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The impact the atmospheric air dust fractions and toxic metals on external respiratory function among chronic obstructive pulmonary disease patients

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Abstract. The study is dedicated to the potential risk determination of external respiratory function (ERF) disorders among chronic obstructive pulmonary disease (COPD) patients under dust fractions and toxic metals influence in Vladivostok atmosphere. The risk assessment included the environmental ERF trigger factors identification among COPD patients by regression analysis, the number of patients responding to factor exposure determination and the analysis of the possible ERF disorders individual risk among COPD patients. It is found that Vladivostok air pollution by dust aerosols and toxic metals directly affects COPD patients' ERF. The most significant effect on the bronchial mucosa, aggravating bronchial patency (r=11.6%) and lung hyperinflation (r=10.7%) have ultrafine suspended particulate matter (SPM) fractions (0-1 μm). Fine SPM fractions (1-10 μm) affect ERF parameters characterizing bronchial patency only and less than ultrafine fractions (r=10.2%). Toxic metals (Ni, Zn) equally influence bronchial patency and lung tissue hyperinflation indicators among COPD patients (r=29.8% and r=29.1% respectively).

1. Introduction

Suspended particulate matter (SPM) or particulate matter (PM) is a complex mixture of solid particles and liquid drops in the air. PM with an aerodynamic diameter ≤10 μm (PM10) is associated with hospitalization and mortality increase [1, 2, 3, 4]. The particles with aerodynamic diameter ≤2.5 μm (PM2.5) are the most dangerous as they can penetrate deeper and have greater toxicity than PM10 [5, 6, 7, 8].

Chronic obstructive pulmonary disease (COPD) belong to the ecologically dependent respiratory diseases group. A number of studies have noted that a long living (for four or more years) in the areas with high industrial air pollution without recreation in relatively favorable environmental conditions of suburban areas is a respiratory pathology risk factor.

Only 15-20% of smokers have a high sensitivity to tobacco exposure, despite the fact that smoking is recognized as the main risk factor for COPD in 90% of cases. Besides, not all big cities residents working in harmful industries develop bronchial obstruction [9].

People inhale not only toxic gases, but also dust, which partially settles on the nasal cavity mucous membranes and bronchi during expiration. Dust particles with a diameter of 0.3-0.5 μm are the easiest to penetrate into the lungs and to persist there. The precise mechanism of PM impact on lung function has not yet been revealed. Studies have shown that PM mediate adverse health effects by forming reactive oxygen species, activating cellular signaling pathways and impacting antioxidant defense and barrier function of the airways. These effects can lead to airway inflammation and changes in lung function [10, 11, 12].

Sub-microscopic dust, being suspended in the air for a long time, is the most unsanitary for humans. So, the concept of "risk assessment" of the population health in cities with unfavorable ecological situation has become widespread. This assessment includes the determination of the quantitative and/or qualitative characteristics of harmful effects that cause an individual (a particular person) or a group (population) risk for the pathology under adverse factors influence.

The population risk determination method is widely used to assess the potential risks, while individual risk assessment is associated with the difficulty of cross-disciplinary comparison of the particular person health status with characteristics of his habitat.

The aim of the study was to determine the external respiratory function (ERF) disorders potential risk among chronic obstructive pulmonary disease (COPD) patients under the dust fractions and toxic metals influence in Vladivostok atmosphere.

2. Materials and methods

The objects of the study were COPD patients living in Vladivostok. Patients lived in areas with adverse environmental conditions associated with the proximity to highways, road junctions, heat plants, an incineration plant, high residential building density and other pollution sources, as suppliers of this type of pollution.

We have examined 147 people to study the potential risk of ERF disturbance under the dust fractions and toxic metals influence in Vladivostok atmosphere. A group of patients with mild and moderate stable COPD included 112 people. The mean age of the patients was 56.5 ± 4.8 years. A control group consisted of 35 practically healthy volunteers, nonsmokers, with normal respiratory function; the mean age was 52.0 ± 3.4 years. The diagnosis of COPD was made in accordance with the Global Initiative for Chronic Obstructive Pulmonary Disease (GOLD, 2017). Informed consent was obtained from all patients and the study conformed to the standards of the Declaration of Helsinki (2013). The protocol was approved by local Committee on Biomedical Ethics.

The inclusion criteria were mild and moderate stable COPD, smokers or former smokers with index of smoking exposure at least 10 packs/year, subjects living in Vladivostok at least 5 years.

The exclusion criteria were severe and extremely severe COPD, exacerbation of COPD, bronchial asthma, severe decompensated internal organs diseases. All COPD patients received basic therapy with long-acting M-cholinolytics. The clinical and laboratory examination was carried out in accordance with the standards of pulmonary patient’s examination.

Patients ERF was studied by Master Screen Body equipment (Care Fusion, Germany). The postbronchodilation parameters such as forced vital capacity (FVC), forced expiratory volume in 1 second (FEV_1) and ratio of these parameters (FEV_1/FVC) were evaluated to determine the degree of COPD severity. The degree of airway obstruction reversibility was assessed using an inhaled bronchodilator salbutamol (400 µg). Static lung volumes and capacities: functional residual capacity (FRC), residual volume (RV), total lung capacity (TLC), ratio of RV to TLC (RV/TLC) and bronchial resistance during inhalation and expiration, were studied by body plethysmography.

The patients were examined during winter period (2014-2017), because air pollution was assessed by snow cover pollution. City air pollution was assessed by the analysis of solid particles aerosol suspensions collected as precipitation (snow). Snow samples were analyzed by the laser particle analyzer Analysette 22 NanoTech (Germany), which can identify particles size and shape distribution. The content (%) of fractions 0-1, 1-10, 10-50, 50-100, 100-400, 400-700, >700 µm and the levels (µg/l) of "toxic metals" Pb, Cr, Mn, Fe, Co, Ni, Cu, Zn in the air (15 factors) has been determined [13].

As a result, a database for studying air pollution by various dust particles fractions and toxic metals, adsorbed on them, according to places of residence of the COPD patients, was created. The risk assessment included 3 stages:

1. The finding of environmental trigger factors influencing ERF of COPD patients. The purpose of this stage was to determine the expected functional connections (Y=f(X)), Y is ERF parameter; X is the atmospheric pollution factor.

2. The goal of the second stage was to evaluate the number of COPD patients who responded to the trigger factor.

3. The calculation of the individual risk of ERF disorders and the relation of selected COPD patients to the total number of examined patients, including the control group, were made by the integration of the results of previous stages of the study. The aim of the third stage was to assess the possible individual risk of ERF disorders among COPD patients as a response to the impact of the air trigger factors.

The module "Multiple regression" of program STATISTICA 8 was used at *the first stage* of the assessment. It allowed determining the response of ERF parameters to the effect of certain factors of city air pollution. We studied only the most potent air pollutants in respect to ERF (dust fractions with toxic metals adsorbed on them), since the influence of the environment on ERF is extremely complex and have different intensity, nature and force. The revealing of trigger factors was carried out using functional connections with low values of regression coefficient ($R_{regres.}$>0.2) and high statistical significance of the results ($p<0.05$) proceeding from the assumption that action of these factors is fragmented against common environmental influence.

The second stage of the study included the analysis of the results obtained in the first stage. ERF parameters, which reacted to air pollution factors, were selected for the database. Then, COPD patients with deviation of selected ERF parameters exceeded 15-20% from the normal value were chosen.

The development of individual disturbances of ERF under the action of trigger factors was evaluated at *the third stage*. The individual risk (r) for ERF disorders in COPD patients was assessed by the analysis of the selected COPD patients percentage against the total number of subjects, including healthy volunteers.

3. Results and discussion

Table 1. The response of ERF parameters ($R_{regres.}$) in COPD patients to the impact of air pollution factors.

ERF parameters (Y), % of normal	Trigger factors of air pollution (X)			
	Fractions of suspended particulate matter (SPM)		Toxic metals	
	0-1 μm	1-10 μm	Ni μg/l	Zn μg/l
FVC	$R_{regres.}$=0.239 *p=0.01*	$R_{regres.}$=0.221 *p=0.03*	$R_{regres.}$=0.212 *p=0.03*	$R_{regres.}$=0.229 *p=0.01*
FEV_1	$R_{regres.}$=0.201 *p=0.04*	$R_{regres.}$=0.200 *p=0.04*	$R_{regres.}$=0.239 *p=0.01*	$R_{regres.}$=0.215 *p=0.03*
FEV_1/FVC	$R_{regres.}$=0.201 *p=0.04*	$R_{regres.}$=0.212 *p=0.03*	$R_{regres.}$=0.221 *p=0.02*	$R_{regres.}$=0.212 *p=0.03*
FRC	$R_{regres.}$=0.204 *p=0.04*		$R_{regres.}$=0.202 *p=0.04*	$R_{regres.}$=0.208 *p=0.034*
RV	$R_{regres.}$=0.200 *p=0.04*		$R_{regres.}$=0.237 *p=0.01*	$R_{regres.}$=0.209 *p=0.031*
RV/TLC	$R_{regres.}$=0.212 *p=0.03*		$R_{regres.}$=0.201 *p=0.04*	$R_{regres.}$=0.216 *p=0.025*

R_{regres}. – regression coefficient

Vladivostok is the administrative center of Primorsky Region. The city has a high level of air pollution by automobile transport (the number of cars per person in the city is one of the highest in Russia), power stations, incineration plant, etc., forming the state of the city's air environment. These urban objects make the greatest contribution to the atmospheric pollution by dust aerosols of various fractions and toxic metals adsorbed on them that have the strongest impact on the human respiratory function. So, the main objective of the study was to establish a change of the pulmonary ventilation under the influence of air pollution.

The regression analysis carried out at the first stage of the study has made it possible to identify 6 main ERF parameters responded to the effect of trigger factors of air pollution with statistically significant results (table 1).

The analysis of the selected trigger factors of air pollution showed a different activity of ERF response ($R_{regres.}$=0.200-0.239) to a fine fraction of dust particles and 2 toxic metals (Ni, Zn) (table 1).

It was established that among patients with COPD ultrafine (0-1 μm) and fine (1-10 μm) SPM fractions have the greatest pathogenic effect on ERF parameters that describe bronchial patency (FVC, FEV_1, FEV_1/FVC), worsening bronchial obstruction ($R_{regres.}$=0.200-0.239). Besides that, ultrafine (0-1 μm) SPM fractions influence on body plethysmography parameters, that characterize «air traps» (RV, RV/TLC) and lung hyperinflation (FRC) ($R_{regres.}$=0.200-0.212). The studies have shown that the long-term impact of SPM may be associated with a decrease in lung function of COPD patients. For instance, exposure of SPM less than 2.5 μm in diameter was associated with a decrease in FEV_1 [14]. Lagorio et al. have found that elevated concentrations of SPM with diameter of less than 2.5 μm and less than 10 μm in the atmosphere are related to a lower lung function (FEV_1 and FVC) of COPD patients [15]. However, other studies have not identified a link between SPM and short-term changes in lung function of COPD patients [16]. Thus, nowadays it is believed that relatively low concentrations of SPM can adversely affect lung function and have significant health effects [15].

Table 2. The risk (r) for ERF disorders in COPD patients under the impact of air pollution factors.

ERF parameters (Y), % of normal	Trigger factors of air pollution (X)			
	Fractions of suspended particulate matter (SPM)		Toxic metals	
	0-1 μm	1-10 μm	Ni μg/l	Zn μg/l
	$R_{regres.}$ (Y=f(X)), p<0,4			
FVC	$R_{regres.}$=0.239 *p=0.009*	$R_{regres.}$=0.221 *p=0.03*	$R_{regres.}$=0.212 *p=0.03*	$R_{regres.}$=0.229 *p=0.01*
r (%)	4.7	3.1	6.1	5.7
FEV_1	$R_{regres.}$=0.201 *p=0.04*	$R_{regres.}$=0.200 *p=0.04*	$R_{regres.}$=0.239 *p=0.01*	$R_{regres.}$=0.215 *p=0.03*
r(%)	3.1	2.9	5.9	6.5
FEV_1/FVC	$R_{regres.}$=0.201 *p=0.04*	$R_{regres.}$=0.212 *p=0.03*	$R_{regres.}$=0.221 *p=0.02*	$R_{regres.}$=0.21 *p=0.03*
r (%)	3.8	4.2	4.8	4.0
FRC	$R_{regres.}$=0.204 *p=0.04*		$R_{regres.}$=0.202 *p=0.04*	$R_{regres.}$=0.208 *p=0.034*
r (%)	2.4		5.1	3.9
RV	$R_{regres.}$=0.200 *p=0.04*		$R_{regres.}$=0.237 *p=0.01*	$R_{regres.}$=0.209 *p=0.031*
r (%)	4.2		3.9	5.1
RV/TLC	$R_{regres.}$=0.212 *p=0.03*		$R_{regres.}$=0.201 *p=0.04*	$R_{regres.}$=0.216 *p=0.025*
r (%)	4.1		4.0	3.9
∑ r of ERF parameters	22.3	10.2	29.8	29.1

Note: r – risk for ERF disorders (%)
$R_{regres.}$ – regression coefficient

In the present study 2 toxic metals (Ni, Zn) of 8 studied ones were distinguished in the atmosphere of Vladivostok. These metals had the most negative effect on ERF parameters characterizing bronchial patency (FVC, FEV_1, FEV_1/FVC) and hyperinflation of lung tissue (FRC, RV, RV/TLC) among COPD patients ($R_{regres.}$=0.201-0.239). It is known that the inhalation of smoke or dust containing salts of heavy metals can lead to a decrease in lung function and an increase in risk of developing cancer.

The determination of risk of ERF disturbance under the influence of atmospheric pollution was carried out by individual selection of COPD patients with parameters that responded to environmental effects, taking into account that $R_{regres.}>0.2$ and $p<0.04$ (table 2).

As a result, COPD patients (112 people), showing deviation of selected 6 ERF parameters from normal values in the range of 15-20%, were selected from the total number of patients (147 people), including healthy subjects.

The greatest effect on the bronchial mucosa is exerted by ultrafine SPM fractions (0-1 μm), which aggravate the bronchial patency (r=11.6%) and the lung hyperinflation (r=10.7%). Fine SPM fractions (1-10 μm) affect only ERF parameters characterizing bronchial patency (FVC, FEV_1, FEV_1/FVC). It should be noted that these SPM fractions have lower impact (r=10.2%) on ERF parameters than ultrafine SPM fractions. The toxic metals (Ni, Zn) equally influence the indicators characterizing bronchial patency and hyperinflation of lung tissue among COPD patients (r=29.8 and r=29.1%, respectively).

4. Conclusions

Thus, air pollution in Vladivostok by dust aerosols and toxic metals directly impacts ERF of COPD patients. The long-term exposure of ultrafine (0-1 μm) and fine (1-10 μm) SPM fractions and salts of heavy metals (Ni, Zn) in the atmosphere lead to a toxic effect on bronchial mucosa, aggravating bronchial obstruction and lung hyperinflation and promoting bronchial remodeling.

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