Short Communication

Manifestation of Bronchial Hyperreactivity from Exposure to Heavy and Precious Metal Vapors among the Ore Smeltery Workers of Zveçan, Kosovo

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Abstract

Context: Kosovo is a region in the Western Balkans that is rich in minerals and coal, so pollution is a serious public health problem there. Workers in the heavy and precious metal smeltery in Zveqan, Kosovo, were studied with regard to the roles that vapor from the smelting of metals (Pb, Zn, Au, Ag, P, and Cu) and particulate matter play in causing bronchial hyperreactivity. **Objectives:** The purpose of the article was to measure the parameters of lung function as determined by body plethysmography, diagnosis of respiratory diseases, and assessment of respiratory function using a histamine bronchoprovocation test. **Settings and Design:** The present study was conducted in two groups of participants: A control group, which included 25 healthy persons, and a smeltery worker group, which included 45 mine workers (15 smokers and 30 nonsmokers) holding permanent jobs in the mineral foundry of Zvecan, Kosovo. **Subjects and Methods:** Pulmonary function parameters (specific airway resistance [Raw] and intrathoracic gas volume) were measured and used to calculate the specific resistance (SRaw) and specific conductance (SGaw) of the airways, and a histamine bronchoprovocation test was conducted. **Statistical Analysis Used:** The data were entered and analyzed using the Microsoft Excel and INSTAT 3 software. **Results:** Airway specific resistance (SRaw) was significantly higher in the smeltery worker group ($P < 0.01$) as compared to the control group ($P > 0.1$). **Conclusion:** These results suggest that occupational exposure to vapors during the metal refining process poses a risk to the workers' health and can cause bronchial hyperreactivity, bronchial asthma, or chronic obstructive pulmonary disease.

Keywords: Bronchoprovocation test of the respiratory system, employees of the metal refining smeltery, respiratory diseases

Introduction

Inflammation is currently known to play an important role in the development of bronchial hyperreactivity and asthma. Data from the analyses of histopathological material from patients (e.g., large numbers of eosinophils, neutrophils, and lymphocytes from bronchoalveolar lavage) or from autopsies of deceased status asthmaticus patients indicate that these diseases are inflammatory in nature. There are several etiological factors that influence pathohistological changes in the bronchial walls, including chemicals, metal vapors, frequent infections, and physical, hormonal, and psychogenic factors. The inflammatory process involves bronchi from the trachea to the respiratory bronchioles[1] and progressively restricts airflow as a result of the action of harmful antigens, gases, and microparticles (particulate matter [$PM_{2.5}$] and PM_{10}) on the respiratory system. Chronic inflammatory processes can be accompanied by bronchial asthma and result in remodeling of the small airways. The lumen of the airways then becomes obstructed due to increased mucus production, thickening of the airway wall from edema, and collagen formation that result in fibrosis and airway narrowing. Persistent inflammation also destroys lung tissue, results in loss of alveolar connections and small airways and reduces the elasticity of lung retractions.[2]

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Research conducted at the smeltery premises on the vapors produced from smelting ores indicates that the vapors have a significant effect in causing bronchial reactivity and COPD. The development of these respiratory diseases is also affected by the factors such as environmental conditions in the workplace, working habits, and smoking. For this reason, a study to assess workers' occupational exposure to heavy and precious metals, such as Pb, Zn, Au, Ag, P, and Cu, and PM, which can cause bronchial hyperreactivity and affect their lung function.

Subjects and Methods

The study focused on assessing bronchial reactivity and the presence of chronic obstructive pulmonary disease (COPD) using the questionnaire for chronic respiratory diseases devised by the Medical Research Council (MRC)[3] and by measuring target respiratory parameters using body plethysmography on ore smeltery workers in Zvecan, Kosovo.

The selection of workers was done randomly, and all research participants were informed about the procedures and the purpose of the study. Two groups of participants were recruited. The control group included 25 healthy people, and the smeltery worker group included 45 workers (15 smokers and 30 nonsmokers) who held permanent jobs in the ore smeltery in Zvecan, Kosovo. All participants were instructed to not take any medication for at least 48 h before the examination not to interfere with the results of our tests.

The lung function of the participants was measured at resting condition. The specific airway resistance (Raw) and intrathoracic gas volume (ITGV) were then measured using the body plethysmography technique. From the measurements obtained for Raw and ITGV, the values of specific airway resistance (SRaw) and specific conductance (SGaw) were calculated using the following equations:

$$SRaw = Raw \times ITGV$$

$$SGaw = 1/SRaw$$

In both groups of participants, a test to experimentally provoke bronchoconstriction using a histamine aerosol (1 mg/mL) was performed.

Analysis of respiratory symptoms, changes in lung function, and bronchial reactivity in workers who were exposed to high concentrations of air contamination showed that they had impaired lung function at the level of gas exchange, as manifested by a decrease in DLCO, which is statistically significant ($P < 0.05$), compared to the control group ($P > 0.1$).

Statistical analysis

Statistical processing included the determination of the mean (X), standard deviation, and standard error of the mean, as well as testing of statistical differences in parameters between the workers and the control group. The parameters were summarized using Microsoft Excel. The INSTAT 3 and Statistica software (Graphpad, California, USA) were used for statistical processing.

Results

Healthy individuals have minimal bronchial reactivity in the respiratory system and were used as a control group to assess the condition of the experimental group (Tables 1,2).

Statistical analyses with the *t*-test showed that there was no significant difference in healthy individuals before and after provocation with histamine aerosol ($P<0.05$).

There was a significant difference in airway SRaw and SGaw between the control and smeltery worker groups ($P < 0.01$), and there was elevated bronchial hyperreactivity in the smeltery worker group. The values of the SRaw and SGaw parameters for both groups are presented graphically in Figures 1 and 2.

In the smeltery worker group, there was a statistically significant reduction in DLCO compared to the control group [$P < 0.05$, Figure 3], which implies difficulty in the circulation of gases through the alveolo-capillary membrane.

With increasing duration of exposure after the age of 20 years, there were significant increases in bronchial hyperreactivity and COPD ($P < 0.01$).

Discussion

Bronchial hyperactivity refers to an increased airway response to specific and nonspecific stimuli. This is a condition in which the airways react restrictively to small doses of provocative agents. In afflicted individuals, this reaction can be caused by smaller amounts of irritation than is the case for normal healthy people. This sensitivity results in constriction of the smooth bronchi muscles, increased mucus secretion, and inflammatory reactions (swelling, vasodilation, the effects of inflammatory cells, desquamation of epithelial cells, and the release of chemical mediators such as histamine, serotonin, bradykinin substances with clumsy action [SRS], leukotrienes, platelet-activating factor, and free radicals).[4] The symptoms of this condition include cough, shortness of breath, and wheezing.

Bronchial reactivity can arise from a reaction to nonspecific inducing agents (e.g., cold air, physical exertion, $PM_{2.5}$, and PM_{10}) as well as from exposure to specific stimulants (e.g., allergens or occupational exposure). Usually, bronchial hyperreactivity manifests as the onset of asthma.[5] Bronchial hyperreactivity may also occur transiently in healthy persons after long-term exposure to sulphur dioxide, ozone, and nitrogen oxides in the workplace (e.g., power plants and mines) or after frequent viral infections.[6]

This study included 70 workers of the heavy and precious metals foundry in Zvecan, Kosovo. All participants were given a histamine bronchoprovocation test, which confirmed the presence of bronchial hyperreactivity in the smeltery worker group and resulted in the necessity to administer bronchodilators to relieve symptoms.

By analyzing the function of the respiratory system without provocation, we obtained baseline values in both groups. After provocation with histamine, there was pronounced

Table 1: General characteristics of the researched persons

Group	*n*	Age (years)	Height (cm)	Weight (kg)	VC (L)	FEV_1 (L)
Control	25	23.5±0.2	176±0.12	69.2±1.7	3.77±0.22	3.55±0.22
Experimental	45	38.34±1.12	179±0.21	73.50±1.22	3.68±0.45	3.45±0.52

Generalized mean values for: Control group *n*=25, X±SEM, Experimental group *n*=45, X±SEM. The general starting values for: VC (L) and FEV_1 (L) are also given. VC=Vital capacity expressed in liters, FEV1: Enhanced expiratory volume in the 1 s, expressed in liters, SEM: Standard error of the mean

Table 2: Body-plethysmography features of the people involved in this study

Group	*n*	Raw (kPa × s/L)	ITGV (L)	SRaw (kPa×s)	SGaw (kPa × s)
Control	25	0.19±0.7	3.15±0.8	0.59±0.4	1.69±0.15
Experimental	45	1.25±0.3	3.23±0.9	4.03±0.9	0.25±0.13

Raw (kPa × S/L), ITGV (L), SRaw=Raw × ITGV, SGaw=1/SRaw. Raw: Airway resistance expressed in kilopascal/s/L, SGaw can also be referred to as specific airway passage or conductivity. ITGV: Volume of intrathoracic gas expressed in liters, SRaw: Specific airway resistance which is the relationship between resistance and the volume of intrathoracic gas, SGaw: Expresses the relationship between 1/specific resistances

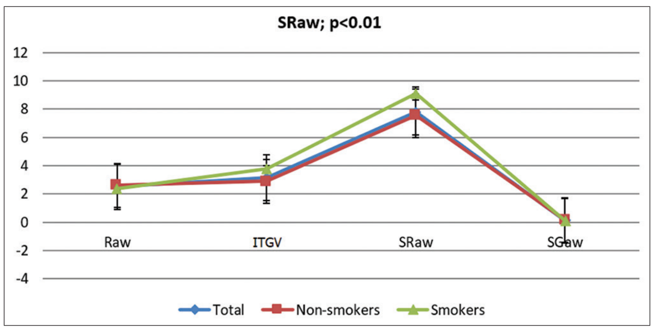

Figure 1: Researched as per categories of nonsmokers and smokers (before provocation with histamine-aerosol). Comparison of SRaw and SGaw values between nonsmokers and smokers; prior provocation with histamine-aerosol ($n = 45$; X ± standard error of the mean)

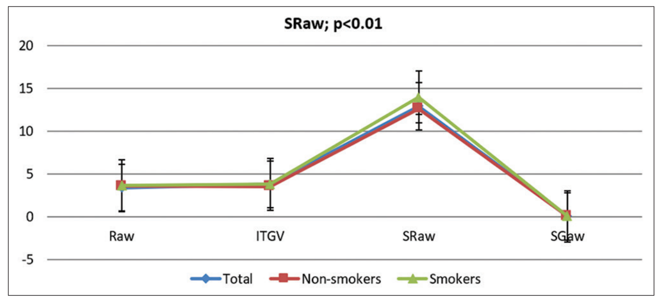

Figure 2: Researched as per categories of nonsmokers and smokers (after provocation with histamine). Comparison of SRaw and SGaw values between nonsmokers and smokers; prior provocation with histamine-aerosol 1 mg/ml ($n = 45$; X ± standard error of the mean)

hyperreactivity in the smeltery worker group, as demonstrated by an increase in SRaw and reductions in SGaw and DLCO, which were statistically significant when compared to the control group.[7] At the beginning of the study, both groups had parameters within the limits of normal values. Some studies indicate that there is a direct correlation between respiratory parameters (SRaw and SGaw) and bronchial hyperreactivity in response to histamine or methacholine.[8]

Many studies have indicated that even after therapy, bronchial reactivity does not return to normal levels, and that the number of eosinophils in the sputum is elevated in these patients.[9]

Fujimura *et al*. demonstrated that patients treated only with bronchodilators did not improve clinically, but instead experienced deterioration after long-term treatment; in other words, this therapy may actually promote the development of classic bronchial asthma.[10] Conversely, timely application of anti-inflammatory medications such as corticosteroids significantly reduces bronchial hyperreactivity and thus reduces the risk of developing classic bronchial asthma.

Bronchial reactivity is mainly determined by the sensitivity of the smooth musculature in the pars membranacea of the tracheobronchial system, but this cannot be explained by genetic factors. This increase in bronchial hyperreactivity occurs in the presence of an inflammatory reaction throughout the tracheobronchial system, except in the pars membranacea.[11]

The analysis of heavy metal vapors released during the process of ore exploiting and their effects on the respiratory system (e.g., damage, inflammatory reactions, remodeling of airways, and alveolo-capillary membranes), as well as decisions on preventive measures, diagnosis, or treatment, are comprehensive measures that are necessary to fully mitigate the impact of air pollutants on the health of workers and the general population.[12,13]

Conclusion

This study indicates that occupational exposure to heavy metals such as Pb, Zn, Au, Ag, P, and Cu, as well as PM, causes bronchial hyperreactivity, which manifests as a reduction in DLCO and is associated with difficulties in the circulation of gases through the alveolo-capillary membranes; these changes were statistically significant in the group of exposed smeltery workers when compared to the control group.

Given these results, preemptive surveillance of respiratory function and early detection of bronchial hyperreactivity are crucial, especially with regard to inflammatory reactions, which occur following inhalation (absorption) of the metal vapors.

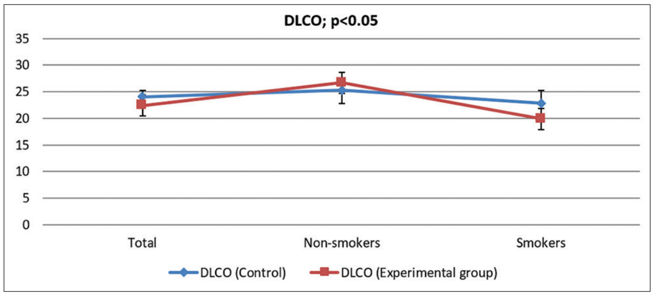

Figure 3: Expressed transfer factor (DLCO) of control and experimental group (mmol/s/1 kPa). (n = 45; X ± standard error of the mean)

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Conflicts of interest

There are no conflicts of interest.

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