Abstract

**Background:** Asthma is a chronic inflammatory disease of the respiratory tract and strong evidence suggests that environmental factors may induce or exacerbate it via irritants or sensitizers. About 10-15% of all asthma cases occur due to occupational exposures which makes asthma the most important work-related respiratory disease. It is interesting to study biological markers of inflammation as an intermediate phenotype in order to understand the pathophysiologic mechanisms and how environmental determinants may cause asthma. The role of a systemic inflammation which is present in asthma has scarcely been studied with regard to occupational exposures.

**Methods:** We analysed 894 participants (37.0% current asthmatics, 52.3% women) of the follow-up of the French Epidemiological Study on the Genetics and Environment of Asthma study (EGEA2). The study included information about asthma characteristics, occupational exposures and measurements of two biological markers (C-reactive protein (CRP), a marker of inflammation, and Club Cell protein (CC-16), a sensitive marker for lung injury). Current asthma was further characterised by asthma control, allergy and asthma treatment (inhaled corticosteroids - ICS) using standard definitions. Occupational exposure during the last professional activity was estimated via an asthma specific Job-Exposure-Matrix. CRP and CC-16 values were described in dependence of asthma, occupational exposures and other confounding factors using univariate statistics and linear mixed models.

**Results:** CRP levels were significantly increased with increasing age, in women and with increasing BMI and were higher in male heavy smokers. Asthmatic women had higher CRP values compared to non asthmatic women ($p = 0.02$), but this difference was not observed in men. Subjects with partially controlled or uncontrolled asthma had significantly higher CRP values compared to non asthmatics ($p < 0.01$). Allergic asthmatics had increased CRP values compared to non allergic asthmatics ($p = 0.04$) and compared to non asthmatics ($p < 0.01$). We found an increase of CRP in asthmatics using ICS compared to untreated asthmatics ($p = 0.02$) and compared to non asthmatics ($p < 0.01$). Regarding occupational exposures, no association with CRP was observed.

Increasing CC-16 concentrations were associated with a higher age, lower BMI, and an acute exposure to tobacco smoke in men, whereas a chronic exposure to tobacco smoke decreased CC-16 levels ($p < 0.01$). Asthma status, control and treatment were not associated to CC-16 levels, but allergic asthmatic women had significant lower CC-16 values compared to non allergic asthmatic women ($p = 0.04$). This association was not observed in non asthmatic women or in men. CC-16 levels were higher in subjects exposed to high molecular weight agents. This increase reached significance in subjects exposed to latex compared to subjects exposed to other high molecular weight agents and to non exposed persons ($p < 0.01$).

**Conclusion:** We confirm known relations between CRP, CC-16 and variables like age, sex, BMI and tobacco consumption. CRP is increased in allergic asthma and ICS treated asthmatics. CC-16 is increased after acute exposure to tobacco smoke, but decreased after chronic exposure. For the first time in the literature an increase of CRP in uncontrolled asthma, a decrease of CC-16 in allergic asthmatic women and an increase of CC-16 levels after occupational exposures to latex is described.