

Methylisothiazolinone Contact Allergy Prevalence in Western Canada: Increased Detection With 2000 ppm Patch Test Allergen

Journal of Cutaneous Medicine and Surgery

1-4

© The Author(s) 2017

Reprints and permissions:

sagepub.com/journalsPermissions.nav

DOI: 10.1177/1023475417690307

journals.sagepub.com/home/jcms

Canadian
Dermatology
AssociationAssociation
canadienne de
dermatologie

Jessica E. Wilford¹ and Gillian C. de Gannes^{1,2}

Abstract

Background: Contact allergy to methylisothiazolinone (MI) or to the combination of methylchloroisothiazolinone and MI (MCI/MI) is an important and increasing cause of allergic contact dermatitis, with prevalence rates higher than 10% in some centers.

Objectives: The objective of this retrospective chart review is to provide a western Canadian perspective on whether the positive patch testing rate to MCI/MI or MI increased during the testing period of 2008 to 2015 and whether the addition of MI at 2000 ppm resulted in increased detection.

Methods: We conducted a retrospective chart review of patients who tested positive ($n = 104$) of 2177 total patients who were patch tested for MCI/MI or MI at a community dermatology clinic in Vancouver, British Columbia, Canada, from January 2008 through April 2015.

Results: One hundred and four patients had positive patch testing results for MCI/MI, MI, or both. Positive results increased over the study period, with the highest prevalence in 2015 at 9.41% for MCI/MI, 12.94% for MI, and 15.29% for either. When testing for MI at 2000 ppm was introduced in 2013, the initial positive patch testing prevalence was 6.6%, followed by 10.1% in 2014, and 12.9% in 2015.

Conclusions: We demonstrate an increasing prevalence of MCI/MI and MI allergy between 2008 and 2015, with the highest prevalence of 15.29% in 2015 for MCI/MI and/or MI allergy. The addition of MI 2000 ppm greatly increased the positive patch testing yield for MI. Our results support the importance of continued efforts to monitor and regulate these preservatives.

Keywords

methylisothiazolinone, methylchloroisothiazolinone, contact, allergy

Introduction

Methylisothiazolinone (MI) and the combination of methylchloroisothiazolinone (MCI) with MI (MCI/MI) in a 3:1 ratio are well-known allergens used as preservatives in personal care and industrial products. Methylisothiazolinone was recognized as the American Contact Dermatitis Society Contact Allergen of the Year for 2013.¹ Methylisothiazolinone has been used in personal care products since 2005 and in industrial products since 2000. Over the past several years, due to the awareness of contact allergy to MCI/MI and the opinion that MCI was the much greater sensitizer than MI, the use of MI alone increased.² Recent studies have supported the notion that MI alone is a significant cause of allergic contact dermatitis (ACD) as well as a sensitizer to MCI/MI, and its increased use has contributed to the rising incidence of MCI/MI allergy.³⁻⁵

These findings led to suggestions to reduce the concentration and use of both MI and MCI/MI in personal care

products⁶ as well as to add MI to the North American Contact Dermatitis Group (NACDG) screening series at a concentration of 2000 ppm to reduce the incidence of false negative results for MI allergy when only MCI/MI 100 ppm or 200 ppm was tested. Recent studies have indicated an increasing detection of MI-induced allergic contact dermatitis since the introduction of MI 2000 ppm to the screening series.⁶⁻¹¹

Until recently, in Canada, MCI/MI was permitted in leave-on products in concentrations up to 0.00075% (7.5

¹Department of Dermatology and Skin Science, University of British Columbia, Vancouver, BC, Canada

²Division of Dermatology, Department of Medicine, St. Paul's Hospital and Providence Health Care, Vancouver, BC, Canada

Corresponding Author:

Jessica E. Wilford, Department of Dermatology and Skin Science, University of British Columbia, 835 West 10th Avenue, Vancouver, BC V5Z 4E8, Canada.

Email: jessicawilford@gmail.com

Table 1. Prevalence of MCI/MI and MI Positive Patch testing, 2008-2015.

	2008	2009	2010	2011	2012	2013	2014	2015	Total
Total No. of patients tested for MCI/MI or MI	25	251	557	413	287	273	286	85	2177
Positive patch testing to MCI/MI, MI, or both, n (%)	0 (0.0)	3 (1.2)	19 (3.4)	6 (1.5)	5 (1.7)	23 (8.4)	35 (12.2)	13 (15.3)	104 (4.8)
Positive patch testing to MCI/MI, n (%)	0 (0.0)	3 (1.2)	19 (3.4)	6 (1.5)	5 (1.7)	14 (5.1)	18 (6.3)	8 (9.4)	73 (3.4)
Total No. of patients tested for both MCI/MI and MI						273	286	85	644
Positive patch testing to MCI/MI alone (MI negative), n (%)						5 (1.8)	6 (2.1)	2 (2.4)	13 (2.0)
Positive patch testing to MI, n (%)						18 (6.6)	29 (10.1)	11 (12.9)	58 (9.0)
Positive patch testing to MI alone (MCI/MI negative), n (%)						9 (3.3)	17 (5.9)	5 (5.9)	31 (4.8)

Abbreviations: MCI/MI, combination of methylchloroisothiazolinone and MI; MI, methylisothiazolinone.

ppm). In December 2015, Health Canada responded to the evidence of increasing sensitization to MCI/MI and resolved that after June 14, 2016, MCI/MI will no longer be included in products intended for use in children under the age of 3. After December 31, 2016, MCI/MI will not be permitted in any leave-on products. It may still be used in rinse-off products to a maximum concentration of 0.0015% or 15 ppm. Methylchloroisothiazolinone is only permitted in combination with methylisothiazolinone, not alone. Methylisothiazolinone continues to be permitted as a preservative at a maximum concentration of 0.01% (100 ppm).^{12,13} Since July 2015, the European Commission Cosmetics Regulation has restricted use of both MCI/MI and MI to rinse-off cosmetic products only at a maximum concentration of 0.0015% (15 ppm).^{2,14,15} There is no regulation of MCI/MI or MI in industrial or consumer cleaning products in Canada although these sources have been identified as a significant source of sensitization.^{12,16}

The objective of this retrospective chart review is to provide a western Canadian perspective on whether the positive patch testing rate to MCI/MI and/or MI increased during the testing period and whether the addition of MI at 2000 ppm resulted in an increased detection of MI allergy beyond the rate detected by MCI/MI 100 ppm in the NACDG screening series.

Materials and Methods

This retrospective chart review included patients assessed by patch testing for allergic contact dermatitis in a community dermatology clinic in Vancouver, British Columbia, Canada, between January 2008 and April 2015. Patients included in the review had a recorded positive reaction (+, ++, or +++) to MCI/MI or MI at either the initial or the delayed readings.

From January 2008 to April 2015, 2310 patients were evaluated for ACD with patch testing. Of these, 2177 patients were tested with panels that included MCI/MI 100 ppm (January 2008 to June 2012) or MCI/MI 200 ppm and MI 2000 ppm (January 2013 to April 2015). Patch testing was not conducted at the clinic between July 2012 and January

2013. Patients were patch tested according to the NACDG protocol.¹⁷ Allergens were obtained from AllergEAZE (SmartPractice Canada, Calgary, Alberta, Canada) and Chemotechnique Diagnostics (Dormer Laboratories, Inc, Toronto, Ontario, Canada) and applied using IQ Ultra chambers reinforced with Scanpore tape (Chemotechnique Diagnostics). A 45 allergen North American Standard Series was used from 2008 through August 2009, a 70 allergen North American Contact Dermatitis Group Screening Allergens Series from August 2009 to June 2012, and an 80 allergen American Contact Dermatitis Society Core Allergen Series from January 2013 to April 2015. A total of 104 patient records were identified with positive patch testing results to MCI/MI, MI, or both.

Information gathered from patient records included patch test allergens applied, positive or equivocal results, body location of dermatitis, and demographics including the patient's sex, age, occupation, and personal or family history of atopy.

Results

Of 2177 patients who were tested for MCI/MI or MI, 104 patients with positive patch testing results for MCI/MI, MI, or both were identified. Both MCI/MI and MI positive patch test results increased over the study period, with the highest prevalence in 2015 at 9.41% for MCI/MI, 12.94% for MI, and 15.29% for either (Table 1). Between 2008 and 2012, the prevalence of MCI/MI allergy ranged from 0.0% to 1.7%. From 2013 to 2015, it steadily increased, from 5.1% to 9.4%.

When testing for MI at 2000 ppm was introduced in 2013, the initial positive patch testing prevalence was 6.6%, followed by 10.1% in 2014, and 12.9% in 2015. When both MCI/MI and MI were tested, during 2013 to 2015, a subset of patients in each year reacted positively to one allergen but not the other, ranging from 1.8% to 2.4% for MCI/MI and 3.3% to 5.9% for MI.

Of the 104 patients with a positive patch testing result to MCI/MI or MI, 76 (73.1%) were female and 28 (26.9%) male. The mean age of females was 49 years (range, 16-73

Table 2. Patient Characteristics: Positive Reactions to MCI/MI or MI (n = 104).

	No.	%
Female	76	73.1
Male	28	26.9
Anatomical site		
Females		
Upper extremities	40	52.6
Head and neck	37	48.7
Trunk	22	28.9
Lower extremities	9	11.8
Males		
Upper extremities	21	75.0
Trunk	8	28.6
Head and neck	6	21.4
Lower extremities	6	21.4
Personal history of atopy	47	45.2
Allergic rhinoconjunctivitis	35	33.7
Atopic dermatitis	25	24.0
Asthma	17	16.3
Family history of atopy	34	32.7

Abbreviations: MCI/MI, combination of methylchloroisothiazolinone and MI; MI, methylisothiazolinone.

Table 3. Occupations of Patients With Positive Reactions to MCI/MI or MI (n = 104).

	No.	%
Female		
Not recorded	21	27.6
Administration/office	20	26.3
Hairstylist	8	10.5
Retired/not working	8	10.5
Health care	7	9.2
Child care	4	5.3
Food services	3	3.9
Education	2	2.6
Exercise facility	1	1.3
Laboratory	1	1.3
Retail	1	1.3
Male		
Not recorded	8	28.6
Mechanic	11	39.3
Trades	7	25.0
Health care	1	3.6
Retired	1	3.6

Abbreviations: MCI/MI, combination of methylchloroisothiazolinone and MI; MI, methylisothiazolinone.

years) and of males was 52 (range, 32-81 years). The most common anatomical sites of dermatitis were upper extremities (52.6%) and head and neck (48.7%) in females and upper extremities (75.0%) and trunk (28.6%) in males. Forty-seven patients (45.2%) had a history of atopy, and 34 patients

(32.7%) reported a family history of atopy. The most common occupations for females were administrative (27.6%), hairstylist (10.5%), retired or not working (10.5%), health care (9.2%), and child care (5.3%). The most common occupations for males were mechanic (39.3%) and trades (25.0%). Patient characteristics are summarized in Tables 2 and 3.

Discussion

We report a prevalence of contact allergy to MI, MCI/MI, or both of 4.8% for the 2008-2015 period and 11.0% for 2013 to 2015, after the addition of MI 2000 ppm to the testing panel. The highest prevalence in an individual year was 15.3% in 2015. Recently Ham et al⁹ reported an MCI/MI allergy prevalence of 7.5% in another Canadian center, and Yu et al¹¹ reported prevalence of 8.1% in a clinic in the United States. However, clinics in Europe¹ and Thailand¹⁸ have noted prevalence of 10% or greater.

In our cohort, the sensitization rate for MI alone increased from 3.3% in 2013 to 5.9% in 2015. During this period, 31 patients (4.8%) were sensitized to MI but not to MCI/MI. Of the 71 patients who reacted to MCI/MI, MI, or both, 31 reacted only to MI, indicating that 43.7% of the patients sensitized to MI would have had false negative results prior to the addition of MI 2000 ppm to the testing panel. During the same period, 13 patients (2.0%) reacted to MCI/MI but not to MI, reinforcing the need for both MCI/MI and MI to remain in standard screening series. As found in other recent studies, the most commonly affected body sites for ACD in patients with positive patch testing to MCI/MI or MI were the upper extremities.^{9,11}

Our retrospective study confirms that the addition of MI 2000 ppm to the patch testing series in 2013 detected a much higher level of positive patch test reactions than had been detected with MCI/MI alone from 2008 to 2012. Patch testing was ceased at our clinic in April 2015, so it is unclear if and when the peak prevalence will be reached in our population. Our findings are in concordance with other studies from various geographic locations that MCI/MI and MI are significant and increasing causes of positive patch testing and that the addition of MI to the testing series increases the positive yield.^{5,11,19,20} These findings support Health Canada's prohibition of MCI/MI in leave-on products and in leave-on or rinse-off products intended for children under 3 and restriction to 0.0015% (15 ppm) in rinse-off products. However, in contrast to Europe, Canada continues to permit MI at a 0.01% (100 ppm) concentration.

We found a predominance of female patients affected by MCI/MI or MI allergy. In the female patient population, specific occupations were not consistently highly represented, suggesting the exposure may have been due to personal care products. However, among male patients, mechanics and other trades were the predominant occupations, suggesting an industrial exposure to these preservatives. Canada does not monitor or regulate the use of MCI/MI or MI in industrial

products, which leaves patients working in certain occupations vulnerable to sensitization and/or reaction to workplace exposures.

Conclusion

We have demonstrated an increasing prevalence of MCI/MI and MI allergy between 2008 and 2015 in a Vancouver, British Columbia, Canada, dermatology clinic, with the highest prevalence of 15.29% in 2015. From 2008 to 2015, MCI/MI and MI contact allergy has increased in a Vancouver, British Columbia, Canada, dermatology clinic. The addition of MI 2000 ppm greatly increased the positive patch testing yield for MI. Our results support the continued inclusion of both MCI/MI and MI in a screening series as well as the importance of continued efforts to monitor and regulate these preservatives in personal care and industrial products.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

References

1. Castanedo-Tardana MP, Zug KA. Methylisothiazolinone. *Dermatitis*. 2013;24:2-6.
2. Schwensen JF, Bregnbak D, Johansen JD. Recent trends in epidemiology, sensitization and legal requirements of selected relevant contact allergens. *Expert Rev Clin Immunol*. 2016;12(3):289-300.
3. Ali FR, Shepherd EL, Yell LC, et al. Escalating methylisothiazolinone/methylchloroisothiazolinone allergy probably attributable to methylisothiazolinone in leave-on body cosmetics. *Contact Dermatitis*. 2014;70:316-317.
4. Ackermann L, Aalto-Korte K, Alanko K, et al. Contact sensitization to methylisothiazolinone in Finland: a multicentre study. *Contact Dermatitis*. 2011;64:49-53.
5. Latheef F, Wilkinson SM. Methylisothiazolinone outbreak in the European Union. *Curr Opin Allergy Clin Immunol*. 2015;15:461-466.
6. Urwin R, Wilkinson M. Methylchloroisothiazolinone and methylisothiazolinone contact allergy: a new "epidemic." *Contact Dermatitis*. 2013;68:253-255.
7. Bruze M, Engfeldt M, Goncalo M, et al. Recommendation to include methylisothiazolinone in the European baseline patch test series on behalf of the European Society of Contact Dermatitis and the European Environmental and Contact Dermatitis Research Group. *Contact Dermatitis*. 2013;69:263-270.
8. Geier J, Lessmann H, Schnuch A, et al. Recent increase in allergic reactions to methylchloroisothiazolinone/methylisothiazolinone: is methylisothiazolinone the culprit? *Contact Dermatitis*. 2012;67:334-341.
9. Ham K, Posso-De Los Rios CJ, Gooderham M. Methylisothiazolinone testing at 2000 ppm: a sensitizer for allergic contact dermatitis. *Dermatitis*. 2015;26(4):166-169.
10. Lundov MD, Krongaard T, Menne TL, et al. Methylisothiazolinone contact allergy: a review. *Br J Dermatol*. 2011;165:1178-1182.
11. Yu SH, Sood A, Taylor JS. Patch testing for methylisothiazolinone and methylchloroisothiazolinone-methylisothiazolinone contact allergy. *JAMA Dermatol*. 2016;152(1):67-72.
12. Health Canada cosmetic ingredient hotlist. <http://www.hc-sc.gc.ca/cps-spc/cosmet-person/hot-list-critique/hotlist-liste-eng.php#tbl2>. Accessed July 6, 2016.
13. Informing Canadians of risks related to certain preservatives in cosmetic, non-prescription and natural health products. <http://www.healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2016/58290a-eng.php>. Accessed July 6, 2016.
14. Public consultation on Methylisothiazolinone (MI) in the framework of Regulation (EC) No. 1223/2009—rinse-off cosmetic products. http://ec.europa.eu/growth/tools-databases/newsroom/cf/itemdetail.cfm?item_id=8740. Accessed July 6, 2016.
15. Scientific Committee of Consumer Safety-SCCS, Giménez-Arnau AM. Opinion of the Scientific Committee on Consumer safety (SCCS)—opinion on the safety of the use of methylisothiazolinone (MI) (P94), in cosmetic products (sensitisation only). *Regul Toxicol Pharmacol*. 2016;76:211-212.
16. Goossens A, Giordano-Labadie F, Aerts O. Contact allergy caused by methylisothiazolinone: the Belgian-French experience. *Eur J Dermatol*. 2015;25(3):228-233.
17. Pratt MD, Belsito DV, Deleo VA, et al. North American Contact Dermatitis Group patch-test results, 2001-2002 study period. *Dermatitis*. 2004;15(4):176-183.
18. Puangpet P, Chawarung A, McFadden JP. Methylchloroisothiazolinone/methylisothiazolinone and methylisothiazolinone allergy. *Dermatitis*. 2015;26(2):99-102.
19. Goncalo M, Goossens A. Whilst Rome burns: the epidemic of contact allergy to methyl isothiazolinone. *Contact Dermatitis*. 2013;68:257-258.
20. Scherrer MAR, Rocha VB, Andrade ARC. Contact dermatitis to methylisothiazolinone. *An Bras Dermatol*. 2015;90(6):912-914.