Impact evaluation of environmental factors on respiratory function of asthma patients living in urban territory

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Abstract
Background: Environmental pollution, local climatic conditions and their association with the prevalence and exacerbation of asthma are topics of intense current medical investigation.
Materials and methods: Air pollution in the area of Vladivostock was estimated both by the index of emission volumes of “air gaseous components” (nitrogen oxide and nitrogen dioxide, formaldehyde, hydrogen sulfide, carbon monoxide) in urban atmosphere and by mass spectrometric analysis of precipitates in snow samples. A total of 172 local asthma patients (101 controlled-asthma patients—CAP and 71 non-controlled asthma patients—nCAP) were evaluated with the use of spirometry and body plethysmography. Airway obstruction reversibility was evaluated with the use of an inhaled bronchodilator. Using discriminant analysis the association of environmental parameters with clinical indices of asthma patients is explored and thresholds of impact are established.
Results: CAP presented high sensitivity to large-size suspended air particles and to several of the studied climatic parameters. Discriminant analysis showed high values of Wilks’ lambda index ($\lambda = 0.69–0.81$), which implies limited influence of environmental factors on the respiratory parameters of CAP. nCAP were more sensitive and susceptible to the majority of the environmental factors studied, including air suspended toxic metals particles (Cr, Zn and Ni). Air suspended particles showed higher tendency for pathogenicity in nCAP population than in the CAP, with a wider range of particle sizes being involved. Dust fractions ranging from 0 to 1 $\mu$m and from 50 to 100 $\mu$m were additionally implicated compared to CAP group. Considerably lowest thresholds levels of impact are calculated for nCAP.

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1. Introduction

The prevalence of respiratory diseases in urban environments is constantly growing and is largely determined by the high levels of technogenic air pollution (Golokhvast et al., 2015). It is believed that asthma occurs mainly among residents of industrialized regions world-wide and its prevalence is influenced by climatic changes, the degree of environmental pollution and even lifestyle habits (To et al., 2013; Villeneuve et al., 2007). At the same time it is found that asthma is less frequent in developing countries. However, there are only limited data on environmental factors...
interaction with the initiation or exacerbation of asthma (Bokov and Delclaux, 2016).

Major recent epidemiological studies are focused in delineating environmental and air pollution relation to asthma and cardiopulmonary mortality (Wong and Lai, 2004). Ambient air in urban environments contain a vast number of pollutants including ozone, nitrogen oxides and sulfur dioxide and particles of different sizes (Wong and Lai, 2004). In an observational prospective birth cohort study it was found that air pollutants were correlated with asthma diagnosis until the age of 2 years old. (Brauer et al., 2002). In a study in Netherlands, it was also discovered that proximity to highways was associated with increased cardiopulmonary mortality due to augmented exposure to traffic air pollution (Hoek et al., 2002).

The respiratory function plays a major role in body’s adaptation to environmental conditions. On one hand, the respiratory system maintains homeostasis and even minor functional changes lead to a homeostasis shift. On the other hand breathing variations can occur even during small muscular exercise. It is thought that asthma development and the degree of the disease control depend greatly on the influence of environmental factors (Harris et al., 2017; Walker et al., 2003).

Snow precipitates are regarded as one of the main forms of wet atmospheric deposition and could be used to study the deposition of pollutants from the atmosphere and evaluate environmental air pollution (Francova et al., 2017). Snowflakes are more capable to absorb air pollutants than raindrops due to their larger surface area and their slower deposition (Cereceda-Balic et al., 2012). In addition, accumulation of chemical species in snow cover is found to have an impact on human health (Siudek et al., 2015).

Vladivostok is located in the south of the Russian Far East and has a monsoon climate, which in combination with urban technogenic emissions and air pollution associated with high road traffic, has a detrimental effect on physiological external respiration function (ERF) parameters. Aim of the present study was to investigate the impact of several environmental factors on ERF in asthma patients with varying degrees of disease control living in Vladivostok and to calculate thresholds concentrations of impact.

2. Materials and methods

Snow precipitates were analyzed to collect data on air pollution. More specifically snow samples were collected during snowfall periods in winter (2005–2015) in 13 districts of Vladivostok. The upper layer (5–10 cm) of fresh snow from a 1 m² area was collected into 3 L sterile containers that had been prewashed with double-distilled water. This collection method was chosen to avoid secondary contamination by anthropogenic aerosols (Golokhväst et al., 2015).

The study population comprised of 172 asthma patients (79 men and 93 women, aged 20–45 years old) living in the same 13 districts of Vladivostok, where snow sampling was performed. The majority of the patients enrolled in the study inhabited areas with unfavorable environmental conditions (proximity to highways, road junctions, thermal plants, an incinerator, high residential building density). There were 101 patients with controlled asthma (CAP) and 71 patients with non-controlled asthma (nCAP) among the study population. All patients received standard therapy with inhaled corticosteroids in combination with long-acting beta2-agonists according to their personal physicians’ prescription. 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 the Committee on Biomedical Ethics of Vladivostok branch of Far East Scientific Center of Physiology and Pathology of Respiration – Research Institute of Medical Climatology and Rehabilitation Treatment.

Asthma was diagnosed in accordance with the Global Strategy for Asthma Management and Prevention criteria (GINA, 2016). ACQ-5 test (Asthma Control Questionnaire) (Juniper et al., 1999) was used to assess asthma control level; patients with a score above 1.5 were thought to suffer from uncontrolled asthma, while patients with a score ranging from 0 to 0.75 were thought to have controlled asthma. Exclusion criteria included partial control of asthma, chronic obstructive pulmonary disease, occupational respiratory diseases, cardiovascular diseases (coronary heart disease, hypertension) and their complications, diabetes and acute and chronic respiratory diseases during the stage of decompensation.

Respiratory function was studied with the use of Master Screen Bodi equipments (Care Fusion, Germany) at standard conditions; airflow as well as several air volume indicators were recorded during a forced expiratory action, along with a series of body plethysmography parameters. Type and degree of pulmonary ventilation disorders were evaluated by spirometry. The static lung volumes, functional residual capacity (FRCplet, %), total lung capacity (TLC, %), residual volume (RV, %), ratio of residual volume to total lung capacity (RV/TLC), resistance to inhalation (Rin) and resistance to exhalation (Rex) were monitored by body plethysmography (Luo et al., 2017). The degree of airway obstruction reversibility was evaluated using an inhaled bronchodilator (salbutamol 400 µg).

Among the atmospheric pollutants monitored, the most common urban technogenic emissions (nitrogen oxide, nitrogen dioxide, formaldehyde, suspended substances) are included. Six stationary observation posts of the Federal State Budgetary Institution « Primorsky Department of Hydrometeorology and Environmental Monitoring » (Golokhväst and Shvedova, 2014; Veremchuk et al., 2016) are located in the areas of Vladivostok with high environmental loads.

Air suspended toxic metals concentrations were assessed with the use of a Hitachi S–3400N scanning electron microscope with an Ultra Dry (Thermo Scientific, USA) energy-dispersive spectrometer. The sample deposition for the electron microscopy was made of platinum. A high resolution inductively coupled plasma mass spectrometry (HR-ICP-MS) employing Element XR (Thermo Fisher Scientific, USA) was used (1). A total number of 19 air suspended particles sizes and metals were measured.

At the same time suspended aerosol particles were analyzed from snow precipitants. A laser particle size analyzer supplied with Fritsch MaS software (Analysette 22 NanoTec Fritsch, Idar-Oberstein, Germany) was used to determine particle size distribution. This technology can analyze particulate matter (PM) size distribution of the wet or dry dispersion units separately or simultaneously with automated switching features. Optimal dispersion was achieved using the NanoTec integral wet dispersion unit with a combination of a robust, variable speed centrifugal pump with powerful ultrasonification, according to the manufacturer’s manual. The sample was added in the open dispersion chamber on the top of the instrument. The samples (60 ml) were diluted with water (150 ml) and then analyzed (Bateson and Schwartz, 2008). Based on particles size distribution (0–1, 1–10, 10–50, 50–100, 100–400, 400–700, >700µm) (%) and «toxic metals» (Pb, Cr, Mn, Fe, Co, Ni, Cu, Zn) concentration (µmol/l) in the air, several fractions for statistical analyses were assigned.

A sharp change in climatic parameters causes a negative reaction of the human organism, especially in patients with respiratory pathology (Voronin, 1981). Nine (9) basic meteorological parameters (wind speed, wind direction, temperature, dew point, effective temperature, air humidity, air pressure, atmospheric conditions, amount of precipitation) were included in the study. These parameters were studied as gradient values with regards to 1 day and
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