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ALLERGIC CONTACT DERMATITIS from NAIL ACRYLATES IN EUROPE. An EECDRG STUDY.

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Abstract

Allergic contact dermatitis (ACD) from nail acrylates is increasingly reported.

Methods: A retrospective study in 11 EECDRG clinics between 2013-15 collected information on cases of ACD from nail acrylates diagnosed by aimed testing.

Results: Among 18228 studied patients, 136 had ACD from nail acrylates (0.75%; 95%CI 0.6–0.9), representing 67.3% (95%CI 60.4–73.7) of ACD from acrylates. They were 135 females, aged 36.7±12.2 years, 59 (43.4%) exposed as consumers and 77 (56.6%) occupationally exposed. Occupational cases were more frequent in Southern Europe (83.7%), were younger (mean 33.4±8.9), most developed during the 1st year at work (65.0%) and at least 11.7% had to quit the job.

Skin lesions involved the hands in 121 patients (88.9%) and the face in 50 (36.8%), with the face as the only affected site in 14 (10.3%).

Most patients reacted to 2 or more acrylates on patch testing, mainly to 2-hydroxyethyl methacrylate (HEMA) (92.5%), 2-hydroxypropyl methacrylate (88.6%), ethylene glycol dimethacrylate (69.2%) and ethyl cyanoacrylate (9.9%).

Conclusions: Nail cosmetics cause most cases of ACD from acrylates and frequently affect nail beauticians or consumers, therefore urging more strict regulations and preventive measures. As HEMA detects most cases and isolated facial lesions may be overlooked it might be worth including this allergen in the Baseline series.

Introduction

Acrylates, methacrylates and cyanoacrylates, further reported as acrylates in this manuscript, are small chemicals that polymerize either spontaneously or with catalysts, like ultraviolet (UV) light, giving rise to very resistant polymers. They are used in multiple industrial settings (plastics, fibreglass, glues, adhesives, coatings, lacquers, paints and printing inks), in medicine (dental restoration, oral prosthesis, contact and intraocular lens, bone cement, surgical glue and wound care dressings) and in aesthetics (nail aesthetics and eyelash or hair extensions)(1)(2). Acrylate monomers are potent sensitizing chemicals and cause allergic contact dermatitis (ACD) mostly in occupational settings (2) Dental workers were mainly affected but within the last decade nail aesthetics has become the main occupation suffering from acrylate allergy (3)(4)(5). ACD to nail acrylates is also frequently affecting consumers with an increasing exposure to this rather popular fashion(4-11).(4)(5)(6)(7)(8)(9)(10)(11)

The technique for sculpturing “acrylic nails” or “porcelain nails”, based on a powder polymer and a liquid monomer that polymerized in the presence of a catalyst is now seldom used as it is time-consuming and causes a disagreeable smell during the procedure(12). Today, main techniques used are based either on acrylates that need UV curing (sculptured gel nails and long lasting acrylate based nail varnish) or on cyanoacrylate (glued nail tips or dipping nails). Mixed techniques can sometimes be used, namely gluing nail tips and applying long-lasting UV-cured nail varnish(5)(12). Any of these techniques can cause ACD both in the beauticians, who also often complain of respiratory problems (2)(6)(7), and in the consumer, who may also suffer paraesthesia, pain, onycholysis and long lasting and severe nail dystrophy (2)(8)(9), sometimes mimicking psoriasis(10).

Many reports have been recently published from European and non-European countries, particularly from the United Kingdom(4),(13) Portugal(3)(11)(14)(15), Spain(5)(16), Germany (17) suggesting an almost epidemic of ACD from nail aesthetics. Also, a safety concern has been raised by the authorities in Denmark and Sweden restricting the use of home kits for nail aesthetics (9).

Objective

Evaluate the panorama of ACD from nail aesthetics across Europe and characterize the clinical manifestations, main allergens detected by patch testing, the occupational or non-occupational origin of the dermatitis and the impact on the occupation.

Methods

A retrospective study was performed reviewing all cases of ACD from acrylates related to cosmetic nail procedures (artificial gel nails, glued nails, dipping nails and acrylate nail varnish) diagnosed during 3 years (2013-2015) in 11 EECDRG (European Environmental Contact Dermatitis Research Group) clinics from several European countries – Bari (Italy), Barcelona (Spain), Coimbra (Portugal), Copenhagen and Odense (Denmark), Heidelberg (Germany), Helsinki (Finland), Leeds (Great Britain), Leuven (Belgium) and Malmö (Sweden).

All patients were patch tested with the European Baseline series and, according to history, also with the acrylate series used in the respective centres (Chemotechnique Diagnostics, Vellinge, Sweden or Trolab allergens, SmartPractice, Europe). Allergens were applied in the back for 48h using 8 mm Finn Chambers on Scanpor Tape™ (Smartpractice, Europe), IQ or IQ-ultra™ patch test chambers (Chemotechnique Diagnostics, Vellinge, Sweden) or Al Test® (Euromedical, Calolziocorte (LC), Italy). Readings and relevance were assessed according to the ESCD (European Society of Contact Dermatitis) guidelines for diagnostic patch testing(18). Only 1+ or more intense patch test reactions were considered.

We retrieved the following data from the files of patients with positive reactions to acrylates with relevance for nail aesthetics: age and gender, history of atopy, localization and characteristics of cutaneous and nail lesions, type of exposure to nail acrylates (occupational v. non-occupational) and reactive chemicals on patch testing. In occupational cases we registered the time at work before developing cutaneous lesions and the future outcome at work.

Data were statistically analysed with SPSS software (Version 21.0; IBM, Armonk, NY, USA). The *t*-test for independent samples was used to compare quantitative variables (eg. age) between groups (eg. occupational v. non-occupational exposure). We used Fisher's exact test and chi-square test to compare nominal variables between different groups. *p*-values <0.05 were considered to be significant. The confidence intervals for proportions were set at 95%.

Results

During the 3 years of the study a total of 18228 patients were patch tested in the 11 clinics involved in the study, 6084 males (33.4%) and 12144 females (66.6%), 57.7% older than 40 years. MOAHLFA distribution is presented in Table 1. ~~Each clinic contributed with 306 to 3113 patients.~~

Positive reactions to acrylates observed during aimed testing occurred in 202 patients (1.11%). Among these ACD from nail acrylates was diagnosed in 136 patients, representing 0.75% of all patch-tested patients (95% Confidence Interval (CI) 0.6–0.9), with percentages varying from 0.07% in Bari to 4.01% in Coimbra, and between 0.68 and 0.86% in the 3 years of the study (Table 2).

Nail acrylates were responsible for 9.1 to 100% (mean 67.3%, 95% CI 60.4–73.7)

of all cases with ACD from acrylates (Table 3), with the lowest percentages observed in the departments devoted to occupational Dermatology, namely Helsinki and Heidelberg.

ACD from nail acrylates occurred in 135 females and one male, with a mean age of 36.7 ± 12.2 years (range 16 to 79). A total of 50 had personal atopy (36.8%), 31 with allergic rhinitis (22.8%), 23 with present or past atopic dermatitis (16.9%) and 20 with asthma (14.7%). Atopy was more frequent among nail acrylate cases than in the whole population tested (36.8% v. 26.8%; $p=0.0112$, Chi-square with Yates correction, two-sided).

Fifty nine patients (43.4%) were exposed to nail acrylates only as consumers, aged 17 to 79 (mean 40.9 ± 14.4 years). Exposure in an occupational setting occurred in 77 cases (56.6%), 76 females and one male, aged 16-59 years (mean 33.4 ± 8.9 years). Occupational cases were significantly younger than consumer cases ($p<0.001$, *t*-test for independent samples).

An occupational origin was observed in 83.7% of the cases from southern Europe (Portugal, Spain, and Italy) while the corresponding figure for the other European countries was 43.5% (36/43 vs 40/92; $p<0.001$, Fisher's exact test, two-sided). At least 39 of the 77 occupational cases (50.6%, 95% CI 39.5–61.8) also reported exposure to nail acrylates as consumers, varying between 100% in the few cases from Odense, Helsinki and Heidelberg to none in Bari (Table 2).

Occupational cases occurred mostly in nail beauticians, 32 of them working only as part-time in this job, often in association with hairdressing. One hairdresser developed symptoms only by sharing the occupational venue with a nail beautician. The only male patient was a complementary therapist applying nail acrylates to clients. Cutaneous lesions developed during the training period in 3 patients or within the first year of work in 26 (65.0%) of the 40 cases that had this information available. In 6 cases there was concomitant or previous occupational exposure to dental acrylates with symptoms developing also in relation with occupational or non-occupational nail aesthetic procedures.

Consumers were performing the technique in nails saloons, at home or among friends and alternating between sculptured gel nails, glued nails and long-lasting gel nail varnishes. No information was collected on the number of sessions before the development of skin lesions, neither on the precise technique used by each of these individuals.

Skin lesions developed mostly on the fingers, hands and/or wrists (121 – 88.9%). Pulpitis with fissures observed in 84 patients (61.7%) was the main presentation in nail beauticians. Concomitant or isolated acute or subacute eczema was observed on the distal parts of the fingers (78 patients – 57.3%), in 1 one case with bullae, on the palms (15 – 11.0%) or wrists/forearms (13 – 9.6%). The face was involved in 50 patients (36.8%), affecting particularly the eyelids (8 cases), lips (4 cases) or cheeks (3 cases). Twenty six of the 50 cases with facial

lesions occurred in an occupational setting. The neck was involved in association with the face in 16 patients (11.8%). Lesions were localized exclusively in the face/neck area in 14 patients (10.3%). In one case lesions were localized on the trunk. Three technicians reported respiratory symptoms during work with nail acrylates.

Subungual hyperkeratosis and long lasting onycholysis or nail dystrophy were also reported but this aspect was not specifically looked for.

The acrylate series tested varied in the different clinics but mostly included 2-hydroxyethyl methacrylate (HEMA), 2-hydroxypropyl methacrylate (HPMA), ethylene glycol dimethacrylate (EGDMA), triethylene glycol dimethacrylate (TEGDMA), methyl methacrylate (MMA) and ethyl cyanoacrylate (Table 4). Positive reactions were observed mainly to HEMA (91.9%), HPMA (83.2%), EGDMA (69.2%), TEGDMA (31.6%), MMA (26.3%) and ethyl cyanoacrylate (9.9%) (Table 4), with a similar distribution among occupational and non-occupational cases. Positive reactions were observed also to 2-hydroxyethyl acrylate (17 cases), ethyl acrylate (16 cases), tetraethyleneglycol dimethacrylate (13 cases), urethane dimethacrylate (10 cases) butyl acrylate and triethyleneglycol diacrylate (9 cases each) and 1,4-butanediol diacrylate (4 cases)

Most patients reacted to 2 or more acrylates, often with 2+ or 3+ reactions (Table 5). A single reaction was observed in 17 patients, to HEMA in 5 cases, to HPMA, ethyl cyanoacrylate, butyl methacrylate and ethylacrylate in 2 cases each, and to ethyl methacrylate, butyl acrylate, triethylene glycol dimethacrylate and tetraethyleneglycol dimethacrylate in 1 case each. None of the patients reacted exclusively either to EGDMA or MMA and 7 patients reacted to acrylates outside the main group of allergens tested in most centres.

HEMA and/or many other acrylates were present in the gels used for nail sculpting procedures and for long-lasting gel nail lacquers, that belonged to many different brands, mostly depending on the country of origin. Although there was no information on the precise technique used by each patient, the use of dipping nails or nail tips glued to the nail plate with a glue based on ethyl cyanoacrylate was frequently reported among UK consumers in association with long-lasting nail gel varnishes and in this subgroup of patients reaction to ethyl cyanoacrylate was particularly frequent (8 of 40 cases – 20.0%). Two of the other 3 patients reactive to ethyl cyanoacrylate reported concomitant occupational exposure to glues used for eyelash extensions.

Apart from acrylates, 56 patients (41.2%) reacted to allergens from the baseline series, mainly to nickel sulphate (33 – 24.3%), methylisothiazolinone and/or methylchloroisothiazolinone/methylisothiazolinone (14 – 10.3%), fragrance mix I and/or II (12 – 8.8%), para-phenylenediamine (8 – 5.8%), thiuram mix or other rubber additives (4 – 2.9%).

Out of 77 beauticians diagnosed with occupational ACD, we have information on the outcome on 46 cases: 9 (11.7%) had to abandon the job, 34 (44.2%) kept working with skin lesions and only 3 (3.9%) managed to keep working without skin lesions, one of them using two pairs of gloves. Customers improved on removal of the artificial nails/acrylate nail varnish but some reported long-lasting nail dystrophy or onycholysis.

Discussion

Nail aesthetics, responsible for 67.3% of positive patch tests to acrylates, confirms that ACD from these chemicals is shifting from industry or dental technicians to nails aesthetics in most countries, as previously reported (3).

ACD from nail-related acrylates has long been known (8)(19) (20), but it seems to be increasing in the last years in many countries, almost in an epidemic trend (5), with a recent report of 230 cases collected from Portugal in 5 years (15). In the present study, 0.75% of all tested patients and 1.1% of females had ACD from nail acrylates. The percentage of patients diagnosed did not increase during the 3 years of the study, suggesting a possible stabilization of these cases.

ACD occurred in all European countries, although the frequency of cases varied in the different centres, with less than 0.1% in Bari, Italy, between 0.2 and 0.8% in most countries and, according to the frequency of previously reported cases (3-7, 9), 1.7% of patch tested patients in Leeds, UK and 4% in Coimbra, Portugal had ACD from nail acrylates. However, the actual nail acrylate contact allergy frequencies in consecutively tested dermatitis patients at the various clinics are not known as the figures presented here represent results from aimed testing. Moreover, these clinics may not fully reflect the panorama of their country.

ACD from nail acrylates is mostly a problem of young females (13), but all age groups can be affected. In this study age ranged from 16 to 79 years, but mean age was 33.6 years whereas most of the patch-tested population was older than 40 years (57.7%). Actually, young females all over Europe had a good adherence to this fashion, that needs repeated exposure to acrylates, in some cases using home kits that were introduced around 2010 (9).

More than half cases were related to occupational exposure, but in large studies these values vary from 25%, as in Israel in 2007, and 31% more recently in the UK (4) to 75.6% in Portugal in 2017 (15) and >90% in Spain, both in 2008 and 2017 (16)(5). Interestingly, an occupational origin was significantly more frequent in southern Europe (Portugal, Spain, Italy) than in the other European countries (83,7 v. 43.5%). About half of the beauticians were also consumers which is lower than in other series (15), although underreporting of personal use of nail acrylates might have occurred.

Cumulative exposure as consumers, with the nail beauticians performing the technique on themselves, potentially with more acrylate spill over during the application, may enhance sensitization. Moreover many of these beauticians have other jobs, namely hairdressing, which may cause hand dermatitis and also

favour further sensitization to acrylates. As previously reported, ACD affects mainly young workers, with some cases beginning still during apprenticeship or during the first year of work, reinforcing the high sensitizing properties of these acrylates (1) and certainly also the inadequate information on their sensitization hazards and adequate preventive measures (17). Atopic dermatitis and atopy, more frequent among nail acrylate cases, as in other studies ((5), may be another possible individual susceptibility factor.

ACD from nail acrylates can have a significant impact on the occupation, with many workers having to quit the job, sometimes choosing a new one where acrylate exposure was highly predictable (dental assistants or dental prosthesis manufacture). Most workers prefer to go on with their profession with mild dermatitis. Correct procedures to prevent acrylate spill-over and direct contact with contaminated objects or working surfaces and frequent glove replacement, possibly with additional cotton or 4H fingertips, allowed continued work with improved lesions, as often reported (5). Acrylates permeate gloves easily but regular change after each client may prevent that acrylates reach the number of molecules within the skin required to elicit ACD, as shown by patch testing acrylates over gloves for limited periods of time (21).

In the present study 87.5% of the patients had two or more positive reactions to acrylates, mostly associated with HEMA and/or HPMA. These are explained either by concomitant or cross-sensitization that is, nevertheless, not extensive to cyanoacrylate. Reactions to ethyl cyanoacrylate in 9 of the 11 patients in this study, observed mostly from UK, are probably explained by the frequent association of different nail aesthetic techniques (cyanoacrylate-based glued nails + long-lasting UV-cured nail varnish). This association was also frequent in other reports from UK (8),(16), but less frequent in other studies(3) (5) (15).

Alone, HEMA or HPMA were able to diagnose, respectively, 91.9% or 83.2% of the cases of ACD from nail acrylates, but unable to detect allergy to ethyl cyanoacrylate. Therefore, in agreement with previous works and to prevent many intense reactions when patch testing suspected patients we can recommend to patch test first with HEMA and ethyl cyanoacrylate, further supplemented with an extended series when these 2 allergens are negative.

As usually reported, skin lesions localized both on areas in direct contact with the acrylates (fingers, hands or wrists) and on ectopic or air-exposed areas (eyelids, face, neck). This can occur by allergen transport by contaminated tools/hands but acrylate evaporation can also explain these skin lesions as well as respiratory complaints reported in a few occupational cases (5). Nail acrylates as the cause of ACD exclusively of the face and neck, observed in 14 patients in this study, may be overlooked if acrylates are not included in a cosmetic series or in the Baseline series. As more than 1% of females are diagnosed with nail-acrylate allergy only with aimed testing and an additional 30% react to other acrylates, this percentage of positive patch tests to acrylates, their frequent

relevance and occasional atypical cases with ectopic localization, may support the introduction of HEMA in the European Baseline series (22), (23).

Conclusions

This retrospective study collecting a large series of cases of ACD from nail acrylates diagnosed all over Europe shows this is a relevant and frequent problem. It affects both consumers and nail beauticians, with significant consequences for the workers: most keep working with dermatitis or abandon the job and have limitations for further occupations. Moreover, although there are contradictory studies (24), some consumers and workers with ACD from acrylates may suffer adverse reactions when further exposed to medical procedures using acrylates (dental restoration, dental prosthesis, bone cement, earing devices, surgical glues, insulin-pumps)(2).

Therefore, in order to prevent sensitization, authorities that regulate cosmetic use should propose a more strict regulation on the use of these highly sensitizing chemicals for aesthetic purposes. Also, consumers and, particularly, workers during their apprenticeship, deserve more correct information on the potential risk of sensitization to acrylates and the most adequate preventive measures.

Table 1 – The total number of patch-tested patients/year and their MOAHLFA distribution in 11 European clinics and positive reactions/allergic contact dermatitis (ACD) to all acrylates and to nail acrylates during aimed testing.

	2013	2014	2015	2013 - 15	%
Total tested	5603	6156	6469	18228	
Male	1869	2150	2065	6084	33.4
Occupational	904	964	967	2835	15.5
Atopy	1430	1661	1801	4892	26.8
Hand eczema	1753	1988	1909	5650	30.9
Leg dermatitis	429	597	540	1566	8.6
Face dermatitis	1392	1578	1627	4597	25.2
Age > 40 years	3255	3744	3517	10516	57.7
Total cases of ACD to acrylates	59 1.05%	78 1.27%	65 1.00%	202 1.11%	
ACD to nail acrylates	39 0.69%	53 0.86%	44 0.68%	136 0.75%	

Table 2. The total number of patch-tested patients in each center, the number and % of patients reacting to nail acrylates, the number and % of those representing occupational cases and those occupational cases who had concomitant exposure to nail acrylates as consumers.

Centre	Patch-tested patients	Nail acrylate cases		Occupational cases		Occupational cases with consumer exposure	
		n	%	n	%	n	%
Barcelona	1258	3	0.24 %	3	100%	2	66.7%
Bari	2731	2	0.07%	2	100%	0	
Coimbra	948	38	4.01%	31	78.8%	18	58.1%
Copenhagen (Gentofte)	3113	18	0.58%	6	33.3%	4	66.7%
Copenhagen (Bispebjerg)	1600	2	0.13%	0	0%	0	
Heidelberg	306	2	0.65%	1	50.0%	1	100%
Helsinki	374	1	0.27 %	1	100%	1	100%
Leeds	2383	40	1.68%	18	45.0%	6	33.3%
Leuven	1601	12	0.87 %	7	58.3%	4	57.1%
Malmö	2263	11	0.49%	6	54.5%	1	16.7%
Odense	1651	7	0.42 %	2	28.6%	2	100%
Total	18228	136	0.75 %	77	56.6%	39	50.6%

Table 3 – Total number of cases of ACD from acrylates among the patch-tested patients in 10 departments, and the number and % of cases related with nail aesthetics.

Centre	Patch-tested patients	Total number of cases of ACD from acrylates	Cases of ACD from nail acrylates	% of nail cases among acrylate allergy
Barcelona	1258	3	3	100%
Bari	2731	4	2	50.0%
Coimbra	948	45	38	84.4%
Copenhagen (Gentofte)	3113	22	18	81.8%
Copenhagen (Bispebjerg)	1600	4	2	50.0%
Heidelberg	306	9	2	22.2%
Helsinki	374	11	1	9.1%
Leeds	2383	46	40	86.9%
Leuven	1601	22	12	54.5%
Malmö	2263	27	11	40.7%
Odense	1651	9	7	77.8%
Total	18228	202	136	67.3%

Table 4. Main allergens tested, with the number of patients tested, number and percentage of positive reactions.

Allergens	Patch-tested patients	Positive reactions	
		n	%
2-Hydroxyethyl methacrylate 2% pet	135	124	91.9%
Hydroxypropyl methacrylate 2% pet	119	99	83.2%
Ethylene glycol dimethacrylate 2% pet	117	81	69.2%
Triethylene glycol dimethacrylate 2% pet	98	31	31.6%
Methyl methacrylate 2% pet	114	30	26.3%
Ethyl cyanoacrylate 10% pet	111	11*	9.9%

- *8 of the 11 cases reacting to ethyl cyanoacrylate were observed among UK consumers; isolated reactions were observed in 2 cases

Table 5 – Main allergens tested with the total number of patients tested with each allergen and the number of positive, negative and concomitant reactions

Allergens	Total tested /reactivity	HEMA			HPMA			EGDMA			TEGDMA			MMA	
		pos	neg	nt	pos	neg	nt	pos	neg	nt	pos	neg	nt	pos	neg
HEMA total tested	135														
HEMA-pos	124	124	0												
HEMA-neg	11	0	11												
HEMA-n.t.	1	0	0	1											
HPMA total tested	119														
HPMA-pos	99	97	2	0											
HPMA-neg	20	11	9	0											
HPMA-n.t.	17	16	0	1											
EGDMA-total tested	117														
EGDMA-pos	81	81	0	0	68	3	10								
EGDMA-neg	36	27	9	0	23	9	4								
EGDMA-n.t.	19	16	2	1	8	8	3								
TEGDMA-total tested	98														
TEGDMA-pos	31	30	1	0	26	1	4	23	5	3					
TEGDMA-neg	67	57	10	0	56	7	4	28	27	12					
TEGDMA-n.t.	38	37	0	1	17	12	9	30	4	4					
MMA-total tested	114														
MMA-pos	30	29	1	0	22	4	4	24	3	3	13	16	1		
MMA-neg	84	80	4	0	61	15	8	41	29	14	14	41	29		
MMA-n.t.	22	15	6	1	16	4	5	16	4	2	4	10	8		
ECA - total tested	111														
ECA-pos	11	9	2	0	8	3	0	9	1	1	3	7	1	5	4
ECA-neg	100	97	2	1	87	7	6	66	19	15	26	55	19	20	64
ECA-n.t.	25	18	7	0	4	10	11	6	16	3	2	5	18	5	16

HEMA: 2-hydroxyethyl methacrylate; HPMA: 2-hydroxypropyl methacrylate;
EGDMA: ethylene glycol dimethacrylate; TEGDMA: triethylene glycol
dimethacrylate; MMA: methyl methacrylate; ECA: ethyl cyanoacrylate; n.t. – not
tested.

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