SHORT REPORT

Exposure-response relations for work related respiratory symptoms and sensitisation in a cohort exposed to α-amylase

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Aims: To explore relations between exposure to fungal α-amylase and the risk of new work related respiratory symptoms or sensitisation.
Methods: A prospective cohort study among 300 bakers and millers was followed up for a maximum of seven years. Exposure to α-amylase was estimated by air measurements and questionnaires and classified into three categories. Symptoms were recorded with a self-administered questionnaire and skin sensitisation assessed using skin prick test (SPT).
Results: There were 36 new cases of chest symptoms, 86 of eyes/nose symptoms, and 24 of a positive SPT to α-amylase. There were exposure-response relations for chest and eyes/nose symptoms and for sensitisation, and a significantly increased prevalence ratio for chest symptoms in the highest exposure category.
Conclusion: A reduction in α-amylase exposure is likely to reduce the risk for respiratory morbidity in bakery workers.

Respiratory symptoms, including asthma, may occur in bakery and mill workers. IgE mediated sensitisation to fungal α-amylase is one cause of respiratory symptoms in bakers and millers.[1] Exposure-response relations for sensitisation by α-amylase were found in two cross-sectional studies.[2 3] For α-amylase, neither exposure-response relations for respiratory symptoms, nor any cohort studies have been reported.

Previously, a longitudinal data set was analysed for exposure-response relations of exposure of flour aeroallergen and total dust and the outcome of new-onset sensitisation or work related symptoms using a case-control design.[4] As in other studies, they showed a good exposure-response relation. Here we use the same dataset to study relations between exposure to α-amylase and the risk of work related respiratory symptoms or sensitisation.

METHODS

This was a study of exposure-response relations within a prospective cohort study on new work related cases.

Subjects

The cohort has been described previously.[4] Briefly, it comprised 300 bakers and millers in the UK. In 1990 they had worked for a maximum of four years and a minimum of one month in a job with exposure to flour dust. At six-monthly intervals between 1990 and 1993 all subject still employed were surveyed—a total of seven visits. Subjects who became employed were also included in the cohort after one month of flour exposed work. Persons with exposure to flour in a previous job were excluded. The median time of follow up from 1986 was 40 months (range 1–91). About 80% of all eligible workers were seen at each time point.

All participants completed a self-administered questionnaire at each survey visit. ''Chest symptoms'' were defined as at least one positive answer to questions on chest tightness, breathing difficulties, wheezing, or whistling in the chest. ''Eyes/nose symptoms'' were defined as at least one positive answer to questions on eyes being itchy or runny or the nose being blocked, itchy, runny, or sneezing (without having a cold or flu). Symptoms were regarded as work related if improved during weekends or holidays or if provoked by contact with flour or grain. Symptoms were regarded as ''new'' if they started after employment at the site. Only new work related symptoms were used in the analyses. Workers were classified as smokers if they had smoked at least one cigarette daily for a year while employed at the site during the follow up—that is, between 1990 and 1993.

Skin prick tests (SPT) were carried out at every survey visit. Positive and negative control solutions, three common inhalant allergens (grass, cat, and *Dermatophagoides pteronyssinus*), fungal α-amylase (10 mg/ml, Novo Nordisk), and an extract of wheat flours were used. A positive test was defined as a mean weal diameter at least 3 mm greater than that of the negative control. Subjects were classified as atopic when having a positive response to at least one common allergen.

Workers were questioned for work tasks from the time of joining the bakery/mill and at every survey. With this information and results of previous measurements of α-amylase aeroallergen, each worker was assigned an exposure concentration, as described previously.[3] If the worker reported any change of work during follow up, the highest exposure ever worked in was used in the analyses. The population was divided into three exposure categories of α-amylase based on the average exposure by exposure group; <5 ng/m^3; 5–15 ng/m^3, or >15 ng/m^3, as described previously.[3] Forty persons (13%) were not classified due to missing information (table 1).

Analyses

The associations between exposure and the probability of reporting a respiratory symptom or having a positive SPT to α-amylase during follow up were analysed with a proportional hazards model (Cox regression) using the Stata software package, version 5. The lowest exposure category was used as referent. Age, sex, atopy, and smoking were introduced as potential confounders. Sex and atopy were significant confounders and thus retained in the final model.

RESULTS

There were 36 cases of chest symptoms, 86 of eyes/nose symptoms, 24 of a positive SPT to α-amylase, and 21 of a

Main messages

- There were clear trends for exposure-response relations between the exposure of α-amylase and the response of respiratory symptoms or sensitisation.
- Sensitisation to fungal α-amylase was more common than sensitisation to flour in this cohort, underscoring the allergenic capacity of this enzyme.

Policy implications

- A reduction in α-amylase exposure is likely to reduce the risk for respiratory morbidity in bakery workers.

positive SPT to flour over the study period. Demographic details of the cases have been reported previously.[4]

A significantly increased prevalence ratio (PR) was observed for chest symptoms in the highest exposure category to α-amylase (PR 3.0, 95% CI 1.1 to 8.1) (table 1). There were trends towards increased PRs for eyes/nose symptoms, and for a positive SPT to α-amylase by increasing exposure.

The predictive value of a positive SPT to α-amylase was 29% (7/24) for chest symptoms and 42% (10/24) for eyes/nose symptoms.

DISCUSSION

Our longitudinal analysis indicated that there are clear exposure-response relations between α-amylase allergen exposure and work related respiratory symptoms. To our knowledge, this has not been reported before. In addition, our results support the findings of the two cross-sectional studies on exposure and sensitisation to α-amylase.[2 3] Sensitisation to fungal α-amylase was more common than sensitisation to flour in our cohort, underscoring the allergenic capacity of this enzyme.

The cohort was dynamic—that is, some workers left employment during the study period and even though we tried to survey them before leaving, this was not always possible. If those were more often symptomatic or sensitised, the exposure-response relation might have been underestimated. Newly employed workers also entered the cohort. No systematic pre-employment screening was reported at any of the work sites, and those newly employed could be assigned to any exposure category. One of the limitations of the cohort is its size. Even though it is the largest cohort of flour and amylase workers with good exposure data, the cohort is still fairly small, resulting in imprecise risk estimates.

The categorisation of exposure was based on analysis of work tasks. The participants were not aware of the categorisation and recall bias is improbable. However, there is variability in exposure within the categories and some misclassification of exposure is probable. As such misclassification is based on task and not on outcome it is probably random, leading to an attenuated exposure-response relation.

The highest exposure ever worked in was used in order to reduce misclassification of exposure; it is biologically more plausible that workers develop symptoms and are sensitised at the highest exposure level. Subsequently they may move to a lower exposure group. Nieuwenhuijsen and colleagues[3] reported the best exposure-relations using this approach.

Table 1 Prevalence ratios for chest and eyes/nose symptoms and a positive SPT to fungal α-amylase in relation to exposure categories for fungal α-amylase allergen

Exposure category	Low	Medium	High
α-amylase allergen level (ng/m^3)			
Arithmetic means (SD)	0.7 (0.8)	10.7 (2.2)	46.7 (16.6)
Number of measurements	225	22	13
Chest symptoms			
Prevalence ratio	1	1.7	3.0
95% CI		0.6 to 4.9	1.1 to 8.1
Number of incident cases	22	5	5
Eyes/nose symptoms			
Prevalence ratio	1	1.9	1.9
95% CI		0.9 to 3.8	0.9 to 4.2
Number of incident cases	56	10	7
SPT positive to α-amylase			
Prevalence ratio	1	3.1	4.0
95% CI		0.6 to 17	0.9 to 18
Number of incident cases	18	2	4

Sex and atopy were confounders in the model.

Sex, atopy, age, and smoking were evaluated in the model as potential confounders. The first two were of significant importance and were retained in the analyses.

The distribution of α-amylase exposure was highly skewed, with 86% of workers in the low exposure category. This makes the precision of the estimates low in the other exposure categories. There were trends for increased PRs in the second exposure category, with an arithmetic mean of 10.7 ng/m^3, and still higher PRs in the highest exposure category with a mean of 46.7 ng/m^3. In the discussion on prevention of respiratory allergy to fungal α-amylase, levels in the low ng/m^3 range have been considered as possible occupational limit values.[5 6]

Conclusion

There were clear trends for exposure-response relations for exposure to fungal α-amylase, and respiratory symptoms and sensitisation. A reduction in α-amylase exposure is likely to reduce the risk for respiratory morbidity in bakery workers.

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Additional data is available on the *OEM* website (www.occenvmed.com/supplemental)

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ECHO

Mental health of emergency ambulance workers

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Dealing with acutely ill people is undoubtedly stressful. Some patients will inevitably have a bad outcome and there is the possibility of self recrimination among emergency staff. Studies have suggested a prevalence of post-traumatic stress disorder (PTSD) among emergency ambulance staff of around 20% and some degree of psychiatric morbidity in about one in three. Researchers in south Wales and the west of England, UK have performed the largest study yet reported.

Questionnaires were sent to all 1029 emergency medical technicians (EMTs) and paramedics working for one ambulance service covering a population of three million people. To preserve anonymity no record was kept of the names corresponding to questionnaire numbers. Six hundred and seventeen questionnaires (60%) were returned by 513 men, 91 women and 13 respondents who did not declare their sex. There were 380 paramedics, 194 EMTs, and 43 respondents who did not declare their grade.

Two yes/no items on the questionnaire asked about intrusive work related memories. Respondents who had had such memories for a month or more completed a validated diagnostic scale (the Posttraumatic Diagnostic Scale (PDS)) that has shown an 82% concordance with psychiatric interview. All respondents completed the Hospital Anxiety and Depression Scale (HADS). Around 45% of respondents reported current troubling memories and another 15% reported having had them in the past. Twenty two per cent of respondents had a PDS score indicative of PTSD. The rate of PTSD was similar in paramedics and EMTs but higher in men (23%) than in women (15%). The rates of clinically significant anxiety (23%) or depression (9%) were similar in paramedics and EMTs and in men and women.

Among emergency ambulance workers who responded, 22% had evidence of PTSD and a similar proportion had evidence of anxiety. Almost 10% had probable clinical depression. No rates are quoted for comparison groups.

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