ASSESSMENT OF HEALTH EFFECTS RELATED TO FIBER GLASS EXPOSURE IN FIBER GLASS WORKERS: EXHALED BIOMARKERS eCO, FE_{NO} AND THEIR USEFULNESS IN THE OCCUPATIONAL ENVIRONMENT TESTING

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Abstract

Introduction. *Numerous epidemiological animal model studies have been conducted in order to assess the health effects of man-made vitreous fibers. They have been shown to be responsible for producing lung fibrosis and lung and peritoneal cancer in animal models. A few large cohort studies were conducted in Europe and the US to assess the health effects of fiber glass in production workers and a higher cancer incidence was evidenced.*

Aim. *The aim of the study is to assess the usefulness of exhaled biomarkers measurements: exhaled nitric oxide and exhaled carbon monoxide in fiber glass workers as indicators of an inflammatory airway response .*

Material and method. *A total of 42 fiber glass workers were included in this study with a minimum of 5 year exposure period in which FE_{NO} and eCO values were measured. Also spirometry chest X ray, C reactive protein , fibrinogen, total IgE serum and IL8 serum levels were determined.*

Results. *Increased values of exhaled nitric oxide (over 25 ppb) were found in 43% of the fiber glass workers and increased values of exhaled carbon monoxide (over 6 ppm) were determined in 26% of the fiber glass workers. A positive correlation was found between the exposure period and FE_{NO} values and total IgE values ($p<0.05$). A negative correlation coefficient was found between FEF 25-75 predictive values and FE_{NO} and total IgE values.*

Conclusion. *These results suggest that exhaled biomarkers can be useful to assess an inflammatory airway response in the occupational environment.*

Keywords: fiber glass, exhaled biomarkers.

Abbreviations: FeNO - fraction of exhaled nitric oxide, eCO - exhaled carbon monoxide.

Introduction and aim

A number of epidemiological studies of the potential health effects of man made vitreous fibers have been carried out. The main concern is that because these fibers are structurally very similar to the asbestos fibers MMVS can also cause respiratory disease such as occupational related asthma, interstitial pneumonia, pulmonary fibrosis and especially lung cancer [1].

Exposure to fiber glass has been shown to induce pleural and lung disorders such as emphysema, fibrosis and lung and peritoneal cancer [2].

Two large epidemiological studies were conducted between 1986-1992 in Europe [3] and one in the US between 1982-1990 [4]. In the European cohort an increased lung cancer risk was suggested for the workers employed for a short time.

The research on MMVS is still continuing today. The most recent large studies were conducted in the US in the months following the collapse of the World Trade Center towers. These studies have shown high concentration of MMVS in the dust collected from ground zero and was concluded that it was responsible for at least the early pulmonary symptoms observed in the ground zero workers [5].

Nitric oxide (NO) in orally exhaled air mainly originates from the respiratory epithelium . NO is produced by inducible NO synthase (iNOs). Several studies have shown increased values of NO in exhaled air in asthmatic

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patients due to airway inflammation. Considering that occupational exposure to fiber glass can produce chronic inflammation, FE_{NO} and eCO values were determined [6,7].

Exhaled carbon monoxide levels represent the sum of the endogenous production of the gas and airway contamination from environmental exposure. In the absence of high background exposure eCO may correlate with cellular haem oxigenase derivated CO production induced by oxidative stress and may reflect an inflammatory response in human disease [7,8,9].

Material and method

Patient group

A prospective observational study in fiber glass workers was conducted: 42 patients were included in the study. The assessment included a bronchial symptoms questionnaire, exposure history, complete blood work, determination of exhaled biomarkers, fibrinogen, PCR, spirometry, chest X ray, total IgE, serum IL8 levels.

We selected workers in a fiber glass factory with a minimum of 5 years exposure time. All the patients included in the study were non smokers or ex smokers, had not underwent corticosteroid topic or systemic treatment and/or non steroidial anti-inflammatory treatment within a month prior to the study.

FE_{NO} measurement was performed after a 10 minute resting period, prior to spirometry testing, at total lung capacity with exhalation flow rate at $50mL \cdot s^{-1}$ for at least 6 seconds [10]. A device based on electrochemical sensor was used. A single breath method was used, the patients were seated comfortably with the mouthpiece at proper height and position and a nose clip was used. The patients were instructed to inhale 3 seconds through the mouth to total lung capacity and then exhale immediately without breath holding. The analyzer used was designed to accept test results only if the air flow rates were held constant at 50 ml per second which was indicated by the display on the monitor of a cloud centered within a black box accompanied by a constant sound that meant breathing out at the right rate. For the interpretation of the FE_{NO}, values between 5-25 ppb show unlikely inflammation, values >25 ppb were considered evocative for the presence of mild inflammation and values >50 ppb evocative for significant inflammation [11].

For the eCO measurement an electrochemical device was used in the parts per million ranges. The measurement was performed with a Smorkerlyzer, the test was performed after a 15 second period of holding their breath. Abnormal values were considered >6 ppm [12].

Demographic data of the subjects and exposure period are represented in Table I.

Table I. Demographic data of the subjects and exposure period.

Age (mean+/-SD)	40+/-7 years
Gender F/M	20/22 (number)
Exposure period (mean=/-SD)	12=/-2 years

Ethical Issues

All the patients were included in the study after they gave their informed consent. The study was conducted according to the Helsinki Declaration on human experimentation and was approved by the ethical committee of Medical University of Cluj-Napoca.

Results

All the patients agreed to participate in the study. SigmaPlot 12.0 was used for the statistical analysis of the collected data. The Kruskal-Wallis One Way Analysis of Variance on Ranks was used to determine the mean values which are shown in table II.

Table II. Mean values of exhaled biomarkers.

eCO (mean+/-SD)	2.095=/-2.097
FE_{NO} (mean+/-SD)	24.238+/-9.060

Increased FE_{NO} values >25 ppb were found in 38% of the patients and >55 in 5% of the patients. Increased eCO values >6 ppm were found in 26% of the patients. Spearman correlation test was used to determine if there was any correlation between the exposure period and the FE_{NO} and eCO values. No correlation was found between the exposure period and FE_{NO} and eCO values. FE_{NO} values and eCO values versus the exposure period are represented in figure 1 and figure 2.

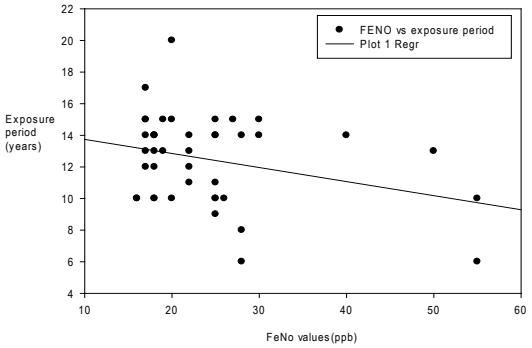

Figure 1. The FE_{NO} versus exposure period.

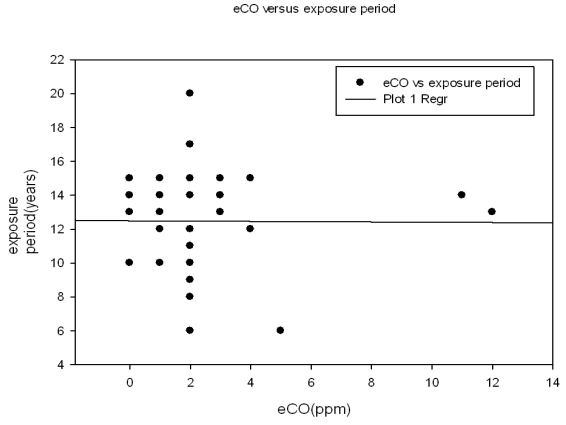

Figure 2. Exhaled eCO values versus exposure period.

The methodology also included chest X ray which evidenced no significant findings.

The spirometry was performed in all the patients included in the study and revealed small airway obstruction in 22 patients (53%) with predictive values of FEF 25-75 ranging between 53-79.

C reactive protein and fibrinogen levels were also determined, the protein C levels were negative for all the subjects included in the study and the fibrinogen values were slightly elevated in 6 patients (14.2%).

Total serum IgE levels were increased in 33 patients (78%) with mean value of 136.42.

The interleukin 8 levels were determined and were found elevated in the study group compared to a control group with mean values of 14.2 pg/ml for the controlled group and mean value of 94 for the study group.

The Pearson Product Moment correlation test was used for the statistical analysis and showed a positive correlation between exposure period, FE_{NO} and total serum IgE levels ($p<0.05$) and a negative correlation between FEF 25-75, FE_{NO} and total serum IgE levels.

Discussion and conclusion

This is an exciting area in which determining the exhaled biomarkers might be of help in the diagnosis and the evaluation of the occupational lung disease. The data available currently on FE_{NO} and eCO monitoring in occupational respiratory disease are limited and show conflicted results. In this study we have found increased values of FE_{NO} and eCO in nonsmokers fiber glass workers.

These increased values of FE_{NO} and eCO may reflect an inflammatory response and could predict the onset of a pulmonary occupational disease.

The statistical analysis has shown a negative correlation between FE_{NO} values and FEF 25-75 predictive values.

Several studies have shown increased FE_{NO} values and concluded that FE_{NO} measurement could have the potential to assess and monitor effects of air pollution and this increase in FE_{NO} is most often accompanied by a slight decrease in spirometric values [13,14,15]. Increased FE_{NO} values were described in shoe and leather workers at the end of a workday when exposed to solvents [16] and in farmers, bakers and healthcare workers [17].

The limitations of this study include a small number of subjects and the lack of serial testing. Testing for FE_{NO} at different flow rates could also be useful to assess the inflammatory response. Further studies in a larger population are needed to establish if exhaled biomarkers are of added value in occupational respiratory distress.

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