate the frequency of preservative allergy among patients with contact dermatitis in Turkey.

Patients and Methods

From 2000 to 2004, 308 patients with the diagnosis of contact dermatitis were patch tested in the Department of Dermatology, Ankara University School of Medicine. The age, sex and occupation of the patients, duration and localization of the lesions were recorded. All patients were patch tested with European standard series. In addition to the 4 preservatives included in the standard series (formaldehyde, quaternium 15, methylchloroisothiazolinone/methylisothiazolinone (MCI/MI) and paraben mix), patients were also tested with DMDM hydantoin, imidazolidinyl urea, bromonitropropane diol, diazolidinyl

urea, thimerosal, propylene glycol, chlorocresol, chloroxylonol, methylidibromoglutaronitrile/phenoxyethanol (MDBGN/PE) and benzalkonium chloride.

The allergens were applied with Finn Chambers on Scanpor tape to the upper back of the patients. The strips were removed after 2 days, and the reading was noted after 30 min. The sites were re-examined after 4 days. Two experienced dermatologists participated in reading the tests. The results were evaluated according to the standard scoring system recommended by ICDRG (3).

Results

One hundred and ninety-seven patients were female (63.9%) and 111 patients were male (36.1%). Male/female ratio was 0.56. The patients were from 6 years to 76 years of age (mean age 37.03 ± 14.48 years). Out of the 308 patients suspected of having contact dermatitis, 23 patients were found to have positive reactions to one or more preservatives. Preservatives that were the most frequent cause of positive reactions were thimerosal (1.6%), benzalkonium chloriden

(1.6%), and formaldehyde (1.3%). The frequency of positive patch test reactions to the 14 preservatives is shown in Table 1. Concomitant patch test reactions were noted to DMDM hydantoin and formaldehyde, imidazolidinyl urea and diazolidinyl urea and MDBGN/PE and thimerosal (one patient each). Sensitivity to bromonitropropane diol, propylene glycol, chlorocresol and chloroxylenol was not seen in any of our patients. Irritant patch test reactions were noted to benzalkonium chloride in 5 patients and to MDBGN/PE in 3 patients.

Discussion

Preservatives are among the most frequent causes of allergic contact dermatitis. So far, it has not been possible to identify a biocide that is non-sensitizing but also capable of destroying all microorganisms responsible from spoilage of products. Today, lower than 1% sensitization rate for a biocide that adequately preserves the product is found acceptable.

In our study, out of the 14 preservatives tested, only 3 preservatives; thimerosal, benzalkonium chloride and formaldehyde caused positive patch test reaction in more than 1% of the patients. Thimerosal is used as a preservative in some cosmetics, ophthalmologic and otic preparations, contact lens solutions, vaccines, anti-toxins, desensitization solutions and intradermal tests. Several studies have revealed a high rate of thimerosal sensitivity in the range of 1.6%–15.3% (4–9). Due to the decreasing use of this preservative in cosmetics and topical medications, thimerosal sensitivity is thought to be mainly induced by thimerosal containing vaccines (7, 10, 11). In our study, 1 patient out of the 5 thimerosal-sensitive patients had had a desensitization therapy for

allergic rhinitis. In the remaining patients, thimerosal sensitivity could have been induced by immunizations. Although in previous studies, high rates of thimerosal sensitivity was detected, making thimerosal one of the most common sensitizers, clinical relevance could not be shown in most of the patients and the real nature of positive reactions to thimerosal is still unknown (6, 7, 10–12). In our study, we could not find clinical relevance in any of the patients.

Benzalkonium chloride is widely used as a disinfectant in the hospitals. It is also used as a preservative in cosmetics, toothpastes and ophthalmic preparations (2, 13). Although it is considered a rare sensitizer, sensitization rates between 0.2% and 5.5% have been found in different studies (4, 8, 9, 13). In a German multicentre study, it was one of the most common causes of allergic patch test reactions in a preservative series (8). Because of the high-irritancy potential of benzalkonium chloride, positive patch test reactions must be interpreted with great caution (8, 9, 14, 15). We found contact sensitivity to benzalkonium chloride in 1.6% of our patients. In 5 patients, irritant patch test reactions were noted which regressed at 96 hr.

Methyldibromoglutaronitrile/phenoxyethanol, marketed under the trade name Euxyl K 400, was first introduced to the European market in 1985 as a replacement for MCI/MI. Due to its widespread use in cosmetic industry, the incidence of positive patch test reactions to methyldibromoglutaronitrile increased from a European average level of 0.7% in the early 1990s to 2.4%–4% in the year 2000, the source of exposure being both wash-off and leave-on products (16–20). In our study, positive reactions to MDBGN/PE were found in 0.9% of our patients. Although MDBGN/PE was one of the most common cause of positive patch

Table 1. Positive patch test reactions to preservatives

	% Vehicle	Number of positive reactions	% <i>n</i> = 308
Formaldehyde	1% aqueous	4	1.3%
Quaternium 15	1% petrolatum	2	0.6%
Paraben mix	16% petrolatum	2	0.6%
MCI/MI	0.01% aqueous	1	0.3%
DMDM hydantoin	2% aqueous	2	0.6%
Imidazolidinyl urea	2% petrolatum	1	0.3%
2-Bromo-2-nitropropane-1,3 diol	0.25% petrolatum	–	–
Diazolidinyl urea	2% petrolatum	1	0.3%
Thimerosal	0.1% petrolatum	5	1.6%
Propylene glycol	5% petrolatum	–	–
4-chloro-3-cresol	1% petrolatum	–	–
4-chloro-3-xyleneol	0.5% petrolatum	–	–
Methyldibromoglutaronitrile/phenoxyethanol	1.5% petrolatum	3	0.9%
Benzalkonium chloride	0.1% aqueous.	5	1.6%

test reactions, 0.9% sensitivity rate is much lower than the high levels of sensitivity that are now being seen in Europe.

MCI/MI is widely used as a preservative in cosmetics and various industrial products based on its broad antimicrobial spectrum at low concentrations (21, 22). During the 1980s, increased use of MCI/MI led to high-sensitization rates in Sweden, Finland, Germany and Italy in the 3.4%–5.0% range (23–27). Currently, it is included in both European and American standard series allergens. Wilkinson et al. (19) analysed the levels of preservative sensitivity between the years 1991–2000 in 16 centres in 11 countries. The results of this study revealed that the levels of patch test sensitivity to MCI/MI remained stable between 2% and 5% throughout the decade. In our study, positive patch test reaction to MCI/MI was recorded in only one of our patients. The patient was a painter, and he had occupational hand dermatitis due to MCI/MI used as a biocide in the paints he used.

Formaldehyde is among the most important allergens in Europe and the USA. Exposure commonly occurs through contact with products such as cosmetics or medicated creams which contain formaldehyde or formaldehyde releaser as a preservative and with formaldehyde released from resins used as treatment for textiles. Formaldehyde sensitivity is found in 1%–9% of patients patch tested with standard series allergens (8, 9, 19, 20, 28, 29). We found formaldehyde sensitivity in 1.3% of our patients. On the other hand, formaldehyde-releasing preservatives had relatively low-sensitivity rates ranging from 0.3% to 0.6%. No positive reaction was seen to bromonitropropane diol. 1 patient who reacted to DMDM hydantoin was also positive to formaldehyde, and 1 patient allergic to imidazolidinyl urea also reacted to diazolidinyl urea.

In our study, only formaldehyde out of the 4 preservatives included in the European standard series scored more than 1% positive reaction. In another study, conducted in Turkey, Hillenbrand and Beyazit had also reported low-sensitivity rates to quaternium 15 (0.6%), formaldehyde (0.6%) and MCI/MI (0.2%). No positive reactions were observed to paraben mix (30). These similar findings from two studies carried out in Turkey may be explained by the less frequent use of perfumed products and cosmetics in Turkey compared with most of the European countries. On the other hand, 65% of the positive reactions were caused by allergens not present in the standard series. Thimerosal may not be considered an important allergen, because clinical relevance could not be found in any of the patients.

However, benzalkonium chloride and MDBGN/PE caused higher rates of positive reactions than standard series allergens paraben mix, MCI/MI and quaternium 15. This finding has to be kept in mind when evaluating patients with suspected contact dermatitis to cosmetics in Turkey.

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