ROLE OF AIR POLLUTION ON PATHOGENESIS OF ASTHMA AND ALLERGIC DISEASES

Arman Hashemi1, Afshin Shirkani2, Mohammad Hashemi1, Mohammad Davood Salimi1, Shayan Behzadi1, Alireza Fakharian1, Shokrollah Farrokhi2*

1 Student Research Committee, School of Medicine, Bushehr University of Medical Sciences, Bushehr, Iran
2 Department of Immunology, Asthma and Allergy, The Persian Gulf Tropical Medicine Research Center, Bushehr University of Medical Sciences, Bushehr, Iran

Abstract:
Air pollution is one of the prevalent causes of respiratory disorders. The main air pollutants are NOx, SOx and O3 that affect quality of life and health. Therefore, assessment of air pollutants effects on the pathogenesis of asthma and allergic diseases may lead to reach a better quality and reduce the prevalence of the diseases. The sample size of this study was according to the index articles containing the terms “Air pollution, Asthma and Allergy”. For writing of this review, 55 articles were studied. Air pollutants induced nonspecific immune and allergic inflammation with enhancing the production of IL - 4, IL - 5, and IL - 13 by Th2 lymphocytes. Our present research demonstrates that, there is significant relationship between air pollution and asthma and allergic diseases. Therefore, air pollution plays role in the pathogenesis and exacerbation of the allergic diseases.

Review
Air pollution is one of the main concerns of developed countries especially in large cities. These days, air pollution is a general health problem which has adverse effect on the quality of life specially in large cities and cities with high traffic rate [1]. The main biogenic sources include volcanic activities, natural fire, desert dust and human activities (anthropogenic sources). Other air pollution sources related to human’s activity are divided into two categories, which are motile and immotile sources. Motile sources include motor vehicle exhaust gases, and immotile sources are home appliances using fuel, industrial facilities and power stations [1, 2]. Generally, outdoor pollutants are two types: primary contaminants such as carbon monoxide (CO) emitted by vehicles and sulfur dioxide (SO2) which enters to environment from industrial activities. Secondary pollut-
ants are ones which are produced as the result of chemical activities on primary contaminants in atmosphere. These kinds of pollutants are produced by sunrays and air humidity. For example, ozone (O$_3$) is produced from effect of sunrays on volatile hydrocarbons or secondary micro particles in the atmosphere such as sulfates. The result of all these processes is production of gases such as ozone (O$_3$), carbon monoxide (CO), carbon dioxide (CO$_2$), nitrogen monoxide (NO), nitrogen dioxide (NO$_2$), nitrogen trioxide (NO$_3$), sulfur dioxide (SO$_2$) and all other particles (PM$_{0.1}$, PM$_{2.5}$, PM$_{10}$) which are floating in air [3, 4]. Air pollution caused by car traffic in many cities and specially in urban areas is a giant source of air pollution which includes benzene from lead - free diesel, organic chemical material released from diesel exhaust, NO$_2$, SO$_2$, O$_3$ as actuator gases and PM [2]. In addition, secondary pollutants are produced due to the exposure of CO, PM$_{2.5}$, NO$_2$, NO$_3$ with sunlight. NO, NO$_2$ and NO$_3$ are the air pollutants which are mainly produced from diesel engines and fuel based machines in power stations or factories which run by coal or oil [2]. Among these gases, NO and NO$_2$ play an important role in air pollution because of their heavy destructive effect on human health [3, 4]. Ozone (O$_3$) is a very active gas which is produced primarily by the effect of sun light on hydrocarbons and NOx released by burning of fossil fuels [2]. Exposure to ozone gas in animal model can cause the toxicity during fetal development period [5]. CO is a primary pollutant which competitively inhibits oxygen (O$_2$) transfer by producing carboxyhemoglobin which is a complex of CO and hemoglobin [6]. CO gas is mainly produced from public transport in big cities [7]. SO$_2$ is another example of primary pollutants which is harmful for human and environment [8]. This gas is produced from oxidation of sulfur in fuel or from the industrial activities, which use sulfur components [5, 9, 10]. So, thermal power planets are the main sources of SO$_2$ emission compared to the other industries in IRAN [11]. PMs include chemical or physical solid and liquid particles which are divided into fine and ultrafine according to the aerodynamic diameter [2]. Lead, as one of the air pollutants, is mostly found in soil and painting materials [12, 13]. Industrial sources like battery making factories and metal melting stations emit huge amount of lead to environment [14]. In some areas where lead is still used in fuel, vehicles in traffic enter the huge amount of lead into air [15]. The highest concentration of lead is in the dust suspended in air [16]. Studies in some US institution centers, showed the lead exposure for 18 percent of children aged between 1 to 5, so that the toxicity was observed in 6.6 percent of them [9]. According to some studies in England and USA on children aged between 1-5 and Iran (province: Semnan), the amount of lead pollution was reported 8.6 %, 6.3 %, 8.7 % respectively [11, 17, 18].

**Research method**

To present this paper, the relevant articles indexed in reliable data bases such as Pubmed, Elsevier, Trip, Embase, Black Cochrane, New spring link, Ovid, SID were studied. Among the 86 articles, 57 studies were reviewed for this paper.

**Studies review**

According to the studies on asthma immunopathology, approximately 70 % of atopic asthma cases are associated with rapid reaction of IgE with allergens. In remaining 30 % may also occur due to the non-immunological stimuli such as medications, cold temperature and exercise. Asthma, a chronic inflammatory disease, occurs as a result of the activation of mast cells in response to the allergen binding to IgE and is affected by the response to Th2 contributing T cell. It has been empirically proven that other subunits cells such as Th1, Th17 and also involvement of IL-9 cytokine secreted from T-cell play an important role in inflammation. In addition, mast cells,

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basophils and eosinophils produce all of mediators, such as LTC4, LTD4 and LTE4 which all are leukotrienes, can cause contraction of smooth muscles in respiratory tract [19].

Air pollution caused by dust which occurs in east and west Asia can accentuate asthma symptoms. It seems that some factors and mineral elements such as SiO$_2$, which is the main component of soil particles in Asia, stimulate secretion of cytokines in Th2 cells (IL-4, IL-5, IL-13). The result of a study showed that increase in serum levels for IL-4 and IL-3 in individuals which are under exposure of air dust may stimulate B cells which cause production of IgE antibody for specific antigens and also exacerbate the allergic inflammation. Microorganisms, pollen of plants, trees and fungi are found in air dust in western states of Iran [20 - 22].

In a study done in Iran (province: Bushehr), it is reported that the number of B- lymphocytes (CD19 +) and T- lymphocytes (CD4 + and CD25 +) in individuals which are exposed to air dust pollution has been significantly increased [23]. In recent years, epidemiologic studies showed that the prevalence of allergic disease in children and adolescents is increasing [24 - 26]. Children, elders and individuals with some specific diseases such as asthma are more affected by air pollution. As children spend more time in outdoor compared to adults, they inhale more volume of air pollutants per pound of body weight. A study in Europe reported that air pollution is significantly associated with the number of B-cells, CD 4+ and CD8+ T-cells, NK cells during childhood ages [27].

Another study showed that exposure to PM$_{2.5}$ and aromatic hydrocarbons such as polycyclic aromatic hydrocarbons (PAH) during the last two weeks of pregnancy, significantly increased the number of B cell lymphocytes and decreased the number of T cell lymphocytes in placenta and umbilical cord [28]. According to WHO report in 2008, air pollutions in cities was responsible for annual death of 13 million people [29]. Also some evidences showed air pollution caused by traffic in cities plays important role in prevalence of asthma [30, 31]. In addition, recent epidemiologic studies have shown that Asian dust can worsen the allergic diseases such as asthma [32 - 34]. It was also showed in a experimental study that rats had bronchal and pulmonary inflammation after frequent exposure to Asian dust. It means that Asian dust increases the number of neutrophils by chemokines and cytokines such as IL -12, IL -1 b, TNF-α, IL -6, IL -12, IL -17A in air ways which can be proven in Broncho alveolar Lavage Fluid (BALF) [20]. Also pollutants such as exhaust particles from diesel engines may have synergistic effects with allergens in upper respiratory tract mucoid tissue, which increase the production of specific IgE of the allergen following increase in Th2 dependent cytokines [6]. During a study which done by Ozcan and Cubukcu in 2012, they found a significant relation between number of individuals suffering from asthma and urban air pollution level in Turkey (Province: Izmir) between years 2007-2010, which was due to the high volume of SO$_2$ and PM$_{10}$[14]. In other study, voluntaries were exposed to a diesel exhaust particle (DEP) for an hour. The Experiments showed the increase in number of peripheral blood mononuclear cell and the increase in vascular cell adhesion molecules (VCAM-1) and epithelial cell adhesion molecule in lungs tissue. Also in adults, elevated C-reactivated protein (CRP) level and markers for acute inflammation can be observed after exposure to air pollution [6, 9, 15, 16, 18-38]. Based on studies done in Netherland, Uk and Italy, elevated incidence of wheezing, chronic cough and asthma can be seen more in urban areas. In fact, diesel engines exhaust gases, can increase inflammatory response followed by increase in sensitivity to antigenic agents [30, 31, 39-50]. Due to the variation in air pollutants, various effects have been reported, so that in Sweden there is a strong connection be-
tween asthma exacerbation, and increasing NO$_2$ in air in the same day [51]. Also large amount of NO$_3$ in air was associated with increasing the number of patients in emergency department for asthma during summer and winter in Spain (Barcelona) [52]. Based on studies in Paris, there was strongest connection between asthma exacerbation and increasing sulfur dioxide on the same days [53]. Also recent studies on asthmatic patients in 12 hospital in London reported that the main reason of referring these patients to hospital is significant increase in level of NO$_2$ and SO$_2$ in air [54]. In addition, many reports indicated increase in respiratory disease symptoms in children is due to the exposure to NO$_2$ resulting from gas oven in kitchens [55].

Epidemiologic and clinical studies showed that O$_3$ radiation is associated with impairment athletes performance, decrease in lungs function and respiration, chest pain with deep inhalation, wheezing, cough and asthma exacerbation [56]. Since 2005, approximately 35 million people have lost their lives during next 10 years (until 2015) due to the chronic pulmonary disease such as asthma and chronic obstructive pulmonary disease (COPD) in all around the world and mortality rate due to these chronic diseases has increased 17 % in Turkey. According to this fact, all these studies and reports demonstrated the relationship between air pollution with the development and exacerbation of asthma and allergic diseases [57].

**CONCLUSIONS**

Various epidemiological studies have shown that air pollution exacerbates pulmonary disease in human. Many of these contaminants have oxidant effects and exacerbate respiratory tract inflammation. It has also been suggested that air pollution will change the type of response to allergens and increase the sensitivity to these allergens. In fact this type of immunological response, stimulates Th2 lymphocytes and increases the production of IL-4, IL-5, IL-13 and cytokines by these cells. Therefore, air pollution plays an important role in stimulation of symptoms of asthma and allergy.

**FINANCIAL SUPPORTS**

The authors would like to thank the facility support by Vice-Chancellery Research & Technology Affairs of Bushehr University of Medical Sciences.

**COMPETING INTERESTS**

All authors declare that they have no conflicts of interest.

**ACKNOWLEDGEMENTS**

Vice-Chancellery Research & Technology Affairs of Bushehr University of Medical Sciences financially supported this study. We acknowledge the critical comments from anonymous reviewers and editor.

**ETHICAL CONSIDERATIONS**

The authors state that they have no ethical consideration and all ethical issues have been completely observed by authors.

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