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Influence of air pollution on exhaled carbon monoxide levels in smokers and non-smokers. A prospective cross-sectional study

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ABSTRACT

Background: The poor air quality and cigarette smoking are the most important reasons for increased carbon monoxide (CO) level in exhaled air. However, the influence of high air pollution concentration in big cities on the exhaled CO level has not been well studied yet.
Objectives: To evaluate the impact of smoking habit and air pollution in the place of living on the level of CO in exhaled air.
Methods: Citizens from two large cities and one small town in Poland were asked to complete a survey disclosing their place of residence, education level, work status and smoking habits. Subsequently, the CO level in their exhaled air was measured. Air quality data, obtained from the Regional Inspectorates of Environmental Protection, revealed the differences in atmospheric CO concentration between locations.
Results: 1226 subjects were divided into 4 groups based on their declared smoking status and place of living. The average CO level in exhaled air was significantly higher in smokers than in non-smokers ($p < 0.0001$) as well as in non-smokers from big cities than non-smokers from small ones ($p < 0.0001$). Created model showed that non-smokers from big cities have odds ratio of 125.3 for exceeding CO cutoff level of 4 ppm compared to non-smokers from small towns.
Conclusions: The average CO level in exhaled air is significantly higher in smokers than non-smokers. Among non-smokers, the average exhaled CO level is significantly higher in big city than small town citizens. These results suggest that permanent exposure to an increased concentration of air pollution and cigarette smoking affect the level of exhaled CO.

1. Introduction

The continuous growth of the world population in the 21st century aggravates contamination problems and air pollutants seem to play a significant role in the process (Senechal, et al.. 2015; Briggs, 2003). Some of the contributing factors include a higher number of vehicles and dynamic industrial development, coupled with inadequate protective measures, such as lack of chimney filters and failure to implement new, environmentally compatible technologies. (Levy, 2015.) One of the most common toxic gases contaminating the atmosphere is carbon monoxide (CO). This odorless, tasteless and colorless gas is the third most frequent reason for intoxication after drugs and ethanol (Bleeker, 2015; Blumenthal, 2001). The origin of carbon monoxide can be both endo- and exogenous. The main endogenous source of CO in the human body is the oxidative degradation of heme, catalyzed by heme oxygenase (HO); an additional supply can be provided by pathological conditions, such as lipid peroxidation, photooxidation of organic compounds as well as the activity of intestinal bacteria (Pouokam et al., 2011; Baranano et al., 2002; Bełtowski et al., 2004; Singer et al., 1996). The most commonly described exogenous sources include: cigarette smoke, traffic exhaust, gas ovens, wood stoves, an incomplete combustion of fossil fuels, mining industry and power plants.

The pathophysiology of CO is complex as this entity is characterized by a multidirectional bioactivity. Due to its greater affinity for Hb, CO displaces oxygen (O_2) from its complexes with hemoglobin and forms carboxyhemoglobin (COHb). Although the reaction is reversible, the

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reverse reaction time is almost 10 times longer than O_2-hemoglobin dissociation, which results in impaired O_2 delivery and growing hypoxia. Moreover, COHb increases the stability of oxygen-hemoglobin connection, additionally impeding O_2 release in peripheral tissues. Another toxic mechanism of CO activity is associated with its binding to cytochrome *C* oxidase and interruption of cellular respiration (Kajimura et al., 2010; Wu and Wang, 2005).

The studies conducted so far have shown that a long-term exposure to low concentration of CO affects predominantly cardiovascular, nervous, respiratory, digestive and immune systems (Evans et al., 2014; European Environment Agency, 2011; Jasnos et al., 2014; Pope et al., 2015; Cuinica et al., 2015). Carbon monoxide modulates vascular wall tension, inhibits platelet aggregation and supports lipid migration through damaged endothelium. All of this leads to the increased risk of myocardial infarction and stroke. The impact of CO on the nervous system is associated with its participation in neurotransmission, which may generate many neuro-psychiatric symptoms. Furthermore, maternal exposure to CO was reported to be associated with Hypertensive Disorder of Pregnancy (Mobasher et al., 2013), the slowed down fetal growth (Ritz et al., 2013), reduced birth weight (Yucra et al., 2013; Rich et al., 2015; Wylie et al., 2016) and preterm birth (Li et al., 2016). The most important factors which determine the severity of the damage include the following: CO level in exhaled air, duration of exposure to its increased concentration, coexistence of other toxic gases as well as overall health status and age of the subject.

The objective of the present study was to examine the level of carbon monoxide in the air exhaled by people who have different smoking habits (smokers and non-smokers) and who live in places with different levels of air pollution. So far such correlations have not been well investigated.

2. Material and methods

The study was conducted in three locations: two biggest Polish cities (Warsaw and Krakow) and the small town (Kozienice). The data were gathered in shopping malls as part of the nationwide public health project called “Health under control”, supervised by the International Federation of Medical Students Association (IFMSA). Participation in the study was voluntary and written informed consent was obtained from all the enrolled individuals. Any person above 18 years old was eligible to participate. The exclusion criteria comprised the following: a history of chronic obstructive pulmonary disease, lung cancer, asthma, chest deformation and infection on the day of the test.

The study protocol consisted of two parts. At first, the subjects were asked to complete a questionnaire, addressing the following issues: the number of citizens in their place of residence, level of education, work status as well as active and passive smoking habits, including the frequency and length of smoking history. The passive smoking was assessed by the average time, which participants spend accompanied by cigarette smoke, both in the house, workplace or any other places, where subjects spent their time with people smoking cigarettes. It could be the co-workers, spouse, other family members or friends. We did not take this data into further consideration. In the second part, the level of CO in exhaled air as well as the body mass index (BMI; kg/m^2) of each subject were measured. The main social role of the project was to inform smokers and individuals with BMI over 25 about their health status and associated risk factors.

Volunteers were divided into four groups:

- Group 1 – non-smokers living in small towns/villages (citizens < 100,000, air pollution level expected to be low)
- Group 2 – smokers living in small towns/villages
- Group 3 – non-smokers living in big cities (citizens > 100,000, air pollution level expected to be high)
- Group 4 – smokers living in big cities

The CO levels in exhaled air were compared between the groups.

The level of CO in exhaled air was measured with the use of *PiCO+ Smokerlyzer* tools (Bedfont Scientific Ltd, England); all devices were calibrated in the same licensed company – Synecpol S.C. The subjects were examined by qualified medical students who had undergone professional training prior to the test. The examination proceeded according to the following scheme: after a period of normal breathing, subjects were asked to hold breath during a 15-s countdown and, after hearing the machine beep, to blow continuously and slowly into the smokerlyzer mouthpiece (Bedfont Scientific Ltd. 2014). Following the instructions of the tool's manual, the subjects were tested at least 30 min after the last cigarette or exposure to passive smoking. The results were entered into the second part of the protocol and the subjects were informed about their test results.

The data concerning CO levels in ambient air were obtained from local air quality monitoring stations run by the Regional Inspectorate of Environmental Protection. Such data are available on demand and free of charge. In the analyses assessing correlations with pollution level only people living in the above-mentioned cities were included. The mean values of CO levels in each city, reported in the month of the testing, were subjected to final analysis. In order to provide a wider picture of air pollution trends in the investigated locations, the mean values of CO levels measured in the three preceding months were also presented. [Suplementary Material].

2.1. Statistical analysis

The quantitative data were reported as mean ± standard deviation (SD) or median/interquartile range, according to a normal distribution status fit. For the qualitative data, frequencies and percentages were calculated. Mean differences between the two groups were compared by the Student’s *t*-test while the Mann–Whitney *U* test was applied for comparisons of median values. The multiple analyses were performed using analysis of variance (ANOVA) with Bonferroni correction or Kruskal-Wallis test with post-hoc multiple comparison. According to the available literature, the standard CO level in exhaled air should not exceed 4 ppm and this value was selected as the cutoff point in the further analysis. (Cropsey et al., 2014) A generalized linear model with logit link for a binary response with interaction between covariates was performed to verify whether higher CO concentrations at the level of 4, 5, 6 and 7 ppm depend on smoking habits and place of living. Being a non-smoker and living in the rural place was set as a baseline. Odds ratios (ORs) and 95% confidence intervals (95%CI) were calculated in relation to the baseline (group 1) for each of the groups (2, 3, 4). The Receiver-Operating Characteristic (ROC) curves were used to assess the optimal cutoff points that discriminate between smokers and non-smokers, as well as people living in small towns and big cities. Area Under the Curve (AUC) with standard error (SE) and CO level cutoff points were reported, as they provide the best balance between sensitivity and specificity. Also Spearman correlation between the number of smoking cigarettes smoked per day and CO level in exhaled air was performed. The data were analyzed using StatSoftStatistica 12.0 PL with Medical bundle add-in for Microsoft Windows 10. The results with $p < 0.05$ were considered as statistically significant.

3. Results

Exhaled CO levels were assessed in a total of 1226 subjects (515 men, 711 women) with a mean age of 41.2 ± 18.1 years. 955 of subjects were non-smokers or passive smokers (62% and 16% of a study group, respectively) while 271 (22%) were active smokers (mean time of smoking was 16.1 ± 15.1 years). 408 of subjects lived in a city with less than 100,000 citizens (318 non-smokers, 90 smokers; 22% of subjects from a small town were smokers) and 818 lived in a city with a population of 100,000 or more, such as Krakow or Warsaw (637 non-smokers, 181 smokers; 22% of subjects from a big city were smokers).