CUMULATIVE EXPOSURE TO MINERAL DUSTS, BRONCHIAL REACTIVITY AND FEV1 DECLINE

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Abstract: *The aim of this study is to assess the main symptoms of bronchial hyperreactivity (BHR) in relation with cumulative exposure to mineral dusts (CE) and FEV1 decline, in a longitudinal study over a period of 3.7 years. We examined a group of 105 employees of a company producing metallic reinforcements. A respiratory symptoms questionnaire ECRHS II was applied, we calculated the annual decline in FEV1 (ΔFEV1) and we noted the CE. The suggestive symptoms for BHR were: wheezing, morning chest tightness and sudden shortness of breath after an exhausting effort. We observed a significantly increased rate of ΔFEV1 in subjects with BHR compared with the ΔFEV1 in asymptomatic subjects. ΔFEV1 was in a linear relation with the CE and the smoking status. ECRHS II questionnaire is an effective and easy to apply instrument, allowing, together with the ΔFEV1 evaluation, an early selection of subjects likely to develop chronic airway obstruction.*

Cuvinte cheie: *chestionar de simptome respiratorii ECRHS II, declin VEMS, expunere cumulativă la pulberi minerale*

Rezumat: *Scopul lucrării constă în evaluarea pricipalelor simptome de hiperreactivitate bronşică (HRB) în relaţie cu expunerea cumulativă la pulberi minerale (EC) şi declinul VEMS (ΔVEMS) într-un studiu longitudinal pe durata a 3,7 ani. A fost vizat un grup de 105 angajaţi dintr-o societate producătoare de armături metalice. S-a aplicat chestionarul de simptome respiratorii ECRHS II, s-au calculat ΔVEMS şi EC. Simptomele sugestive de HRB au fost: prezenţa fenomenului de wheezing, senzaţia de constricţie toracică matinală şi dispneea instalată brusc după terminarea unui efort epuizant. HRB, apreciată ca probabilă, s-a asociat cu o rată semnificativ crescută a ΔVEMS comparativ cu declinul funcţional al subiecţilor asimptomatici. ΔVEMS s-a aflat într-un model de relaţie lineară cu EC şi statutul de fumător. Chestionarul ECRHS II este un instrument eficient şi uşor de aplicat, care permite, concomitent cu evaluarea ΔVEMS, o selectare precoce a subiecţilor susceptibili de a contracta obstrucţie cronică a căilor aeriene.*

INTRODUCTION

The chronic airway obstruction recorded worldwide a worrying increase in frequency and some studies predict it as the third cause of death for the years 2020.(1) It is an entity with several etiological agents in addition to individual genetic factors that are more and more well-known. Air pollution increases the frequency of respiratory symptoms and that of the lung function decline.(2,3) The main polluting agents are smoking and occupational exposure to dust. In an official document of the American Thoracic Society in 2003, the risk for COPD attributable to occupational factors was evaluated as the main cause in 15% of the diagnosed patients.(4) FEV1, the most representative of the ventilation parameters has a physiological decline with age. It reaches a peak value between 20-30 years of age and then gradually declines (5), with an estimated annual decline rate of 25 ml/year.(6) An accelerated annual FEV1 decline rate (Δ FEV1) leads to a decrease in FEV1 calculated values (reported to the prediction values) under 80% and to a decrease in FEV1/VC index values below 70%. These threshold values certify the onset of COPD. Knowing the Δ FEV1 value before the onset of chronic obstruction is essential in order to prevent the damage of the respiratory function, but for this it is necessary to better understand the mechanisms underlying the ventilatory decline.

Recent research tends to associate the presence of an accelerated functional decline with a bronchial hyperreactivity (BHR) that is caused by chronic inflammation of the airways following the exposure to risk factors. Thus, the BHR can be considered a predictor for an increased rate of functional decline (7), anticipating chronic airway obstruction. It is also an aggravating factor by its persistence in the case of a continuous exposure to the incriminated risk factors. Some studies on asymptomatic subjects with normal ventilatory function, but hyperreactive, show an increase in the rate of decline under continuous exposure to the etiological agents.(8)

To constitute a target group on which effective means of prevention must be implemented, the ideal situation would be the investigation of bronchial reactivity. Since this investigation is generally not appreciated by asymptomatic individuals, the application of respiratory symptoms questionnaires is recommended to practitioners as an alternative. To this end we conducted a validation study of the ECRHS II questionnaire, to a group of subjects with respiratory symptoms, who were submitted to a histamine challenge test, which concluded that the presence of wheezing outside recurrent infections, morning chest tightness and sudden shortness of breath after an exhausting effort, are strongly suggestive of BHR.(9)

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PURPOSE

The purpose of this study is to evaluate the main symptoms of FEV1 decline in BHR, in relation with the cumulative exposure to mineral dusts.

METHODS

Our investigated lot includes 105 employees working in foundry and machining departments of a company producing metallic reinforcements with a similar qualitative exposure to mixed dust (metal oxides, silicates, and a small proportion of free SiO_2). The concentrations, measured gravimetrically as total dust, were different from one job to another. Irritant gases (nitrogen oxides, sulphur dioxide), determined using a Triple Plus analyzer (Crowcon Instruments LTD) equipped with electrochemical sensors, were below the quantifiable limit, and formaldehyde determined by molecular absorption spectrophotometer was on average 10 times below the permissible limit. For these reasons the exposure to mineral dusts was considered as the dominant risk factor.

The major inclusion criteria in the lot were the agreement of the subjects to give an honest response at every item of the questionnaire administered and the activity in the company of at least 12 months, with at least two functional investigations performed (at the beginning and at the end of the observation period).

The exclusion criteria were the presence of arterial hypertension, ischemic heart disease and poor cooperation when performing the functional tests, translated by differences that exceeded 20 to 30 ml in the three attempts made during the test.

Collection of symptoms, duration of the activity in one or more work departments and practice of active or passive smoking were obtained by going through items Q1-Q29 of the ECRHS II questionnaire.(10)

Ventilatory function testing was performed with a Japanese manufactured equipment Microspiro HI - 501, calibrated on the day of use with a 1000 ml syringe. To each subject, three tests were performed in order to include in the study the best performed values recorded as absolute values and as percentage values (reported to predictive values ERS - 93 - European Respiratory Society - 1993). Functional testing was done by the same person, a physician, and the subject was tested in orthostatic position with a nose clamp. We stated that the chronic obstructive subjects are those with FEV1 values below 80% of the prediction value and with FEV1 / VC index less than 0.7 (11), and that subjects with chronic bronchitis, are those who answered "yes" to items Q8.1 and Q10.1 (chronic cough with expectoration for at least 3 successive months per year in two consecutive years). The mean observation time was 44.88 ± 14.14 months (3.7 years) ranging from 12 to 84 months. The Δ FEV1 calculation was done using the formula: *[FEV1 (1) – FEV1 (2)] x12 / observation interval in months*, and was expressed in ml / year [FEV1 (1) = the absolute value from the trial admission, FEV 1 (2) = the absolute value at the end of the observation period].

The cumulative exposure to dust (CE) was calculated as the product of the dust concentration with the number of years working in these conditions. When employees had more jobs, cumulative exposure was calculated as the sum of the corresponding products. CE was expressed as dust years. Bronchial hyperreactivity was considered as present with high probability in subjects who answered “yes” to items Q1 (wheezing), Q2 (morning chest tightness) and Q4 (sudden dyspnea after an exhausting effort).

In every subject a standard chest X-ray was performed to determine the presence of silicosis.

Qualitative variables were summarized as percentages and their 95% confidence intervals (95%CI) calculated with an optimized binomial formula (12, 13). Z-test was used to compare proportions. The main characteristics of the metric variables were expressed as mean and standard deviation (m ± stdev) whenever data were normally distributed; otherwise median and interquartile range (median [Q1; Q3], where Q1 = 25^{th} percentile, Q3 = 75^{th} percentile) were used. Student’s t test was applied to compare normal distributed continuous variables; otherwise, the Mann-Whitney U-test was applied. The General Linear Model technique was applied to analyze the link between dependent variable (FEV1 decline) and independent variables (cumulative exposure to dust and smoking status).

The statistical analyses were conducted with Statistics software at a 5% significance level.

RESULTS

The percentage representation of men / women is 81% and, respectively, 19%. The proportion of male was significantly higher compared to the proportion of female (Z statistics = 16.1945, p-value < 0.0001). This reflects the global gender structure of the employees. The mean age of the whole group is 46.44 ± 6.77 years with no significant differences between the means observed in males and females (Mann-Whitney test = 704).

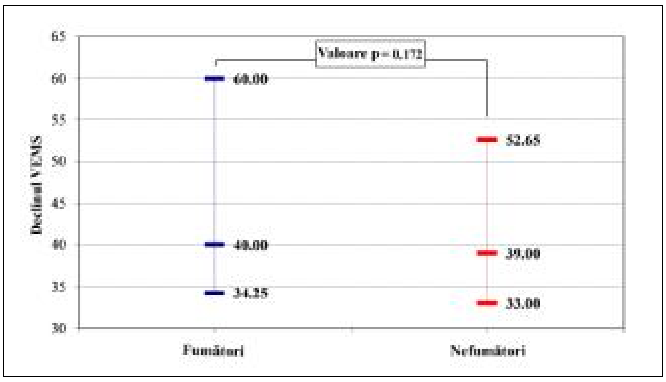
The prevalence of chronic bronchitis was 14% on the entire lot, being higher in smokers (19%) compared with non-smokers, the differences not being statistically significant (Z statistics = 1.1075, p-value = 0.2681). The overall prevalence of COPD was 8%, with 12% in smokers and 5% in non-smokers, without statistically significant differences (Z statistics = 1.2244, p-value = 0.2208) (table no. 1).

Table no. 1. Prevalence of chronic bronchitis and COPD

Diagnosed entity	Prevalence (%) [95%CI]	Z statistics (p-value)
Chronic bronchitis All Smokers (n=42) vs Non-smokers (n=63)	 14 [8-21] 19 [10-33] vs 11 [5-22]	 1.1075 (0.2681)
COPD All Smokers (n=42) vs Non-smokers (n=63)	 8 [7-9] 12 [5-26] vs 5 [2-13]	 1.2244 (0.2208)

Δ FEV1 ranged between 21.67 and 90.00 ml / year, with an average value of 44.73 ± 15.68 ml/year. There were no significant differences in Δ FEV1 comparison between smokers and non-smokers (Mann-Whitney test = 1114.5) (figure no. 1)

Figure no. 1. Δ FEV1 comparison between smokers and non-smokers



The relationship between Δ FEV1 and the presence/absence of symptoms, suggestive of BHR, is illustrated in Table 2, was seen in the high FEV1 decline, significantly higher for the symptomatic subjects.

Table no. 2. FEV1 decline (ml / year) related to the presence of symptoms

Subcategories depending on the answer „YES" to items Q1, Q2, Q4	**No. obs.**	**ΔVEMS (ml/year)**	**Statistical significance**		
A: two or three symptoms present	31	61,73±12,9	**A/B:** t=3,946 p<0,002	**B/C:** t=0,960 p>0,05	**A/C:** t=9,656 p<0,001
B: one symptom present	9	41,23±12,8			
C: without symptoms	65	36,72±9,3			

Q1: Have you had wheezing or whistling in your chest at any time in the last 12 months?
Q2: Have you woken up with a feeling of tightness in your chest at any time in the last 12 months?
Q4: Have you had an attack of shortness of breath that came on following strenuous activity at any time in the last 12 months?

The cumulative exposure to dust was similar in smokers and non-smokers (109.4 ± 59.89 vs 106.88 ± 59.068) (p = 0.832). There was a linear model linking Δ FEV1 and two independent variables: cumulative exposure to dust and smoking status ($F = 546.4$, $p = 1.13 \times 10^{-62}$, eta-square = 0.941, observed power = 1). Both independent variables were statistically significant (cumulative exposure to dust: $F = 82.15$, $p = 9.57 \times 10^{-15}$, eta-square = 0.446, smoking status: $F = 61.07$, $p = 3.65 \times 10^{-18}$, eta-square = 0.545).

DISCUSSIONS

The prevalence of nonspecific lung diseases lies in the context of known literature data regarding the risk of occupational exposure. The fact that prevalence differences are insignificant when comparing smokers with non-smokers, suggests an important dust pollution that "deletes" the differences attributable to the smoking status. This phenomenon is well known from the extensive research done in the 70s by Lambert and Reid.(14)

The functional decline observed by us is much higher than the physiological FEV1 decline and close to the decline stated by Bake et al. (15) in the underground workers performing drilling operations for the construction of tunnels. Even higher levels of Δ FEV1 (65 ml/year) were communicated, over a short period of exposure in coal mines, an average of 11 months.(7) In our study group, Δ FEV1 was not significantly correlated with the smoking status, something explainable perhaps, also by the high level of pollution. Other studies mention an excess of functional decline in smokers at risk compared with non-smokers.(11)

The main symptoms that suggested a BHR were wheezing (most common), morning chest tightness and sudden shortness of breath after an exhausting effort. Other data in the literature indicates that the main symptom of BHR is wheezing.(16,17,18)

BHR, considered in our observations as probable, was associated with an increased rate of Δ FEV1, representing a true "prelude" of the functional decline. A recent study of fire-fighters engaged in the events at the World Trade Center on September 11, 2011 confirmed a clear relationship between the FEV1 decline and BHR.(19)

The cumulative exposure to dust is a relevant indicator in studies about long-term respiratory effects.(11,20) In our study, Δ FEV1 was in a linear relationship with the CE and the smoking status.

Based on the current knowledge, the sequence of phenomena that lead to functional decline begins with airway inflammation caused by mineral dust and mediated by the noradrenergic, noncholinergic system (18,21) that generates neuropeptides. This neurogenic inflammation leads to the phenomena of bronchial remodelling, including the hypertrophy of the airway contractile substrate, expressed through hyperreactivity. Even an asymptomatic BHR is associated with the remodelling phenomena.(22)

Our study indicates the importance of recording respiratory symptoms using a standardized questionnaire and the dynamic Δ FEV1 follow-up as methods for selecting candidate employees for programs of respiratory function preservation.

CONCLUSIONS

The ECRHS II questionnaire is an effective, convenient and accepted instrument that can be used to highlight with high probability the presence of BHR.

The suggestive symptoms for BHR were: wheezing, morning chest tightness and sudden shortness of breath after an exhausting effort. The coexistence of at least two of these symptoms was associated with an increased rate of FEV1 decline.

The FEV1 decline was in a linear relation with the CE and the smoking status.

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