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Original Article

Air pollutants and asthma

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Prevention of asthma occurrence and exacerbation requires attention to indoor and outdoor air pollution. The aim of this paper is to describe common asthma-related pollutants in Taiwan, including nitrogen oxides, sulfur oxides, ozone, particulate matter, formaldehyde and environmental tobacco smoke, and to provide recommendations for reducing exposure to these pollutants. Such recommendations include staying indoors, keeping windows and doors closed, and using air purifiers or high-efficiency particulate arrestor air filters. Prohibition of smoking in indoor spaces can reduce the levels of indoor air pollutants. Individuals with asthma should also avoid exertion outdoors when the levels of outdoor air pollutants are high.

Keywords: asthma, nitrogen oxides, sulfur oxides, ozone, particulate matter, formaldehye, environmental tobacco smoke

Asthma

Asthma is a chronic inflammatory disease of the airways. Airway exposure to allergens[1,2] or non-allergic irritants (such as cigarettes and certain air pollutants)[3,4] induces inflammation[5], leading to chronic mucus plug formation, swelling and deformation of the bronchiolar wall, airflow obstruction and hyperinflation. Airway obstruction-associated bronchial disorders are a feature of asthma, accompanied by recurrent breathing difficulty (dyspnea) and bronchoconstriction causing wheezing[6]. These symptoms often occur at night, early in the morning, or during vigorous exercise.

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Asthma epidemiology

Individuals with asthma should avoid exertion outdoors when the levels of air pollutants are high[7]. The prevalence of asthma varies widely around the world, ranging from 1% to 18%[8]. It is worth noting that asthma prevalence in some countries is growing[7-12]. However, geographic variation and growth trends cannot be fully explained by genetic factors. In addition to the burden of medical costs, patients with asthma suffer a negative impact on quality of life. The World Health Organization (WHO) has estimated that the number of disability-adjusted life years (DALYs) lost due to asthma worldwide is about 15

million per year. Asthma accounts for around 1% of all DALYs lost worldwide[8].

Asthma has a two-peaked prevalence curve[13]. Childhood asthma is mainly provoked by allergy and temporarily stops before adulthood, whereas adult asthma due to hyperreactivity gradually increases in prevalence until 60-70 years of age. In Taiwan, the asthma prevalence among schoolchildren was 5.1% in 1985, an increase from 1.3% in 1974[14]. Another investigation found that asthma prevalence among elementary schoolchildren in southern Taiwan rose from 6.5% in 1993 to 8.5% in 1997[15]. Kao et al.[16] noted that the asthma prevalence of children in Taiwan was 12.2% in 2002. Hwang et al.[17] analyzed the National Health Insurance Database from 2000 to 2007 and showed that the asthma prevalence of the general population was 11.9%, but that the prevalence among children and adolescents was 15.7% during that period.

The development of a standardized questionnaire for the International Study of Asthma and Allergies in Childhood (ISAAC) has allowed for some international comparisons[18]. From the data obtained from the ISAAC questionnaire, prevalences in Australia and New Zealand are higher than in European countries; while prevalences in European countries are higher than in Asia. Countries with higher asthma prevalence in children may also have higher prevalence of people sensitized to pollen in their living environment.

Environmental factors for asthma

The mechanism underlying the pathogenesis of asthma is multi-factorial. In addition to genetic factors, environmental factors play a very important role in the occurrence of asthma. Possible associated factors are: 1) Exposure to allergens such as dust, cockroaches, pet dander, and mold in the domestic environment[1,2] and pollen in the outdoor air[19]. 2) Exposure to air pollutants such as nitrogen oxides (NOx), sulfur oxides (SOx), ozone (O3), particulate matter (PM), and formaldehyde. Several studies have pointed out that the higher the concentration of these substances, the higher is the risk of asthma occurrence[3,20-23]. 3) Smoking habit and exposure to environmental tobacco smoke (ETS). Cigarette smoke can cause respiratory epithelial inflammation[24], decrease the adherence of epithelial cells, and increase detachment[25]. Turnover of epithelial adhesion is a critical contributor to airway remodeling in asthma[26]. 4) Occupational exposure such as to dust in the workplace. This can cause airway obstruction or injury, resulting in airway inflammation[27,28]. 5) Socioeconomic status and educational level of the family. However, epidemiological evidence is conflicting[22,29]. 6) Allergies to foods such as seafood, eggs, milk, beans, and peanuts. Such allergies have been indicated in childhood asthma [30,31]. 7) Viral respiratory infections[32]. Viruses can enter macrophages and replicate in cells, causing airway epithelial cells to produce a variety of inflammatory mediators in response to infection. An animal study found that recurrent infections of respiratory syncytial virus in dust mite-sensitized mice augmented hyperresponsiveness and expression of immunoglobulin (Ig) E, which are responsible for airway inflammation and obstruction[33].

Asthma-related air pollutants are present in both indoor and outdoor environments. It is worth mentioning that the onset of asthma may be more relevant in the indoor environment, as people spend a large proportion of their time indoors, such as in the home, in the workplace or at school. In contrast to the outdoors, there is a greater ability to reduce specific indoor hazards. In the following sections, we will introduce specific air pollutants that are most relevant to asthma development in the Taiwanese population, regardless of occupation. Further, we will make recommendations for preventing asthma occurrence.

Air pollutants

Some air pollutants can affect the development of asthma. In general, individuals have little control over the outdoor environment. Therefore, asthma sufferers are recommended to stay indoors in an air-conditioned environment, if feasible, or to avoid exertion when specific pollutant levels are

high. Asthma-related air pollutants include NOx, SOx, O3, PM[3,20-22], formaldehyde[23], and ETS[24-26]. People who live in urban and industrial areas generally have a higher proportion of respiratory symptoms, due to exposure to air pollution, compared to those living in rural areas. SOx, O3 and acid aerosols are possible bronchoconstrictors. Airway inflammation can be induced by inhalation of low concentrations of pollutants. At high concentrations, pollutants directly cause toxicity to the respiratory epithelium. Altering of the immune response can trigger allergic reactions in asthma patients. In theory, air pollutants increase the risk of asthma occurrence or enhance the severity of asthma[34].

Furthermore, adverse health effects caused by air pollutants may be additive[35,36] without the existence of a threshold[37]. Even low levels of air pollutants can damage human respiratory health. During a 3-year period, from 1987 to 1989, Ponka[38] studied the relationship between low levels of air pollutants and hospital admissions among a total of 4,209 asthmatic patients in Helsinki. After adjusting for the effects of temperature, admissions rates were associated with ambient nitric oxide (NO), nitrogen dioxide (NO2), SOx, O3, and particulates. Further regression analysis revealed that NO and O3 are most strongly associated with admission for asthma. In the following subsections, we introduce the frequently reported air pollutants relevant to asthma development.

Nitrogen oxides (NOx)

NOx include NO and NO2 mainly produced from the reaction of nitrogen and oxygen during high-temperature combustion. They have many indoor sources, such as gas stoves, space heaters, furnaces, and fireplaces[39]. Automobile exhaust is the main outdoor source of NOx in most urban areas[40]. Other sources include industrial and power plants. Evidence has shown that a reduction in traffic density in a local region decreases asthma morbidity, most likely due to the lowering of NO2 exposure[40,41]. Exposure to NOx has been demonstrated to impair host resistance to respiratory viruses and bacteria, by weakening bacterial clearance and impairing innate immunity[42,43]. However, studies of the relationship between NOx and respiratory health have led to inconsistent results[44,45]. A growing number of studies have found a positive association between indoor NO2 concentrations and asthma morbidity[46-50]. Ambient NOx has also been suggested to be associated with the occurrence and exacerbation of asthma, as well as the number of asthma-related hospitalizations and decline in lung function, especially among vulnerable populations, such as children and the elderly[51-53].

Given the uncertain relationship between NOx and the occurrence of asthma, more research is needed. For NOx control, general strategies include source modification and ventilation[54].

Sulfur oxide (SOx)

SOx is mainly formed by the combustion of high-sulfur coal or oil. However, indoor sources are not common, because SOx is rapidly adsorbed into household surfaces. Thus, SOx exposure is mainly due to ambient air pollutants in the household. Earlier experimental evidence has shown that SO2 decreases lung function in asthmatic adults during exercise[55,56]. Therefore, it is recommended that asthmatic patients avoid outdoor exercise on days when levels of air pollutants, including SOx, are high[54].

Ozone (O3)

Ozone is a highly reactive gas that is generated by photochemical reactions involving sunlight on mixtures of NO2 and hydrocarbons from the combustion of fossil fuels. Its major sources are vehicular traffic and power plants. Sunlight and hot weather can also increase ground-level ozone, which is the major constituent of "summertime smog"[57].

Since O3 has limited solubility in water, it is poorly absorbed by airway mucosa. Rather, it is deposited in the terminal airway and alveolar tissue. Ozone can react with epithelium lining fluid along the whole airway and produce many diffusible products such as formaldehyde, hydrogen peroxide and free radicals which can cause toxicity[36]. Such toxicity is reflected in the cilia loss of airway epithelial cells, damage to alveolar macrophages, increases in edema and inflammation, and impairment of lung function, resulting in

weakening host resistance and higher susceptibility to microbial infection. Epidemiological studies have shown that exposure to ozone is associated with reduced pulmonary function, increased respiratory symptoms, increased medication use, and increased risk of asthma exacerbation[20,58]. Therefore, outdoor exercise or exertion should be avoided when the O_3 level is high[54].

The level of indoor O_3 is usually high only in warmer months, which is largely influenced by the penetration of outdoor O_3[59]. Although indoor O_3 is uncommon, sources include negative air ionizers, air purifiers, air-cleaning devices, and xerographic copy machines[60].

It has been shown that there is a significant relationship between ambient O_3 level and asthma-related morbidity[61-63]. However, the association of indoor O_3 and asthma morbidity has not been fully studied. Indoor O_3 level can be reduced by keeping windows and doors closed. Since O_3 is a highly reactive gas, the O_3 level is generally much lower indoors than outdoors, even in peak O_3 season[64].

Particulate matter (PM)

PM comes from a variety of natural and manmade sources. Natural sources include pollen, spores, bacteria, plant and animal debris, sea salt, and dust from the earth's crust. Manmade sources are the combustion by-products of factories, motor vehicles, and power plants. In terms of indoor PM, smoking is a significant contributor. Other indoor sources include cooking fumes, wood-burning stoves and fireplaces, as well as outdoor particles that can penetrate the indoor environment[65].

PM is characterized on the basis of particle size. PM with a diameter of less than 10 μm (PM10) can enter the respiratory system and PM with a diameter of less than 2.5 μm (PM2.5) can reach the alveoli. "Coarse particles" (PM2.5-10) that are too large to involve the alveoli are deposited in the proximal airway[65]. In addition, PM often contains high proportions of toxic metals and acid sulfide. Therefore, special attention has been paid to the harmful effects of PM[65]. Evidence from pediatric asthma patients has revealed that higher levels of indoor PM are linked to reduced lung function[66,67], increased respiratory symptoms and increased use of medication[68]. In particular, exposure to PM may cause irritation or provoke airway inflammation[67]. Notably, the levels of PM in some indoor settings are higher than in outdoor settings.

Smoking, frequent sweeping and stove use can raise the levels of indoor PM[69,70]. Increased ventilation by opening of windows and use of (high-efficiency particulate arrestor [HEPA]) air filters can effectively prevent indoor PM exposure[54,71].

Formaldehyde

Increasing attention has been paid to the relationship between formaldehyde exposure and respiratory symptoms[23,72]. Formaldehyde emissions occur in certain occupational settings, but exposure via formaldehyde-emitting products in the home such as particle board, urea formaldehyde insulation, carpeting, and furniture, is common[73]. Importantly, long-term inhalation of formaldehyde has been linked to asthma[74]. Children may be particularly sensitive to formaldehyde exposure. Younger children may be even more vulnerable due to the small caliber of their airways[75].

Evidence has suggested an association between formaldehyde exposure and the development of airway hyperresponsiveness and asthma[72,75,76]. Several possible mechanisms have been proposed[77]: 1) Formaldehyde is a known irritant, which can provoke transient decline in pulmonary function. 2) Formaldehyde may be able to create newly synthesized antigenic moieties, to induce formation of specific IgE antibodies that cause degranulation of mast cells. 3) Formaldehyde can induce mucosal inflammation in airways.

Formaldehyde is released into indoor air from construction materials and a variety of consumer products[73]. Therefore, formaldehyde levels can be reduced by 1) keeping the home well ventilated; 2) limiting the use of pressed wood or sealing unfinished pressed wood products; and 3) washing new clothes before wearing. It is worth mentioning that formaldehyde is a component of tobacco smoke and smoking in enclosed spaces should be avoided[73].

Environmental tobacco smoke

In addition to the common air pollutants, several studies have suggested that indoor exposure to ETS

is associated with asthma symptoms in susceptible individuals[78,79]. Importantly, gas-phase of cigarette smoke contains 1020 oxidant molecules per puff[80] that can cause airway epithelial inflammation[24]. Imbalance in oxidative and anti-oxidative statuses might lead to increased permeability of epithelial cells in individuals exposed to cigarette smoke[81]. Moreover, cigarette smoke can decrease the adherence of epithelial cells and increase detachment[82]. Air cleaners should be considered if ETS exposure cannot be avoided as such devices can effectively reduce PM generated from ETS[54].

Conclusions

The mechanism underlying the pathogenesis of asthma is multi-factorial. In addition to genetic factors, air pollution likely plays a key role in the occurrence of asthma in Taiwanese patients. Therefore, avoiding exposure to air pollutants is crucial for the prevention of asthma. It has been proposed that levels of air pollution below current standards might still be unhealthy, particularly for vulnerable populations, such as children and individuals with respiratory disease. Therefore, current regulations for several air pollutants might be inadequate and should be reevaluated. Importantly, the public health sector should instigate an interdisciplinary approach to prevent air pollution, by engaging with and supporting the work of other sectors (i.e. transportation, housing, energy, and industry) to develop and fulfill long-term policies and programs aimed at reducing air pollution and improving health. Here, individual-level recommendations include reducing exposure by staying indoors, keeping windows and doors closed, and using air purifiers. In addition, prohibition of smoking in indoor spaces can reduce the levels of indoor air pollutants. Individuals with asthma should avoid outdoor exertion when the levels of outdoor air pollutants are high. Future research on environmental and genetic interactions should be conducted to help us to further understand the mechanism involved in the development of asthma.

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