

Adverse Effects of Air Pollution on Pulmonary Diseases

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Abstract

Environmental exposure to air pollution is known to have adverse effects on various organs. Air pollution has greater effects on the pulmonary system as the lungs are directly exposed to contaminants in the air. Here, we review the associations of air pollution with the development, morbidity, and mortality of pulmonary diseases. Short- and long-term exposure to air pollution have been shown to increase mortality risk even at concentrations below the current national guidelines. Ambient air pollution has been shown to be associated with lung cancer. Particularly long-term exposure to particulate matter with a diameter <math><2.5\ \mu\text{m}</math> ($\text{PM}_{2.5}$) has been reported to be associated with lung cancer even at low concentrations. In addition, exposure to air pollution has been shown to increase the incidence risk of chronic obstructive pulmonary disease (COPD) and has been correlated with exacerbation and mortality of COPD. Air pollution has also been linked to exacerbation, mortality, and development of asthma. Exposure to nitrogen dioxide (NO_2) has been demonstrated to be related to increased mortality in patients with idiopathic pulmonary fibrosis. Additionally, air pollution increases the incidence of infectious diseases, such as pneumonia, bronchitis, and tuberculosis. Furthermore, emerging evidence supports a link between air pollution and coronavirus disease 2019 transmission, susceptibility, severity and mortality. In conclusion, the stringency of air quality guidelines should be increased and further therapeutic trials are required in patients at high risk of adverse health effects of air pollution.

Keywords: Air Pollution; Chronic Obstructive Pulmonary Disease; Asthma; COVID-19; Idiopathic Pulmonary Fibrosis; Lung Cancer; Mortality

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Introduction

Air pollution, contaminated water, soil, food, and occupational exposure to various harmful materials are well-known environmental risk factors with potential adverse effects on human health¹. These environmental exposures are known to induce a number of cellular and molecular processes, including oxidative stress, inflammation, genetic alterations, mutations, epigenetic alterations, mitochondrial dysfunction, endocrine disruption, and altered intracellular communication¹. Exposure of lung epithelial cells to particulate matter

(PM) consisting of mixtures of transition metals and other secondary substances produced from gaseous pollution, induces the production of reactive oxygen species, resulting in inflammation, cell death, and organ damage^{2,3}. Furthermore, somatic mutations and epigenetic alterations, such as DNA methylation, induced by environmental exposures can affect the development of chronic diseases or cancer^{4,5}. In the pulmonary system, immune cell interactions, altered lung microbiome, and virus activation are also important pathogenetic processes that result in the increased incidence of infectious lung diseases, such as pneu-

monia and bronchitis, as well as exacerbation of respiratory diseases¹. In addition, there is evidence that air pollution affects all organs through these processes, including the occurrence and exacerbation of chronic diseases, such as cancer, cardiovascular, cerebrovascular, and metabolic diseases¹.

The World Health Organization (WHO) has estimated that 12.6 million deaths are attributable to environmental factors annually around the world⁶. Among these environmental risks, the burden of disease caused by air pollution is increasing, and PM was estimated to be responsible for 9 million premature deaths, representing to one in six deaths globally every year⁷.

The main ambient air pollutants for which there is accumulating evidence of adverse health effects include PM, nitrogen oxides (NO_x and NO₂), ozone (O₃), sulfur dioxide (SO₂), and carbon monoxide (CO)⁸. PM is classified according to particle size as PM_{2.5} and PM₁₀ with particle diameters of <2.5 μm and <10 μm, respectively⁹. The levels of these pollutants are continuously monitored worldwide as a means of determining air quality in a given area. Indoor air pollution represents household air pollution from multiple sources, such as cooking and heating using solid fuels or burning of biomass⁸.

Here, we present a review of recent studies regarding the effects of ambient and indoor air pollution on the development, morbidity, and mortality of pulmonary diseases.

Air Pollution and Mortality

Many previous studies performed around the world have yielded convincing evidence for associations of short- and long-term exposure to air pollution with mortality. In 1992, Dockery et al.¹⁰ reported increases of 16%–17% in daily mortality risk for each 100 μg/m³ increase in PM, and Pope et al.¹¹ reported that an increase in 5-day moving average PM₁₀ level of 100 μg/m³ was associated with an estimated increase in daily mortality rate of 16%. A recent systematic evaluation of time-series studies regarding the association of PM₁₀ and PM_{2.5} with daily mortality in more than 600 cities around the world indicated that an increase of 10 μg/m³ in the 2-day moving average of PM₁₀ concentration was associated with increases of 0.44% in daily all-cause mortality rate and 0.47% in daily pulmonary mortality rate, with corresponding increases of 0.68% and 0.74% in daily mortality rates for the same change in PM_{2.5} concentration, respectively¹².

A study in six cities in the United States reported that long-term exposure to PM_{2.5} was associated with

increases of 1.26-fold in all-cause mortality rate and 1.37-fold in the cardiopulmonary mortality rate for the cities with the highest versus the lowest levels of air pollution¹³. Recently, Di et al.¹⁴ reported increases in annual all-cause mortality rates of 7.3% per increase of 10 μg/m³ in PM_{2.5} and 1.1% per increase of 10 ppb in O₃. These authors reported that air pollution can have adverse effects at low concentrations, below the current national standards¹⁴. Similar to this study, exposure to air pollution at concentrations below the WHO guidelines has been shown to affect mortality. A population-based study of Medicare beneficiaries over 65 years old in the southeastern USA suggested that long-term exposure to low levels of NO₂ at concentrations below the guidelines can increase mortality risk by 4.7%¹⁵.

A recent study based on the Effects of Low-level Air Pollution Study in Europe (ELAPSE) cohort, which extended the European Study of Cohorts for Air Pollution Effects (ESCAPE) cohort from six European countries, suggested that the increase in mortality due to long-term PM_{2.5} exposure is most likely due to vanadium¹⁶.

Air Pollution and Lung Cancer

The ESCAPE study evaluated the association between long-term exposure to ambient air pollution and incidence of lung cancer, and showed significant hazard ratios (HRs) for PM₁₀ of 1.22 for all lung cancers and 1.51 for adenocarcinoma¹⁷. Based on these results, the International Agency for Research on Cancer (IARC) has classified PM as group 1 carcinogen to humans¹⁸.

Recently, results from the ELAPSE study about the relations of low-level air pollutants, including PM_{2.5}, NO₂, black carbon, and O₃, with the incidence of lung cancer were reported^{19–21}. The risk of lung cancer was shown to increase with higher levels of exposure to PM_{2.5}, with a HR of 1.13¹⁹. However, NO₂, black carbon, and O₃ showed no associations with the development of lung cancer¹⁹. A prospective study using data from the UK Biobank reported significant associations between the incidence of lung cancer and air pollutants, with HRs of 1.63 per increase of 5 μg/m³ in PM_{2.5}, 1.53 per increase of 10 μg/m³ in PM₁₀, 1.10 per increase of 10 μg/m³ in NO₂, and 1.13 per increase of 20 μg/m³ in NO_x²⁰.

Air Pollution and Chronic Obstructive Pulmonary Disease

Although the most important risk factor for the onset of chronic obstructive pulmonary disease (COPD) is smoking, about 30% of patients are never-smokers²².

Air pollution has been considered another risk factor for the incidence of COPD; urban PM significantly decreases cell viability and increased oxidative stress and autophagy levels on human bronchial epithelial cells²³. However, there was still insufficient direct epidemiological evidence linking long-term air pollution exposure to the onset of COPD²².

Many studies have shown positive relations between pollutants and COPD incidence, with long-term exposure to air pollution associated with impairment of lung function²⁴⁻²⁸. However, other studies, such as those using data from the ESCAPE cohort, showed no such associations²⁹. A recent study of ELAPSE project data reported the incidence of COPD according to long-term exposure to low concentrations of air pollution³⁰. Of the total of 98,058 participants with a mean follow-up period of 16.6 years, 4,928 developed COPD, and the excess risks of COPD occurrence were 17% per increase of 5 $\mu\text{g}/\text{m}^3$ in $\text{PM}_{2.5}$, 11% per increase of 10 $\mu\text{g}/\text{m}^3$ in NO_2 , and 11% per increase of $0.5 \times 10^{-5} \text{ m}^{-1}$ in black carbon³⁰. In a population-based cohort study performed in Canada, Shin et al.³¹ also reported that the risk of COPD increased by 7%, 4%, and 4% per interquartile range (IQR) increase of 3.4 $\mu\text{g}/\text{m}^3$ in $\text{PM}_{2.5}$, NO_2 , and O_3 , respectively.

In a trial performed in UK, to evaluate individual exposure, to allow precise evaluation of the effect of air pollution on patients with COPD, personal monitoring of exposure to pollutants and their effects in 115 COPD patients showed that higher levels of NO_2 , NO , and CO exposure increased exacerbation risk, and exposure to O_3 was related to dyspnea and peak expiratory flow³².

Furthermore, recent studies have evaluated improvements in respiratory morbidity of COPD after interventions to reduce indoor pollution³³. In a blinded randomized controlled trial, Hansel et al.³³ reported a significant difference in St. George's Respiratory Questionnaire score between a group using a portable high-efficiency particulate air (HEPA) filter and a control group using a sham filter for 6 months. This was the first environmental intervention study in patients with COPD, and the results suggested that improvement of air quality can improve symptoms in these patients.

Air Pollution and Asthma

$\text{PM}_{2.5}$, NO_2 , and O_3 are the major pollutants related to airway inflammation and oxidative stress: NO_2 and O_3 produce airway hyperresponsiveness. Through these several responses and pathways, air pollution is associated with exacerbations, mortality, and even the development of asthma³⁴.

The association air pollution and incidence of asthma has been well known in children that meta-analysis study showed statistically significant associations for black carbon, NO_2 , $\text{PM}_{2.5}$, and PM_{10} exposures and risk of asthma onset³⁵. Furthermore, Garcia et al.³⁶ reported that decreases in the levels of NO_2 and $\text{PM}_{2.5}$ for 10 years were associated with lower asthma incidence among children in United States. Additionally, ELAPSE project showed that long-term exposure to $\text{PM}_{2.5}$, NO_2 , and black carbon was associated adult-onset asthma³⁷.

A case-crossover study was performed to assess the association between short-term exposure to air pollution and asthma mortality in China³⁸. The study provided that each IQR increase of $\text{PM}_{2.5}$, NO_2 , and O_3 was associated with asthma mortality, with odds ratios of 1.07, 1.11, and 1.09, respectively.

There was a randomized clinical trial about effect of classroom air filter purifiers on asthma symptoms in students with active asthma³⁹. The number of symptom-days with asthma during a 2-week period in the group used HEPA filter purifiers was 1.6 and the mean was 1.8 symptom-days in children with asthma used sham HEPA filter purifiers. However, results showed that use of HEPA filters in the classrooms did not significantly reduce symptom-days with asthma. Further interventional study may need to consider allergen levels, other source of particle exposure, and asthma symptom at baseline.

Air Pollution and Idiopathic Pulmonary Fibrosis

Acute exacerbations and worsening of idiopathic pulmonary fibrosis (IPF) have been shown to be associated with exposure to O_3 , NO_2 , and PM , but the association between chronic exposure to air pollution and incidence of IPF was not clear.

Consistent with the results of earlier epidemiological studies, a recent study in a population of 1,114 IPF patients in Korea showed a 17% increase in mortality in association with an increase of 10 ppb in NO_2 level estimated based on residential address⁴⁰.

The results of a study by Conti et al.⁴¹ suggested a weak association between NO_2 and IPF incidence. Furthermore, pollution factors, such as metal and wood dust, were shown to have meaningful effects on occupational and environmental risks of IPF⁴². Further detailed studies are required to elucidate the associations between pollution and the incidence of IPF.

Air Pollution and Infectious Lung Disease

The risks of infectious lung diseases, such as pneumonia and bronchiolitis, are increased by exposure to air pollution, especially in childhood⁴³. The ESCAPE study investigated the associations of air pollutants, such as NO₂, NO_x, PM_{2.5}, PM₁₀, with pneumonia⁴³. The adjusted odds ratios of pneumonia increased significantly for 1.3 per increase of 10 µg/m³ in NO₂ and 1.76 per increase of 10 µg/m³ in PM₁₀⁴³. Children have greater susceptibility to the effects of environmental pollution than adults due to their less developed immune system, small-sized airways, higher respiratory rates, and longer-term exposure to air pollution of the lower respiratory tract. In a time-series study of ambient PM pollution and adult hospital admissions for pneumonia in China, short-term increases of 10 µg/m³ in 3-day moving average levels of PM_{2.5} and PM₁₀ were shown to be associated with 0.31% and 0.19% increases in hospital admissions due to pneumonia, respectively⁴⁴.

A recent study showed associations between indoor air pollution and susceptibility to tuberculosis infection⁴⁵. Briefly, higher levels of indoor air pollution exposure were shown to increase the odds ratio of latent tuberculosis infection in a cohort of 107 children living with 71 patients with active tuberculosis⁴⁵. Based on these results, further studies regarding the associations of pollution with transmission risk of transmittable diseases, such as tuberculosis, and evaluation of the underlying mechanisms are required.

Both long-term and short-term air pollution may play an important role in the airborne spreading of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and may enhance the incidence of coronavirus disease 2019 (COVID-19). Recently, many studies have reported the influence of PM_{2.5} and PM₁₀ on SARS-CoV-2 transmission⁴⁶⁻⁵¹. PM could aggravate neurological symptoms of SARS-CoV-2 and exacerbate respiratory and cardiovascular injuries of COVID-19⁵²⁻⁵⁴. Moreover, there was a report that air pollution is an important co-factor increasing the risk of mortality from COVID-19⁵⁵. Some studies proposed that PM operates as a virus carrier, promoting its transport through the air^{56,57}.

However, most studies showing an association between air pollution and COVID-19 infection did not consider potential confounding factors in the correlation analysis. Therefore, more rigorous studies considering several additional confounding factors, such as individual age, population density, and pre-existing comorbidities, should be conducted to determine the impact of air pollution on COVID-19 infection.

Conclusion

Recent large-scale cohort studies have confirmed the correlations of long-term exposure to air pollution with the incidence and clinical exacerbation of respiratory diseases. New findings have shown that exposure to pollution at levels below the WHO guidelines can have adverse health effects, suggesting the necessity of revising the guidelines for air quality.

More precise exposure evaluation, such as individual monitoring, is required to clarify the underlying mechanisms and develop suitable interventions to reduce the adverse health effects of air pollution. Recent studies involving precise monitoring of air pollutant exposure levels in patients with COPD reported that interventions to improve indoor air quality can improve COPD symptoms. Thus, such precise evaluation of exposure and trials to improve air quality are meaningful for patients with chronic pulmonary diseases who are at increased vulnerability to the adverse effects of air pollution.

Recent studies have provided evidence supporting the association between PM and lung cancer incidence risk. From observations showing vulnerability to respiratory infection, it should be considered that infants, children, and people with weakened immune systems are vulnerable to the adverse effects of air pollution.

Authors' Contributions

Conceptualization: Kyung SY. Methodology: Kyung SY. Investigation: Kyung SY. Writing - original draft preparation: Ko UW. Writing - review and editing: Kyung SY. Approval of final manuscript: all authors.

Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

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