

Contact sensitivity to 2-hydroxyethyl methacrylate in consecutive patients: a one-year multicenter SIDAPA study



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Acrylates and methacrylates, here referred to as (meth)acrylates, are reactive monomers that polymerize into polymer plastics (1). They are well known sensitizers in occupational (e.g. dental materials) (2) and non-occupational settings (e.g. dressings and wound care products) (3). An increasing source of contact sensitivity are (meth)acrylate-containing nail products (4); emerging sources of (meth)acrylate allergy are medical devices (5). 2-Hydroxyethyl methacrylate (2-HEMA) has previously been suggested as a marker of contact allergy to (meth)acrylates (6). Recently, addition of 2-HEMA 2% pet. to baseline patch test series was recommended by the British Society for Cutaneous Allergy in July 2018 (7) and by the ESCD in January 2019 (1). In this study, the prevalence of 2-HEMA contact allergy as a marker of (meth)acrylate allergy in an Italian population sample was analyzed.

### Materials and Methods

Between November 2017 and October 2018, data were collected from 8 Italian dermatology departments homogeneously distributed in Italy. Consecutive patients (n= 4025, 1499 men, 2526 women; mean age 47.2 years) underwent routine patch testing with the SIDAPA (Società Italiana Dermatologia Allergologica Professionale Ambientale) baseline series containing 2-HEMA 2% pet. since 2016. In patients with a history of (meth)acrylate exposure and clinical and/or anamnestic data suggestive of contact sensitivity to (meth)acrylates but negative to 2-HEMA, 5 additional (meth)acrylates were patch tested: ethyleneglycol dimethacrylate (EGDMA), methyl methacrylate (MMA), triethyleneglycol dimethacrylate (TREGDMA) (all 2.0% pet.), and ethyl acrylate (EA) and triethyleneglycol diacrylate (TREGDA) (both 0.1% pet.).

Patch testing was performed with the Haye's Test Chambers (Haye's Service, Alphen aan den Rijn, The Netherlands) on Soffix tape (Artsana, Grandate, Italy), and allergens from FIRMADiagent (Florence, Italy). Readings were performed on day (D)2, D4, and D7 according to ESCD recommendations; patients were asked to return in case of late reactions. The  $X^2$  test with Yates' continuity correction and Fisher's exact test were used to analyze categorical variables. Statistical analysis was performed using IBM-SPSS version 25.0 (IBM Corp., Armonk, New York). In all analyses, a two-sided  $P$ -value  $\leq 0.05$  was considered significant.

### Results

Among the 4025 patch tested patients, 61 (1.5%) reacted to 2-HEMA. This prevalence was higher in females (2.1%; mean age 43.5 years) than in males (0.5%; mean age: 51.0 years) ( $P<0.0001$ ) (Table 1). No late reactions were observed. Strong (++) and extreme (+++) positive reactions were observed in 72.1% of patients (44/61), more frequent in females than in males (73.6% and 62.5%, respectively). Clinical relevance (41/61, 67.2%) was more frequent in females than in males (71.7% and 37.5%, respectively). Moreover, ++ and +++ reactions resulted more frequent in patients who presented clinical relevance than in those without clinical relevance (80.5% and 55.0%, respectively).

Among patients with clinical relevance, non-occupational exposure to (meth)acrylates was documented in 63.4% (Table 2). In both non-occupational and occupational settings, sensitivity to 2-HEMA was mainly caused by nail (meth)acrylates (88.9% and 64.3%, respectively), and in 86.8% of females and in none of males ( $P=0.005$ ). Nine patients negative to 2-HEMA but with a history suggestive of contact sensitivity to (meth)acrylates reacted all to at least 1 (meth)acrylate: 5 (55.5%) to EGDMA, 3 (33.3%) to TREGDA and TREGDMA, and 2 (22.2%) to EA and MMA.

## Discussion

In this one-year study of a large Italian sample of 4025 consecutively tested patients, 2-HEMA yielded a substantial contact sensitization prevalence of 1.5%. Therefore, this frequency of contact sensitization being greater than the 1% threshold, its inclusion in the baseline series (as SIDAPA has done since January 2016) appears appropriate (8). This prevalence is similar to that recently observed in 5920 UK patients (1.7%) (7) and greater than that previously observed in 2790 Swedish and Singaporean patients consecutively patch tested with 2-HEMA from 2005 to 2007 (0.6%) (6), confirming the increasing role of (meth)acrylate allergy in the general population (9).

Our 2-HEMA positive patients presented mean age and range of age consistent with previous studies (4, 10). Regarding gender, prevalence in females was fourfold compared to males; the share of females (86.9%) was similar to other recent studies (6, 11) but higher than in a 13-year study (2002-2015) (3), probably owing to changes of (meth)acrylate allergy sources. Interestingly, we observed ++ and +++ positive reactions more frequently in females than in males, especially concerning relevant reactions. The higher frequency of relevant reactions in females has previously been described (12).

Non-occupational sources of exposure were identified in 63.4% of our patients, more than previously reported (10, 13). Among the relevant reactions, allergy to artificial nails is dominant in our patients (80.5%), especially in non-occupational setting (88.9%), confirming its increasing trend highlighted by recently published literature (3, 4, 14, 15). Despite the well-known concerns about active sensitization to acrylates (11), in our experience, consecutive patch testing with 2-HEMA is safe. In fact, we did not observe any late appearing reaction to 2-HEMA in our patients, as recently reported (1).

In conclusion, our data support the inclusion of 2-HEMA in the baseline patch test series. However, patch testing with a short (meth)acrylate series should be performed in cases with suspected (meth)acrylate allergy, as recently proved by Rolls et al (7).

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**Table 1** Positive reactions to 2-HEMA in 4025 consecutive patch tested patients

Scores	Positive reactions (%)			Relevant positive reactions (%)			Non-relevant positive reactions (%)				
	+	++	+++	+	++	+++	+	++	+++		
N. patients 61 (1.5)	17 (27.9)	28 (45.9)	16 (26.2)	N. patients 41 (67.2)	8 (19.5)	20 (48.8)	13 (31.7)	N. patients 20 (32.8)	9 (45.0)	8 (40.0)	3 (15.0)
Females 53 (2.1)	14 (26.4)	25 (47.2)	14 (26.4)	Females 38 (71.7)	7 (18.4)	19 (50.0)	12 (31.6)	Females 15 (28.3)	7 (46.7)	6 (40.0)	2 (13.3)
Males 8 (0.5)	3 (37.5)	3 (37.5)	2 (25.0)	Males 3 (37.5)	1 (33.3)	1 (33.3)	1 (33.3)	Males 5 (62.5)	2 (40.0)	2 (40.0)	1 (20.0)

**Table 2** Relevant positive reactions to 2-HEMA in 41 patients: non-occupational and occupational exposure

	N. patients (%)	M (%)	F (%)
<b>Non-occupational</b>	<b>27 (63.4)</b>	<b>1 (3.7)</b>	<b>26 (96.3)</b>
Artificial nails	24 (88.9)	-	24 (92.3)
Dental prosthesis	2 (7.4)	-	2 (7.7)
Glues	1 (3.7)	1 (100.0)	-
<b>Occupational</b>	<b>14 (36.6)</b>	<b>2 (14.3)</b>	<b>12 (85.7)</b>
Artificial nails	9 (64.3)	-	9 (75.0)
Dental prosthesis	3 (21.4)	2 (100.0)	1 (8.3)
Glues	2 (14.3)	-	2 (16.7)
<b>Total</b>	<b>41 (100)</b>	<b>3 (7.3)</b>	<b>38 (92.7)</b>
Artificial nails	33 (80.5)	-	33 (86.8)
Dental prosthesis	5 (12.2)	2 (66.7)	3 (7.9)
Glues	3 (7.3)	1 (33.3)	2 (5.3)