

ORIGINAL RESEARCH

Allergic contact dermatitis to methylisothiazolinone: Exposure from baby wipes causing hand dermatitis

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ABSTRACT

Background/Objectives: Methylchloroisothiazolinone/methylisothiazolinone (MCI/MI) is a preservative used in both cosmetic and industrial settings. In Europe it is allowed to be used in rinse-off cosmetics only because of its propensity to cause allergic contact dermatitis (ACD). No such legislation exists in Australia. In recent years MI without MCI has been used. In August 2010 the first cases of MI causing non-occupational ACD were reported in Europe. The objective here was to present a case series of ACD to MI occurring in the Australian setting.

Methods: We retrospectively reviewed positive reactions to MI and MCI/MI from the Skin and Cancer Foundation patch test clinical database. MI was added to our baseline test series in January 2011.

Results: In total 653 patients were tested for MI and there were 43 reactions, of which 23 were relevant, based on a history of exposure to MI. Seven were parents of young children with hand dermatitis caused by ACD to MI contained in baby wipes. The remaining patients reacted to MI in shampoos, conditioners, deodorants, moisturisers, a skin cleanser and a facial wipe. Three patients had ACD to MI associated with occupational exposure to hand cleansers.

Conclusions: These data demonstrate for the first time that MI is an emerging, important allergen in both cosmetic and occupational settings in Australia. An important source of exposure was baby wipes, which was predominantly associated with hand

dermatitis in parents. We believe that it is important to test for MI, not just MCI/MI, in the baseline series.

Key words: allergy, cosmetic, hand, isothiazolinone, methylchloroisothiazolinone, moist wipe, Kathon CG, occupational, preservative, wet wipe.

INTRODUCTION

Methylchloroisothiazolinone/methylisothiazolinone (MCI/MI), also known by its trade name Kathon CG (Dow Chemical, Midland, MI, USA), is a non-formaldehyde releasing preservative used in both cosmetic and industrial settings.¹ Both MCI and MI can cause allergic contact dermatitis (ACD).² The sensitising potential of MCI is higher than MI, however MI is still classed as a strong sensitiser.³ The maximum concentration of MCI/MI in leave-on cosmetics has been regulated in Europe because of increasing reports of ACD.⁴

Presumably in an attempt to reduce the frequency of ACD occurring with MCI/MI, MI alone has been used as a preservative. It was first permitted for use in industrial products in Europe in the early 2000s, including in paints, varnishes and inks.⁵ The first reports of ACD to MI alone in occupational settings were published in 2004 and 2006.⁵ MI alone was approved for use in cosmetic products in 2005 at a maximum concentration of 100 ppm.^{4,5} This is more than 25-fold the permitted concentration of MI in the MCI/MI combination (3.75 ppm MI in 15 ppm MCI/MI). In August 2010 the first cases of ACD to MI in non-occupational settings began to emerge.⁵

In Australia there are currently no formal restrictions on the use of MI or MCI, either in the National Industrial Chemicals Notification and Assessment Scheme or the

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Conflict of interest: none

Submitted 8 February 2013; accepted 20 March 2013.

Abbreviations:

ACD	allergic contact dermatitis
MCI	methylchloroisothiazolinone
MI	methylisothiazolinone

Standard for the Uniform Scheduling of Medicines and Poisons. There have been no published reports of ACD to MI in Australia.

MATERIALS AND METHODS

A search was performed on the clinical database of patients assessed at the Occupational Dermatology Clinic and Contact Dermatitis Clinics at the Skin and Cancer Foundation, Victoria from 1 January 2011 to 30 June 2012. Routine patch testing to the Australian baseline series containing 60 allergens, including MI, commenced in January 2011 (R Nixon, personal comm.). The clinics' consultant dermatologists (RN, MT, BT together with AL of Monash Medical Centre) had agreed to include MI in the Australian baseline series, based on concerns emanating from Europe that MI on its own was a cause of allergy. MI was tested at a concentration of 200 ppm and was obtained from Chemotechnique Diagnostics (Malmo, Sweden). MCI/MI was also obtained from Chemotechnique Diagnostics and was tested at dilutions of 100 ppm in the baseline series and 200 ppm in the plastics series, with its composition being 1 : 3 (MI : MCI).

Patches were applied to the upper back using Finn chambers on Scanpore (Smart Practice, Phoenix, AZ, USA) and left on for 48 h. Reactions were recorded at 48 h and 96 h, according to the International Contact Dermatitis Research Group guidelines. Only patients with positive reactions (+, ++ or +++) were used for the analysis. Positive reactions were classified as relevant, of past relevance or of unknown relevance. Relevance was determined by the patch test clinic consultant dermatologist at the time of patch testing.

Details of patients' exposure to MI were ascertained from their attending clinicians and medical records. Data were also collected on patients' characteristics, history of atopy, anatomical location of the dermatitis, additional positive patch test reactions (to MCI/MI and other allergens) and source of exposure to MI.

RESULTS

There were 43 positive patch test reactions in 653 patients patch tested to MI (7%), of which 23 (4%) were found to be relevant, in that a source of exposure to MI was identified. The other reactions were of unknown relevance. In total, 17 of the patients were identified from the contact dermatitis clinic and six were identified from the occupational dermatology clinic.

Of the reactions that were relevant, 17 patients were female and six were male. Their age range was 5 to 79, with a mean age of 44 years. In all, 14 (61%) patients had a background history of atopy (defined as a history of atopic eczema, asthma or hay fever). The most common sites of involvement were the hands (12 patients) and face (11 patients). The dermatitis in eight patients was so severe that it required treatment with oral prednisolone. The characteristics of the patients are displayed in Table 1.

Clinically relevant ACD to MI present in baby wipes involving the hands occurred in seven patients, all of whom

were parents of young children. One patient was a 5-year old girl with facial dermatitis caused by MI contained in baby wipes, after they were used to wipe off food.

ACD to MI found in cosmetics included exposure from shampoos or conditioners (six patients), deodorants (four patients), moisturising creams (two patients), a cleanser (one patient) and a facial wipe (one patient). Three patients had ACD to MI associated with occupational exposure to hand cleansers.

It was noted that the time to presentation for hand dermatitis was often quite long, up to 2–3 years. However, for moisturising creams and deodorants the allergic response was often faster, even occurring after only a few applications. There was no noticeable time trend with the shampoos and conditioners.

During the period when MI was tested, 660 patients were also patch tested to MCI/MI. Table 2 compares the results of testing of MI and MCI/MI during this time period, both in the occupational dermatology and contact dermatitis clinics.

Of the 43 patients reacting to MI, 34 (79%) had concomitant reactions with MCI/MI, of which 25 (58%) were relevant, the remainder being of unknown relevance. Of the 52 reactions to MCI/MI, 34 (65%) had concomitant reactions with MI, of which 23 (44%) were relevant. All but three patients had positive reactions to other chemicals tested in the Australian baseline series. The most common relevant comorbid reactions aside from MCI/MI were fragrance mix, colophonium and formaldehyde.

DISCUSSION

Isothiazolinones are preservatives commonly used in cosmetic and occupational settings. It was recently reported that 25% of cosmetics and 28% of detergents contained isothiazolinones.⁶ Several European studies in the 18 months prior to the time of writing have shown that MI alone is an emerging cause of ACD in both cosmetic and industrial settings.^{4,5,7–9}

Our study demonstrates for the first time that MI is also an emerging and important allergen in Australia and we have detected a surprising number of relevant reactions in the relatively short time that MI has been routinely tested. This reinforces the need to test for MI alone in standard patch testing, as only 79% of the patients who reacted to MI also reacted to MCI/MI, and only 65% of patients who reacted to MCI/MI also reacted to MI. This finding has been confirmed in a recent study.⁸ Testing MI as a sole allergen detects the relevant allergy missed by testing the MCI/MI mix, thus its presence in the current baseline series. MI is not present in True Test (Smart Practice, Hillerød, Denmark)¹⁰ and therefore cases of allergy are likely to be missed unless it is specifically tested for. It is likely that MI in Australia is used in products at a higher concentration than in the MCI/MI combination, which has occurred in Europe.⁴

Our study also shows for the first time that MI contained in baby wipes and facial wipes is an important cause of hand dermatitis in carers. Previous studies have described ACD of the hands caused by MCI/MI in parents using moist baby

Table 1 Patients with allergic contact dermatitis caused by methylisothiazolinone (MI)

Patient	Age at testing, sex	Personal history of atopy	Primary site(s) involved	Source of MI	Relevant comorbid reaction to MCI/MI
1	58, F	N	Hands	Huggies baby wipes	Y
2	53, F	N	Face, neck	Algologie France Optimal Cream and Moisturising Rich Cream	N
3	35, F	Y	Hands	Huggie baby wipes	Y
4	53, M	Y	Face, neck	Natures Organics Organic Care Normal Balance Shampoo	Y
5	54, F	Y	Face, hands, forearms	Garnier deodorant [‡]	N
6	35, F	N	Face, hands	Mamia baby wipes	Y
7	30, F	Y	Hands	Huggies baby wipes	N
8	45, M	Y	Hands	Huggies baby wipes	N
9	28, F	N	Face, neck	John Frieda shampoo/conditioner Dove cleanser/toner	Y
10 [†]	34, M	Y	Hands	Deb Suprega Plus Heavy Duty Hand Cleaner	Y
11	35, F	Y	Hands	Huggies baby wipes	Y
				Herbal Essence Shampoo	
12 [†]	57, M	N	Hands	Permatex Fast Orange Hand Cleanser	Y
13	62, F	Y	Face, scalp, neck, chest	Natures Organics Fruits shampoo and conditioner	N
				Dove shampoo	
14	55, F	N	Elbow, ankle	Huggies baby wipes [§]	Y
15	61, F	Y	Axillae, perioral	Garnier deodorant	N
16 [†]	26, M	Y	Hands	Permatex Fast Orange Hand Cleanser	Y
17	33, F	Y	Hands	Huggies baby wipes	Y
18	37, M	Y	Hands, face	Natures Organics Fruits shampoo and conditioner	Y
19	56, F	N	Face, neck	Natures Organics Natural Skin Expert Light Moisturiser	Y
20	62, F	Y	Axillae, face, forearms	Garnier deodorant	N
21	46, F	N	Axillae	Garnier deodorant	N
22	5, F	Y	Face, scalp	Mamia baby wipes	Y
				Natures Organics Fruits conditioner	
23	79, F	N	Face	Nivea facial wipes	N

[†]Denotes occupational exposure. [‡]Also relevant reaction to fragrance mix (geraniol in India Hicks Body Wash). [§]Also relevant reaction to colophonium (shoes, Pine O Cleen wipes). MCI, methylchloroisothiazolinone. Algologie France Optimal Cream and Moisturising Rich Cream, Algologie, Brittany, France; Clairol Herbal Essences Shampoo, Procter & Gamble, Bangkok, Thailand; Deb Suprega Plus Heavy Duty Hand Cleaner, Deb Group, Sydney, New South Wales, Australia; Dove cleanser/toner, Dove shampoo, Unilever, Melbourne, Victoria, Australia; Garnier deodorant, Garnier, Paris, France; Huggies baby wipes, Kimberly-Clark, Neenah, WI, USA; India Hicks Body Wash, India Hicks, Melbourne, Victoria, Australia; John Frieda shampoo/conditioner, John Frieda, Cincinnati, OH, USA; Mamia baby wipes, Aldi Stores, Melbourne, Victoria, Australia; Natures Organics Organic Care Normal Balance Shampoo, Natural Skin Expert Light Moisturiser, Natures Organics Fruits shampoo and conditioner, Natures Organics, Ferntree Gully, Melbourne, Australia; Nivea facial wipes, Beiersdorf, Hamburg, Germany; Permatex Fast Orange Hand Cleanser, Permatex, Ballarat, Victoria, Australia; Pine O Cleen wipes, Reckitt Benckiser, China.

Table 2 Results of patch testing to methylisothiazolinone (MI) and methylchloroisothiazolinone (MCI/MI from 1 January 2011 to 30 June 2012

	Total tested (n)	Total positive reactions	Relevant reactions (n, % of total positive)	Unknown relevance
MI	653	43	23 (53)	20
Occupational clinic	259	13	6	7
Contact clinic	414	30	17	13
MCI/MI	660	52	35 (67)	17
Occupational clinic	241	15	12	3
Contact clinic	419	37	23	14

wipes but have not tested MI alone.^{11,12} Our study showed that in three of the 10 patients reacting to baby wipes there was no concomitant relevant reaction to MCI/MI. Studies of ACD to MI alone in moist toilet wipes have been reported

but these have caused an ACD of the perineal and perianal region rather than the hands.^{13,14} It has been thought that the non-keratinised and occluded sites might facilitate the development of ACD to MI in these areas. Our study, however, finds that hands are also at risk of developing ACD. Our study has also shown for the first time that moist wipes can cause facial dermatitis in children.

The use of MI and MCI/MI in baby wipes will mean an increased risk of exposure of and sensitisation to MI and MCI/MI in infants and children, which may lead to increased rates of allergy to these preservatives in adults. The substitution of MI for MCI/MI will not reduce this problem, particularly if a higher concentration of MI is allowed.

There are several reports of MI causing ACD in occupational settings, particularly as an allergen in paint,^{5,15,16} but also in cleaning products, chemicals, glues and cutting oils.⁵ In our study, all three cases of occupational exposure to MI occurred from hand cleansers.

CONCLUSION

Clinicians need to be aware of the possibility of ACD from MI, particularly as a cause of hand dermatitis in parents from use of baby wipes, as well as from other cosmetic products. We add our concerns to those voiced in Europe^{4,5,7} that the allowable concentration of MI in both leave-on and rinse-off products needs urgent review by regulators. We also believe that it is important to test for MI alone in the baseline series.

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