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Can patch testing with methylchloroisothiazolinone/methylisothiazolinone be optimized using a new diagnostic mix? – A multicenter study from the Swedish Contact Dermatitis Research Group

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Abstract

Background: Methylchloroisothiazolinone/methylisothiazolinone (MCI/MI) and methylisothiazolinone (MI) are tested to detect contact allergy to these isothiazolinones.

Objectives: To study if an aqueous patch test preparation with MCI and MI in a mix of 0.015% and 0.2%, respectively, detects more contact allergies than the commonly used preparations of MCI/MI in 0.02% aq. and MI in 0.2% aq.

Methods: A total of 1555 patients with dermatitis in five Swedish dermatology departments were tested consecutively with MCI/MI 0.215% aq., MCI/MI 0.02% aq., and MI 0.2% aq.

Results: The share of contact allergy to MCI/MI 0.215% aq., MCI/MI 0.02% aq., and MI 0.2% aq. varied in the test centers between 7.9% and 25.9%, 3.2% and 10.3%, and 5.8% and 12.3%, respectively. MCI/MI 0.215% aq. detected significantly more patch-test positive individuals than both MCI/MI 0.02% aq. ($P < .001$) and MI 0.2% aq. ($P < .001$), as well as either one of MCI/MI and MI ($P < .001$). In the patients only reacting to MCI/MI 0.215% aq., 57.7% were recorded as having a dermatitis that was explained or aggravated by exposure to either MCI/MI or MI.

Conclusion: The results speak in favor of replacing the preparations MCI/MI 0.02% aq. and MI 0.2% aq. with MCI/MI 0.215% aq. as the screening substance in the Swedish baseline series, which has been implemented in 2020.

KEYWORDS

allergic contact dermatitis, contact sensitization, delayed hypersensitivity, methylchloroisothiazolinone/methylisothiazolinone (MCI/MI), mix, patch testing

1 | INTRODUCTION

In the early 1980s a preservative called Kathon CG was introduced on the market. It contained a mixture of methylchloroisothiazolinone (MCI) and methylisothiazolinone (MI). Due to the conditions present during synthesis of this preservative, MCI was formed and found at a

three times higher concentration than MI. MCI/MI in the ratio 3:1 has been patch tested in Sweden in the concentration 0.02% aq. since the mid-1980s.¹ It has been shown to be an extreme sensitizer in both humans and animals.^{2,3} In the early 2000s, MI by itself was introduced as a preservative in industrial products. The first cases of occupational allergic contact dermatitis from MI in industrial products were

reported in 2004.⁴ In 2005, MI by itself was allowed as a preservative in cosmetics. Because MI is a weaker preservative and also a less-potent sensitizer than MCI, a higher concentration was allowed in cosmetics compared to MCI/MI. However, the use of MI became widespread and it was soon evident that the allowed concentration indeed did cause sensitization, as an unprecedented rise in the contact sensitization frequencies to MCI/MI and MI was seen, for example, in Europe.⁵⁻⁷

In 2012, the Swedish Contact Dermatitis Research Groups (SCDRG) conducted a study in which MI 0.2% aq. was tested in parallel with MCI/MI 0.02% aq.⁸ It showed that by only testing with MCI/MI at 0.02% there is a risk that those with a weak MI sensitization are missed because the concentration of MI is too low in the test preparation (50 ppm). The SCDRG concluded that because several repeated open application studies had shown that also patients with weak allergies risk developing dermatitis if exposed under prolonged conditions,⁹⁻¹¹ it is necessary to test with MI separately, and thus SCDRG recommended that MI 0.2% aq. (60 µg/cm²) should be included in the Swedish baseline series from January 2014.⁸ This is the same concentration/dose as the one recommended in the European baseline series.¹² Thereby, at present there are two patch-test preparations containing MI in the Swedish and European baseline series.

The aim of the present study was to explore the possibility of patch testing with an MCI/MI mix with an MI concentration high enough to detect also those with a weak MI sensitization. Thereby, only one preparation is needed in the screening of MCI and MI sensitization, which would save space on the patient's back and thus enable a wider screening of other contact allergens.

2 | METHODS

The study was conducted by the SCDRG. Five Swedish dermatology clinics took part during the period from January 1, 2014 until December 31, 2014. The participating clinics were located in Malmö, Gothenburg, Uddevalla, Stockholm, and Umeå. Results are based on the consecutive patch testing of 1555 patients with suspected allergic contact dermatitis, 1069 female and 486 male patients (mean age 45.1 years; range 9-95 years; female/male 68.7/31.3%).

2.1 | Substances

Patch test preparations used in the study are listed and specified with regard to their content of MI in Table 1. All participating clinics used patch test preparations from the same batches. The preparations containing MCI/MI 0.02% (w/w) aq. and MI 0.2% (w/w) aq. were purchased from Chemotechnique Diagnostics (Vellinge, Sweden) by the Malmö department and distributed to the participating clinics. MCI/MI 0.215% (w/w) aq. was prepared by the Malmö department by spiking the commercial preparation of MCI/MI 0.02% (w/w) aq. (Chemotechnique Diagnostics) with Neolone 950 (Rohm and Haas, Croydon, UK). The MI content in Neolone 950 was analyzed with high-performance liquid

TABLE 1 Specification of aqueous patch test preparations used, their methylchloroisothiazolinone (MCI) and methylisothiazolinone (MI) content as well as the frequency of positive patch tests in the study population

Patch-test preparation	MCI content (ppm)	MI content (ppm)	Contact allergy prevalence (%)
MCI/MI 0.02% v/v	150	50	7.3
MCI/MI 0.215% v/v	150	2000	13.2
MI 0.2% v/v	-	2000	8.4

chromatography prior to the preparation to ensure that the right concentration was obtained. The method is described in detail elsewhere.¹³

2.2 | Patch testing

The patch testing and reading of the patients followed the routine of the participating clinics. Finn Chambers (8 mm diameter; SmartPractice, Phoenix, Arizona) on Scanpor tape (Norgesplaster, Vennesla, Norway) was used in all centers except Uddevalla and Gothenburg, which used IQ Ultra chambers (8 × 8 mm; Chemotechnique Diagnostics) on a hypoallergenic surgical tape. The doses 15 µL (30 µL/cm²) for the Finn Chamber¹⁴ and 20 µL (31 µL/cm²) for the IQ Ultra were applied. Micropipettes were used to apply the correct dose for the test system of choice. The chambers were applied on the back and stayed occluded during 48 hours. Readings were classified according to the International Contact Dermatitis Research Group (ICDRG) guidelines.¹⁵ All patients were read twice, on day (D)3 or D4 and on D7. An individual test protocol designed for the study was filled in for each patient with patch test reactions (allergic, doubtful, or irritant) to at least one of the following test preparations: MCI/MI 0.02%, MI 0.2%, or MCI/MI 0.215%. It was emphasized that all patch test reactions without an obvious morphology of an allergic or irritant nature must be classified as doubtful. Also known, probable, or unknown exposure to MCI/MI or MI was to be recorded. In all patch testing centers, an assessment of clinical relevance of the contact sensitization to MI and/or MCI/MI was to be registered. When the reading dermatologist judged the clinical relevance, he/she had one of four options to tick, that is, explains the dermatitis, aggravates/contributes to the dermatitis, has no influence on the dermatitis, or has unknown influence on the dermatitis. Whether the skin problems were work-related or not also was to be commented on. Late reactions beyond D8 were also to be reported. A dermatologist read all patch tests on both days in all centers except Umeå, where a nurse trained in patch test readings did the first reading and a dermatologist the second one.

2.3 | Statistics

McNemar's two-sided test was used to compare the frequency of contact sensitization to (a) MCI/MI 0.215% aq. and MCI/MI 0.02%

aq., (b) MCI/MI 0.215% aq. and MI 0.2% aq. as well as (c) MCI/MI 0.215% aq. and MCI/MI 0.02% aq., and/or MI 0.2% aq. Fisher's exact test, two-sided, was used to compare the number of contact sensitization cases in female and male patients for the three patch test preparations. In addition, 95% confidence intervals of frequencies of contact sensitization were calculated using the Mid-P exact test by OpenEpi (<http://openepi.com>). A *P*-value of $<.05$ was considered to be significant.

3 | RESULTS

The number of patch-tested individuals in each center, the prevalence of contact sensitization to the investigated preparations, and patch test readings are shown in Tables 2 and A and B3. Overall, the proportion of contact sensitization to MCI/MI 0.02% aq., MCI/MI 0.215% aq., and MI 0.2% aq. varied in the five test centers between 3.2% and 10.3%, 7.9% and 25.9%, and 5.8% and 12.3%, respectively. MCI/MI 0.215% aq. detected significantly more patch-test positive individuals than both MCI/MI 0.02% aq. ($P < .001$) and MI 0.2% aq. ($P < .001$) when compared separately. The preparation of MCI/MI 0.215% aq. detected significantly more positive reactions than the two other preparations did together ($P < .001$), even if this mix did not pick up all allergic individuals; 6 were missed (0.4%). Statistically significantly

more women than men were positive to MI 0.2% aq. ($P = .023$), whereas no statistically significant differences could be seen between the sexes for MCI/MI 0.215% aq. ($P = .11$) or MCI/MI 0.02% aq. ($P = .092$).

In Figure 1 the distribution of exclusive and concurrent reactions to the three preparations is presented in an area-proportional Venn-diagram, plotted using euler APE v 3.¹⁶ In Figure 2 the distribution of patch test reactions to MCI/MI 0.215%, MCI/MI 0.02% aq., and MI 0.2% aq. on D3/4 versus D7 is shown for all five participating clinics. When assessing the results from the five clinics it was shown that 4.9% (10/206) of the individuals who were patch-test positive to MCI/MI 0.215% aq., 5.4% (7/130) who were patch-test positive to MI 0.2% aq., and 2.7% (3/113) who were patch-test positive to MCI/MI 0.02% aq. would have been missed if readings had only been performed on D3/4.

In total, eight irritant reactions in four patients were reported (Tables 3A and B). Of these, two irritant reactions were registered for MCI/MI 0.215% aq. on D7 in two patients with a registered IR reaction and doubtful reaction, respectively, on D3/4. The patient with a doubtful reaction on D4 and irritant reaction on D7 had a positive reaction on D13. This patient was not retested to try to rule out patch-test sensitization.

The percentage of doubtful reactions to MCI/MI 0.215% aq. seen on D3/4 was 2.5% in the whole population (Table 3A), whereas the figure for D7 was 1.8% (Table 3B). The percentage of doubtful

TABLE 2 Positive patch test reactions on day 3/4 and/or day 7 when patch testing with methylchloroisothiazolinone/methylisothiazolinone (MCI/M) 0.02% (w/w) aq., MCI/MI 0.215% (w/w) aq., and methylisothiazolinone (MI) 0.2% (w/w) aq. In five different patch test centers, stratified by gender

	Total number of tested (n)		MCI/MI 0.02% aq. n (%), CI		MCI/MI 0.215% aq. n (%), CI		MI 0.2% aq. n (%), CI		MCI/MI 0.02% aq. and/or MI 0.2% aq. n (%), CI	
	♀	♂	♀	♂	♀	♂	♀	♂	♀	♂
Center 1 Malmö	489	238	46 (9.4) 7.0-12.4	14 (5.9) 3.3-9.6	72 (14.7) 11.6-18.4	19 (8.0) 4.9-12.2	47 (9.6) 7.1-12.7	14 (5.9) 3.3-9.6	61 (12.5) 9.6-15.9	16 (6.7) 4.0-10.7
Center 2 Gothenburg	242	100	10 (4.1) 2.1-7.4	1 (1.0) 0.05-4.9	21 (8.7) 5.5-13.0	6 (6.0) 2.4-12.5	16 (6.6) 3.9-10.5	4 (4.0) 1.3-9.6	18 (7.4) 4.5-11.5	4 (4.0) 1.3-9.6
Center 3 Stockholm	122	52	11 (9.0) 4.7-15.7	7 (13.5) 5.9-26.6	27 (22.1) 14.9-31.8	18 (34.6) 21.2-53.7	15 (12.3) 7.1-19.8	6 (11.5) 4.7-24.0	16 (13.1) 7.8-20.8	8 (15.4) 7.1-29.2
Center 4 Uddevalla	95	43	13 (13.7) 7.6-22.8	1 (2.3) 0.12-11.5	23 (24.2) 15.7-35.8	4 (9.3) 3.0-22.4	14 (14.7) 8.4-24.1	3 (7.0) 1.8-19.0	16 (16.8) 10.0-26.8	3 (7.0) 1.8-19.0
Center 5 Umeå	121	53	6 (5.0) 2.0-10.3	4 (7.5) 2.4-18.2	9 (7.4) 3.6-13.7	7 (13.2) 5.8-26.1	9 (7.4) 3.6-13.7	2 (3.8) 0.63-12.5	10 (8.3) 4.2-14.7	4 (7.5) 2.4-18.2
Total	1069	486	86 (8.0)	27 (5.6)	152 (14.2)	54 (11.1)	101 (9.4)	29 (6.0)	121 (11.3)	35 (7.2)
CI			6.5-9.9	3.7-8.0	12.1-16.6	8.4-14.4	7.7-11.4	4.1-8.5	9.4-13.5	5.1-9.9

Abbreviations: ♀ = women; ♂ = men; CI = 95% confidence interval.

TABLE 3 (A), Number of all patch test reactions on day 3 or 4 when patch testing with methylchloroisoethiazolinone (MCI/M) 0.02% (w/w) aq., MCI/MI 0.215% (w/w) aq., and methylisothiazolinone (MI) 0.2% (w/w) aq. in five different patch test centers. (B), Number of all patch test reactions on day 7 when patch testing with methylchloroisoethiazolinone/ methylisothiazolinone (MCI/M) 0.02% (w/w) aq., MCI/MI 0.215% (w/w) aq., and methylisothiazolinone (MI) 0.2% (w/w) aq. in five different patch test centers

Center (A)	MCI/MI 0.02% aq.n, (%)						MCI/MI 0.215% aq. n, (%)						MI 0.2% aq. n, (%)					
	Neg	?+	+	++	+++	IR	Neg	?+	+	++	+++	IR	Neg	?+	+	++	+++	IR
1 Malmö	660 (90.8)	8 (1.1)	18 (2.5)	29 (4.0)	11 (1.5)	1 (0.1)	636 (87.5)	4 (0.6)	31 (4.3)	33 (4.5)	23 (3.2)	0 (0)	664 (91.3)	6 (0.8)	18 (2.5)	26 (3.6)	13 (1.8)	0 (0)
2 Gothenburg	330 (96.5)	1 (0.3)	6 (1.8)	4 (1.2)	1 (0.3)	0 (0)	317 (92.7)	1 (0.3)	9 (2.6)	11 (3.2)	4 (1.2)	0 (0)	322 (94.2)	2 (0.6)	6 (1.8)	8 (2.3)	4 (1.2)	0 (0)
3 Stockholm	147 (84.5)	9 (5.2)	4 (2.3)	8 (4.6)	6 (3.4)	0 (0)	108 (62.1)	24 (13.8)	23 (13.2)	11 (6.3)	8 (4.6)	0 (0)	147 (84.5)	6 (3.4)	8 (4.6)	6 (3.4)	7 (4.0)	0 (0)
4 Uddevalla	122 (88.4)	2 (1.4)	3 (2.2)	7 (5.1)	4 (2.9)	0 (0)	110 (79.7)	1 (0.7)	12 (8.7)	9 (6.5)	6 (4.3)	0 (0)	118 (85.5)	3 (2.2)	8 (5.8)	4 (2.9)	5 (3.6)	0 (0)
5 Umeå	163 (93.7)	2 (1.1)	7 (4.0)	2 (1.1)	0 (0)	0 (0)	148 (85.1)	9 (5.2)	11 (0.6)	5 (2.9)	0 (0)	1 (0.6)	155 (89.1)	8 (4.6)	6 (3.4)	4 (2.3)	0 (0)	1 (0.6)
Total no of reactions, (%)	1422 (91.4)	22 (1.4)	38 (2.4)	50 (3.2)	22 (1.4)	1 (0.1)	1319 (84.8)	39 (2.5)	86 (5.5)	69 (4.4)	41 (2.6)	1 (0.1)	1406 (90.4)	25 (1.6)	46 (3.0)	48 (3.1)	29 (1.9)	1 (0.1)
Center (B)																		
1 Malmö	673 (92.6)	17 (2.3)	17 (2.3)	16 (2.2)	3 (0.4)	1 (0.1)	655 (90.1)	10 (1.4)	36 (5.0)	18 (2.5)	8 (1.1)	0 (0)	675 (92.8)	9 (1.2)	25 (3.4)	14 (1.9)	4 (0.6)	0 (0)
2 Gothenburg	332 (97.1)	2 (0.6)	4 (1.2)	3 (0.9)	1 (0.3)	0	317 (92.7)	0 (0)	13 (3.8)	11 (3.2)	1 (0.3)	0 (0)	325 (95.0)	0	9 (2.6)	8 (2.3)	0 (0)	0 (0)
3 Stockholm	158 (91.0)	2 (1.1)	4 (2.3)	7 (4.0)	3 (1.7)	0	132 (75.9)	13 (7.5)	15 (8.6)	6 (3.4)	8 (4.6)	0 (0)	156 (89.7)	1 (0.6)	6 (3.4)	5 (2.9)	6 (3.4)	0 (0)
4 Uddevalla	123 (89.1)	2 (1.4)	3 (2.2)	6 (4.3)	4 (2.9)	0	113 (81.9)	2 (1.4)	10 (7.2)	7 (5.1)	6 (4.3)	0 (0)	120 (87.0)	2 (1.4)	7 (5.1)	5 (3.6)	4 (2.9)	0 (0)
5 Umeå	165 (95.0)	0	7 (4.0)	2 (1.1)	0	0	158 (90.8)	3 (1.7)	7 (4.0)	4 (2.3)	0 (0)	2 (1.1)	160 (92.0)	3 (1.7)	6 (3.4)	3 (1.7)	0 (0)	2 (1.1)
Total no of reactions, (%)	1451 (93.3)	23 (1.5)	35 (2.3)	34 (2.2)	11 (0.7)	1 (0.1)	1375 (88.4)	28 (1.8)	81 (5.2)	46 (3.0)	23 (1.5)	2 (0.1)	1436 (92.3)	15 (1.0)	53 (3.4)	35 (2.3)	14 (0.9)	2 (0.1)

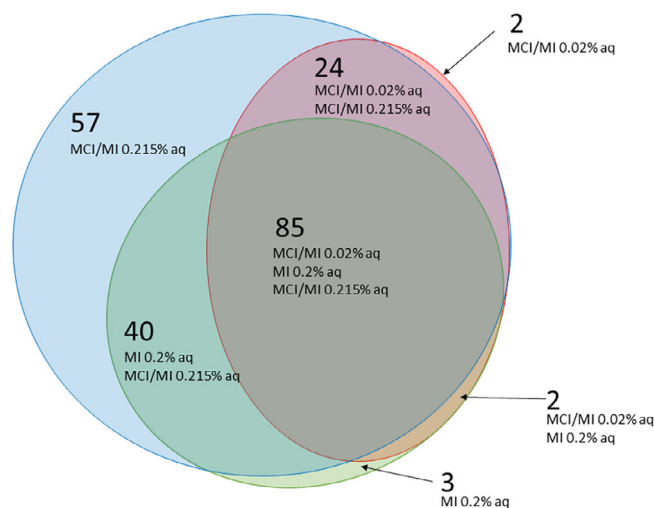


FIGURE 1 The distribution of exclusive and concurrent reactions to methylchloroisothiazolinone/methylisothiazolinone (MCI/MI) 0.02% aq., MCI/MI 0.215% aq., and methylisothiazolinone (MI) 0.2% aq. presented in area-proportional Venn diagrams plotted using euler APE v3. The numbers in the circles represent the number of patients with a positive test reaction to the respective test substance

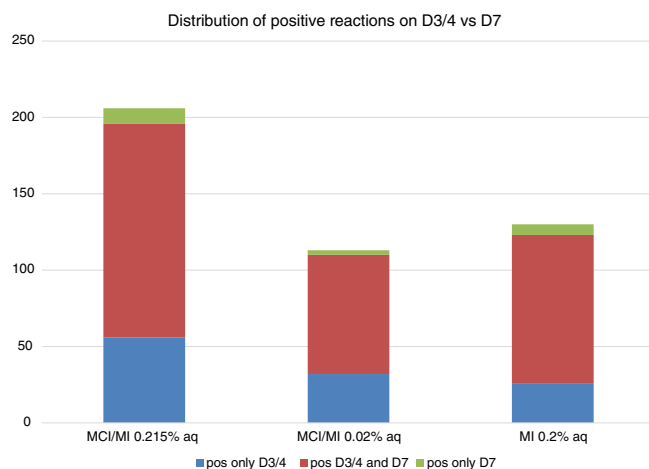


FIGURE 2 The distribution of number of individuals who (a) only reacted on day (D)3/4, (b) reacted on both D 3/4 and 7, and (c) who reacted only on D7 to methylchloroisothiazolinone/methylisothiazolinone (MCI/MI) 0.215% aq., MCI/MI 0.02% aq., and methylisothiazolinone (MI) 0.2% aq., respectively

reactions to MCI/MI 0.215% aq. seen on D3/4 varied from 0.3% to 13.8% and for D7 from 0% to 7.5% in the five departments (Tables 3A and B). In seven patients with a doubtful reaction to MCI/MI 0.215% on D3/4 and D7 the other two haptens were negative, and in another five patients with a doubtful reaction to MCI/MI 0.215% on D3/4 and D7, MI 0.2% was doubtful.

Of the 254 cases with a positive, doubtful, or irritant reaction to any of the three test preparations, 81 patients (32%) were reported to have a known current exposure to MCI/MI, 35 (14%) had no such

exposure, 76 (30%) had a probable exposure, and in 62 (24%) there was no information available. Concerning MI, 62 individuals (24%) had a known current exposure to MI, 36 (14%) had no such exposure, 86 (34%) had a probable exposure, and in 70 (28%) no information was available. Regarding the offending cause in 254 noted cases, in 23 cases (9.1%) the exposure was occupational. In 11 of these patients (48%) the dermatitis could be explained by exposure to either MI or MCI/MI, and the offending relevant causes were reported to be putty, dishwashing liquid, paints, wall-covering glue, and cleaning liquids. In another 11 patients (48%), in whom the dermatitis was considered to be aggravated by such exposure, the offending causes were much the same, but in addition more personal hygiene products were noted. In one patient (4%) in contact with cleaning products and a hair conditioner exposure to MI or MCI/MI was considered having an unknown influence.

In 94 cases (37.0%), exposure was non-occupational. In 16 of these patients (17%) the dermatitis could be explained by exposure to either MI or MCI/MI. The offending relevant causes were reported to be personal hygiene products and washing-up liquid. In 52 cases (55%) the dermatitis was considered to be aggravated by such exposure and the offending relevant causes were similar to the former group. In two cases (2%) the exposure was considered probable and in 24 cases (26%) the exposure to MI or MCI/MI was considered having an unknown influence on the dermatitis. In 137 cases occupational/nonoccupational was not registered.

In the 57 patients only reacting to MCI/MI 0.215% aq., there were data on clinical relevance in 26 cases. In two patients (7.7%) exposure to MCI/MI or MI explained the dermatitis, in 13 patients (50%) the dermatitis was aggravated by such exposure, in three patients (11.5%) the exposure to MCI/MI or MI had no influence on the dermatitis and in eight patients (30.8%) the exposure had an unknown influence on the dermatitis.

4 | DISCUSSION

MCI/MI in the ratio 3:1 is well-known for its steep dose-response curve when patch tested in serial dilutions, and a slight change in concentration can affect the patch-test reactivity and irritancy significantly.¹ At present, the recommended patch test concentration in most baseline series is 0.02% aq.^{17,18} Patch test sensitization rates of ~1% have previously been shown when MCI/MI in the ratio 3:1 has been tested at 0.025 and 0.03% aq. using the Finn chamber technique, with application of 15 μ L.¹⁷ To minimize the risk of active sensitization when testing with an MCI/MI mix with a high content of MI (i.e., MCI/MI 0.215%) a pre-study was conducted at the Malmö department. In this study the concentration of MI was increased in the MCI/MI mix to 2000 ppm and patch tested in consecutively patch tested dermatitis patients in a step-wise manner, ensuring that no adverse effects were seen before proceeding with a higher concentration. Thus, at first 79 patients were tested with only a preparation consisting of 0.015% MCI and 0.05% MI (MCI/MI 0.065%); thereafter 46 patients were tested with MCI/MI 0.065% and an additional

preparation consisting of 0.015% MCI and 0.1% MI (MCI/MI 0.115%), and finally another 191 patients were tested with MCI/MI 0.065% aq., MCI/MI 0.115%, and MCI/MI 0.215%. Because no adverse effects were observed in the pre-study, it was concluded that MCI/MI 0.215% aq. could be used in the larger multicenter study.

The results show that MCI/MI 0.215% aq. detects a significantly higher number of patch-test positive individuals than the preparations of MCI/MI 0.02% aq. and MI 0.2% aq. do individually or together. The fact that women more often tested positive to MI 0.2% aq. than men has been reported previously, and one explanation is sensitization from cosmetics preserved with MI.

In the guidelines for patch testing published by the ESCD it is recommended that patch-test readings are performed on D3/4 and D7.¹⁹ As pointed out in the guidelines, D4 is the reading day that traces most contact sensitization; however, to trace all contact sensitization, a second reading is necessary. For some allergens, such as corticosteroids, gold, and isocyanates, this is particularly important, since positive reactions from these substances are known to appear late.²⁰⁻²² However, based on the results from this study, MCI/MI and MI do not seem to belong to the group of allergens that appear late (Figure 2).

Of note, major differences in the frequency of contact sensitization among the five centers were seen. There are many possible explanations. Differences in referrals of patients for patch testing and differences in exposure habits may have prevailed. One center with a very high sensitization frequency to MCI/MI 0.215% had a very long waiting list why only patients with the worst eczema were admitted for patch testing, and obviously they had been sensitized to products containing these preservatives. Another explanation may be differences in evaluation of the morphology of a test reaction (Tables 3A and B). One can see that the percentage of doubtful reactions noted for MCI/MI 0.215% aq. seen on D3/4 and on D7 varied considerably among the centers, between 0.3% and 13.8% and 0% and 7.5%, respectively (Tables 3A and B). This variation implies that standardization is warranted not only for the dose of the patch test but also when various combinations of morphological features should be ascribed as irritant, doubtful, or weak reactions. Concerning irritant reactions, only eight such reactions in four patients were reported, which is a low number.

In addition, differences in gender, age, the number of occupational cases, atopy, and hand, leg, and face dermatitis may also contribute to the results, as well as technical aspects of the patch test procedure. In this study we only had information on gender and age. None of those factors can explain the differences. In this multicenter patch test study there was a high standardization of the patch test methodology. In a recent publication on how to improve the quality of multicenter patch test studies, 16 factors of possible significance for the patch test result in multicenter patch test studies were discussed.²³ In addition to listing the 16 factors, a scoring system is also suggested with various scores based on the relative importance of each factor for the quality of the multicenter patch test study. In the current study, the highest scores were obtained for all factors except for different patch test techniques, lack of control of occlusion after

48 h, no calibration of the test reading, and no monitoring. Despite this, the total score was 23, which rendered this study to be classified as a multicenter patch test study with a high quality.²³

In 95.7% of the occupational cases the exposure to MCI/MI and/or MI was considered clinically relevant, which is a very high figure. The offending relevant causes were similar to what other studies have shown. This is in contrast to the nonoccupational cases, in which 72.3% were considered clinically relevant. Causes were personal hygiene products. However, even this figure is very high.

In the 26 patients with information on specific exposure to these preservatives and only reacting to MCI/MI 0.215% aq. and not to the other two haptens tested simultaneously, two were recorded as having a dermatitis that was explained, and 13 aggravated, by exposure to either MCI/MI or MI, that is, in 57.7% the dermatologist having had the patient noted clinical relevance. In the remainder of the 31 patients, there was not enough information to judge clinical relevance.

The results from this multicenter study are in line with a similar study performed within the International Contact Dermatitis Research Group (ICDRG) (to be published), and in the updated ICDRG baseline series from 2019, MCI/MI 0.02% aq. and MI 0.2% aq. will be replaced by MCI/MI 0.215% aq.²⁴ Based on the results from the present Swedish study, the preparations MCI/MI 0.02% aq. and MI 0.2% aq. will be replaced by MCI/MI 0.215% aq. as the screening substance in the Swedish baseline series from 2020, since the latter preparation yields significantly more positive reactions, a high share of clinical relevance, and a low number of irritant reactions. No cases of patch test sensitization were reported.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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