

Short-term prognosis of occupational asthma in a Finnish population

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Abstract

Background: Causative agents of occupational asthma (OA) are well described in literature but far less is known about factors affecting the outcome of OA. Short duration of exposure, early diagnosis when symptoms appear and further avoidance of exposure have been suggested as good prognostic factors. This study was designed to investigate a short-term outcome of OA.

Methods: The medical records of 47 Caucasian patients from a Finnish population diagnosed with OA in year 2003 were reviewed retrospectively. Employment status at 6-month follow-up of all patients was determined. We assessed the following potential predictors of unemployment at follow-up: the causative agents of OA, asthma medication, spirometry results, smoking status, gender, age, occupation, atopy status, bronchial hyperresponsiveness and time to diagnosis. We calculated odd ratios (ORs) to predict employment status at follow-up.

Results: At the follow-up examination, 23 persons (49%) were not working. At the time of follow-up there were no significant differences in pulmonary function between those employed and those who discontinued to work. Atopy at baseline predicted diminished lung function at the 6-month follow-up. In addition, atopy was the only prognostic factor and was inversely related to the work discontinuation at the follow-up [OR 0.18, 95% confidence interval (CI) 0.04–0.79]. Work continuation as an OA outcome at 6 months could not be predicted by gender, age, occupational status, exposure antigen, smoking habits or duration of symptoms before diagnosis.

Conclusions: The socio-economic short-term prognosis of OA was relatively poor since half of the patients were not at work at the 6 months follow-up.

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Key words

occupational asthma – prognosis – socio-economic factor

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Contributions

Paula Kauppi: collection of data and writing of the manuscript.

Timo Hannu: writing of the manuscript.

Eva Helaskoski: collection of data.

Pauliina Virtema: statistical analysis.

Riitta Sauni: collection of data and writing of the manuscript.

Ethics

This study was approved by the Ethics Committee of the Finnish Institute of Occupational Health.

Conflicts of interest

The authors have stated explicitly that there are no conflicts of interest in connection with this article.

Introduction

Occupational asthma (OA) is the most commonly reported occupational lung disease in industrial countries. In a national surveillance scheme in United Kingdom, OA was responsible for 25% of all the cases, the most often reported causative agents being isocyanates, metals, grains, wood dusts, solders and welding

fume (1). In Finland, the prevalence of OA has been reported to be 5% of the new cases of asthma (2). According to the Finnish Register of Occupational Diseases, 306 cases of OA were diagnosed and financially compensated in year 2002. Of those, 25.8% were caused by moulds, 14.1% by flours, 7.2% by animal epithelia, 6.2% by storage mites, 3.3% by wood dust and organ plants, 0.7% by other unspecified organic

materials, 14.3% by chemicals and 28.4% by other causes (3).

Regardless of the prevalence of OA, little is known about its outcome and factors affecting it. The outcome can be evaluated by different measures, which include persistence of symptoms, employment rate, non-specific bronchial hyperresponsiveness and lung function (4). The prognostic determinants that have been studied are, e.g. age at the time of diagnosis, duration of exposure, time from cessation of exposure and the agent causing OA (5–9). The findings concerning the agents causing OA have been inconclusive, since both low-molecular weight compounds (LMW), such as diisocyanates and reactive dyes, and high-molecular weight compounds (HMW) such as detergent enzymes have been reported to associate with continuous symptoms after cessation of exposure (10, 11).

A systematic review on outcome of OA after cessation of exposure found that the recovery rates based on the reported respiratory symptoms were lower for older subjects, whereas the patients with the shortest durations of exposure had the highest recovery rate (8). However, there was considerable heterogeneity in the findings of the outcome in different studies. The review covered 39 studies and 1681 subjects with a median follow-up of 31 months. The authors concluded that a part of the patients do not recover. However, more knowledge is needed about the determinants affecting the outcome. More detailed information is needed especially for evaluating the effects of OA on the patients' employment status.

This study was focused on the outcome of OA 6 months after the diagnosis and on factors affecting employment status and work continuation.

Study material and methods

We retrospectively reviewed 47 records of Caucasian patients from a Finnish population diagnosed with OA in 2003 at the Clinic of Occupational Medicine at the Finnish Institute of Occupational Health (FIOH), Helsinki. The patients were randomly selected from all the patients with confirmed OA at the FIOH in 2003. Patients throughout Finland are referred to FIOH, Helsinki, for the specialist examinations (e.g. the specific inhalation challenge tests) needed for an official diagnosis of OA, in order to receive the financial compensation from the insurance companies. The diagnostic criteria for OA include an appropriate work history with a relevant exposure to a sensitizing antigen, and asthma symptoms that are aggravated at work or caused by work. Serial peak expiratory flow (PEF)

measurements at work and off work were performed when possible (12). Spirometry was performed according to the recommendations of the European Respiratory Society, and forced vital capacity (FVC), forced expiratory volume in 1 s (FEV_1) and the FEV_1 /FVC ratio ($FEV_1\%$) were measured. The diagnostic criteria for asthma include reversible obstruction of airways (bronchodilator effect of 15% or more in PEF recording, or diurnal variation of 20% or more in PEF, or 12% or more bronchodilator response in FEV_1) or moderate to severe bronchial hyperresponsiveness in the histamine challenge test. A histamine challenge test was performed according to the method of Sovijärvi (13); the provocative dose (PD) of 1.6% histamine diphosphate causing a 15% reduction in FEV_1 (PD_{15}) was measured. Mean values, absolute number and proportion of patients with lower than normal results were analysed for FVC, FEV_1 and FEV_1 /FVC ratio (14, 15). Bronchial hyperresponsiveness was graded as strong with a $PD_{15} < 0.10$ mg, moderate with a PD_{15} 0.11–0.40 mg and mild with a PD_{15} 0.41–1.6 mg. Skin prick tests and specific Immunoglobulin E (IgE) measurements were used to measure allergy/hypersensitivity to the causing agent. Atopy was defined as total serum Immunoglobulin E (S-IgE) > 110 kU/L (16, 17). The clinical diagnosis of OA was finally confirmed by the specific inhalation tests. All our study patients fulfilled the American College of Chest Physicians criteria for a medical case definition for OA (18).

The patients diagnosed with OA at the FIOH participate in a follow-up examination 6 months after their diagnosis of OA. In the present study, the patients were divided into two groups based on their employment status at this follow-up: i.e. employed and non-employed persons. The groups were studied with respect to age, gender, occupational status (blue- or white-collar worker), exposure agent (HMW allergen, LMW allergen or moulds), spirometric results at the time of OA diagnosis and 6 months later, bronchial hyperresponsiveness and asthma medication at the 6-month follow-up. Factors affecting employment status and work ability as well as pulmonary function measured by spirometry were analysed at the 6-month follow-up.

Statistical analyses

Comparison between the groups was done by cross tabulation and chi-square tests. The continuous variables of the groups of employed and non-employed persons were examined by a one-way ANOVA or *t*-test. The median delay to diagnosis was analysed by the

Mann–Whitney test. Odds ratios (ORs) for different factors affecting employment status and work ability as well as pulmonary function test results at 6 months were calculated with logistic regression analysis. Crude model was calculated with univariate logistic regression and multivariate model adjusted for age, gender, smoking and atopy. The analyses were performed using the SPSS 15.0 software package (SPSS Inc., Chicago, IL, USA). A *P* value of <0.05 was considered significant.

Results

At the time of the OA diagnosis, the mean age of the study patients was 46 years [standard deviation (SD) 8.5 yrs] and 20 (43%) of them were males (Table 1). The median time to OA diagnosis after the first asthmatic symptoms was 3.2 years [interquartile range (IQR) 2.0–7.5]. Majority of the patients were blue-

collar workers (68%). Causative agents of OA were similar in both study groups (Table 1).

At the follow-up examination, 24 (51%) individuals with diagnosed OA were employed and 23 (49%) were not working. Of those not at work, 4 (17%) had retired, 12 (52%) were on sick leave, 5 (22%) were in retraining for a new occupation and only 2 (9%) were actually unemployed. Among those who had been able to continue in their work, the exposure of 4 (17%) had been limited by the use of respiratory protective equipment and in 3 (13%) by improving the work hygiene. The work tasks had been limited of 5 (21%) of the subjects with OA and changed in 6 (25%) cases.

There were significantly more current smokers (48% vs 13%, *P* = 0.010) and more patients with atopic tendency (61% vs 26%, *P* = 0.017) in the employed group than in the non-employed group. The groups did not differ with respect to age, gender, occupation or causative agent of OA (Table 1).

Table 1. Comparisons of the characteristics of subjects employed and not employed at 6 months follow-up after the diagnosis of occupational asthma

	Total (<i>N</i> = 47)	Not employed (<i>n</i> = 23)	Employed (<i>n</i> = 24)	<i>P</i> value
Gender, <i>n</i> (%)				
Male	20 (43)	9 (39)	11 (46)	NS
Female	27 (57)	14 (61)	13 (54)	
Age (years), mean (SD)	45.9 (8.5)	44.7 (10.0)	47.1 (6.9)	NS
Occupation, <i>n</i> (%)				
White-collar worker	15 (32)	7 (30)	8 (33)	NS
Blue-collar worker	32 (68)	16 (70)	16 (67)	
Smoking*, <i>n</i> (%)				
Current or ex-smoker	31 (67)	15 (65)	16 (70)	NS
Non-smoker	15 (33)	8 (35)	7 (30)	
Pack years†, median (IQR)	9.0 (0–15.0)	1.5 (0–10.0)	10 (0–18.8)	NS
Atopy*, <i>n</i> (%)				
No	26 (55)	17 (74)	9 (39)	0.017
Yes	20 (43)	6 (26)	14 (61)	
Bronchial hyperreactivity†‡, <i>n</i> (%)				
No	15 (36)	9 (41)	6 (30)	NS
Mild	11 (26)	5 (23)	6 (30)	
Moderate or strong§	16 (38)	8 (36)	8 (40)	
Time to diagnosis (years)*, median (IQR)	3.2 (2.0–7.5)	3.4 (1.7–8.8)	3.2 (2.1–7.1)	NS
Causative agent of OA, <i>n</i> (%)				
Moulds	18 (38)	10 (42)	8 (35)	NS
Low-molecular weight	15 (32)	6 (25)	9 (39)	
High-molecular weight	14 (30)	8 (33)	6 (26)	

*Data missing on one patient.

†Data missing on five patients.

‡Bronchial hyperreactivity at the time of diagnosis.

§Strong hyperreactivity in 3 individuals of which 1 is unemployed and 2 are employed.

Statistical analysis was made with Mann–Whitney or *t*-test for continuous variables and chi-square test for categorical data.

IQR, inter quartile range; NS, not significant; SD, standard deviation; OA, occupational asthma.

Table 2. Results of spirometry at the time of diagnosis of occupational asthma and at 6 months follow-up according to the employment status

	Employed at follow-up <i>n</i> = 24		Not employed at follow-up <i>n</i> = 23	
	At time of diagnosis	At follow-up	At time of diagnosis	At follow-up
FVC				
% of predicted, mean (SD)	89.0 (16.5)	88.7 (15.9)	93.3 (15.8)	91.1 (14.3)
<80% of predicted, <i>n</i> (%)	9 (38)	4 (17)	4 (17)	4 (17)
FEV ₁				
% of predicted, mean (SD)	84.9 (17.9)	84.7 (15.7)	90.4 (15.5)	90.4 (12.1)
<80% of predicted, <i>n</i> (%)	9 (38)	8 (33)	4 (17)	4 (17)
FEV ₁ /FVC				
Ratio (% of predicted), mean (SD)	95.5 (9.6)	95.4 (9.4)	96.9 (9.4)	99.7 (8.4)
FEV ₁ /FVC < 88% of predicted, <i>n</i> (%)	6 (25)	7 (29)	5 (22)	3 (13)

Mean values, absolute number and proportion of patients with lower than normal results are given for the studied parameters FVC, FEV₁ and FEV₁/FVC ratio.

FVC, forced vital capacity; FEV₁, forced expiratory volume in 1 s; SD, standard deviation.

Nearly all (98%) of the patients were either on inhaled steroids or on combination therapy (long-acting bronchodilators and inhaled steroids) in order to achieve the adequate asthma control (data not shown). Despite of the diagnosis of OA, and when exposure was limited or avoided, asthma was classified to be mild persistent in 45% of the cases (regular use of inhaled steroids) and moderate persistent in 53% of the cases (combination therapy). None used oral steroids on a regular basis while 17% of the patients used nasal steroids.

At the time of diagnosis, the average values for FEV₁, FVC and FEV₁/FVC ratio were in the normal range in both the employed and the non-employed group (Table 2). At the follow-up, there were no statistically significant changes/differences in the pulmonary function in either group.

Current smokers had significantly more often [OR 8.8, 95% confidence interval (CI) 1.0–76.2] diminished FEV₁ values at the follow-up visit. Similarly, those with atopy had increased risk of lowered lung function at the follow-up (OR 7.7, 95% CI 1.7–34.0) (Table 3). When the model was adjusted for age, gender, atopy and smoking, atopy predicted abnormal lung function results (OR 5.0, 95% CI 1.0–25.2). Contrary to this, atopy was inversely associated with work discontinuation (OR 0.18, 95% CI 0.04–0.79).

Discussion

The short-time socio-economic prognosis of OA was poor, since half of the patients were not at work at the 6-month follow-up. However, only two patients were

truly unemployed, whereas the rest were either in vocational rehabilitation, retired or on sick leave. Finnish occupational insurance companies pay for the cost of vocational rehabilitation as compensation for an occupational disease (19). Sick leave was the most often found reason for work discontinuation (30% of the patients). The occupational insurance companies in Finland also pay compensation to the patients up to 1 year after they have been diagnosed with OA. It should be noted, however, that the compensation systems for OA claims are different from one country to another (19). In France, e.g. the risk of unemployment for persons submitting a claim was 25% on average 3.1 years after their diagnosis (20).

Age, gender, duration of symptoms, exposure agent or occupational status before OA diagnosis did not predict the employment status at the short-term follow-up in our study. According to a systematic review of the outcome of OA, when the median duration of follow-up was 31 months, the recovery rate of asthma was significantly lower with increasing age (8). The same review also indicated that a short duration of symptomatic exposure was associated with a better prognosis and recovery (8). In previous studies, the mean time to diagnosis of occupational asthma has been 3.8–4.9 years (9, 21, 22). In our study, the median delay for the diagnosis of OA due to various causative agents was 3.2 years (IQR 2.0–7.5).

Pulmonary function did not differentiate the employed patients and those not working, which indicates that unemployment or work discontinuation is not merely a result of medical factors, as shown also by Eisner *et al.* (23). Partial work disability resulting from

Table 3. Factors associated with employment status and lung function at 6 months follow-up after the diagnosis of occupational asthma

	Not employed 6 months after diagnosis of OA		FEV ₁ ≤ 80%	
	Crude model OR (95% CI)	OR (95% CI)	Crude model OR (95% CI)	OR (95% CI)
Gender				
Male	1.0	1.0	1.0	1.0
Female	1.3 (0.4–4.2)	1.1 (0.3–4.4)	0.54 (0.15–1.9)	1.2
Age				
<46 years	1.0	1.0	1.0	1.0
≥46 years	0.40 (0.12–1.3)	0.35 (0.10–1.3)	3.8 (0.88–16.1)	3.1 (0.62–15.8)
Occupation				
White-collar worker	1.0	–	1.0	–
Blue-collar worker	1.1 (0.24–3.9)		0.67 (0.18–2.5)	
Smoking				
Non-smoker	1.0	1.0	1.0	1.0
Current or ex-smoker	0.75 (0.24–2.8)	2.2 (0.4–10.8)	8.8 (1.0–76.2)	4.6 (0.43–50.0)
Pack years				
<10 pack years	1.0	–	1.0	
≥10 pack years	1.3 (0.13–1.6)		7.1 (1.3–38.8)	
Atopy				
No	1.0	1.0	1.0	1.0
Yes	0.23 (0.07–0.79)	0.18 (0.04–0.79)	7.7 (1.7–34.0)	5.0 (1.0–25.2)
Bronchial hyperreactivity*				
None	1.0	–	1.0	–
Mild	0.56 (0.12–2.7)		8.0 (0.75–85.7)	
Moderate to severe	0.67 (0.16–2.8)		6.4 (0.65–62.7)	
Time to diagnosis				
<3,2 years	1.0	–	1.0	–
≥3,2 years	1.2 (0.37–3.8)		2.5 (0.64–10.0)	
Exposure antigen				
Low-molecular weight	1.0	–	1.0	–
High-molecular weight	0.50 (0.11–2.2)		3.6 (0.57–22.9)	
Mould	0.53 (0.13–2.1)		3.3 (0.55–19.3)	

Crude model calculated with univariate logistic regression and multivariate model adjusted for age, gender, smoking and atopy.

*Bronchial hyperreactivity at the time of diagnosis.

OA, occupational asthma; FEV₁, forced expiratory volume in 1 s; OR, odds ratio; CI, confidence interval.

severe adult asthma has been related to exposure at work (23). In the same study, however, the most effective determinant for complete withdrawal from work life was ex-smoker status (OR 3.17; 95% CI 1.54–6.54), whereas a higher level of education, i.e. college degree or higher, protected against complete withdrawal from work (OR 0.30; 95% CI 0.10–0.89). In our study with a relatively small study population, smoking status did not predict employment status at the short-term follow up.

In a Finnish study of diisocyanate asthma with an average 10 years follow-up, unemployment was remarkably low (14%) and 50% of the unemployment was caused by asthma (24). Moreover, symp-

tomatic asthma with nocturnal asthma symptoms (OR 10.9) or increased PEF variability (OR 8.5) was associated with unemployment. In our present results, atopy was associated with lower than normal FEV₁ but was still inversely associated with unemployment or work discontinuation. In a Norwegian study, only 3% of OA patients were unemployed at the follow-up after 2–6 years (25). Most of the patients with OA were symptomatic and 60%–78% of them were on asthma medication at the follow-up. In our study, 98% of the patients had regular asthma medication.

In a review of socio-economic impact of work-related asthma, unemployment was found in 8%–38%

of the studied OA populations (26). The rates of unemployment and income loss in work-aggravated asthma were estimated to be similar to OA. In addition, adult asthma was reported with partial work disability and impairment in self-reported work effectiveness in more severe asthma. In our study, we have no data on work-aggravated asthma.

In the study on long-term effects of acute irritant-induced asthma in 35 individuals, no significant improvements were seen in FEV₁ or FEV₁/FVC, and 68% of the subjects were on inhaled steroids after a mean follow-up of 13.6 years (27). In the present study, the medication needed to control asthma did not differ in the employed and unemployed group (those not at work), whereas having smoked for more than 10 pack-years was associated with abnormal FEV₁ results. Atopy was a risk factor for lowered FEV₁ value at the follow-up, but it was, nevertheless, inversely associated with unemployment or work discontinuation. We used elevated level of serum total IgE values as a marker of atopy. Another commonly used definition for atopy is skin prick test results. Because such data were partly lacking in our study population and because serum IgE levels are known to associate with skin prick test results, we consider that the definition used for atopy was reasonable.

It has been suggested that follow-up studies conducted in specialist clinics may be biased, because the diseases of their patients may be more severe and present with more persistent symptoms (1). This kind of bias is not probable in the present study, because patients throughout Finland are referred to FIOH, Helsinki, for the specialist examinations (e.g. specific inhalation challenge tests) required for an official diagnosis of OA, regardless of the severity of the symptoms. Also, a follow-up 6 months after the diagnosis is routine practice for every patient receiving the OA status. In addition, our study was based on the data collected with a structured formula and obtained from the patient files, which reduces the reporting bias common in questionnaire studies. A limitation is that our series consisted of a relatively small number of patients that might restrict the generalization of our results. In addition, these results might not be generalized into non-Caucasian populations.

In conclusion, the short-time prognosis of OA was relatively poor in our series of patients whose OA was confirmed by the inhalation challenge test. Atopy and current smoking were more common in the group of employed. After adjustment for smoking, atopy, age and gender, atopy predicted abnormal lung function results, but in contrast to this, atopy was inversely associated with unemployment or work discontinuation.

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