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Laboratory animal allergy reduction from 2001 to 2016: An intervention study

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ABSTRACT

Exposure to laboratory animals (LA) can cause allergic sensitization and symptoms as rhinitis, conjunctivitis, asthma, anaphylaxis and dermatitis. In 2000, a program was instituted at Trieste Universities to decrease LA allergy among scientists and technicians working with animals. The aim of our study was to investigate LA allergy in workers exposed to LA from 2001 to 2016, and to verify the effects of a preventive program.

Four hundred sixty seven people underwent pre-employment screening for a job with laboratory animals at Universities of Trieste consisting in a medical examination, a full respiratory and allergy anamnesis, using a standardized questionnaire, skin prick test with common and occupational allergens, and spirometry. Every year, each worker repeated the medical examination and underwent again tests and questionnaire. Each worker can ask for a medical examination and skin prick test, in case of unset of symptoms. Logistic multivariate analysis and generalized equation estimation were use, to verify factors associated to LA allergy.

Sensitization to LA decreased in years, going from 25.6% in 2001–2004 to 8.2% in 2013–2016 ($p < 0.001$). Multivariate logistic regression analysis confirmed the role of atopy by prick test (OR = 6; IC95% 2.2–16.6), of common allergic symptoms (OR = 2.9; IC95% 1.4–6.39) and of calendar periods. No association was found between LA allergy, years, and hours of exposure. Our study demonstrated a significant reduction of LA allergy after the application of a preventive program.

1. Introduction

Exposure to laboratory animals (LA) can cause allergic sensitization and symptoms. Prevalence estimation of LA allergy ranged between 11 and 44% of workers, with higher figures in old reports and lower prevalence in more recent studies [1–5]. Symptoms included allergic rhinitis, conjunctivitis, asthma, anaphylaxis, and skin symptoms [4–6]. Chest and skin symptoms were associated with increasing intensity to exposure to rat urinary allergy [7] and recent studies [8] demonstrated an increased risk for exposed people to develop symptoms compared to non-exposed, but sensitized to common allergens controls. Occupational asthma decreased from old studies in the 70's to more recent ones, but a further reduction of exposure is needed to prevent the onset of occupational rhinitis [4]. A previous study of our group [9] found that LA allergy ranged from 11.8 to 14.8% according to work seniority, with 5% and 7.9% of subjects that reported work related asthma and rhinitis, respectively. Our figures were low compared with other reports in Brazil [8], in Korea [10] and in USA [11]. Personal atopy and total IgE level are risk factors for the sensitization to LA [3,6,10] and incidence of symptoms is significantly related to exposure in a dose-related matter for some authors [6,7].

LA allergy remains a significant problem for LA workers despite the interventions done to reduce exposure through a better local exhaustion system during animal handling, procedural and personal controls with health surveillance system for workers, and the compulsory use of a protective personal equipment. In 2000, a program was instituted at Trieste Universities to decrease LA allergy among scientists and technicians working with animals. The program included education and training, institution of good work practice to reduce exposure to LA, the use of a local exhaustion system during all working procedures, the use of protective respiratory protection, and a medical surveillance program with symptoms assessments, skin prick test for common and occupational allergens including latex (as researchers can wear latex gloves) and animal danders. Work practice modification included the institution of wet cleaning practices, and wet-shaving practices (i.e. using water or a foam shaver), the avoidance for researchers to go into stabularies, and the use of local exhaustion system during the work with animals. Environmental controls were implemented including high efficiency particulate air-filtered room ventilation and use of dust-free bedding [12]. All workers had to wear a mask with high efficiency (PP3) to limit the inhalation of allergens.

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The medical surveillance assessment with skin prick test and spirometry were performed before the start of the work with animals and every year or before, if occupational symptoms occurred during the course of their job. Educational training to increase knowledge on LA was undergone by every worker, with the aim to recognize mild symptoms occurring and ask for medical control.

The aim of the study was to evaluate LA allergy in workers exposed to LA from 2001 to 2016, and to verify the effects of a preventive program.

2. Methods

Between 2001 and 2016, 467 people underwent pre-employment screening for a job with laboratory animals at University of Trieste and SISSA (Scuola Internazionale Superiore di Studi Avanzati). Pre-employment screening was done by the Unit of Occupational Medicine at University of Trieste, and consisted in a medical examination, a full respiratory and allergy anamnesis using a standardized questionnaire [9,13], skin prick test with common and occupational allergens and spirometry. Every year each exposed worker repeated the medical examination and underwent skin prick test for LA and questionnaire. Each worker asked for a new medical examination, and were skin prick tested again, in case of unset of symptoms. At baseline, some workers resulted already exposed to laboratory animals, during thesis or training period or in a previous job in other research facilities. The study was inserted in a compulsory program for prevention of occupational diseases following the Italian Low 81/2008, local Ethics Committee was informed about the retrospective analysis performed. Written informed consent was obtained from all subjects after reading and discussing the protocol individually. All workers underwent lung function evaluation using a Biomedin Spiromether (Padua, Italy) with the evaluation of forced expiratory volume in 1 s (FEV1) and vital capacity (VC), Forced Expiratory Flow 25–75 (FEF25-75), according to the American Thoracic Society recommendations [14]. As all values were normal, results are not reported.

2.1. Skin prick test

Skin prick test (SPT) was performed according to the recommendations of the European Academy of Allergology and Clinical Immunology [15], using a panel of common allergens (*Dermatophagoides farinae and Pteronyssinus,* cat and dog, *Alternaria*, pollen of *Graminae, Betula, Corylus, Oleaea, Parietaria* spp) and occupational allergens included latex, rat, mouse, rabbit, guinea pig, hamster extracts (Lofarma Milano, Italy). Histamine dihydrichloride (10 mg/ml) served as positive and the solvent as negative control. A wheel of ≥3 mm in diameter was considered as positive reaction. Atopy was defined when a subject was positive to at least one common allergen.

2.2. Questionnaire

The questionnaire used contained questions on personal (nose, skin and lower respiratory tract symptoms) and familiar allergic diseases, allergic drug intake, smoking habits, exposure to laboratory animals and symptoms in connection with this exposure, usage of safety equipment [9,13]. Allergic symptoms due to working with laboratory animals were defined as the presence of allergy during working hours or after contact with laboratory animals. Allergic symptoms were divided into 4 groups: nasal symptoms defined as sneezing or running nose with production of nasal secretions; eye symptoms, defined as itching or smarting eyes; asthma, defined as the presence of shortness of breath and wheezing; cough, defined as cough without secretions, and skin symptoms, defined as itching and red skin. The sensitization period was defined as the period between the first exposure to laboratory animals and the first occurrence of symptoms of laboratory animal allergy.

2.3. Exposure evaluation

As a surrogate for exposure intensity the mean numbers of hours per month a person was exposed to laboratory animals was used. Four calendar periods, for those entering the cohort, were distinguished with baseline data: 2001–2004, 2005–2008, 2009–2012, 2013–2016. Four periods of exposures were considered: < 1 year; 1 year; 2–3 years, > 3 years.

2.4. Statistical analysis

Statistical analysis was performed using STATA, Inc. (Texas, USA). Comparison between never exposed and exposed workers was done using chi-square technique for categorical data and by *t*-test for age, seniority of work and exposure data. Association between sensitization to laboratory animals, calendar periods, intensity of exposure and related factors were performed using the univariate and multivariate regression analysis. Results are reported as Odds ratio and 95% Confidence intervals. Factors involved in LA allergy during the follow-up were analysed using the Generalized Equation Estimation (GEE). A p value < 0.05 was settled as significant.

3. Results

467 subjects exposed to LA were involved in the study. They represent the 98% of exposed subjects. 145 were never exposed to LA and 322 were already exposed for 4.1 ± 6.2 (95% CI 2.9–5.4) years in men and 3.1 ± 6.9 (95% CI 2.1–4.1) years in women. Hours of exposure to LA ranged from 25.4 to 50.8 per month (95% CI). The Table 1 reports the characteristics of the two groups. The group of “never exposed” resulted significant younger that “already exposed”, as expected, and were represented by students in the 36.5 and 42.7% of cases, in men and women respectively. Women reported to have a higher familiarity for atopy, while men resulted more atopic by prick test (55.6% and 60.1% in men never and already exposed, respectively). Percentage of allergic symptoms was similar between the two groups, but asthma was more prevalent in exposed vs never exposed (12% vs 9.6%), without reaching the statistical significance. LA sensitization resulted significant higher in already exposed subjects with 14.4% and 13.7% vs 7.9% and 4.9% in never exposed, in men and women, respectively ($p < 0.001$). LA allergy involved mainly mouse (11% sensitization in men and 5.9% in women), followed by rat (8.5% sensitization in men and 4.9% in women), rabbit, guinea pig and hamster. Prevalence of latex allergy was low with small differences in groups (0.85–4.9%) without reaching the statistical significance. More than half of subjects used latex gloves during work but gloves were without powder and at low latex release, to minimize the risk of sensitization.

Symptoms in subjects sensitized to LA are reported in Table 2. The 9 workers, never exposed to LA but sensitized to them are all atopic to common allergens and 2 of them reported perennial rhinitis. Thirty subjects (67%) already exposed, and sensitized to LA reported symptoms, 20 had rhinitis (6.2% of exposed), 14 asthma (4.3% of exposed), 5 dermatitis and 2 urticaria. Table 3 reports the univariate logistic regression analysis of factors involved in LA sensitization in never and already exposed to LA. Atopy by prick test was strongly associated to LA sensitization (OR = 9.44; IC95% 3,6–24.6) as well as common allergic symptoms (OR = 4.4; IC95% 2.3–8.4), asthma (OR = 5.9; IC95% 2.9–12.00) and symptoms during work (OR 2.5; IC95% 1.3–9.4). Sensitization to LA decreased in years (Fig. 1) going from 25.6% in 2001–2004 to 8.2 in 2013–2016, with higher percentages in females, but with a significant reduction during time: OR = 0.20; IC95% 0.07–0.53 in subjects evaluated in 2009–2012 and OR = 0.37; IC95% in those evaluated in 2013–2016, compared to those exposed in 2001–2004. No association was fount between years and hours of exposure. Multivariate logistic regression analysis confirmed the role of atopy by prick test (OR = 6; IC95% 2.2–16.6), of common allergic