



Review article

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AIR POLLUTION AND COPD: SHORT-TERM HEALTH EFFECTS

SUMMARY

Chronic obstructive pulmonary disease (COPD) is a major and increasing global health problem. According to World Health Organization estimates, 80 million people in the world have severe COPD. It is predicted to become the third most common cause of death and the fifth most common cause of disability in the world by 2020. The health effects of air pollution have been subject to intense study in the recent years. These effects have been found in short-term studies, which relate day-to-day variations in air pollution and health, and long-term studies, which have followed cohorts of exposed individuals over time. Epidemiological studies on the short-term effects of air pollution have consistently shown that COPD patients are susceptible to the acute effects of air pollution, and that COPD explained an important part of the total number of deaths attributed to air pollution. Epidemiological research has identified more exacerbations during periods of increased pollution. Increases in black smoke particulate matter, sulphur dioxide, ozone, and nitrogen dioxide are associated with increases in respiratory symptoms, admissions for exacerbations, and COPD-associated mortality. Frequent exacerbations appear to be associated with worsening health outcomes, and efforts should focus on preventing these episodes or prompt effective treatment. Treatment options are limited and to estimate the potential public health benefit of reducing air pollution to below various thresholds is important.

Key words: air pollution, chronic obstructive pulmonary disease, short-term effects

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is one of the leading causes of morbidity and mortality in the industrialized and the developing countries (1). COPD is currently the fourth leading cause of death in the world, and further increases in the prevalence and mortality of the disease can be predicted in the coming decades. It is predicted to become the third most common cause of death and the fifth most common cause of disability in the world by 2020 (2).

The World Health Organization (WHO) has published data placing the worldwide prevalence of COPD at 0,8% (3). Other reports place the prevalence of COPD substantially higher, at approximately 4 to 6% (4,5). COPD is more frequent in industrialized countries than in developing ones. As all chronic diseases, COPD is also strongly associated with age: thus, the prevalence and incidence have risen constantly over the last decades, as the population aged (1).

The European Respiratory Society (ERS) defines COPD as a disorder characterized by chronic nonreversible airflow limitation, and airway obstruc-

tion is present when the $FEV_1/FVC < 0.7$ (6). The air-flow limitation is usually both progressive and associated with an abnormal inflammatory response of the lungs to noxious particles or gases (7). In addition to inflammation, two other processes thought to be important in the pathogenesis of COPD are an imbalance of proteinases and antiproteinases in the lungs and oxidative stress (8).

RISK FACTORS FOR COPD

Risk factors for COPD include both host factors and environmental exposures, and the disease usually arises from an interaction between these two types of factors. Cigarette smokers have a higher prevalence of lung-function abnormalities and respiratory symptoms, a higher annual rate of decline in FEV_1 , and higher death rates for COPD than nonsmokers. Exposure to particulate matter, irritants, organic dust, and sensitizing agents can cause an increase in airway hyperresponsiveness, especially in airways already damaged by other occupational exposures, cigarette smoke, or asthma (7). There is good evidence that outdoor air pollution is important risk factor for COPD, after both acute and chronic exposure (Table 1).

and fine-particulate air pollution $< 10 \mu m$ in diameter (PM_{10}) (9).

Severe episodes of air pollution in Europe and North America before 1960s provided evidence that high levels of air pollution have important short-term effects on human health, including a significant increase in mortality (10). Recent studies indicate that effects exist around and below the current national and international air quality guidelines and standards. Air pollutants may interact between one another as well as with other environmental factors, resulting in different effect estimates depending on local or regional conditions (11).

Relation with mortality and morbidity at current levels of exposure has become apparent with recent improvements in analytical tools, including the use of time series methods. Time series studies assess the effects of short-term changes in air pollution on acute health effects by estimating associations between day-to-day variations in both air pollution and in mortality and morbidity counts. The data for daily time series analysis include daily measures of the number of health events (e.g., daily mortality count), concentrations of pollutants, and weather variables for a given area. Short-term effects are estimated by use of regression models where the

Table 1. Risk factors for COPD

Degree of certainty	Environmental factors	Host factors
Certain	-Tobacco smoke -Some occupational exposures	- α -antitrypsin deficiency
Good evidence	-Outdoor air pollution -Low socioeconomic status -Alcohol intake -Environmental tobacco smoke in childhood -Other occupational exposures	-Low birth weight -Childhood respiratory infection -Atopy (high IgE) -Bronchial hyperresponsiveness -Family case-history
Supposed	-Adenovirus infection -Dietary deficiency of vitamin C -Indoor air pollution	-Genetic predisposition -Blood group A

Modified from Siafakas et al. (6)

SHORT-TERM HEALTH EFFECTS OF AIR POLLUTION

Air pollution as a trigger for exacerbations of COPD has been recognized for more than 50 years, and has led to the development of air quality standards in many countries that substantially decreased the levels of air pollutants derived from the burning of fossil fuels, such as black smoke and sulfur dioxide (SO_2). However, the recent increase in motor vehicle traffic has produced a relative increase in the levels of newer pollutants, such as ozone (O_3)

concentration of pollutants is included in the model lagged for 0 to a few days. This procedure included modelling all potential confounders (seasonal and long term patterns, daily temperature, humidity, day of the week, influenza epidemic, and other unusual events), choosing the best air pollution models, and applying diagnostic tools to check the adequacy of the models (12).

A multi-city analysis of the short-term health effects of air pollution on mortality and hospital admissions was initiated within the European Union Environment 1991-1994 Programme (Air Pollution and Health: a European Approach: the APHEA

project). This study investigated the effects of several air pollutants in 15 European cities in 10 countries (11). In a part of APHEA project (results from the 12 European cities), in western European cities it was found that an increase of $50 \mu\text{g}/\text{m}^3$ in sulphur dioxide or black smoke was associated with a 3% (95% confidence interval (CI) 2% to 4%) increase in daily mortality from all causes and the corresponding figure for PM_{10} was 2% (95% CI 1% to 3%). In central eastern European cities the increase in mortality from all causes associated with $50 \mu\text{g}/\text{m}^3$ change in sulphur dioxide was 0.8% (95% CI -0.1% to 2.4%) and in black smoke 0.6% (95% CI 0.1% to 1.1%). Cumulative effects of prolonged (two or four days) exposure to air pollutants resulted in estimates comparable with the one day effects (12).

In 20 US cities in National Mortality and Morbidity Air Pollution study (NMMAPS) it was found that an increase of $10 \mu\text{g}/\text{m}^3$ in PM_{10} was associated with a 0.48% (95% CI 0.09-0.88%) increase (lag 0), and 0.58% (95% CI 0.34-0.87%) increase (lag 1) in respiratory and cardiovascular mortality (13).

In a ten-year study in East Germany (Erfurt), a significant logarithmic relationship was found between SO_2 or particulates and daily mortality. Comparing the 5th percentile to the 95th percentile, an increase of 23 to $929 \text{ g}/\text{m}^3$ in SO_2 leads to an increase in mortality of 10%, whilst 15 to $331 \text{ g}/\text{m}^3$ in suspended particulates causes a 22% increase (14).

Several studies from the USA (15,16) indicated small, statistically significant increases in mortality as a result of short-term exposure to air pollution, especially to "inhalable" particulate matter (PM_{10}). These studies use data from cities and areas with different socioeconomic, geographic and climatic characteristics, and different levels and mixtures of air pollutants.

Studies on daily admissions in emergency rooms and hospital admissions were specific for COPD. Studies conducted during the 1980s and 1990s in different cities in Europe and Australia have consistently observed that admissions due to COPD increased on days with high pollution values (17,18).

In APHEA 2 project, In 8 European cities, it was found that an increase of $10 \mu\text{g}/\text{m}^3$ in SO_2 was associated with a 0.6% (95% CI 0.0-1.2%) increase in emergency room admissions for COPD and asthma at ages 65+ years (19).

The Barcelona study on emergency admissions for COPD was extended to a five-year period, and the results confirmed those of the previous analyses. In this study, an increase of $25 \mu\text{g}/\text{m}^3$ in SO_2 was associated with a 6% to 9% increase in emergency room admissions for COPD (20).

POTENTIAL BIOLOGICAL MECHANISMS

Particulate matter has now been linked to a broad range of adverse health effects, in epidemiologic and toxicologic research. The diversity of effects may reflect the complexity of airborne particulate matter, which is made up of a rich mixture of primary and secondary particles. Physical and chemical properties of particulate matter have been postulated to be determinants of toxicity: for example, metal content, oxidative potential, or being in the ultrafine size mode ($<0.10 \mu\text{m}$) (21).

Particles are thought to be involved in complex inflammatory responses in animals and humans, which could lead to pulmonary and/or cardiovascular effects, and possibly to pulmonary and/or cardiovascular events (22,23). Experimental studies have shown that exposures to concentrated air particles induce pulmonary inflammatory response, such as alveolar cytokine release, responsible for bronchospasms, and reduction of pulmonary function (24). Increased reactive oxygen species in the lung and heart have been produced by exposure to concentrated air particles as well (25).

Numerous studies have shown that particulate matter exposure activates inflammatory pathways in the respiratory system. For example, in vitro exposure of normal human bronchial epithelial (NHBE) cells stimulates release of oxidants, and cytokines (26). Experimental 2-h human exposures to particulate matter increases the numbers of neutrophils in lavage fluid (27).

COPD patients have a systemic deficit in their antioxidant defenses, and particles could have produced a significant additive oxidative stress as a response to the inflammation of the lungs (8). An alternative explanation of the COPD susceptibility was that lung deposition of inhaled fine particles was much higher in patients with obstructive airways diseases than in normal subjects (28).

Mucus hypersecretion and ciliary damage are features of COPD (29) and would be expected to impair clearance of inhaled particles or soluble gases. This may make the patient more susceptible to the pro-inflammatory effects of inhaled pollutants which, in turn, would lead to more mucus secretion, airway oedema, and neutrophil recruitment and activation, all of which are features of acute exacerbation of COPD.

A better understanding of molecular and cellular pathogenic mechanisms of COPD should lead to many new directions for both basic and clinical investigations.

CONCLUSION

There is consistency in the findings that relate the acute increases in urban air pollution and the short-term health effects on patients suffering from COPD. Frequent exacerbations appear to be

associated with worsening health outcomes, and efforts should focus on preventing these episodes or prompt effective treatment. Treatment options are limited and to estimate the potential public health benefit of reducing air pollution to below various thresholds is important.

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AEROZAGAĐENJE I HOBP: AKUTNI ZDRAVSTVENI EFEKTI

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SAŽETAK

Hronična opstruktivna bolest pluća (HOBP) je važan i rastući globalni zdravstveni problem. Prema proceni Svetske zdravstvene organizacije, 80 miliona ljudi u svetu ima ozbiljnu HOBP. Procenjeno je da će do 2020. godine HOBP biti na trećem mestu uzroka smrti i na petom mestu uzroka invaliditeta u svetu. Zdravstveni efekti aerozagađenja su poslednjih godina bili predmet istraživanja velikog broja studija. Postojanje negativnih zdravstvenih efekata dokazano je i u studijama akutne i u studijama hronične izloženosti aerozagađenju. Epidemiološke studije akutnih efekata aerozagađenja su pokazale da su pacijenti koji boluju od HOBP osetljivi na akutni uticaj aerozagađenja i da je HOBP jedan od značajnih uzroka mortaliteta koji je povezan sa aerozagađenjem. U periodu povećanog aerozagađenja utvrđeno je povećanje broja akutnih egzacerbacija HOBP. Porast koncentracija čestica čađi, sumpor dioksida, ozona i azot dioksida povezani su sa porastom respiratornih simptoma, hospitalnih prijema i prijema u hitnu pomoć zbog egzacerbacije, kao i porastom mortaliteta od HOBP. S obzirom da učestale egzacerbacije dovode do pogoršanja zdravstvenog stanja, trebalo bi usmeriti napore na prevenciju ovih epizoda i sprovesti efikasnu terapiju. Zbog limitiranih terapijskih mogućnosti HOBP, procena potencijalnih koristi od redukcije aerozagađenja od velikog značaja je za javno zdravlje.

Ključne reči: aerozagađenje, hronična opstruktivna bolest pluća, akutni efekti