

Contact allergy to acrylates and methacrylates in consumers and nail artists – data of the Information Network of Departments of Dermatology, 2004–2013

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Summary

Background. Allergic contact dermatitis caused by (meth)acrylates used in artificial nails is a relevant problem in both nail artists and consumers.

Objective. To analyse the frequency of this problem in the contact allergy surveillance network Information Network of Departments of Dermatology in 2004–2013, and address possible time trends and patterns of co-sensitization.

Methods. A retrospective analysis of patch test results with (meth)acrylates, along with clinical and demographic data, was performed. These were used to subdivide patients according to (i) a potentially exposed occupation and (ii) nail cosmetics as the suspected cause of contact dermatitis.

Results. Among the 114 440 patients patch tested, 72 244 were female and were considered further. Eighty-seven patients both worked as nail artists/cosmetologists and suspected nail cosmetics as the cause of dermatitis. Among these, 47.1% reacted to at least one (meth)acrylate, most often to 2-hydroxyethyl methacrylate ($n = 27$), 2-hydroxypropyl methacrylate, and hydroxyethyl acrylate ($n = 26$ each), with marked coupled reactivity. In other subgroups of interest, frequencies of sensitization to (meth)acrylates were less elevated but higher than in all remaining female patients ($n = 69\,419$).

Conclusions. The results indicate a not entirely common, but potentially serious, problem, especially concerning occupationally exposed, and sensitized, nail artists. Adequate protective measures should be taught as part of the vocational training.

Key words: acrylates; contact sensitization; cosmetics; methacrylates; nail sculpturing.

Acrylates and methacrylates are a large group of chemically reactive monomers that are (co-)polymerized into

acrylic plastics. These have very broad application as glues, as coatings, and in various plastic materials (1). Both acrylates and methacrylates are well known for their sensitizing potential, and for causing – sometimes severe (2) – allergic contact dermatitis in those exposed to the monomers, be it as consumers or patients, or, in particular, professionally. Occupational exposure, particularly in dental technicians, attracted attention quite early (3). Subsequently, enhanced personal protection and the use of ‘non-touch’ techniques have helped to reduce the burden of contact allergy in this field. Among the many other occupations with regular contact with (meth)acrylates, which will not be discussed here (see, for

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example, 1, 4, 5), cosmetologists involved in either modelling or gluing of artificial nails have received some attention (4, 5). This prompted us to analyse the database of the Information Network of Departments of Dermatology (IVDK, www.ivdk.org), covering 10 recent years, with the objective of identifying the number of patients affected by this problem, sensitization patterns, and a possible time trend.

Methods

The IVDK as a network dedicated to the clinical surveillance of contact allergy has been described elsewhere (6). For the present analysis, data of all patients patch tested between 2004 and 2013 in the IVDK in the course of 114 440 consultations were considered. In cases of multiple consultations by one patient, only the first consultation was chosen. According to the documented (i) occupation and (ii) 'contactants' (product categories presumably causing or worsening dermatitis), patients were subdivided into four groups:

- Patients in whom nail care/sculpturing material was considered to be causative ($n = 89$) and who worked either as nail artists ($n = 31$) or as cosmetologists ($n = 58$)
- Patients who worked as nail artists ($n = 31$) or cosmetologists ($n = 307$), but in whom nail materials were not explicitly mentioned as culprit products [$n(\text{total}) = 338$]
- Patients who worked neither as nail artists nor as cosmetologists, but in whom nail cosmetics/materials were documented as culprit product ($n = 325$)
- Finally, all remaining patients ($n = 110\,289$)

The prevalence of positive patch test reactions to each one of the (meth)acrylate allergens, and the concomitant reactivity between different substances, were analysed following pertinent guidelines (7). Age-adjusted time trends were analysed with log-binomial regression analyses. The demographic and clinical profile of patients in the four above-mentioned subgroups was described according to the MOAHLFA index (8). For data management and analysis, R statistical software, version 3.1.1, was used (9).

Results

The characteristics of patients according to the MOAHLFA index are shown in Table 1. As patients in the three subgroups of interest were almost exclusively female, the following analyses, focusing on the pattern of sensitization, are restricted to female patients.

In the 10-year period, the proportion of female patients tested with the special series containing (meth)acrylates increased by some percentage points ($p < 0.0001$, Cochran–Armitage trend test): whereas 10.5% had initially been patch test with at least one of the acrylates considered, this share was 13.7% in 2013. Concerning patch testing with at least one of the methacrylates, the proportions were 14.9% and 17.6%, respectively. Although the number of patients reacting to acrylates or methacrylates also increased significantly in a univariate analysis ($p = 0.025$, Cochran–Armitage trend test), a log-binomial regression showed no indication of a significant increase in the proportion of positive reactions.

The frequencies of positive reactions to the set of (meth)acrylates considered and the epoxy resin (bisphenol A diglycidyl ether) tested in the baseline series are shown in Table 2. Evidently, all three subgroups showed higher proportions of patients sensitized, compared to the comparison group except for epoxy resin and bisphenol A-glycidyl methacrylate (Bis-GMA), for which sensitization prevalences did not differ significantly between the four groups of female patients ($p = 0.99$ and $p = 0.85$, respectively, χ^2 test). Moreover, with the (non-significant) exception of pentaerythritol triacrylate (PETA), the subgroup 'Occ+ Cont+' (patients working as cosmetologists or, particularly, nail stylists, and claiming that nail cosmetics caused their dermatitis) had the highest observed prevalences. This also holds true if the summary measures 'at least one positive reaction' are considered, as shown at the bottom of Table 2.

Finally, the pattern of cross-reactivity between different compounds was assessed in the subset of female patients in whom nail care/sculpturing material was considered to be causative ('Occ–, Cont+' and 'Occ+, Cont+') and who were patch tested with all of the substances of interest. The results concerning those six allergens tested in the general 'plastics and glues' test series are shown in Table 3. Comparison of the number of patients reacting to both respective allergens in the table cells with the number of positive reactions to each single allergen shows some 'asymmetry' of reactivity. Table 4 includes a similar cross-tabulation of results of the other four (meth)acrylates tested only in a 'dental technician' test series, which had been applied only to a minority of patients, and two marker allergens from the previous set, namely, 2-hydroxyethyl methacrylate (2-HEMA) and methyl methacrylate (MMA). All 41 patients in this subgroup with contact allergy to at least one methacrylate or acrylate could hypothetically have been identified as sensitized with the following set of allergens: hydroxyethyl acrylate (HEA) (with five isolated reactions), MMA, triethyleneglycol dimethacrylate (TEGDMA), ethyl acrylate, PETA (with

Table 1. Distribution of MOAHLEA factors in the four subgroups defined by (i) occupation with potential exposure to acrylic nails (Occ+) and (ii) nail materials having caused dermatitis (Cont+), patch tested in the Information Network of Departments of Dermatology 2004–2013

	Occ–, Cont–	Occ–, Cont+	Occ+, Cont–	Occ+, Cont+
Number	110 289	325	338	89
Male	37.1	4.3	1.2	2.2
Occupational	15.5	18.2	42.6	75.3
Atopic eczema	20.1	25.2	29	19.1
Site: hand	27.3	43.4	51.8	70.8
Site: leg	11.1	1.2	2.1	0
Site: face	15.9	32.3	16.3	15.7
Age ≥ 40 years	71.8	57.5	44.4	42.7

Table 2. Frequency of positive reactions to potentially important (meth)acrylate allergens and epoxy resin [bisphenol A diglycidyl ether (BADGE)] from the baseline series in the four subgroups (female patients only)

Allergen acronym	%	Occ–, Cont– Positive/tested % positive (95% CI)	Occ–, Cont+ Positive/tested % positive (95% CI)	Occ+, Cont– Positive/tested % positive (95% CI)	Occ+, Cont+ Positive/tested % positive (95% CI)
2-Hydroxyethyl methacrylate	1	227/9770 2.3 (2–2.6)	39/172 22.7 (16.6–29.7)	16/73 21.9 (13.1–33.1)	27/74 36.5 (25.6–48.5)
2-Hydroxypropyl methacrylate	2	218/8112 2.7 (2.3–3.1)	36/166 21.7 (15.7–28.7)	16/70 22.9 (13.7–34.4)	26/75 34.7 (24–46.5)
Ethyleneglycol dimethacrylate	2	189/8418 2.2 (1.9–2.6)	31/170 18.2 (12.7–24.9)	14/70 20 (11.4–31.3)	24/75 32 (21.7–43.8)
Triethyleneglycol dimethacrylate	2	89/8416 1.1 (0.9–1.3)	17/170 10 (5.9–15.5)	3/70 4.3 (0.9–12)	11/75 14.7 (7.6–24.7)
Methyl methacrylate	2	148/10 008 1.5 (1.3–1.7)	13/175 7.4 (4–12.4)	2/77 2.6 (0.3–9.1)	10/75 13.3 (6.6–23.2)
Ethyl methacrylate	2	72/5029 1.4 (1.1–1.8)	6/65 9.2 (3.5–19)	2/34 5.9 (0.7–19.7)	6/30 20 (7.7–38.6)
Tetrahydrofurfuryl methacrylate	2	34/4998 0.7 (0.5–0.9)	1/61 1.6 (0–8.8)	2/34 5.9 (0.7–19.7)	4/29 13.8 (3.9–31.7)
Hydroxyethyl acrylate	0.1	108/4309 2.5 (2.1–3)	31/133 23.3 (16.4–31.4)	12/45 26.7 (14.6–41.9)	26/64 40.6 (28.5–53.6)
Ethyl acrylate	0.1	73/5035 1.4 (1.1–1.8)	11/64 17.2 (8.9–28.7)	7/35 20 (8.4–36.9)	9/31 29 (14.2–48)
Pentaerythritol triacrylate	0.1	43/5028 0.9 (0.6–1.2)	0/62 0 (0–5.8)	2/35 5.7 (0.7–19.2)	1/31 3.2 (0.1–16.7)
Bisphenol A-glycidyl methacrylate	2	39/5348 0.7 (0.5–1)	1/154 0.6 (0–3.6)	0/53 0 (0–6.7)	1/74 1.4 (0–7.3)
Epoxy resin (BADGE)	1	715/61 543 1.2 (1.1–1.2)	3/274 1.1 (0.2–3.2)	3/287 1 (0.2–3)	1/78 1.3 (0–6.9)
At least one acrylate	–	201/69 419 0.3 (0.3–0.3)	39/311 12.5 (9.1–16.7)	18/334 5.4 (3.2–8.4)	33/87 37.9 (27.7–49)
At least one methacrylate	–	396/69 419 0.6 (0.5–0.6)	53/311 17 (13–21.7)	19/334 5.7 (3.5–8.7)	34/87 39.1 (28.8–50.1)
At least one acrylate or methacrylate	–	467/69 419 0.7 (0.6–0.7)	56/311 18 (13.9–22.7)	25/334 7.5 (4.9–10.9)	41/87 47.1 (36.3–58.1)

CI, confidence interval.

one isolated reaction each), and additionally 2-HEMA or 2-hydroxypropyl methacrylate (2-HPMA).

Discussion

The present analysis of routine clinical surveillance data collected in the IVDK network in the course of 10 years

has identified a considerable number of patients in whom 'nail cosmetics', including artificial nails, were considered to have caused contact dermatitis prior to patch testing, and/or who worked in potentially exposed occupations, as compared with female patients in whom neither criterion was applicable. It is one of the drawbacks of such a compilation of clinical data that case definitions as used

Table 3. Cross-reactivity between six (meth)acrylates, examined in 193 female patients from subgroups 'Occ–, Cont+' and 'Occ+, Cont+' in whom all six allergens had been patch tested

Allergen n (positive)	2-HEMA 51	2-HPMA 52	EGDMA 43	TEGDMA 26	MMA 14	HEA 56
2-HEMA	–	42	41	16	11	42
2-HPMA	–	–	39	19	11	43
EGDMA	–	–	–	17	10	39
TEGDMA	–	–	–	–	9	21
MMA	–	–	–	–	–	11

EGDMA, ethyleneglycol dimethacrylate; HEA, hydroxyethyl acrylate; MMA, methyl methacrylate; TEGDMA, triethyleneglycol dimethacrylate; 2-HEMA, 2-hydroxyethyl methacrylate; 2-HPMA, 2-hydroxypropyl methacrylate.

Table 4. Cross-reactivity between three (meth)acrylates tested in the context of a 'dental technician' test series in only 86 patients, along with 2-hydroxyethyl methacrylate (2-HEMA) and methyl methacrylate (MMA)

Allergen n (positive)	2-HEMA 24	MMA 6	EA 19	EMA 12	TFMA 5
2-HEMA	–	5	15	9	5
MMA	–	–	4	5	3
EA	–	–	–	7	3
EMA	–	–	–	–	4

EA, ethyl acrylate; EMA, ethyl methacrylate; TFMA, tetrahydrofurfuryl methacrylate.

Pentaerythritol triacrylate did not yield a positive reaction in this subsample, and is therefore omitted from the table.

here may not be entirely specific. This is illustrated by the fact that, in the most specific subgroup, 'Occ+ Cont+', 10 patients had neither been tested with acrylates nor tested with the methacrylates considered here – possibly because of a recent previous patch test with these allergens, or for other reasons not available from the standard documentation.

Previous studies have yielded quite similar results in terms of the significance of certain allergens, with, however, a patch test programme that was not entirely identical to that used in the IVDK. For instance, in a study from Malmö, Sweden, 14 acrylate/methacrylate-allergic nail patients were identified, the most common allergens being ethyleneglycol dimethacrylate (EGDMA) (11 positive), 2-HEMA (9 positive), and TEGDMA (9 positive). All 14 'nail patients' would have been detected if these three allergens had been used instead of a very comprehensive (meth)acrylate series (10). In our data, 4 of 34 methacrylate-positive patients from the subgroup 'Occ+ Cont+' did not react to these three methacrylates; hence, they would have been missed had only 2-HEMA, EGDMA and TEGDMA been tested. If acrylate-positive patients of this subgroup are also taken into account, 11 of 41 would have been missed. In a recent study from Coimbra, Portugal, 122 of 2263 patients were tested with the (meth)acrylate series from Chemotechnique Vellinge, Sweden, including 35 patients who were exposed to artificial nails either as aestheticians or as consumers. Of

these, 28 (80%) showed positive reactions, all of which were considered to be relevant. Overall, the most common allergens were 2-HEMA, 2-HPMA, and HEA (5). Bis-GMA obviously plays no role as a contact sensitizer in the context of acrylic nails. As previously shown, it does not cross-react with other methacrylates (11, 12).

Concerning the test methodology, it has been found that the actual concentration in syringes of methyl methacrylate material is lower than the nominal test concentration of 2% in petrolatum (13), for example only ≤ 56% of 2% (14). Hence, false-negative test reactions may have occurred, and thus an underestimation of the true frequency of MMA sensitization. In contrast, the actual concentrations of 2-HEMA have been found to be in the range of the nominal concentration (13). Attempts to rationalize patch testing with a large number of single (meth)acrylates by compounding important substances into a mix have failed, owing to a high proportion of false-positive reactions (15). Hence, a more or less extensive (meth)acrylate series must probably be employed for adequate diagnosis – notwithstanding the notion of 'marker allergens' such as 2-HEMA, which are, however, not sensitive enough to diagnose 'methacrylate allergy'. At any rate, further breakdown testing would be necessary to identify the individual spectrum of contact allergy, also with the aim of possibly identifying substances that are tolerated. However, even if some (meth)acrylates are tolerated, contact allergy to these

may develop later, so that improved working hygiene and 'non-touch' techniques must probably also be promoted in this area of occupational exposure, preferably early during professional training.

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