Respiratory Medicine 118 (2016) 7–14

Contents lists available at ScienceDirect

Respiratory Medicine

journal homepage: www.elsevier.com/locate/rmed

Prolonged occupational exposure leads to allergic airway sensitization and chronic airway and systemic inflammation in professional firefighters

Niki Gianniou [a], Paraskevi Katsaounou [a], Efrossini Dima [b], Chariklia-Eleni Giannakopoulou [b], Matina Kardara [c], Vassiliki Saltagianni [a], Rodoula Trigidou [d], Aggeliki Kokkini [e], Petros Bakakos [b], Evangelos Markozannes [b], Eleni Litsiou [a], Alexandros Tsakatikas [f], Christos Papadopoulos [f], Charis Roussos [a, b, c], Nikolaos Koulouris [b], Nikoletta Rovina [b, *]

[a] Pulmonary and Critical Care Department, Evangelismos Hospital, National and Kapodistrian University of Athens, Greece
[b] 1st Department of Pulmonary Medicine, "Sotiria" Hospital, Athens Medical School, National and Kapodistrian University of Athens, Greece
[c] "M. Simos" Laboratories, Department of Critical Care and Pulmonary Services, National and Kapodistrian University of Athens, Greece
[d] Department of Pathology, "Sotiria" Hospital, Greece
[e] Department of Cytology, "Sotiria" Hospital, Greece
[f] Hellenic Fireforce Department, Greece

ARTICLE INFO

Article history:
Received 21 January 2016
Received in revised form
7 July 2016
Accepted 7 July 2016
Available online 13 July 2016

Keywords:
Firefighters
Airway inflammation
Systemic inflammation
Allergic sensitization

ABSTRACT

Background and objectives: Little data exist on short- and long-term effects of occupational exposure on airway and systemic inflammation in professional firefighters. We aimed to characterize airway and systemic inflammation in training firefighters with a maximum occupational exposure of 1 year compared to the long-term exposure of professional firefighters.
Methods: A questionnaire for symptoms and exposure, pulmonary function, atopy, bronchial hyperresponsiveness, and markers of inflammation in induced sputum, serum, bronchoalveolar lavage (BAL) fluid and bronchial biopsies were assessed in a total of 92 firefighters (63 full-time professionals and 29 trainees).
Results: Professional firefighters showed allergic bronchial sensitization documented by the presence of atopy, and eosinophilia in induced sputum, BAL and bronchial biopsies. IL-8, ECP, VEGF, and TNF-α levels were statistically significantly higher in the sputum supernatants of professional firefighters compared to the trainees ($p = 0.04$, $p = 0.02$, $p = 0.04$, and $p = 0.02$, respectively). Serum IL-8 and TNF-α levels were also statistically significantly higher in the group of professional firefighters ($p = 0.04$, $p = 0.03$, respectively). Finally, there was a linear correlation between the duration of the occupation in Service and the degree of airway and systemic inflammation.
Conclusions: These results indicate a "dose-response" effect of chronic exposure to a polluted environment on bronchial and systemic inflammation in professional firefighters.

1. Introduction

Professional firefighters have prolonged and direct exposure to smoke and to a wide variety of inhaled particles and particulates [1,2] which are inhaled into the respiratory tract. Several epidemiological and toxicological data show the adverse effects of inhaled smoke from the burning of wood and biomass on cardiopulmonary morbidity [3–5]. Exposure to air pollutants (combustion products) may lead to increased sensitization to airway

Abbreviations: FEV_1, forced expiratory volume; FVC, forced vital capacity; TLC, total lung capacity; RV, residual volume; KCO, CO transfer coefficient; PD20meth, provocative dose of methacholine producing a 20% fall in FEV_1; ECP, Eosinophilic cationic protein; IL-8, Interleukin-8; IL-4, Interleukin-4; IL-13, Interleukin-13; TNF-α, tumor necrosis factor-alpha; VEGF, vascular endothelial growth factor; BALF, bronchoalveolar lavage fluid.

* Corresponding author. "Sotiria" Hospital for Diseases of the Chest, 152 Mesogion Ave, Athens, GR-11527, Greece.
E-mail address: nikrovina@med.uoa.gr (N. Rovina).

http://dx.doi.org/10.1016/j.rmed.2016.07.006
0954-6111/

allergens [6,7]. Studies examining respiratory symptoms and pulmonary function in professional firefighters have found increased symptoms, and airways hyper-responsiveness, and declined lung function during fire fighting periods and seasonally [5,8–12].

These observations suggest that firefighting is associated with upper and lower airways inflammation and raise concern about the potential risk of long-term respiratory effects, including asthma, chronic obstructive pulmonary disease (COPD), and upper airways conditions, such as sinusitis [3,13–15]. Furthermore, apart from the inflammatory responses locally in the airways [16–19] a measurable systemic inflammatory response is also induced [20–25], which in turn is associated with an elevation of several cytokines (Interleukin (IL)-6, IL-1b) in the bloodstream [25], as well as increased production and release of polymorphonuclear leukocytes (PMN) and monocytes from the bone marrow [22–25].

Data from the firefighters involved in rescue operations during the World Trade Center attack showed that there is an association between the intensity of the exposure and the decline rate in pulmonary function parameters [8] as well as the persistence of airway hyper-responsiveness [12,26]. Aim of this study was to assess respiratory health and airway and systemic inflammation in young firefighters (trainees) with a part-time occupational exposure in firefighting for a year the most and compare it to that of professional firefighters with chronic occupational exposure.

To address this question we assessed symptoms, pulmonary function, atopy, bronchial hyper-responsiveness, and markers of inflammation in induced sputum, serum, bronchoalveolar lavage (BAL) fluid and bronchial biopsies.

2. Methods

2.1. Study population

A total of 92 male firefighters were included in this study (63 full-time professional firefighters, 29 trainees that had been working on a part-time basis for a year the most and 18 healthy subjects who served as a control group). All firefighters (professional and trainees) participated in similar operations and there was no difference in the use of respiratory protection equipment between the groups.

Firefighters were administered a standardized questionnaire assessing lifetime chronic respiratory conditions, history of tobacco use, history of upper and lower respiratory symptoms during fire fighting and during the interval periods, volunteer firefighter status, and lifetime occupational history.

Subjects underwent spirometry, sputum induction, methacholine provocation test and skin prick tests. Each subject attended the laboratory in two separate visits within one week. On visit one sputum induction was performed after reversibility test. On visit two, patients underwent methacholine provocation challenge and skin prick tests. Bronchoscopy was performed in a subgroup of 20 firefighters who volunteered, after signing an informed consent. There was no interest from the healthy subjects to undergo bronchoscopy.

All subjects gave informed consent for the participation in the study, which was approved by the Ethics Committee of Sotiria Hospital, IRB number: 16750.

2.2. Reversibility test

Lung function (FEV_1, FEV_1/FVC) was measured with a dry wedge spirometer (Masterscreen, Jaeger, Hoechberg, Germany) according to standardized guidelines [27]. Reversibility test was performed 20 min after inhalation of 200 μg salbutamol via a metered dose inhaler.

2.3. Bronchial responsiveness to methacholine

BHR was measured as PD_{20} of methacholine using the dosimeter method by a commercially available system (APS; Viasys Healthcare, Jaeger, Hoechberg, Germany), according to ATS guidelines [28].

2.4. Skin prick tests

Atopic status was measured by skin-prick tests using 13 common aeroallergens applied to the fore-arm. The allergens tested (HAL allergen Lab B. V. Harlem) were house dust mites (*Dermatophagoides pteronyssinus* and *Dermatophagoides farinae*), household pets (cat and dog), pollens (mixed grass, olive, mixed weed, and *Parietaria judaica*) and molds (alternaria, and *Aspergillus fumigatus*). Histamine and glycerinated saline solution were used as positive and negative controls. Atopy was defined as having at least one positive skin prick test. A skin-prick test result was considered positive if the mean wheal diameter was at least 3 mm.

2.5. Sputum induction and processing

Sputum was induced by inhalation of hypertonic saline aerosol and processed as described previously [29], by using an ultrasonic nebulizer (ULTRA-NEB 2000, DeVilbiss Healthcare INC, Somerset, USA). Sputum samples containing >20% of squamous cells and with cell viability <70% were excluded from analysis as indication of poor quality. Sputum supernatants were stored at −80 °C for subsequent assay for interleukin (IL)-4, IL-8, IL-13, TNF-α, vascular endothelial growth factor (VEGF), and eosinophil cationic protein (ECP) concentration.

2.6. Measurement of inflammation biomarkers

IL-8, IL-4, IL-13, VEGF, TNF-α, and ECP concentrations were measured in both serum and sputum supernatants. The concentrations of TNF-α, IL-8, IL-13, VEGF, and IL-4 were determined by ELISA using kits purchased from R & D Systems (Minneapolis, Minnesota, USA). The sensitivities of the assays used were 1.6 pg/ml, 3.5 pg/ml, 32 pg/ml, 9 pg/ml, and 10 pg/ml, respectively. ECP was measured using Unicap ECP kit (Pharmacia Diagnostics; Uppsala, Sweden) with a detection limit of 0.5 ng/ml. In all cases, the assays were carried out according to the manufacturer's recommendations.

2.7. Bronchoscopy

After local anesthesia of the throat, larynx, and bronchi which was achieved with 2% lidocaine, a flexible bronchoscope (BF 1T200; Olympus Optical; Tokyo, Japan) was introduced into the bronchial tree and gently wedged into the segmental bronchi of the right middle lobe. Four to six bronchial biopsies were obtained from segmental divisions of the main bronchi at the end of the bronchoscopic procedure. Collection, processing and microscopic evaluation of histological and cytological specimens were performed according to standard procedures.

2.8. Statistical analysis

Continuous variables are expressed as mean ± SD and categorical variables are expressed as relative frequencies and percentages. Fisher's exact test expanded with the use of linear regression was used for testing differences in the prevalence of respiratory symptoms, the provocative dose of methacholine, and atopy between groups. Differences in markers of inflammation between