

Increasing trend of sensitization to Methylchloroisothiazolinone/methylisothiazolinone (MCI/MI)*

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Abstract: Recent reports have shown increased sensitization to Methylchloroisothiazolinone/methylisothiazolinone. We report a retrospective study conducted at the Hospital das Clínicas - UFMG, based on the results of patch tests with the Brazilian standard series, performed on referred patients. The positive results in 359 patients from November 2009 to October 2012 were analyzed and compared with the previous data collected from March 2006 to October 2009 (447 patients). The data showed 11.14% sensitization to Methylchloroisothiazolinone/methylisothiazolinone during 2009-2012, contrasting with the previous period (3.35%). A positive association was found between its positivity and the period of 2009-2012.

Keywords: Dermatitis, allergic contact; Epidemiology; Preservatives, pharmaceutical

Methylchloroisothiazolinone/methylisothiazolinone (MCI/MI) is a preservative mixture at a fixed combination (ratio 3/1), which is commonly used in cosmetic and industrial applications and can be found in cosmetics, especially shampoos, dermatological products, mainly sunscreens, household cleaning products, paints, moist toilet paper, metalworking fluids.^{1,4}

It is also known as Euxyl K 100 or Kathon CG. In the USA, where it was first introduced in 1980, it is permitted as a preservative for rinse-off products at 15ppm and for leave-on products at 7.5ppm. In Europe, it was used initially in the mid-1970s, and is employed today at 15ppm for leave-on or rinse-off products. In Japan, it is permitted only for rinse-off products, at 15ppm. In Brazil, it is permitted at 0.0015% (15ppm) and is tested at 0.5% in petrolatum (Brazilian standard series).⁵

Recent reports have shown an increase in sensitization to both MCI/MI and MI by itself.^{1,4} The global frequency of sensitization to MCI/MI remained constant at around 2.1% from 1998-2009, but increased to 3.9% in 2011.^{1,2,3} North American Contact Dermatitis Group data from 2009-2010 revealed a frequency of 2.5% among 4,032 patients tested. The allergen was the fifth most positive preservative and had the highest relevance of all. The definite and probable relevance was 54.6%, whereas the possible relevance was 38.9%. Methylisothiazolinone (MI) was the American Contact Dermatitis Society Contact Allergen of the Year for 2013 because its use in cosmetics and toi-

letries is rising.⁵ It is suggested that primary sensitization to MI led to a subsequent rise in MCI/MI reactions.¹

A retrospective study was carried out based on the results of patch tests with the Brazilian standard series, performed on contact dermatitis referred patients. They were patch tested to the Brazilian Standard Tray (FDA Allergenic/Immunotech, Rio de Janeiro, Brazil) with a standardized technique, using Finn Chambers (Epitest Ltd Oy, Tuusula, Finland) on Scanpor tape (Norgeplaster Alpha AS, Vennessla, Norway). Readings occurred on days two and four. The positive results in 359 patients from November 2009 to October 2012 were analyzed and compared with the previous data collected from March 2006 to October 2009 (447 patients). For descriptive characterization of the patient population, the MOHALFA index (an acronym for male, occupational, atopic, hand, leg or face dermatitis and age >40) was used.

The data showed 11.14% sensitization to MCI/MI during 2009-2012, contrasting with the previous period (3.35%). A positive association between MCI/MI positivity and the period 2009-2012 (OR+3,61 CI 95% 1.91-7.16 p<0,001) was detected (the analyses were obtained with the R program, version 2.13.0) (Table 1).

Positive reactions were observed equally in caucasians, black and mulattos. The most afflicted occupations were cleaners and housewives, which were linked to wet work and use of household products,

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Table 1: Differences in the MCI/MI positive reactions during the studied periods analyzed by exact Fisher's test and Odds ratios (CI=95%)

Period	N	Positive reaction	%	OR
2006-09	447	15	3.35	3,61(CI 95% 1,91-7,16) p<0,001
2009-12	359	40	11.14	

while 27.5% of the patients showed occupational correlation with sensitization. The period of evolution of the dermatitis was one year in 60% of the patients. 82.5% of the patients presented disseminated lesions affecting more than three body areas. The most affected sites were the legs (80%) and feet (62.5%), followed by the scalp (57.5%) and neck (50%). 42.5% of the patients had lesions on the hands and 27.5% on the face.

In both groups women were more affected and their ages were similar, but the first group was more associated with occupational exposure (53.3%) (Table 2).

Table 2: MOAHLFA index for the investigated populations

MOAHLFA	2006-2009	Period	2009-2012	Period
	%	N 15	%	N 40
Men	33.3	5	12.5	5
Occupational dermatitis	53.3	8	27.5	11
Atopic dermatitis	26.6	4	17.5	7
Hand dermatitis	80	12	42.5	17
Leg dermatitis	20	3	80	32
Face dermatitis	46.6	7	27.5	11
Age> 40	53.3	8	57.5	23

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The final diagnosis was angry back in 7.5%, allergic contact dermatitis to Kathon in 57.5% and allergic contact dermatitis to Kathon and other contactants in 35% of the patients. The main source was household products and cosmetics.

Our data revealed an increase in the prevalence of MCI/MI, especially after 2009, linked to exposure to cosmetic, household and industrial products, which explains the clinical features described above and confirms previous European studies.

Isothiazolinones do not always cross-react and therefore, allergy to one isothiazolinone does not mean sensitivity to the entire group. Patients sensitized to MI also react to MCI, while the opposite does not necessarily apply. Nevertheless, a study with a stratified data analysis revealed pronounced increases in reactivity to MCI/MI and MI in females, face dermatitis patients and patients tested for suspected cosmetic intolerance. In order to understand the scale of the problem, MI should be considered as a potential suspect allergen in patients sensitized to MCI/MI, and MI should be included in the standard trays.

In conclusion, the positivity to MCI/MI in this series was associated with: females, mainly housewives and cleaners; the presence of dermatitis of at least 1 year's evolution; and disseminated lesions affecting especially the legs. □

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