Austin Environmental Sciences

Open Access

Austin Publishing Group

Original Article

Particulate Matter and Polycyclic Aromatic Hydrocarbons Influence on Respiratory Function and the Possibility of Allergy in Healthy Adults

Chciałowski A[1]; Dąbrowiecki P[1]; Jaskóła-Polkowska D[1*]; Rzeszotarska A[2]; Korsak J[2]; Stańczyk A[3]; Mucha D[4]; Badyda AJ[4]

[1]Department of Internal Medicine, Infectious Diseases and Allergology, Military Institute of Medicine - National Research Institute, Poland

[2]Department of Clinical Trasfusiology, Military Institute of Medicine - National Research Institute, Poland

[3]Department of Cardiology, Military Institute of Medicine - National Research Institute, Poland

[4]Department of Informatics and Environment Quality Research, Warsaw University of Technology, Poland

[*]**Corresponding author: Jaskóła – Polkowska D**

Department of Internal Medicine, Infectious Diseases and Allergology, Military Institute of Medicine - National Research Institute, Szaserow 127 Str, 04-141 Warsaw, Poland.

Tel: +48261818358

Email: djaskola-polkowska@wim.mil.pl

Received: February 14, 2024

Accepted: March 16, 2024

Published: March 22, 2024

Abstract

There is little evidence of the prolonged effects of continuous Particulate Matter (PM) and Polycyclic Aromatic Hydrocarbons (PAHs) pollution exposure on respiratory function and the possibility of allergy occurrence in healthy individuals. We present the results of prospective studies assessing the possible effects of selected PAHs on lung function, possibly inflammatory effect, and impact on allergy development. The research was conducted in a town in the north-central region of Mazovia, with approximately 50.000 inhabitants. The study comprised 73 healthy individuals (23M and 50F, aged 54.95 ± 12.64 years). Pulmonary Function Tests (PFT), serum cytokine concentrations, allergen-specific IgE levels (inhalation panel), and the samples of $PM_{2.5}$ to assess PAH concentrations were performed in the heating and non-heating seasons. In both periods, the values of the PFT parameters were within the normal range. Serum cytokine and PAHs concentrations were higher during the heating season. Correlation analysis of the results of PFT parameters with cytokines level revealed the occurrence of weak but significant ($p<0.05$) associations in the heating season compared to the non-heating season. Negative correlations were observed between increasing concentrations of PAHs (Anthracene, Phenanthrene, Pyrene, and Acenaphthene in particular) and decreasing PFT parameters. Simultaneously, correlations were observed between the rising concentrations of PAHs and concentrations of proinflammatory cytokines IL-4, IL-6, IL-8, and TNF- α. This study revealed the possible impact of PAHs in ambient air on lung function and the development of local and systemic inflammation, and may suggest the possibility of allergy occurrence.

Keywords: Particulate matter; Polycyclic aromatic hydrocarbons; Lung function; Cytokines; Allergy

Introduction

Air Pollution (AP) negatively affects human health and contributes to increased morbidity and mortality [1,2]. Particulate Matter (PM) with aerodynamic diameters of 2.5 μm and smaller, and PAHs penetrate the pulmonary alveoli from where they easily diffuse through the capillaries and move around the body [3]. Epidemiological studies have explicitly shown that short-term exposure to increased concentrations of PM has a negative impact on health, which has been well documented by studies of Lung Function (LF) in pediatric populations receiving excessive exposure to PM_{10} and $PM_{2.5}$. A small increase in its concentration contributed to lower FEV_1 (Forced Expiratory Volume in the first second of exhalation) [3,4]. In healthy individuals, the influence of persistent pollution on LF has been slight, and there is little evidence of prolonged effects of pollution on respiratory function [5,6]. In some publications, massive PM exposure has not changed the LF. However, in others, a slight alteration in Maximal Midexpiratory Flow Rate (MMEF) and modest increases in bronchial resistance have been noted [2,7-9]. Although the effect on healthy individuals may be weak, AP may be a significant issue, and even small changes in a health-related parameter in a large, exposed population may considerably impact public health [1,10-13]. Many publications concern the adverse effects of air pollution on chronic respiratory and cardiovascular diseases [12,14,15]. They have demonstrated the impact of short-term (several days) increased concentration on LF in healthy individuals. Rice et al. have noted the effect of short-term exposure to a relatively low level of $PM_{2.5}$, NO_2, and O_3 on decreasing the value of FEV1, which normalized after 48 hours in 3,262 healthy participants of the Framingham Heart Study [13]. Whereas Faustini et al. have found a significant rela-

Citation: Chciałowski A, Dąbrowiecki P, Jaskóła-Polkowska D, Rzeszotarska A, Korsak J, et al. Particulate Matter and Polycyclic Aromatic Hydrocarbons Influence on Respiratory Function and the Possibility of Allergy in Healthy Adults. Austin Environ Sci. 2024; 9(1): 1103.

tionship between the temporarily elevated concentration of AP and increased mortality [16]. It has provided valuable evidence pointing out that long-term exposure to air pollution, even at low levels, has been associated with a more frequent occurrence of symptoms of respiratory diseases [17].

Poland is one of the most polluted countries in the European Union (EU), where concentrations of PM_{10} and $PM_{2.5}$ as well as benzo(a)pyrene (BaP) exceed, in some cases significantly, the upper limit values established in the appropriate EU directives and WHO recommendations [1,18-20]. High levels of PM and BaP mainly occur in winter because of the everyday use of solid fuels (coal and wood in particular) for heating individual households. Except for the so-called low-stack emission, this problem also results from traffic-related emissions, especially in winter when solid fuel is intensively used with unfavorable meteorological conditions, and smog is often observed [21]. It has also been shown that each increase in the 5-year PM_{10} concentration by 10 μg/m^3 is associated with a decline in FEV_1 of 1.68%, in Peak Expiratory Flow (PEF) of 1.18% and Midexpiratory Flow (MEF) at 50% of Forced Vital Capacity (FVC) - MEF_{50} of 4.61%), but also with an increasing incidence of allergy and Bronchial Asthma (BA), pneumonia, and other pulmonary diseases [22-26].

We present the results of prospective studies assessing the possible effects of selected PAHs on LF, possibly including an inflammatory effect and an impact on allergy development.

Materials and Methods

The Study Area and Population

The study was conducted in a town in the Mazovia region about 30 km northeast of Warsaw, with approximately 50,000 inhabitants and the highest density population among Polish towns (almost 4,000 persons per km^2). Single-family houses constitute the majority of the infrastructure. The buildings are heated using coal boilers, wood and coal-burning cookers, and fireplaces, and in winter, they are heated more intensively, resulting in the emission of pollutants into the ambient air.

In this study, 73 individuals participated, including 23 males and 50 females aged 54.9 ± 12.6 years who had been residents of this town for at least 10 years. None of them smoked cigarettes or had no comorbidities, especially chronic respiratory, cardiovascular or allergic diseases. The study was carried out in autumn and winter (October – March) - the Heating Season (HS), and in spring and summer (May–August) - the non-heating season (nHS). Information about the investigated group is presented in Table 1.

Medical Examination

All subjects underwent PFTs and had venous blood specimens collected to examine the serum cytokine concentration, including Tumor Necrosis Factor (TNF-α), cytokines - IL-1β, IL-4, IL-5, IL-6, IL-8, IL-10 and allergen-specific IgE (Al spIgE) - inhalation panel. PFTs and blood analyses were performed during HS and nHS at the same time of the day (between 8 and 11 a.m.). PFTs were done with the use of the pneumotachometer Masterscreen (Jaeger, Germany). Volume and flow rate values were measured during an expiratory flow maneuver registered as the flow-volume curve. The parameters, including FVC, FVC% (predicted value), FEV_1, FEV_1% (predicted value), rate of FEV_1 related to the current forced vital capacity - FEV_1/FVC, and MEF_{25}, MEF_{50}, MEF_{75} and MEF_{25}%, MEF_{50}%MEF_{75}% (predicted value) were measured. Eligibility criteria for correct performance of the tests were assumed according to the guidelines [27]. The study was carried out in accordance with the ethical standards in the Declaration of Helsinki and approved by the Bioethics Committee of the Military Institute of Medicine. Written informed consent was obtained from all study participants.

Table 1: Basic characteristics of the examined population and pulmonary function tests results.

Variable	Unit	Heating seasons	Non-heating seasons
Patients	Number - n	73	73
Age	X ± SD	54.95 ± 12.64	54.95 ± 12.64
Male/female	n/n	23/50	23/50
FVC	L X ± SD	3.82 ± 0.94	3.87 ± 0.96
FEV_1		2.90 ± 0.77	2.92 ± 0.80
MEF_{25}		0.99 ± 0.59	0.98 ± 0.45
MEF_{50}		3.22 ± 1.19	3.27 ± 1.31
MEF_{75}		5.64 ± 2.01	5.84 ± 2.00
FVC	% of predicted values X ± SD	106.34±14.00	108.44±15.34
FEV_1		98.73±17.96	102.22±18.76
MEF_{25}		78.35±39.31	86.26±39.84
MEF_{50}		95.72±37.72	103.66±42.70
MEF_{75}		91.02±25.03	95.00±26.28
FEV_1/FVC	%	75.73 ± 6.62	75.10 ± 6.90

FVC: Forced Vital Capacity; FEV1: Forced Expiratory Volume in the first second of expiration; MEF25: Midexpiratory Flow at 25% of vital capacity; MEF50: Midexpiratory Flow at 50% of vital capacity; MEF75: Midexpiratory Flow at 75% of vital capacity; FEV1/FVC: Percentage Rate of FEV1 related to the current Forced Vital capacity (the so-called pseudo-Tiffeneau factor); X ± SD: Mean ± Standard Deviation

Cytokines and Allergen-Specific IgE Antibodies Analysis

Cytokines were evaluated with commercially available Procarta Plex Human High Sensitivity kits (Invitrogen, ThermoFisher Scientific, USA), based on the xMAP technology, which enables detection and quantitative determination of various proteins in one specimen [27]. The limits of detectability for human cytokine assays were as follows: IL-1β – 0.20 pg/ml; IL-4 - 0.88 pg/ml; IL-5 – 0.86 pg/ml; IL-6 - 0.94 pg/ml; IL-8 - 0.24; IL-10 – 0.23 pg/ml; TNF-α – 0.72 pg/ml.

Phadiatop (allergy screening) of allergen-specific IgE (Al sIgE) test was analyzed using fluoroimmunoassay. The panels included allergens such as animal dander (dog, cat, horse), pollen (grass, tree, weeds), fungi (*Cladosporium*), and mites (*Dermatophagoides pteronyssimus, D. farinae*). The results are given in kU/l and classes (0 – 6) [27].

Samples Collection and Instrumental Analyses

The $PM_{2.5}$ samples were collected simultaneously with medical procedures in 15 locations inhabited by persons undergo-

Table 2: Serum cytokine concentrations in the considered seasons.

Cytokines	Season	
	Heating seasons	Non-heating seasons
	X ± SD (pg/mL)	
TNF–α	1.11 ± 3.63*	0.55± 1.05
IL–1β	0.60 ± 0.17	0.29 ± 0.80
IL–4	2.16 ± 4.79*	1.34 ± 2.41
IL–5	2.29 ± 1.38	1.11 ± 3.23
IL-6	3.68 ± 2.84*	2.80 ± 1.08
IL-8	0.11 ± 0.47	0.06 ± 0.13
IL–10	0.13 ± 0.44	0.05 ± 0.13

*p<0.05

IL-1β: Interleukin-1β; IL-4: Interleukin-4; IL-5: Interleukin-5; IL-6: Interleukin-6; IL-8: Interleukin-8; IL-10: Interleukin-10; TNF-α: Tumor necrosis factor-α, X ± SD: Mean ± Standard Deviation

ing medical examinations. The concentration of 6 PAHs in the $PM_{2.5}$ samples was evaluated to assess the variability of PAHs exposure of selected residents in the HP and nHP periods. Three samples per season were collected in each location, and all PM samples were collected for three consecutive days. The results were compared with the outcomes of BaP concentration measurements carried out in the air quality monitoring station operated by the Chief Inspectorate of Environmental Protection within the exact location.

$PM_{2.5}$ samples were collected on previously conditioned and weighed quartz fiber filters (QMA, ø25 mm, CAT No. 1851-025; Whatman, GE Healthcare Bio-Sciences Corp.) using GilAir PLUS aspirators (Gilian, Sensidyne, LP). Before extraction, the precleaned filter samples were spiked with the surrogate standard from Cambridge Isotope Laboratories (CIL) and sonicated with 20 mL of dichloromethane from Sigma-Aldrich (HPLC purity).

All samples were analyzed using a Shimadzu gas chromatograph coupled to a mass spectrometer (GCMS-2010 Plus) and processed using the Shimadzu GCMS solution software. A ZB-5MS capillary column (30 m × 0.25 mm i.d. with a 0.25 µm film thickness) was used for chromatographic separation. Ultrahigh-purity helium at a flow rate of 1.5 mL/min was used as the carrier gas. Mass selective detection was conducted in the electron impact mode. In the test, the samples of six PAHs congeners on the US EPA list were determined.

Statistical Analyses

Before the modeling process, the repositories were combined on the basis of the common time domain, and the data were aggregated into months using averages and sums. The strength and direction of the correlation were assessed using the Spearman or Pearson correlation coefficient, depending on the measurement scale of the variables. The Analysis of Variance (ANOVA) model was also used to assess the impact of weak-scale variables on the measurements in the strong measurement scale. Complementary Generalized Regression Models (GRM) were applied for selected variables on a strong scale to identify the influence of significant independent factors on any measurement scale. For all calculation results, the level $p < 0.05$ was considered significant.

Results and Discussion

The mean values and percentages of all PFT parameters were generally within the normal range; however, a non-significant decline in HS compared with nHS was observed. The results are presented in Table 1.

Serum cytokine concentration has also been higher in the HS compared to the nHS, but only in the case of TNF-a, IL-4, and IL-6 has the difference being statistically significant. The outcomes are presented in Table 2.

While analyzing PAHs, higher values in the HS compared to the nHS have been reported, but a significant difference has been noted exclusively for pyrene. The results are included in Table 3.

Correlation analysis of the results of PFT parameters and cytokine levels revealed a weak association between FEV_1 and the levels of IL-8 (r=-0.29), PEF, and IL-8 (r=-0.27), between MEF_{25} and IL-4 (r=-0.26) and IL-6 (r=-0.28), respectively and MEF_{50} and IL–6 (r=-0.21) in the HS. No significant correlation was found during nHS. A strong correlation was observed between increasing concentrations of PAHs (Anthracene, Phenanthrene, Pyrene, Acenaphthene, and Fluorene in particular), PFT parameters, and proinflammatory cytokines. The results are included in Table 4.

The relationship between FVC and MEF_{25} (r=0.83), MEF_{50} (r=0,75) and MEF_{75} (r= 0,77) in HS and with MEF_{25} (r=0.60), MEF_{50} (r=0.62) and MEF_{75} (r=0.73) in nHS has been noticed. A relationship between the FEV_1 values with MEF_{25} (r=0.62), MEF_{50} (r=0.76), and MEF_{75} (r=0.88) in the HS, as well as with MEF_{25} (r=0.78), MEF_{50} (r=0.76) and MEF_{75} (r=0.96) in nHS has also been observed in a similar manner.

Air pollution remarkably impacts human health, increasing morbidity and mortality [28]. Short-term exposure to elevated concentrations of $PM_{2.5}$, or PAHs, has adverse health effects. It increases the risk of some clinical or subclinical symptoms, such as cough, conjunctival irritation, myocardial infarction, and stroke occurrence [29]. In the literature, there are reports on the short- and long-term effects of AP and PAHs on respiratory function, particularly in children and adults with bronchial asthma or COPD [4,5]. There is less information about their potential influence and consequences on healthy individuals [30]. The Framingham Heart Study revealed the impact of short-term exposure to a relatively low $PM_{2.5}$, NO_2, and O_3 concentrations in 3,262 healthy subjects on their LFT, expressed as a lowered FEV_1 that normalized after 48 hours [13]. Research conducted in two urban areas in northern France (Lille and Dunkirk) in healthy, nonsmoking adults exposed to short-term moderate NO2 concentrations has shown associated with lower values of FEV_1/FVC, FEF_{25-75}%, and FEF_{75}%, whereas exposure to PM_{10} resulted in decreased FEF_{75}% values. This indicates the broadened knowledge about the harmful impact of AP on the LFT, even in healthy subjects [30]. Similarly, our study was conducted among healthy individuals on LFT and cytokine concentrations during excessive exposure to AP. No significant correlation

Table 3: Polycyclic aromatic hydrocarbons (PAHs) concentrations in heating and non-heating season.

PAHs	Season	
	Heating seasons	Non heating seasons
	X ± SD (ng/m³)	
Anthracene	25.87±53.32	17.74±44.21
Phenanthrene	5.02±8.47	3.94±5.53
Pyrene	195.56±402.78*	130.12±303.37
Acenaphthene	17.76±53.96	19.90±60.87
Fluorene	6.88±24.94	5.20±11.36
Naphtalene	15.30±53.19	12.26±28.82

*p<0.05, X ± SD - Mean ± Standard Deviation

Table 4: Correlation between polycyclic aromatic hydrocarbons, pulmonary function test parameters and serum cytokine concentration.

PAHs	Spirometric parameters				Cytokines				
	FEV_1	FEV_1%	MEF_{25}	MEF_{50}	IL-4	IL-5	IL-6	IL-8	TNF-□
Anthracene	-0.77	-0.49	-0.46	0.58	0.80	ns	0.75	0.80	0.78
Phenanthrene	-0.71	ns	-0.34	-0.48	0.77	ns	0.68	0.78	0.78
Pyrene	-0.85	-0.63	-0.60	-0.71	ns	0.85	0.84	0.84	0.81
Acenaphthene	-0.73	-0.65	-0.62	-0.69	0.67	ns	0.74	0.66	0.60
Fluorene	-0.64	ns	ns	-0.67	0.73	ns	0.60	0.74	0.76
Naphtalene	ns	ns	ns	ns	ns	0.72	ns	ns	ns

*p<0.05, ns-non significant

PAHs: Polycyclic Aromatic Hydrocarbons; FEV_1: Forced Expiratory Volume in the first second of expiration; FEV_1%: Percentage of Predicted value of forced expiratory volume in the first second of expiration; MEF_{25}: Midexpiratory Flow at 25% of vital capacity; MEF_{50}: Midexpiratory Flow at 50% of vital capacity; IL-4: Interleukin-4; IL-5: Interleukin-5; IL-6: Interleukin-6; IL-8: Interleukin-8; TNF-α: Tumor necrosis factor-α.

was found between the PAH level and the FVC value, whereas such correlation has been discovered in relation to FEV_1, FEV_1%, MEF_{25}, and MEF_{50}. These findings suggest the possibility of airway bronchoconstriction, which may be related to the increase in HS exposure. MMEF provides a complete description of maximum flow and includes the region beyond the first second where the lungs are less inflated. This results in progressive bronchial narrowing as lung volume decreases [31]. MEF_{25} and MEF_{50} are the flows where one-quarter and one-half of FVC remain to be exhaled. It corresponds to FEV_1 at 25% and 50% of FEF and correlates highly with MMEF. Therefore, MEF_{25} and MEF_{50} may indicate obstruction of the small airways and may be suggestive of early small airway disease [31,32]. Thus, it is believed that due to MEF's great daily volatility, the interpretation of the results is of limited usefulness; they are the most reliable with normal values of FVC [33]. In the study subjects, the FVC values remained within the normal range during both HS and nHS, and spirometry was performed with the use of the same device and at the same daytime (between 8 and 11 a.m.), which allows excluding daily volatility of LFT. In addition, remarkable correlations between FVC, FEV_1, and MEF_{25-75}, both in HS and nHS, have been identified, confirming the connection between MEF and FVC. Therefore, a demonstration that the same PAHs and MEF correlate constitutes a crucial value of this study. Most publications have yet to analyze MEF as an essential index of small airway function. However, they have concentrated chiefly on measuring FEV_1, FVC, and FEV_1/FVC in healthy individuals and those with lung diseases [11,13,34-36]. Zhang et al. have held that PM influences more adversely MEF values compared to FEV_1 and FVC - an increase in $PM_{2.5}$ level by five μg/m^3 has been associated with a decline of MEF by 1.65% compared to a decrease in FEV_1 by 1.46% and in FVC by 1.18% [36]. The authors have suggested that prolonged exposure to $PM_{2.5}$ may be more harmful to small airways. It is a fact that the effects of short-time exposure to PM on the lungs are weakly expressed in comparison with long-term or prolonged exposure, which may additionally confirm the occurrence of breathing disturbances as a result of a prolonged or long-term excessive impact of PM and PAHs. Significant correlations between the analyzed PAHs and MEF_{25}, MEF_{50}, FEV_1, and FEV_1% in HS explicitly speak in favor of the negative impact of PAHs on the respiratory system and the possibility of development of subclinical breathing disturbances, which are the result of local inflammatory reaction of the bronchial mucosa. This would be to the outcomes of an experimental study that has assessed the effects of PM of air, including 100 μg of $PM_{2.5}$, collected in the urban area (the presence of a smelter), rich in metals: cadmium, lead, nickel, copper, zinc and in non-industrialized area. In the study, the 100 μg $PM_{2.5}$ suspensions were instilled through a bronchoscope into the lungs of 12 healthy volunteers [37]. The air from the industrial area induced local inflammatory reactions with a greater number of neutrophils and monocytes and a higher concentration of IL-6 and TNF-α in the material collected in the Bronchoalveolar Lavage (BAL). In our study, local inflammation was not assessed using bronchofiberscopy or BAL. Although the mechanism of PM–induced health effects is not fully defined, this persistent inflammatory process may play an important role. Our study found a higher level of the analyzed cytokines in HS. This indicates that PAHs, particularly during HS, promote the development of local inflammation due to the activation of effector cells and bronchial mucosa cells, which synthesize and release proinflammatory and anti-inflammatory cytokines, including IL-1β, IL-4, IL-6, and IL-8 and IL-10. They contribute to the worsening of not only spirometry parameters but also the development of systemic inflammation. In an experimental examination, it has been shown that AP causes a detectable level of proinflammatory effect after inhalation exposure [12,35,38]. In the human bronchial epithelial cell (16HBE 14o-) line, Hussain et al. have shown an increased IL-6 and TNF-α concentration after inhaling carbon black particles [39].

The literature provides the correlation between the PAH metabolites found in the urine and PFT parameters. Cakmak et al. have shown a correlation between Hydroxyphenantrene, Hydroxypyrene, Hydroxyfluorene, and FEV_1, FVC, and FEV_1/FVC in the group of 3,531 individuals [40]. Similarly, Zhou Y et al., in a group of 2,747 subjects from the Chinese population, demonstrated a significant correlation between the level of specific PAH metabolites grouped in classes and lowered values of FVC and FEV_1 [41]. Additional attention has been paid to the fact that more significant effects were reported for the sum of the compound classes. Wang et al. and Nethery et al., who have analyzed specific PAH metabolites, have shown that there was not only a correlation between their level and FVC and FEV_1 but also FEF_{25-75}, in particular in the case of 1–hydroxyphenantrene and 1-hydroxypirene [42,43]. Therefore, it has also been confirmed by our study, as both compounds are the metabolites of phenanthrene and pyrene, which have strongly correlated with individual spirometric parameters. As mentioned at the beginning of the paper, one of the study's objectives was to assess the possible impact of AP on the development of allergic responses. Therefore, all study participants had allergen-specific IgE determined for the 20 most frequent inhalant allergens. In 10 subjects, a positive result in classes 1 and 2 (very low and moderate value of antibodies) has been found, in particular in terms of seasonal allergens such as birch, alder, and hazel, which speaks in favor of the presence of subclinical (asymptomatic) allergy. The tests have been done once, only in the HS, as we had not seen the need to repeat them - the results would be identical. In most cases, allergen-specific IgE has confirmed the allergy diagnosis to inhalant allergens. In some cases, a positive allergy test does not correlate with the severity of symptoms but predicts the likelihood that the specific allergen is responsible for reported symptoms. Study subjects declared no symptoms of allergy in the respiratory tract thus, it is now difficult to unequivocally determine whether their allergy was subclinical or whether the results of allergen-specific IgE could be influenced (which may be likely) by the prolonged-term stimulation of PAHs in the ambient air. Mazzarella et al., in their experimental studies, have shown that PAHs contained in diesel exhaust particles by depositing on the surface of epithelial cells, easily penetrate the cell, bind to a cytosolic receptor, and then affect the cell growth, differentiation, and stimulation of the cell nuclei to morphological modification, with subsequent synthesis and secretion of cytokines, including IL-6 and IL-8 [44]. It is implicitly supposed that PAH promotes the synthesis and secretion of IL-4. Therefore, this question may be answered with caution, i.e., PAH may directly influence IL-4, which, in turn, as is known, is a significant factor inducing synthesis and secretion of the immunoglobulin E by B lymphocytes. As has been shown by Churg et al., Diesel Exhaust Particles (DEP) induce a Th2-mediated immune response by suppressing the expression of IL-12 and increasing IL-10 secretion in antigen-specific cells [45]. Kobayashi et al. have determined that PAHs cause symptoms of nasal mucosal hyperresponsiveness in guinea pigs [46]. Hence, the strong correlation between most PAHs and IL-4 concentration in the HS observed in our study may additionally indicate its remarkable contribution to allergy development. It

may take place in the small bronchi, which is supported by a not very strong but significant correlation between IL-4 and MEF_{25}. In Polish studies, it has been shown that about 20% of persons with positive Skin Pprick Test (SPT) results had no clinical allergic symptoms. In another research, this proportion was even higher and reached 25% [47].

Consequently, when we assume that nearly half of the Polish population may be SPT positive, the fact of finding (in our study that has been carried out in a relatively small group of 73 individuals) positive results of Al sIgE in 13.6% of the subjects, may reflect the natural distribution of allergy symptoms in the Polish society. It may result from prolonged exposure to the air containing PAHs [45]. Accordingly, it may induce a Th2-dependent reaction and stimulate the overproduction of IgE against common allergens in the environment [48].

The available literature has yet to provide much information concerning such correlations. Fluoris et al. have shown that even brief secondhand smoke exposure generates unfavorable changes in the immune mechanism, upregulation of growth factor synthesis, and the production of type 1 procollagen in the small airways [49]. Therefore, PAH inhalation can elicit different breathing patterns, transitional cough reflexes, and transient bronchoconstriction through activation of vagal afferents. Other tests using cigarette smoke and DEP have suggested that it may induce profibrotic growth factor production in the small airway walls through an oxidant mechanism and cause their fibrosis and thickening, particularly in the subepithelial compartment, and, in consequence, lead to airway remodeling [44,45].

Conclusion

This publication has some limitations. This was a one-year and one-center observational preliminary study performed in HS and nHS patients on a relatively small number of healthy individuals. Despite the small number of participants, this study should be continued and include studies conducted over 5 and 10 years. Therefore, based on the research carried out so far, the following conclusions can be drawn: -one-year prolonged exposure to elevated concentrations of PAHs and breathing the air containing some PAHs by healthy people, especially during HS, have, to some extent, a negative impact on LFT and may induce the development of local and systemic inflammatory processes in the lower airways and may probably promote the occurrence of allergy.

Author Statements

Conflicts of Interest

The authors declare no conflict of interest.

Ethical Approval

The ''Polycyclic Aromatic Hydrocarbons (PAHs) influence on Respiratory Function and the Possibility of Allergy in Healthy Adults'' study was approved by the Resolution of the Bioethics Committee (Resolution No. 16/WIM/2018; WIM = Military Institute of Medicine).

Consent to Participate

Informed consent to participate in the study was obtained from all participants.

Consent to Publication

Informed consent to publication was obtained from relevant participants.

Funding

The investigations were funded by subvention of the Polish Ministry of Science and Higher Education.

References

1. World Health Organization: Ambient air pollution: A global assessment of exposure and burden of disease. WHO, Geneva. 2016.
2. Pascal M, Corso M, Chanel O, Declercq C, Badaloni C, Cesaroni G, et al. Assessing the public health impacts of urban air pollution in 25 European cities: results of the Aphekom project. Sci Total Environ. 2013; 449: 390-400.
3. Götschi T, Heinrich J, Sunyer J, Künzli N. Long-term effects of ambient air pollution on lung function: a review. Epidemiology. 2008; 19: 690-701.
4. Zwozdziak A, Sówka I, Willak-Janc E, Zwozdziak J, Kwiecińska K, Balińska-Miśkiewicz W. Influence of PM1 and PM2.5 on lung function parameters in healthy schoolchildren-a panel study. Environ Sci Pollut Res Int. 2016; 23: 23892-23901.
5. McCreanor J, Cullinan P, Nieuwenhuijsen MJ, Stewart-Evans J, Malliarou E, Jarup L, et al. Respiratory effects of exposure to diesel traffic in persons with asthma. N Engl J Med. 2007; 357: 2348-58.
6. Berend N. Contribution of air pollution to COPD and small airway dysfunction. Respirology. 2016; 21: 237-44.
7. Frampton MW, Utell MJ, Zareba W, Oberdörster G, Cox C, Huang LS, et al. Effects of exposure to ultrafine carbon particles in healthy subjects and subjects with asthma. Res Rep Health Eff Inst. 2004: 1-47.
8. Gong H Jr, Linn WS, Clark KW, Anderson KR, Geller MD, Sioutas C. Respiratory responses to exposures with fine particulates and nitrogen dioxide in the elderly with and without COPD. Inhal Toxicol. 2005; 17: 123-32.
9. Holgate ST, Sandström T, Frew AJ, Stenfors N, Nördenhall C, Salvi S, et al. Health effects of acute exposure to air pollution. Part I: Healthy and asthmatic subjects exposed to diesel exhaust. Res Rep Health Eff Inst. 2003: 1-30.
10. Buzzelli M, Jerrett M, Burnett R, Finklestein N. Spatiotemporal Perspectives on Air Pollution and Environmental Justice in Hamilton, Canada, 1985–199. Annals of the Association of American Geographers. 2003: 93. 557-573.
11. Schindler C, Künzli N, Bongard JP, Leuenberger P, Karrer W, Rapp R, et al. Short-term variation in air pollution and in average lung function among never-smokers. The Swiss Study on Air Pollution and Lung Diseases in Adults (SAPALDIA). Am J Respir Crit Care Med. 2001; 163: 356-61.
12. Wu W, Jin Y, Carlsten C. Inflammatory health effects of indoor and outdoor particulate matter. J. Allergy. Clin. Immunol. 2018; 141: 833-44.
13. Rice MB, Ljungman PL, Wilker EH, Gold DR, Schwartz JD, Koutrakis P, et al. Short-term exposure to air pollution and lung function in the Framingham Heart Study. Am J Respir Crit Care Med. 2013; 188: 1351-7.
14. Brook RD, Rajagopalan S, Pope CA 3rd, Brook JR, Bhatnagar A, Diez-Roux AV, et al. Particulate matter air pollution and cardiovascular disease: An update to the scientific statement from the American Heart Association. Circulation. 2010; 121: 2331-78.
15. Pope CA 3rd, Burnett RT, Thurston GD, Thun MJ, Calle EE, Krews-

ki D, et al. Cardiovascular mortality and long-term exposure to particulate air pollution: epidemiological evidence of general pathophysiological pathways of disease. Circulation. 2004; 109: 71-7.

16. Faustini A, Stafoggia M, Colais P, Berti G, Bisanti L, Cadum E, et al. Air pollution and multiple acute respiratory outcomes. Eur Respir J. 2013; 42: 304-13.

17. Ackermann-Liebrich U, Leuenberger P, Schwartz J, Schindler C, Monn C, Bolognini G, et al. Lung function and long term exposure to air pollutants in Switzerland. Study on Air Pollution and Lung Diseases in Adults (SAPALDIA) Team. Am J Respir Crit Care Med. 1997; 155: 122-9.

18. World Health Organization: Evolution of WHO air quality guidelines: past, present and future. WHO Regional Office for Europe, Copenhagen. 2017.

19. Directive 2008/50/EC of the European Parliament and of the Council of 21 May 2008 on ambient air quality and cleaner air for Europe. 2008.

20. European Environment Agency: Air quality in Europe – 2019 report. EEA report, No 10/2019. ISSN: 1977-8449, doi: 10.2800/822355. European Environment Agency, Copenhagen. 2019.

21. Mazurek H, Badyda AJ. (edited by). Smog. Health consequences of air pollution - Smog. Konsekwencje zdrowotne zanieczyszczeń powietrza. PZWL Wydawnictwo Lekarskie, Warszawa 2018. Book in Polish language. 2018.

22. Badyda AJ, Dąbrowiecki P, Czechowski PO, Majewski G, Doboszyńska A. Traffic-related air pollution and respiratory tract efficiency. Adv Exp Med Biol. 2015; 834: 31-8.

23. Badyda AJ, Gayer A, Czechowski PO, Majewski G, Dąbrowiecki P. Pulmonary Function and Incidence of Selected Respiratory Diseases Depending on the Exposure to Ambient PM10. Int J Mol Sci. 2016; 17: 1954.

24. Jakubiak-Lasocka J, Lasocki J, Badyda AJ. The influence of particulate matter on respiratory morbidity and mortality in children and infants. Adv Exp Med Biol. 2015; 849: 39-48.

25. Miller MR, Hankinson J, Brusasco V, Burgos F, Casaburi R, Coates A, et al. Standardisation of spirometry. Eur Respir J. 2005; 26: 319-38.

26. Tang H, Panemangalore R, Yarde M, Zhang L, Cvijic ME. 384-Well Multiplexed Luminex Cytokine Assays for Lead Optimization. J Biomol Screen. 2016; 21: 548-55.

27. Vidal C, Gude F, Boquete O, Fernández-Merino MC, Meijide LM, Rey J, et al. Evaluation of the phadiatop test in the diagnosis of allergic sensitization in a general adult population. J Investig Allergol Clin Immunol. 2005; 15: 124-30.

28. GBD 2016 DALYs and HALE Collaborators. Global, regional, and national disability-adjusted life-years (DALYs) for 333 diseases and injuries and healthy life expectancy (HALE) for 195 countries and territories, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet. 2017; 390: 1260–344.

29. Brunekreef B, Beelen R, Hoek G, Schouten L, Bausch-Goldbohm S, Fischer P, et al. Effects of long-term exposure to traffic-related air pollution on respiratory and cardiovascular mortality in the Netherlands: the NLCS-AIR study. Res Rep Health Eff Inst. 2009: 5-71.

30. Dauchet L, Hulo S, Cherot-Kornobis N, Matran R, Amouyel P, Edmé JL, et al. Short-term exposure to air pollution: Associations with lung function and inflammatory markers in non-smoking, healthy adults. Environ Int. 2018; 121: 610-619.

31. Güder G, Brenner S, Störk S, Held M, Broekhuizen BD, Lammers JW, et al. Diagnostic and prognostic utility of mid-expiratory flow rate in older community-dwelling persons with respiratory symptoms, but without chronic obstructive pulmonary disease. BMC Pulm Med. 2015; 15: 83.

32. Stockley JA, Cooper BG, Stockley RA, Sapey E. Small airways disease: time for a revisit? Int J Chron Obstruct Pulmon Dis. 2017; 12: 2343-2353.

33. Pellegrino R, Viegi G, Brusasco V, Crapo RO, Burgos F, Casaburi R, et al. Interpretative strategies for lung function tests. Eur Respir J. 2005; 26: 948-68.

34. Chang YK, Wu CC, Lee LT, Lin RS, Yu YH, Chen YC. The short-term effects of air pollution on adolescent lung function in Taiwan. Chemosphere. 2012; 87: 26-30.

35. Cakmak S, Dales R, Leech J, Liu L. The influence of air pollution on cardiovascular and pulmonary function and exercise capacity: Canadian Health Measures Survey (CHMS). Environ Res. 2011 Nov;111(8):1309-12.

36. Zhang R, Dai Y, Zhang X, Niu Y, Meng T, Li Y, et al. Reduced pulmonary function and increased pro-inflammatory cytokines in nanoscale carbonblack-exposed workers. Particle and Fibre Toxicology 2014: 11: 73.

37. Schaumann F, Borm PJ, Herbrich A, Knoch J, Pitz M, Schins RP, et al. Metal-rich ambient particles (particulate matter 2.5) cause airway inflammation in healthy subjects. Am J Respir Crit Care Med. 2004; 170: 898-903.

38. André E, Stoeger T, Takenaka S, Bahnweg M, Ritter B, Karg E, et al. Inhalation of ultrafine carbon particles triggers biphasic proinflammatory response in the mouse lung. Eur Respir J. 2006; 28: 275-85.

39. Hussain S, Boland S, Baeza-Squiban A, Hamel R, Thomassen LC, Martens JA, et al. Oxidative stress and proinflammatory effects of carbon black and titanium dioxide nanoparticles: role of particle surface area and internalized amount. Toxicology. 2009; 260: 142-9.

40. Cakmak S, Hebbern C, Cakmak JD, Dales RE. The influence of polycyclic aromatic hydrocarbons on lung function in a representative sample of the Canadian population. Environ Pollut. 2017; 228: 1-7.

41. Zhou Y, Sun H, Xie J, Song Y, Liu Y, Huang X, et al. Urinary Polycyclic Aromatic Hydrocarbon Metabolites and Altered Lung Function in Wuhan, China. Am J Respir Crit Care Med. 2016; 193: 835-46.

42. Nethery E, Wheeler AJ, Fisher M, Sjödin A, Li Z, Romanoff LC, et al. Urinary polycyclic aromatic hydrocarbons as a biomarker of exposure to PAHs in air: a pilot study among pregnant women. J Expo Sci Environ Epidemiol. 2012; 22: 70-81.

43. Wang S, Bai Y, Deng Q, Chen Z, Dai J, Li X, et al. Polycyclic aromatic hydrocarbons exposure and lung function decline among coke-oven workers: A four-year follow-up study. Environ Res. 2016; 150: 14-22.

44. Mazzarella G, Ferraraccio F, Prati MV, Annunziata S, Bianco A, Mezzogiorno A, et al. Effects of diesel exhaust particles on human lung epithelial cells: an in vitro study. Respir Med. 2007; 101: 1155-62.

45. Churg A, Tai H, Coulthard T, Wang R, Wright JL. Cigarette smoke drives small airway remodeling by induction of growth factors in the airway wall. Am J Respir Crit Care Med. 2006; 174: 1327-34.

46. Kobayashi T, Ikeue T, Ito T, Ikeda A, Murakami M, Kato A, et al. Short-term exposure to diesel exhaust induces nasal mucosal hyperresponsiveness to histamine in guinea pigs. Fundam Appl Toxicol. 1997; 38: 166-72.

47. Samoliński B, Namysłowski A, Lipiec A, Zieliński W, Sybilski AJ, Walkiewicz A, et al. Epidemiology of allergic diseases in Poland - ECAP study. Allergy. 2008; 63: 626-627.

48. Czarnobilska E, Obtulowicz K, Dyga W, Wsolek-Wnek K, Spiewak R. Contact hypersensitivity and allergic contact dermatitis among school children and teenagers with eczema. Contact Dermatitis Enviromental and Occupational Dermatitis 2009: 60: 264–269.

49. Flouris AD, Metsios GS, Carrillo AE, Jamurtas AZ, Gourgoulianis K, Kiropoulos T, et al. Acute and short-term effects of second-hand smoke on lung function and cytokine production. Am J Respir Crit Care Med. 2009; 179: 1029-33.