

Patch testing with methylchloroisothiazolinone/methylisothiazolinone—Comparison of results with TRUE Test and 200 ppm aq., and methylisothiazolinone patch test outcome

María Matellanes-Palacios¹  | Javier Sabater-Abad¹ | Laia Bou-Boluda¹ |
Víctor Dios-Guillán¹ | Javier Montoro-Lacomba² | Javier Miquel-Miquel¹

¹Department of Dermatology, Hospital Arnau de Vilanova, Valencia, Spain

²Department of Allergology, Hospital Arnau de Vilanova, Valencia, Spain

Correspondence

María Matellanes-Palacios, Department of Dermatology, Hospital Arnau de Vilanova, C/San Clemente 12, Valencia 46015, Spain.
Email: mariamatellanes@hotmail.com

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Over the last few years the optimal patch test concentration of methylchloroisothiazolinone/methylisothiazolinone (MCI/MI) and methylisothiazolinone (MI) has been a matter of debate. The goal of our study was to compare the performance of MCI/MI in TRUE Test with MCI/MI 0.02% aq., and at the same time, to explore the value of additional patch testing with MI alone.

METHODS

Between February 2016 and June 2019, a total of 722 patients were consecutively patch tested with our baseline series that is composed of the TRUE Test (Mekos, Hillerød, Denmark) and a panel of additional allergens, included in the Spanish baseline series but not available in the TRUE Test. All patients were simultaneously tested with two different MCI/MI preparations: the one included in the TRUE Test, and MCI/MI 0.02% aq. (AllerGEAZE/Marti Tor) and MI 0.2% aq. (AllerGEAZE/Marti Tor) in FinnChambers (Epitest, Tuusula, Finland). The patch tests were applied on the upper back for 48 h under occlusion, and read on day (D) 2, D4, and D7, according to current guidelines. We considered positive only the reactions graded +, ++, and +++, dismissing the doubtful reactions (?+) as nonallergic. Clinical relevance was assessed based on patient history regarding proven exposure and improvement/resolution with avoidance, and defined as unknown/unlikely, possible, and confirmed. Statistical analysis was performed using SPSS (version 23.0; SPSS, Chicago, Illinois) and Epi Info (version 3.0).

RESULTS

The MOAHLFA index for the whole patient group was as follows: Male, 35.9%; Occupational dermatitis, 5.7%; Atopic dermatitis, 27.8%;

Hand, 39.6%; Leg, 2.4%; Face, 19%; and Age ≥ 40 years, 68.7%. The subgroup of MCI/MI and/or MI sensitized patients ($n = 98$, 13.6%) showed significantly higher percentages of women (odds ratio [OR] = 1.55, 95% confidence interval [CI] 1.01–2.36, $P = .041$) and hand eczema (OR = 1.98, CI 95% 1.29–3.04, $P = .002$).

A total of 440 patients (60.9%) of the 722 tested showed positivity to one or more allergens in the baseline series. Among the 98 who had a positive patch test to at least one of the three formulations, 80 (11.1%) had positive reactions to MCI/MI TRUE Test, 76 (10.5%) to MI 0.2% aq., and 71 (9.8%) to MI/MCI 0.02% aq. (Table 1). Of note, only 51 (52.0%) of the 98 patients sensitized to methylisothiazolinones reacted to all three formulations. Three additional patients had only ?+ reactions and were not considered in the statistical analysis. Reactions to MI 0.2% aq. were significantly stronger ($P < .01$), whereas no significant differences in grades were seen between MCI/MI TRUE Test and MCI/MI 0.02% aq. More than 80% of positive reactions had some degree of clinical relevance, without significant differences between the isothiazolinone formulations (Table 1).

Fifteen of the 98 patients (15.3%) tested negative to both MCI/MI formulations and were positive to only MI 0.2% aq., that is, would have been missed if MI 0.2% aq. was not included in the baseline series. Of note, MCI/MI and MI sensitization in our series has dropped dramatically from 17.9% in 2016 to 5.6% in 2019 (Figure 1).

DISCUSSION

Dittmar et al¹ compared the diagnostic performance of MCI/MI TRUE Test and MCI/MI 0.01% aq. in investigator-loaded chambers, and

Grading of patch test results (n = 101)							
	Total negatives ^a	?+	—	+	++	+++	Total positives
MCI/MI 0.02 aq.	30	10	20	50	20	1	71
MCI/MI TRUE Test	21	6	15	44	34	2	80
MI 0.2 aq.	25	8	17	28	32	16	76
Clinical relevance of positive reactions, % (n)							
	Unknown/unlikely		Possible		Confirmed		
MCI/MI 0.02 aq. (n = 71)	16.9 (12)		53.5 (38)		29.6 (21)		
MCI/MI TRUE Test (n = 80)	17.5 (14)		53.7 (43)		28.8 (23)		
MI 0.2 aq. (n = 76)	17.1 (13)		55.3 (42)		27.6 (21)		

Abbreviations: MCI, methylchloroisothiazolinone; MI, methylisothiazolinone.

^aTotal negatives include “—” and “?+” results.

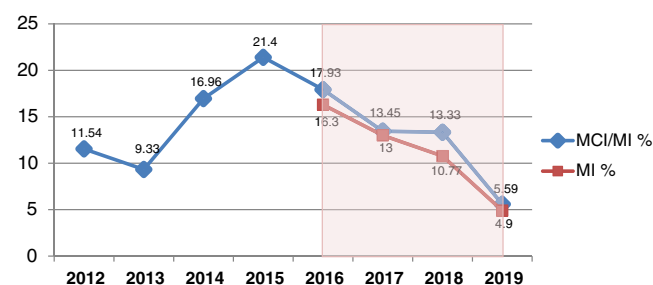


FIGURE 1 Yearly prevalence of sensitization to methylisothiazolinones in our department, from 2012, when we started recording patch test results. The highlighted area corresponds to the period of the current study. The peak of prevalence occurred in 2015, with a progressive declining since then, more pronounced in the last 2 years. MCI, methylchloroisothiazolinone; MI, methylisothiazolinone

their results showed a clear superiority of TRUE Test, which yielded almost twice as high a percentage of positive reactions. The authors explained this finding by the fact that the concentration of MCI/MI in the TRUE Test is 4 $\mu\text{g}/\text{cm}^2$, whereas the concentration achieved in the chambers was 3 $\mu\text{g}/\text{cm}^2$, and the steep dose–response curve of this allergen.

To our knowledge, this is the first study directly comparing MCI/MI in the TRUE Test with MCI/MI 0.02% aq. We have found a slightly higher yield for the TRUE Test (11.8% vs 9.8% positive reactions for MCI/MI 0.2% aq.), although not reaching statistical significance. We conclude from our data that it can be reasonably assumed that the TRUE Test has at least the same sensitivity and specificity as MCI/MI 0.2% aq. in detecting MCI/MI allergic patients, and this should be considered a reassuring finding for all those who use the TRUE Test in their routine clinical practice.

A limitation of our study could be that we did not routinely use micropipettes to load the chambers. The tests were performed in the context of routine clinical practice, and many contact dermatitis practitioners do not use them regularly. Nevertheless, we are able to ensure that the volume loaded in each chamber was at least 20 μL , implying that the final concentration of the allergen was not less than 6 $\mu\text{g}/\text{cm}^2$ for MCI/MI 0.02% aq.

TABLE 1 Patch test results and clinical relevance in the group of patients allergic to methylisothiazolinones (n = 101)

Furthermore, our data speak in favor of maintaining MI 0.2% aq. in the baseline series, as we would have missed approximately 15% of methylisothiazolinone-allergic patients if we had tested only the TRUE Test or MCI/MI 0.02% aq. The similar figures of MCI/MI and MI sensitization in our series, in contrast with older studies,² is in accordance with the hypothesis that, in recent years, most of the “de novo” sensitizations to these isothiazolinones are caused by MI, and not MCI, as apparently was the case when MCI/MI was first introduced as a preservative. Finally, the prevalence of contact allergy to methylisothiazolinones seems to be rapidly declining over the last few years (Figure 1), according to our data, in line with other recent work.³

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AUTHOR CONTRIBUTIONS

María Matellanes Palacios: Conceptualization; data curation; formal analysis; investigation; methodology; resources; software; supervision; validation; visualization; writing-original draft. **Javier Sabater Abad:** Conceptualization; data curation; formal analysis; methodology; project administration; resources; validation; visualization; writing-original draft. **Laia Bou Boluda:** Conceptualization; data curation; formal analysis; investigation; methodology; resources; software; validation; visualization; writing-original draft. **Víctor Dios Guillán:** Conceptualization; data curation; methodology; resources; validation; visualization; writing-original draft. **Javier Montoro Lacomba:** Conceptualization; data curation; formal analysis; investigation; methodology; resources; supervision; validation; visualization; writing-original draft. **Javier Miquel Miquel:** Conceptualization; data curation; formal analysis; investigation; methodology; project administration; resources; supervision; validation; visualization; writing-original draft.

ORCID

María Matellanes-Palacios  <https://orcid.org/0000-0002-6228-3494>

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