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RESEARCH ARTICLE

# Sensitization to Methylisothiazolinone in a group of Methylchloroisothiazolinone/Methylisothiazolinone allergic Patients

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## Abstract

In the EU, Methylisothiazolinone (MI) was approved as a preservative in cosmetics and household products in 2005. Since then, several cases of MI contact allergy have been reported. We studied the prevalence of MI sensitization in patients allergic to Methylchloroisothiazolinone/Methylisothiazolinone (MCI/MI). From a total of 751 patients submitted to patch testing between 2007 and 2011, 26 were sensitized to MCI/MI 100 ppm aq. Fifteen patients were retested with MCI/MI 100 ppm aq, MI 200 ppm aq and personal products, and the relevance of positive results, concerning the use of personal products, was evaluated. Seven of the 15 MCI/MI positive patients were positive to MI: six patients showed an equally intense reaction to MCI/MI and MI alone, and another one presented with a stronger reaction to the latter compound. All positive reactions were relevant. The use of MI alone as a preservative does not seem to be a safe alternative. In this study, the majority of positive reactions to MCI/MI and MI had similar intensity, although primary sensitization to MI has to be considered according to each individual case; moreover, primary sensitization to MCI with cross-reactivity to MI cannot be excluded. Further studies are needed to determine the optimal concentration for MI patch testing.

**Keywords:** Allergic contact dermatitis, Methylisothiazolinone, Methylchloroisothiazolinone, preservatives

## Introduction

Preservatives are necessary to avoid microbiological contamination of products; however, they are frequently causative agents of cosmetic-related allergy (1). The mixture of Methylchloroisothiazolinone (CAS# 26172-55-4) and Methylisothiazolinone (CAS# 2682-20-4) (MCI/MI) was introduced in a 3:1 ratio in the early 1980s (2–4) and, because of its broad-spectrum activity against fungi and bacteria (5), became one of the most used preservatives (2,6). However, since then, numerous cases of MCI/MI sensitization have been reported.

Because MI was believed to be a weaker sensitizer (2,3) and a safe alternative, the EU approved the use of MI on its own as a preservative in cosmetics and household products in 2005 (because MI alone is a less effective biocide, the maximum permitted concentration is 100 ppm) (2,7). Unfortunately, in 2004 (8) and 2006 (9), the first cases of MI contact allergy were reported, caused

by occupational exposure to wallpaper glue and paint, respectively. The first cases of non-occupational sensitization to MI were reported by García-Gavín in 2010 (4), and, since then, Ackermann et al. (3) showed that the prevalence of MI allergic reactions is increasing.

In this study, we evaluated the prevalence of MI sensitization in patients allergic to MCI/MI and the relevance of positive results.

## Materials and methods

Among the 751 patch-tested patients between January 2007 and February 2011, there were 26 patients allergic to MCI/MI 100 ppm aq. Fifteen of those patients were retested with MCI/MI 100 ppm aq, MI 200 ppm aq and personal products containing these preservatives. The patch test substances for MCI/MI and MI were purchased from Chemotechnique Diagnostics (Sweden). Patch testing was performed using Finn Chambers® (Epitest,

Table 1. Methylisothiazolinone (MI)-positive patients and the relevant products containing it.

| Gender | Age | Eczema distribution | MCI/MI 100 ppm | MI 200 ppm | Personal products            | Other positive tests                                                      |
|--------|-----|---------------------|----------------|------------|------------------------------|---------------------------------------------------------------------------|
| Female | 38  | Axilla              | ++             | ++         | Deodorant ++                 | Nickel                                                                    |
| Female | 33  | Hands, axilla       | ++             | ++         | Deodorant +<br>Emollient +   | Thiuram mix<br>Neomycin sulfate<br>Nickel<br>Colophonium                  |
| Female | 38  | Forearms,<br>Hands  | ++             | ++         | Emollient ++<br>Sunscreen ++ | Nickel                                                                    |
| Female | 60  | Hands, wrists       | +              | +          | Shampoo +                    | Nickel                                                                    |
| Male   | 88  | Legs                | ++             | +          | NSAID gel +                  | Formaldehyde<br>Quaternium-15<br>Imidazolidinyl urea<br>Diazolidinyl urea |
| Female | 43  | Hands, wrists       | +              | ++         | Shampoo +                    | Nickel                                                                    |
| Female | 40  | Hands, wrists       | +              | +          | Dishwashing liquid +         | Thimerosal                                                                |

+, palpable erythema; ++, palpable erythema and vesicles; MCI, Methylchloroisothiazolinone.

Finland) and readings according to the guidelines of the International Contact Dermatitis Research Group (10). Leave-on personal products were tested by patch testing (e.g. emollients, sunscreens and deodorants) and rinse-off products were submitted to semi-open testing (e.g. shampoos).

### Results

From the total of 15 patients, 7 were sensitized to MI 200 ppm aq. Six patients showed a similar reaction between MCI/MI 100 ppm and MI 200 ppm, the other one had a stronger reaction to the latter compound. All results were considered relevant. Personal products implicated were: dishwashing liquids, deodorants, shampoos, emollients, wipes, NSAID gel and sunscreens. Only one case had occupational relevance: a female hairdresser for more than 30 years complaining of hand and wrist eczema (Table 1).

### Conclusions

Methylisothiazolinone can potentially induce contact allergy, hence it does not seem to be a safe alternative to the mixture MCI/MI. However, except maybe on cases where MI reaction is more intense than MCI/MI reaction, primary sensitization to MCI with cross-reaction to MI cannot be excluded (4), and it should be evaluated according to each individual case. Although very few data exists concerning cross-reactivity patterns between MCI and MI, Bruze et al. (11) showed that a small percentage of subjects sensitized to MCI/MI also had positive reactions to MI alone. Currently, MI concentration is subject to regulation, mainly in cosmetics, however Lundov et al. (12) showed that, on repeated exposures, many patients allergic to MI reacted to 50 ppm (half of the maximum permitted concentration in cosmetics). Besides, although in the present study cosmetics were the main implicated on MI sensitization, as portrayed before, household products

and occupation exposure are also important sources (12) in which the use of MI is not restricted.

The optimal concentration to MCI/MI and MI patch testing remains a theme of debate. In the baseline series, MCI/MI is tested at 100 ppm concentration, which only contains 25 ppm of MI, leading to possible false-negative results. Two studies proved that, compared to 200 ppm MCI/MI, patch testing with 100 ppm MCI/MI misses about half of the allergic patients (13,14). Ackermann et al. (3) used two different MI concentrations on their study obtaining 1.4 and 0.6% positive reactions to 1000 and 300 ppm, respectively. Other reports used different concentrations (2,15) with equivalent results. In the present study, MCI/MI 100 ppm and MI 200 ppm were the only available test concentrations, hence some relevant sensitizations might have been missed. Currently, a concentration of 2000 ppm is being recommended (12). Therefore, MI and MCI/MI patch testing concentrations, remain important debating issues.

### Declaration of interest

The authors report no declarations of interest.

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