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Two-year follow-up survey of patients with allergic contact dermatitis from an occupational cohort. Is the prognosis dependent on the omnipresence of the allergen?

Running head: Two-year follow-up of occupational epoxy, rubber, and latex allergy

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Conflicts of interest

None declared

What's already known about this topic?

- Skin diseases are the most frequently recognised occupational diseases in Denmark, and contact dermatitis constitutes more than 90% of these.
- The prognosis for occupational contact dermatitis is often poor.

What does this study add?

- QoL was less impaired in patients with relevant occupational contact allergy to a non-ubiquitous allergen, and there was a trend that total clearance of eczema was more frequent for this group.
- Patients with contact urticaria had significantly less frequent clearance, less improvement in eczema and most impairment of QoL at follow-up.
- A significant positive association between job change and improvement was found.

Abstract

Background

Skin diseases are the most frequently recognized occupational diseases in Denmark. The prognosis for occupational contact dermatitis is often poor.

Objectives

The aim of the study was to investigate the prognosis, assessed by eczema- and, job-status, and skin related quality of life among patients allergic to rubber chemicals and latex (ubiquitous allergens) and epoxy (non-ubiquitous allergen), respectively, two years after recognition of occupational allergic contact dermatitis.

Methods

From a cohort based on data from the Danish National Board of Industrial Injuries, and including all patients with recognised occupational dermatitis in 2010 in Denmark, 199 patients with relevant rubber allergy (contact allergy to rubber chemicals or contact urticaria from latex) or epoxy allergy, were included. Follow-up consisted of a questionnaire covering current severity of eczema, employment, exposure, and quality of life.

Results

The response rate was 75%. Clearance of eczema was reported by 11% and 67% reported improvement. 22% of patients with allergy to a non-ubiquitous allergen had total clearance of eczema compared to 10% of cases allergic to ubiquitous allergens and 0% of those with contact urticaria, ($p=0.116$). Improvement was significantly more frequent in those who had changed jobs compared with those who had not ($p=0.010$).

Conclusions

Our study confirms the poor prognosis for occupational allergic contact dermatitis. At follow-up patients with contact urticaria had significantly poorer prognosis than those with contact allergy, and there was a trend towards a poorer prognosis for those with contact allergy to rubber chemicals, representing ubiquitous allergens, than those with allergy to epoxy,

representing a non-ubiquitous allergen. A significant positive association between job change and improvement was found.

Introduction

Skin diseases are the most frequently recognised occupational diseases in Denmark¹, and contact dermatitis constitutes more than 90 % of these². Although irritant contact dermatitis is the most frequent occupational skin disorder, allergic contact dermatitis is involved in 25 % and contact urticaria in 4 % of the recognised cases, respectively.² The prognosis for occupational contact dermatitis is often poor, and more than 70 % of patients are reported still to have eczema after 12 years.³ In a previous study of patients with occupational hand eczema, 25 % had persistent severe or aggravated disease, 41 % improved, and 34 % had unchanged mild/moderate disease at follow-up after one year, independent of contact allergy.⁴ For allergic contact dermatitis allergen, avoidance is naturally crucial, and the prognosis may depend on the ability to avoid further exposure. The traditional clinical impression indicates that contact allergy to ubiquitous (omnipresent) allergens may lead to more severe and prolonged dermatitis. A poor prognosis was previously reported for patients with chromate contact allergy.⁵ This finding is, however, not consistent for all studies^{6,7}, and in most studies contact sensitisation to specific allergens has not been related to prognosis. A poorer prognosis has been reported for patients with contact urticaria compared to patients with contact allergy.⁴

In Denmark rubber chemicals are the most frequent allergens causing occupational allergic contact dermatitis, and epoxy resins the second most frequent.² Rubber chemicals are examples of ubiquitous allergens, which may be difficult to avoid even outside the work place, while epoxy resins are mainly used in industry⁸ and not widespread in the

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environment. Together contact allergy to rubber chemicals and epoxy constitutes nearly 40 % of recognised occupational allergic contact dermatitis cases.²

The aim of the present study was to investigate eczema, job status, and skin related quality of life (QoL) among patients with relevant contact allergies to rubber chemicals and epoxy, as well as patients with contact urticaria caused by natural rubber latex allergy, two years after recognition of occupational allergic contact dermatitis. The focus was on comparing follow-up data for patients with contact allergy to ubiquitous and non-ubiquitous allergens.

Material and methods

From 01 January 2010 to 31 December 2010 1,504 patients had their cases recognised as occupational contact dermatitis in the *Danish National Board of Industrial Injuries* (DNBII). Patients were patch tested with the European baseline series, supplemented with special series when relevant in relation to their jobs.² From this cohort 199 patients were identified and included in the present study; 121 patients with relevant contact allergy to rubber chemicals, 44 to epoxy, 27 to natural rubber latex, and 7 to both rubber chemicals and natural rubber latex. Baseline data on sex, age, specific diagnosis (irritant contact dermatitis, allergic contact dermatitis, or contact urticaria), patch test results, atopic dermatitis, and skin prick tests has previously been described.² The classification of diagnosis and atopic dermatitis (AD) were submitted from the patients' files to the DNBII, and were based on the clinical examination of each patient by a dermatologist. AD was defined as past flexural eczema or current AD diagnosed by a dermatologist.²

A questionnaire was sent by mail to all participants in January 2013. The questionnaire included a question on current severity of the eczema explored with the question 'How is

your eczema now compared to 2010?’ with the answer categories, ‘improved’, ‘unchanged’, or ‘worse’⁴. Since no baseline-values on severity were available, current severity was assessed as relative to severity at time of recognition as an occupational disease. Questions on employment and change of job (including all changes of jobs from baseline to follow-up) were included⁹, as well as questions on current exposure.

The questionnaire also included the Dermatological Life Quality Index (DLQI). The DLQI is a validated dermatology specific questionnaire about quality of life. It is based on ten items on symptoms and feelings, daily activities, leisure, work or school, personal relationships and side effects of treatment. A standardised and validated Danish translated version of the DLQI was used.¹⁰ Missing data on the improvement question were classified as non-improvement (Table 2), missing data on the exposure question led to the exclusion of the patient from the specific analysis (Table 3). Missing data on the DLQI was handled according to guidelines on use of the DLQI.

Statistics

The Kruskal-Wallis test was applied to test for differences between groups for continuous variables. The Chi-Square test was applied for categorical variables, and where the assumptions for the Chi-Square test were not met, the Fisher’s exact test was used. Two-sided p-values < .05 were considered significant. Calculations were performed using SPSS 20.0 (SPSS Inc., Chicago, IL).

Since an aim of the study was to compare the prognosis for patients with ubiquitous allergies to those with non-ubiquitous allergies, it was decided to exclude patients with overlapping allergies (epoxy/rubber chemicals, epoxy/natural rubber latex, rubber chemicals/natural rubber latex) from the statistical analyses.

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The study was approved by the Danish Data Protection Agency (trial number BBH-2012-034).

Results

The response rate to the questionnaire sent two years after baseline to a total of 199 patients allergic to rubber chemicals, epoxy and/or natural rubber latex, was 75 %; 65 % for males and 82 % for females ($p=0.008$), and follow-up data was thus available for 149 patients.

Mean age of respondents at baseline was 42.2 years (range 16-65 years), as compared with 33.7 years for non-respondents ($p<0.001$).

Baseline data for sex, age, and prevalence of AD is given in Table 1.

No patients were found to have epoxy allergy in combination with rubber chemical or natural rubber latex allergy, but seven patients with both rubber chemical and natural rubber latex allergy were identified. Three of these were not working, one was employed in the same job as at baseline, and three were employed in different jobs as compared to 2010. These seven patients are not included in the following tables or statistical analyses, since an aim of the study was to compare the prognosis for patients with different allergies (see above).

Additional non-occupational contact allergies were found in 18 % of patients with epoxy allergy, in 57 % of patients with allergy to rubber chemicals, and in 63 % of patients with allergy to natural rubber latex ($p=0.001$).

Eczema status at follow-up

Current status of eczema stratified by allergen is given in Table 2. In total 11 % of the patients reported clearance of their eczema at follow-up, 15 % men and 9 % women

($p=0.264$). A total of 22 % of patients with epoxy allergy reported total clearance of eczema as compared to 10 % of patients with rubber chemical allergy ($p=0.116$). Overall 67 % of patients reported improvement. With respect to AD, 78 % of patients with previous or current AD reported improvement as compared to 65 % of patients without AD ($p=0.206$). 26 % with epoxy allergy reported no improvement as compared to 30 % with rubber chemical allergy ($p=0.666$). None with natural rubber latex allergy reported clearance of contact urticaria at follow-up, and 42 % reported improvement, which is statistically significantly less than for those with contact allergies to rubber chemicals and to epoxy ($p=0.033$ and $p=0.036$, respectively).

A total of 11 patients, 3 males and 8 females, reported worsening of eczema at follow-up. Median age for this group was 44 years, 3 had epoxy allergy, 4 had rubber chemical allergy and 4 had natural rubber latex allergy. None had AD, and 7 had additional non-occupational contact allergies. 2 were still exposed to the relevant occupational allergen at the job.

Exposure status at follow-up

Overall 31 % of patients employed at follow-up reported current occupational exposure to their relevant allergen; 21 % of patients with epoxy allergy, 32 % of patients with rubber chemical allergy, and 41 % of patients with natural rubber latex allergy ($p=0.463$). Current exposure at work compared to improvement of eczema at follow-up is given in Table 3 for all patients in employment at follow-up. Although the improvement rate was higher in the group which was no longer exposed, no statistically significant difference was found ($p=0.111$).

Employment status at follow-up

Current employment status stratified by allergy type is given in Table 4. In total 27 % of the patients had changed jobs; 41 % were employed in the same job, and 32 % were not

employed at follow-up. 52 % of those with epoxy allergy had changed jobs, as compared to 25 % of those with rubber chemical allergy, and 5 % with allergy to natural rubber latex. Of the 32 % (n=45) who were not employed at follow-up 58 % indicated eczema as the reason for their non-employment, 33 % indicated that it was not due to eczema, and 9 % left the question blank.

Data for improvement of eczema in relation to job change for the patients employed at follow-up is given in Table 5. Improvement was significantly more frequent in those who had changed jobs as compared to those who had not changed jobs ($p=0.010$); this was statistically significant for patients allergic to rubber (rubber chemicals and natural rubber latex) alone ($p=0.020$), but not for epoxy alone ($p=0.262$).

DLQI

Data for DLQI is given in Fig. 1. The mean DLQI score for all patients was 5. A total of 67 % had scores <6 , corresponding to no effect or only a small effect on the patients' quality of life. A severe negative effect on QoL with scores >10 were found in 7 % of patients with epoxy allergy, 17 % with rubber chemical allergy, and 27 % with natural rubber latex allergy. The median DLQI score was lowest for the epoxy allergy patients (median score = 1) and highest for the natural rubber latex patients (median score = 5) ($p=0.016$), illustrating a significant difference in impairment of QoL, dependent on specific triggering allergies.

Discussion

When re-investigating patients with occupational allergic contact dermatitis two years after recognition of occupational disease, we found that 89 % still had active eczema, and that 33 % had experienced no improvement in their skin condition. Patients with contact urticaria from natural rubber latex showed significantly less improvement than the others, and there

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was a tendency for patients with contact allergy to rubber chemicals compared to those with epoxy allergy to have a lower frequency of clearance, although not statistically confirmed. A significant, positive association between job change and improvement was found.

Age and sex for the cohort was similar to other studies of patients with occupational contact dermatitis.^{5,11} The higher number of men with epoxy allergy and women with rubber allergy reflects the fact that males are more often occupationally exposed to epoxy and women to rubber. In the present study AD was less frequent in patients with epoxy than patients with rubber chemical/latex allergy, although not statistically significant. AD has in previous studies been linked to a poorer outcome in occupational dermatitis¹², however, in the present study this was not confirmed. A possible explanation for this is that patients in the present study had work-related allergic contact allergy as their primary diagnosis. The low number of patients with epoxy allergy having AD may reflect that patients with skin problems either do not apply for jobs in the epoxy industry.

With respect to additional, non-occupational contact allergies, the number of these was lower in patients with occupationally related epoxy allergy than in the two other groups. The additional contact allergies should probably be seen as secondary to the occupational eczema, and numbers of additional contact allergies are likely to be related to the severity and duration of the eczema, which explains why the number is higher among patients with rubber allergy. Naturally, increased number of contact allergies may influence the prognosis in a negative direction.

The overall clearance rate of 11 %, as well as the finding that 67 % reported improvement at follow-up, is in line with previous studies of occupational contact dermatitis.^{3,4,12} This high frequency of chronicity strongly underlines the importance of primary prevention and early effective treatment of occupational contact dermatitis.¹³

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Although not statistically significant, there was a trend that total clearance was found more frequently in patients with epoxy allergy as compared to rubber chemical allergy (22 % vs. 10 %, respectively). This was to be expected since non-ubiquitous allergens should theoretically be avoidable after diagnosis. However, avoidance is probably more difficult in practice. Nearly 20 % of those with epoxy allergy were still in the same job (Table 4), and probably still exposed to some degree. The fact that there is persistent eczema in 89 % of the whole patient group after two years indicates that when the eczema is first initiated it takes a perpetual course and becomes chronic.

A poorer prognosis for patients with contact urticaria compared to patients with contact allergy has previously been reported.⁴ This fits well with our findings (Table 2). It is interesting that 41 % of patients with natural rubber latex allergy in our cohort report current occupational exposure, indicating that this allergen is difficult to avoid, and possibly also points to a high degree of awareness of exposure to this specific allergen due to the severe reactions that exposure may lead to. With respect to the small group (11 patients) that had experienced worsening of the eczema during the follow-up period, no specific features were found that could characterize this group.

A particularly interesting finding in the present study is the positive association between improvement at follow-up and change of employment, and that this finding was statistically significant for the whole group, as well as for those with rubber chemical/natural rubber latex allergy alone. Data on the effect of job-change for patients with occupational contact dermatitis is sparse. Some studies report a positive effect^{7,14} while others have not confirmed this^{4,15,16}. The particularly interesting finding in the present study is the positive effect of job change even in patients allergic to ubiquitous allergens (rubber chemicals and natural rubber latex), where this finding would not necessarily be expected.

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Approximately one third of our cohort was not currently employed at follow-up and almost 60 % of these reported that this was due to their eczema, which further underlines the social and economic burden of occupational skin disease, for the patients as well as for society.

There was no significant difference in self-reported current exposure between allergy groups and no significant relationship between current exposure and improvement of eczema.

Exposure was self-reported, and this may cause bias. Perhaps the question regarding exposure in the workplace was not detailed enough, which could lead to under-reporting of exposure.

Exposure can be difficult for participants to assess, because it requires knowledge of both own allergies and contents of the products that the patient comes into contact with. An airborne exposure may not be visible and therefore on-going without the participants' knowledge. This may explain why we did not see an association between improvement and exposure at work. Perhaps a workplace visit by a professional with specific knowledge of exposure could lead to different results.

The DLQI scores are in line with the other findings in the study with significantly higher DLQI scores for the patients with natural rubber latex allergy compared to the patients with epoxy and rubber chemical allergy. The lowest DLQI scores were observed for the epoxy allergy patients and contribute to the overall picture that this group is less affected by their eczema than the other groups.

The high response rate is a strength of this study, and is in line with previous studies of this population.^{11,17} The fact that current exposure is self-reported is a limitation, as is the relatively small sample size limited to a one-year cohort of patients with recognised occupational eczema. The number of patients with contact allergy to non-ubiquitous allergies is particularly limited, which is also a limitation of the study. Unfortunately, the present material does not include data on severity at onset, or information about duration of eczema

before recognition as an occupational disease, which could be other factors influencing improvement at follow-up. The fact that there is no clinical objective measure of disease severity at follow-up is a further limitation. Follow-up data on occupational contact dermatitis is, however, sparse, as is comparison between groups with dermatitis from different allergens. The mean age of respondents was significantly higher than for non-respondents. This may theoretically induce a bias. There is, however, no obvious reason to expect that change of jobs would influence prognosis differently according to age.

In conclusion, our study confirms the poor prognosis reported in previous studies for patients with occupational contact dermatitis. The main new findings are a worse prognosis for those with contact urticaria, and for patients with contact allergy to rubber chemicals as compared to epoxy, although the latter was not statistically significant. A possible explanation for this is that rubber chemicals and epoxy represents ubiquitous and non-ubiquitous allergens, respectively, however this finding needs to be confirmed in future studies. Interestingly, a significant positive association was found between job change during the observation period and improvement of eczema.

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Table 1. Baseline characteristics of patients stratified by allergy type.

		Epoxy (n=27)	Rubber chemicals (n=96)	Natural rubber latex (n=19)	Rubber chemicals and natural rubber latex allergy (n=7)	Total (n=149)
Age (years)	Mean/median	43/42	42/44	44/44	39/42	42/43
Sex						
	Men	24 (89 %)	24 (25 %)	2 (11 %)	2 (29 %)	52 (35 %)
	Women	3 (11 %)	72 (75 %)	17 (89 %)	5 (71 %)	97 (65 %)
Atopic dermatitis	Ever	1 (4 %)	18 (19 %)	4 (21 %)	2 (29 %)	25 (17 %)

Table 2. Eczema at follow-up.

		Epoxy (n=27)	Rubber chemic als (n=96)	Natural rubber latex (n=19)	Total (n=142)	P (Chi-square test)
	No eczema at follow-up	6 (22 %)	10 (10 %)	0 (0 %)	16 (11 %)	Assumptions not met
	Persistent eczema	21 (78 %)	86 (90 %)	19 (100 %)	126 (89 %)	
Eczema in 2013 compared to 2010	Improvement	20 (74 %)	67 (70 %)	8 (42 %)	95 (67 %)	0.044
	No improvement *	7 (26 %)	29 (30 %)	11 (58 %)	47 (33 %)	

* Including one missing answer and one who did not know.

Table 3. Improvement/no improvement in patients currently exposed at work to relevant allergens Only patients employed at follow-up are included.

	Exposed at work (n=30)	Not exposed at work (n=59)*	Total (n=89)	P (Chi-square test)
Improvement	18 (60 %)	45 (76 %)	63 (71 %)	
No improvement	12	14	26	0.111

	(40 %)	(24 %)	(29 %)	
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*One patient with a missing answer and seven who did not know where excluded.

Table 4. Employment status stratified by allergy type.

	Epoxy (n=27)	Rubber chemicals (n=96)	Natural rubber latex (n=19)	Total (n=142)	P (Chi- square test)
Employed in the same job	5 (19 %)	42 (44 %)	11 (58 %)	58 (41 %)	
Employed in a different job	14 (52 %)	24 (25 %)	1 (5 %)	39 (27 %)	
Other (unemployed, sick leave, retired, student)	8 (30 %)	30 (31 %)	7 (37 %)	45 (32 %)	0.006

Table 5. Improvement/no improvement of eczema stratified by job change at follow-up for patients employed at follow-up.

	Employed in a different job (n=39)	Employed in the same job (n=58)	Total (n=97)	P (Chi- square test)
Improvement	33 (85 %)	35 (60 %)	68 (70 %)	
No improvement	6 (15 %)	23 (40 %)	29 (30 %)	0.010

