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Acrylate and methacrylate allergy: When is patch testing with acrylic acid recommended?

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Acrylic monomers are well known contact sensitizers in occupational and non-occupational settings.^{1,2} Since 2016, the SIDAPA (Società Italiana Dermatologia Allergologica Professionale Ambientale) baseline series included 2-hydroxyethyl methacrylate (2-HEMA) 2% pet. as a marker for contact allergy to acrylates and methacrylates,³ from now on referred to as (meth)acrylates. In the last 5 years, allergic contact dermatitis due to monomeric acrylic acid (CAS no. 79-10-7) contained as an impurity in electrode hydrogel for electrocardiogram (ECG) and transcutaneous electrical nervous stimulation (TENS), was reported.⁴⁻⁷ The aims of this study were to estimate the prevalence of acrylic acid contact sensitivity in consecutive patients, the sources of its sensitivity, and if 2-HEMA is a good marker for detecting acrylic acid allergy.

METHODS

Between January and March 2018, in three Italian patch testing clinics, 436 consecutive patients (143 males, 293 females; mean age 46.9 years) with suspected allergic contact dermatitis were patch tested with the SIDAPA baseline series⁸ (FIRMA Diagent, Florence, Italy) and with acrylic acid (Sigma-Aldrich, Steinheim, Germany). Saline solution test

preparation with acrylic acid was made in the laboratory of the Department of Pharmacy-Drug Sciences of the University of Bari (Italy) at 0.1%.

Patch tests were occluded for 2 days with the Haye's Test Chambers (Haye's Service, Alphen aan den Rijn, The Netherlands) on Soffix tape (Artsana, Grandate, Italy), and readings were performed on day (D)2, D4, and D7.⁸ In patients with a history of (meth)acrylate allergy and/or with a positive reaction to 2-HEMA, contained in the baseline series, and/or a positive reaction to acrylic acid, additional patch tests with a (meth)acrylate series⁸ (FIRMA Diagent, Florence, Italy) were performed (Table 1), with readings on day (D)2, D4, and D7.

Qualitative and quantitative analyses of the test preparation of acrylic acid at the end of the study period were performed using proton nuclear magnetic resonance (¹H-NMR) and high performance liquid chromatography (HPLC) techniques, as previously reported.⁵ In particular, samples of the saline solution test preparations with acrylic acid were investigated by HPLC, performed in triplicate using an Agilent1260 Infinity Quaternary LC System. A Phenomenex Synergi 4 mm Hydro-RP 80 Å 250 × 4.6 mm column, thermostated at 40°C, was used and an isocratic separation was performed using 25 mM NaH₂PO₄, with a pH 3 and acetonitrile (98:2, v/v) as mobile phase at

TABLE 1 Sources of (meth)acrylate allergy, occupational and non-occupational exposure and results of patch testing with acrylic acid, 2-hydroxyethyl methacrylate and eight additional (meth)acrylates in eight patients with at least one positive reaction to (meth)acrylates

	Patient no. (gender, age)							
	1 (F, 37)	2 (F, 21)	3 (F, 77)	4 (F, 58)	5 (F, 29)	6 (F, 53)	7 (F, 31)	8 (M, 75)
Source of (meth)acrylate allergy	Artificial nails	Artificial nails	ECG electrodes	Dental prosthesis	Artificial nails	Dental prosthesis	Artificial nails	ECG electrodes
Occupational (O)/non occupational exposure (NO)	NO	O	NO	NO	O	NO	O	NO
(meth)acrylates ^a								
Acrylic acid (0.1%)	-	-	+++ ^b	-	-	-	-	++ ^b
2-Hydroxyethyl methacrylate (2.0%)	++ ^b	++ ^b	++ ^c	++ ^c	++ ^b	+++ ^b	++ ^b	-
Methyl methacrylate (2.0%)	++ ^b	-	NP	+++ ^b	-	++ ^b	++ ^b	-
Ethylene glycol dimethacrylate (2.0%)	NP	NP	+ ^c	++ ^b	+++ ^b	++ ^b	++ ^b	-
Urethane dimethacrylate (2.0%)	NP	NP	-	-	+ ^b	-	-	-
Tetrahydrofurfuryl methacrylate (2.0%)	NP	NP	+ ^c	-	+ ^b	-	++ ^b	-
Triethylene glycol dimethacrylate (2.0%)	-	-	++ ^c	-	+ ^b	-	NP	NP
Hydroxypropyl methacrylate (2.0%)	NP	NP	++ ^c	++ ^c	+++ ^b	-	NP	NP
Triethylene glycol diacrylate (2.0%)	NP	NP	++ ^c	-	-	-	NP	NP
Bisphenol A-glycidyl methacrylate (2.0%)	NP	NP	-	-	NP	NP	-	-

Note: Patient no.1: 2-hydroxyethyl methacrylate and methyl methacrylate were present in data sheet of patient's nail product.

Note: Patient no.2: 2-hydroxyethyl methacrylate was present in data sheets of patient's products used in her work.

Note: Patient no.3: only acrylic acid was demonstrated by HPLC in ECG hydrogel; therefore, 2-hydroxyethyl methacrylate, ethylene glycol dimethacrylate, tetrahydrofurfuryl methacrylate, triethylene glycol dimethacrylate, hydroxypropyl methacrylate, and triethylene glycol were considered cross-reactors.

Note: Patient no.4: methyl methacrylate and ethylene glycol dimethacrylate were present in data sheet of patient's dental prosthesis; therefore, 2-hydroxyethyl methacrylate and hydroxypropyl methacrylate were considered cross-reactors.

Note: Patient no.5: 2-hydroxyethyl methacrylate, ethylene glycol dimethacrylate, urethane dimethacrylate, tetrahydrofurfuryl methacrylate, triethylene glycol dimethacrylate, and hydroxypropyl methacrylate were present in datasheets of patient's products used in her work.

Note: Patient no. 6: 2-hydroxyethyl methacrylate, methyl methacrylate, and ethylene glycol dimethacrylate were present in data sheet of patient's dental prosthesis.

Note: Patient no.7: 2-hydroxyethyl methacrylate, methyl methacrylate, ethylene glycol dimethacrylate, and tetrahydrofurfuryl methacrylate were present in data sheets of patient's products used in her work.

Note: Patient no.8: acrylic acid was demonstrated by HPLC in ECG hydrogel.

^aAll in pet., except for acrylic acid (saline solution); NP, not performed.

^bRelevant positive reaction;

^cCross reaction.

a flow rate of 1 mL/minute. An injection volume of 20 μ L was used. Acrylic acid was detected at 220 nm and quantified from a linear relationship between the peak area and concentration. The total acquisition time was 15 minutes.

RESULTS

Among the 436 consecutive patients, 2 (0.5%) showed positive reactions to acrylic acid 0.1%. Irritant or doubtful reactions were not observed. The positive reactions occurred in one female (0.3%) and in one male (0.7%) (Table 1). Both patients had allergic contact dermatitis due to ECG electrodes and positive patch tests to acrylic acid were judged relevant since its presence was demonstrated in the hydrogel part of ECG electrodes by HPLC (22.3 ± 2.3 μ g of acrylic acid per mg of hydrogel).

Positive reactions to 2-HEMA were observed in seven patients (1.6%); only one of them was also positive to acrylic acid. Thirty

subjects were also tested with eight additional (meth)acrylates and 19 positive reactions in eight patients were observed. Patient no.8 was monosensitized to acrylic acid (Table 1).

In all the eight patients, positive reactions to (meth)acrylates were judged relevant. Non-occupational exposure was documented in five (62.5%) (Table 1): in two subjects (meth)acrylate allergy was induced by dental prosthesis, in two by ECG electrodes, and in one patient by artificial nails. The three remaining patients were nail artists (Table 1). ¹H-NMR and HPLC analyses of the test preparations performed at the end of the 3-month study period showed no degradation product and the intended concentration of 0.1% of acrylic acid was precise and accurate.

DISCUSSION

In this study the prevalence of contact allergy to acrylic acid in 436 patients was 0.5% with two relevant positive reactions, both due to the presence

of this monomer as an impurity in the hydrogel part of ECG electrodes. This observation suggests a role of medical devices as a source of (meth)acrylate allergy, particularly with regard to electrodes.⁴⁻⁷ Recently, acrylic acid sensitivity was also described in a case of allergic contact dermatitis due to isobornyl acrylate contained in glucose sensor.⁹

Recently, Bruze et al tested acrylic acid (1% and 0.1% pet.) and documented the absence of positive reactions, also in patients with (meth)acrylate allergy.¹⁰ As the authors stated, this does not exclude the possibility of false negative results due to the low prevalence of positive patch-test reactions to (meth)acrylates in their consecutive patch tested patients (seven patients, 0.9%).¹⁰ In our study, this prevalence is higher (1.8%), but only two of these eight patients (25.0%) were positive to acrylic acid, of whom one was monosensitized. In this patient, 2-HEMA, now the established useful tool to increase the recognition of a greater number of (meth)acrylate contact allergy cases, failed to act as a marker. Without patch testing with acrylic acid this case would have remained undiagnosed.

We excluded the risk of underestimated contact sensitivity to acrylic acid due to low concentrations in saline solution preparation because of degradation, polymerization, and above all, evaporation. In fact, chemical analyses showed that the concentration was as expected at the end of the study. The stability of the test preparations was evaluated by ¹H-NMR and HPLC techniques, as previously described.⁵ Based on our studies, saline solution test preparation with acrylic acid 0.1% was stable over 8 months when stored in the refrigerator at 4–8°C.

In conclusion, despite the increasing trend of (meth)acrylate contact allergy, we detected a low prevalence of contact sensitivity to acrylic acid. Nevertheless, we suggest patch testing with acrylic acid when the suspected sources of contact dermatitis are electrodes of ECG, TENS, and glucose sensors.

CONFLICT OF INTEREST

All authors declare no conflicts of interest.

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