

**Methyldibromoglutaronitrile in the baseline series: should be tested?
Results of the Skin Allergy Unit of a Fourth Level Hospital in Spain.**

MD García Castro, Rubén (1), MD PhD Velasco Tirado, Virginia (1), MD PhD González de Arriba, Marta (1)

(1) Servicio de Dermatología MQ. y Venereología, Hospital Clínico de Salamanca, Salamanca, España

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Corresponding author:

MD Rubén García Castro
Servicio de Dermatología, Hospital Clínico de Salamanca
C/Paseo de San Vicente, 182, 37007
Teléfono: 923291100
Email: rubengarciacastro.mail@gmail.com

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Methyldibromoglutaronitrile in the baseline series: should be tested?

Results of the Skin Allergy Unit of a Fourth Level Hospital in Spain.

Methyldibromoglutaronitrile (MDBGN) was first introduced in cosmetics in 1985. However, the European Commission banned it in leave-on (2005) and rinse-off (2008) products due to its high sensitization prevalence.(1–5) Thereafter, some reports have found no sensitization with clinical relevance since 2008.(6) However, its use in industrial products is not as restricted.(7) TRUE Test, the Spanish and the European Baseline Series continue to include MDBGN patch tests (5 $\mu\text{g}/\text{cm}^2$ and 0.5% pet., respectively), and Spanish registries report sensitization frequencies of 2.1%.(8)

METHODS

A retrospective study from March 2016 to February 2020 included 455 patients who had been patch tested. All patients had been tested with both MDBGN 5 $\mu\text{g}/\text{cm}^2$ and 0.5% pet. (Marti Tor®, Spain) on Curatest. Additionally, we tested both allergen preparations on 29 healthy controls. Reading criteria followed International Contact Dermatitis Research Group recommendations with readings on day (D) 2 and D4; and morphological criteria were followed to interpret our results. Allergic results included D2 (-) or weak positive, and D4 any positive result (+, ++ or +++) with typical *in crescendo* morphology. Irritant results were all D2 at least weak positive (+) and D4 brownish or vanished (-).

RESULTS

Sixty-seven patients showed a reaction to any of the patches. Two patients showed weak positive reactions (+) to both MDBGN preparations in terms of contact allergy, namely one case of hand eczema in a locksmith, also sensitized to 2-phenoxyethanol, and one case of leg eczema due to topical drugs. Other patch test reactions were weak and more difficult to interpret, as relevance was deemed unknown. We found no strong reaction (++ or +++). Fifty-six irritant reactions (IRR) were seen, appearing as weak positive (+) on D2 and vanishing or decreasing by D4. Most of them corresponded to MDBGN 0.5% pet. In fact, this was the most irritant allergen in our whole series (11.9%). (Fig.1)

All TRUE Test readings were negative in healthy controls. MDBGN 0.5% pet. yielded one weak positive reaction appearing at D4, three doubtful reactions on D2 being negative on D4, and another three (10.3%) which were erythematous and infiltrated on D2 (+) and had vanished on D4.

DISCUSSION

Testing MDBGN using a concentration lower than 0.5% results in a loss of clinically relevant allergic positives.(9) Therefore, testing 0.5% pet. is recommended since 2005, assuming some irritant results will be present.(10) Nevertheless, MDBGN 0.5% pet. has demonstrated both a high share of irritant reactions and scant allergic results, the relevance of which is mainly unknown.(11)

We saw few weak reactions to MDBGN interpreted as allergic. And based on the current legislation, these were hard to explain as we were unable to find any clinical relevance for most of them. MDBGN 0.5% pet. did yield a higher number of cutaneous reactions, but most of them were irritant. In fact, MDBGN 0.5% pet was the most irritant allergen in our series (above others, e.g. 8.7% for carba mix). This percentage exceeds the reported ciphers of other acknowledged irritant allergens, such as carba mix(12) and GST(8), which are no longer tested in the European

nor in the Spanish Baseline Series. Our results on healthy controls support its irritant potential and reveal how arduous its interpretation can be.

In conclusion, regarding the few non-relevant allergic results and the high number of irritative skin reactions, we dispute the need to patch test any MDBGN in a standard series. Assuming it should be tested, finding an optimal concentration seems difficult.

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Patients n=455 (100%)	MDBGN 5 µg/cm ²		INTERPRET.	MDBGN 0.5% pet.		INTERPRET.
	D2	D4		D2	D4	
n=2 (0.4%)	-	+	Weak positive Present relevance	-	+	Weak positive Present relevance
n=3 (0.7%)	-	+	Weak positive Unknown relevance	-	-	-
n=6 (1.3%)	-	-	-	-	+	Weak positive Unknown relevance
n=2 (0.4%)	+	-	IRR	-	-	-
n=54 (11.9%)	-	-	-	+	-	IRR
n=388 (85.3%)	-	-	-	-	-	-

Control g. n=29 (100%)	MDBGN 5 µg/cm ²		INTERPRET.	MDBGN 0.5% pet.		INTERPRET.
	D2	D4		D2	D4	
n=1 (3.4%)	-	-	-	-	+	Weak positive Unknown relevance
n=3 (10.3%)	-	-	-	?+	-	-
n=3 (10.3%)	-	-	-	+	-	IRR
n=22 (75.9%)	-	-	-	-	-	-

Fig.1. Results of MDBGN 5 µg/cm² and 0.5% pet patch tests.

?+: doubtful. +: weak positive. IRR: irritant reactions.