

Methylisothiazolinone as a relevant Contact Allergen

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Introduction

Isothiazolinones are a group of heterocyclic organic compounds with bactericidal, algicidal and fungicidal activity. Two preservatives containing isothiazolinone-derived biocides are approved in the European Union for use in industrial and cosmetic products. The first one, introduced in the beginning of the 1980s, is a mixture in the ratio of 3:1 of methylchloroisothiazolinone and methylisothiazolinone (MCI/MI). It was extensively used for more than a decade until several cases of allergic contact dermatitis limited its use in 1990. Since then, the maximum authorized concentration in cosmetics, previously 30 ppm, was lowered to 15 ppm (11.25 ppm for MCI and 3.75 ppm for MI). The second isothiazolinone, approved since 2005, is the non-halogenated derivative methylisothiazolinone (MI) alone. MI is believed to be a weak sensitizer compared to MCI, however it is also known to be a less effective biocide and hence, requires a high-level usage of concentration. The maximum permitted concentration of MI in cosmetics is 100 ppm, (25-times the concentration of the mixture MCI/MI), while there are no limitations in industrial products. This concentration does not raise in theory a risk to consumer health; however, recently, several cases of MI contact allergy have been reported. Overall three studies on the prevalence of MI contact allergy in dermatological patients reported a prevalence of MI contact allergy around 1.5% suggesting that MI could be an emerging contact allergen to be included by itself in the base line series.^{1,2,3}

Objective

To study the frequency of positive patch test reactions to MI, and its relevance and relation to MCI/MI sensitivity, in the Dermatology Clinic at the Hospital del Mar, Barcelona, Spain.

Material and methods

Patients who attended the Contact Dermatitis Clinic at the Hospital del Mar, Barcelona (Spain) from January 2010 to December 2010 were patch tested following the recommendations of the International Guidelines. MCI/MI (100 ppm in water) and MI (500 ppm) allergens were provided by Hermal Trolab-Almirall. Patch testing results were collected along with basic demographic and clinical data and recorded in the Spanish version of the multilingual "WinAldat®/ESSCA" software (www.essca-dc.org). Allergens were applied using Finn Chambers. Patch test exposure time was 2 days. The standard “positive outcome” (allergic reaction) of the patch test was defined as a morphological + to +++ reaction between day 2 (D2) and day (D4).

Results

From 379 tested patients 21 (5, 5%) showed a positive MCI/MI and MI patch test reaction. Twelve of them only reacted to MCI/MI (3, 1%) and three showed just a MI positive patch test reaction (0.7%) (D4 +++ four and ++ one). Six patients (1, 5%) showed MCI/MI and MI positive patch test reaction and from them five showed a stronger reaction with MI (D4 +++ four and ++ one) compared with the MCI/MI mixture. MI contact allergy was suggested as responsible in the 2.3% of patients patch tested. Relevance was certain in 15 cases. Patch test results for MI and MCI/MI are summarized in table 1.

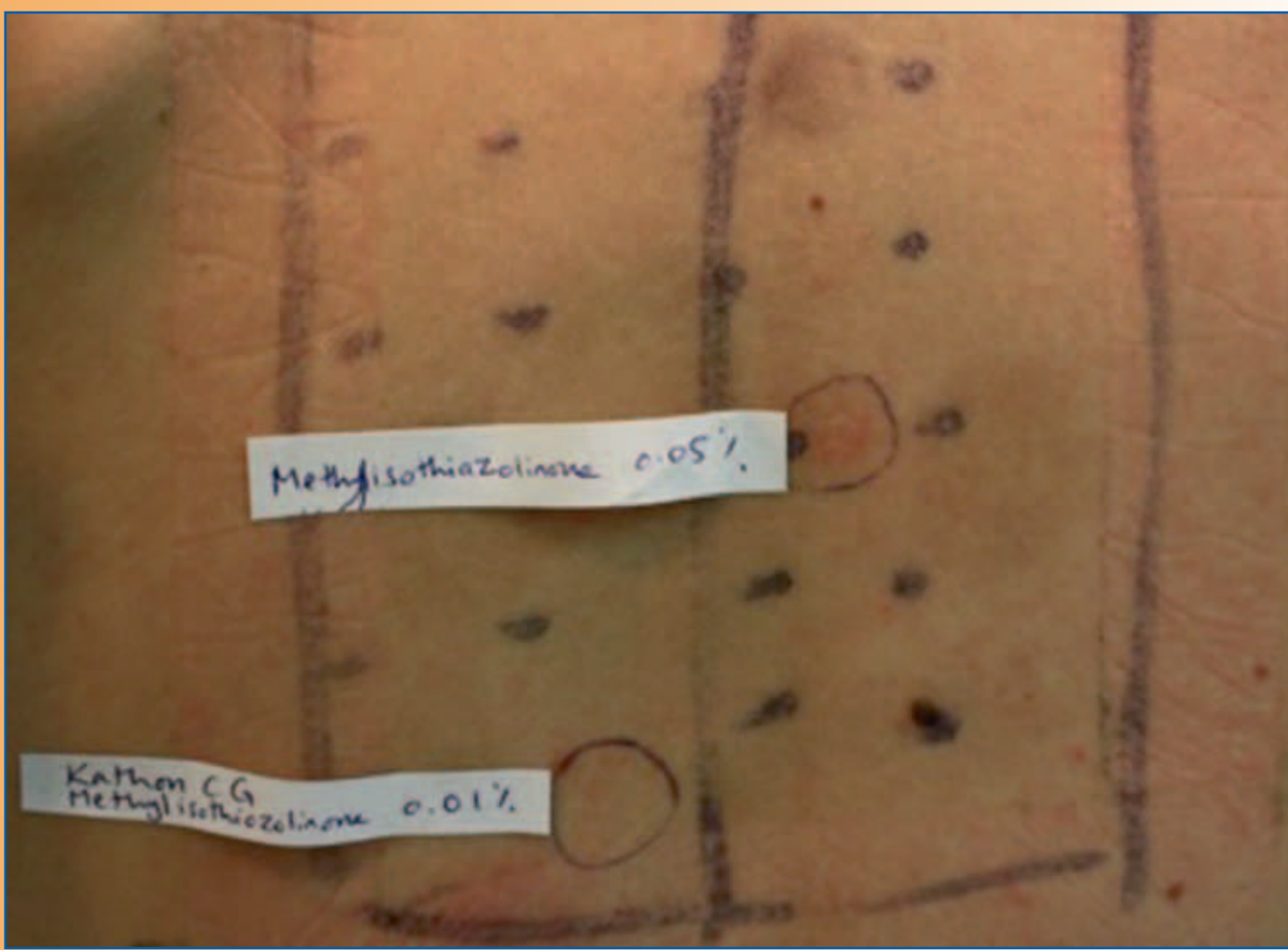


Figure 1. Positive reaction to Methylisothiazolinone 0.05% alone

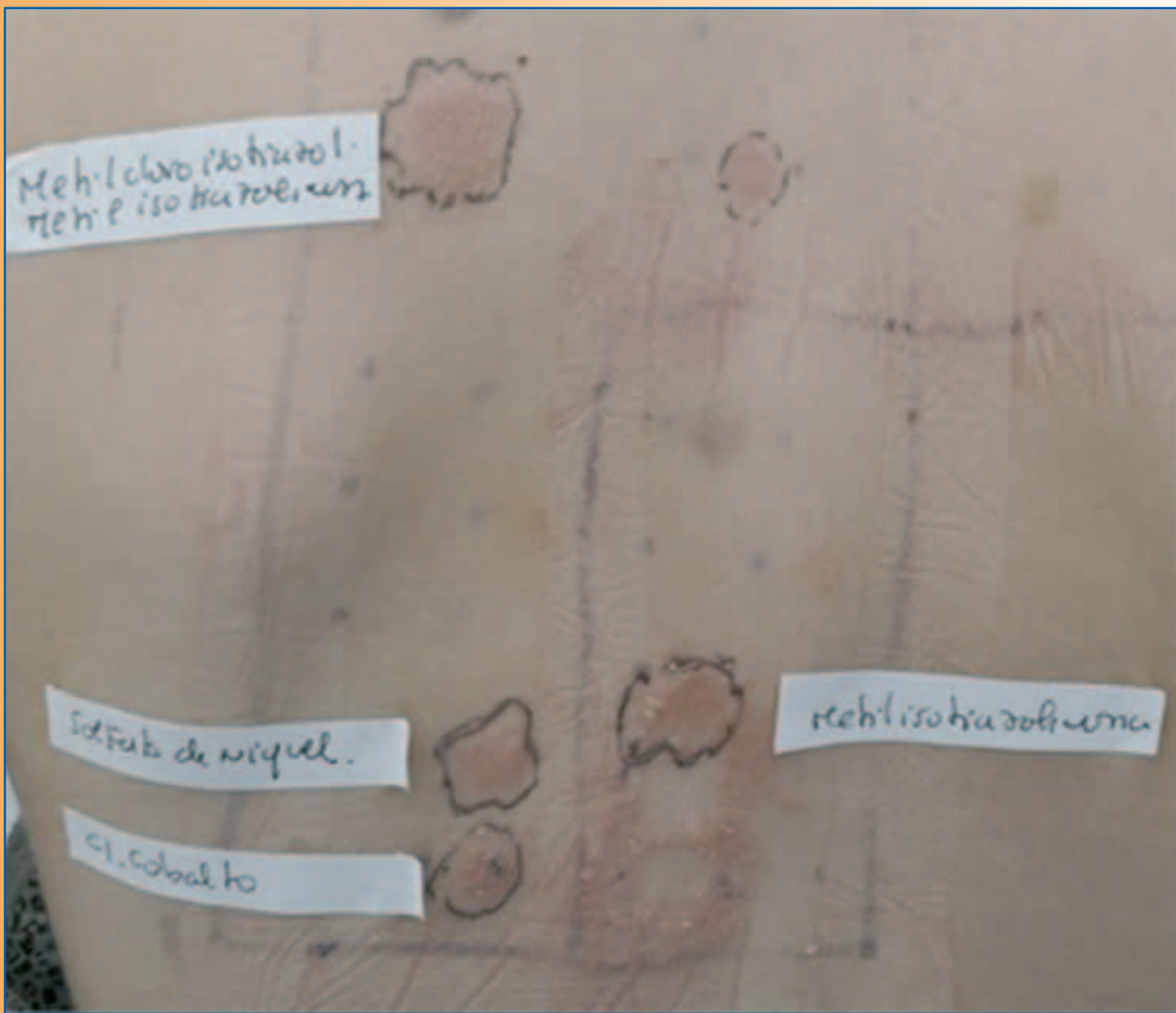


Figure 2 y 3. Positive patch test reaction to Methylchloroisothiazolinone/Methylisothiazolinone and Methylisothiazolinone alone with a stronger reaction with Methylisothiazolinone

Table 1

Case	MCI/MI	MI	Relevance	Exposure	Other positive allergens
1	+++	++	current possible	shoe	BZC
2	++	+++	current occupational	cleaning products	Thi, Ni, Co
3	+++	+++	unknown	unknown	DMDMH, HCTZ
4	++	+++	current certain	cosmetics	PPD, BZC, DMDMH
5	++	+++	unknown	unknown	
6	+	++	current certain	cosmetics	Thi
7	0	+	current possible	cleaning products	
8	0	++	current possible	herbicides, pesticides	FA
9	0	+	current possible	cosmetics	NS, LN, FA,BP, DBCB, IPBC, AM
10	+++	0	current certain	cosmetics	PPD, Co, Ni, Pd
11	+++	0	past probable	cosmetics	NS, FA, CF, BP
12	+++	0	current certain	cosmetics	Ni, LY, Gr, CT
13	++	0	current possible	cosmetics	BP
14	++	0	past possible	unknown	PD, Ni, Co
15	++	0	current certain	cosmetics	
16	++	0	current occupational	cleaning products	Ni
17	+	0	unknown	unknown	
18	+	0	current possible	hair cosmetics	
19	+	0	current possible	cosmetics	BP, BUD, My, Hy
20	+	0	unknown	unknown	
21	+	0	current possible	textile	

Benzocaine: BZC; Thiomersal: Thi; Nickel: Ni; Cloruro de Cobalto: Co; DMDM Hydantoin: DMDMH; Hydroclorothiazide: HCTZ; Paraphenylenediamine: PPD; Formaldehyde: FA; Neomycin sulphate: NS; Lanoline: LN; Balsam of Peru: BP; Dibromodicyanobutane: DBCB; Iodopropynyl: IPBC; Amcinonide: AM; Colophony: CF; Palladium: Pd; Lyril: LY; Geraniol: Gr; Citral: CT; Potassium dichromate: PD; Budesonide: BUD; Methylprednisolone aceponate: My; Hydrocortisone: Hy

Conclusions

These results show that allergic contact dermatitis to MI has still a high prevalence. In order to monitor the development of MI contact allergy and identify cases of MI allergy, which probably otherwise would be undetected, we suggest that inclusion of MI in the European patch test baseline series seems advisable.

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