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The Impact of Air Pollution on Allergic Rhinitis

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Abstract

Recently, air pollution has become more and more severe globally and has decreased the quality of life significantly in subjects with or without allergic diseases. Air pollution more severely affects patients with allergic diseases, including allergic rhinitis (AR); therefore, it could devastate the quality of life. Many epidemiological studies have shown that air pollutants increased outpatient clinic visits as well as the prevalence/severity of AR and decreased quality of life in patients with AR. Traffic-related air pollution also increases the severity and occurrence rate of AR, and heavy traffic is also associated with an increased prevalence of AR. Immunologically, air pollutants increase airway inflammation and mucin production by triggering the generation of reactive oxygen species and inducing the nucleotide-binding domain, leucine-rich repeat protein 3 inflammasome, and apoptosis. Since air pollution affects both the upper and lower airways and is known to be a risk factor for AR, proper diagnosis and treatment should be applied. In this review article, we will address several epidemiological and clinical studies about the effects of air pollution on AR, mechanisms by which air pollutants aggravate AR, and treatment of AR triggered by air pollutants.

Keywords

Air pollution
Allergic rhinitis
Epidemiology
Immunology
Traffic-related pollution

1. Introduction

Recently, there have been various social problems caused by air pollution around the world, and the effects of respiratory diseases have received increasing attention. Among respiratory diseases, allergic rhinitis is a type 1 hypersensitivity reaction in which the nasal mucosa shows IgE antibody-mediated hypersensitivity after antigenic stimulation, with a runny nose, nasal congestion, and sneezing as the main symptoms. The prevalence of allergic rhinitis is reported to be around 10%–30% in adults worldwide, but it is estimated to be higher due to self-diagnosis and treatment [1,2]. In recent years, the prevalence of allergic rhinitis has been gradually increasing due to environmental factors such as air pollution such as fine particulate matter, ultrafine particulate matter, automobile and factory fumes, and

climate change [3]. Domestic air pollution is known to have different proportions of international and domestic influences depending on the season, and the current coronavirus disease 2019 (COVID-19) pandemic has played a positive role in air pollution by reducing particulate matter (PM) and nitrogen dioxide (NO_2) concentrations and indirectly reducing medical insurance claims for allergic rhinitis patients in Korea [4,5], due to movement restrictions, social distancing, and reduced economic activity. In this context, we would like to examine the air pollution-induced changes in allergic rhinitis, which is highly influenced by environmental and seasonal factors, and its clinical implications.

2. Impact of air pollution on allergic rhinitis: an epidemiological analysis

2.1. Air pollutants

Recently, the World Allergy Organization published an expert consensus statement on allergic rhinitis exacerbated by air pollution [8]. Allergic rhinitis affects the quality of life of millions of people worldwide, and air pollution exacerbates its symptoms and increases its morbidity. Meanwhile, it is estimated that around three million people die each year in relation to harmful indoor air pollution.

Air pollutants can be broadly divided into indoor and outdoor pollutants. Indoor pollutants include fine particulate matter, volatile organic compounds, radon, mold, and house dust mites, of which mold and house dust mites are the main antigens that cause allergic rhinitis. Wang *et al.* used enzyme-linked immunosorbent assay analysis of 50 patients with allergic rhinitis to confirm that house dust mites are an important indoor allergen and that long-term exposure to house dust mites exacerbates allergy symptoms [9]. Exposure to mold, an indoor pollutant, has also been linked to the exacerbation of asthma in children and to the development of occupational asthma and rhinitis in adults [10]. Outdoor pollutants include fine particulate matter, nitric oxides, carbon monoxide, sulfur oxides, ozone (O_3), ground-level ozone, traffic-related air pollution (TRAP), and diesel exhaust particles. Particulate matter and volatile organic compounds are both indoor and outdoor pollutants. In industrialized countries, people spend most of their time indoors, so indoor air quality is important. Sources of indoor pollutants include cigarette smoke, space heating, cooking, cleaning, candle and incense use, and furniture and decorations. Sources of outdoor pollutants include fossil fuel-fired factories and vehicles, home heating, and garbage burning. Pollutants are also classified as primary or secondary depending on whether they are emitted into the atmosphere: nitrogen oxides, volatile organic compounds, carbon monoxide, and sulfur oxides are primary, while ozone and diesel particles are secondary.

Particulate matter is classified according to its particle size, as it is distributed differently in the body depending on the particle size. Particulate matter with a diameter of 10 μm or less (PM_{10}) can be distributed in the upper respiratory tract, nasal passages, and throat, while fine particulate matter with a diameter of 2.5 μm or less ($PM_{2.5}$) is mainly distributed in the lungs and affects the lower respiratory tract [11]. Ultra-fine particles ($PM_{0.1}$), with particles of 0.1 μm or less, which can act as carrier vehicles for metals and other organic compounds, are more commonly associated with lower respiratory tract disease and are absorbed and affected systemically [12].

Ground-level ozone is produced by the reaction of nitrogen dioxide and volatile organic compounds with solar radiation and has been shown to have adverse effects on human health and to be epidemiologically associated with allergic rhinitis, asthma, and atopic dermatitis [13,14]. Cabrera *et al.* analyzed the relationship between air temperature and outdoor pollutants such as ozone and fine particulate matter and seasonal allergic rhinitis in the Madrid region of Spain, comparing 1996 and 2009, and found that allergy symptom scores were higher in 2009 and attributed this to increases in air temperature and ozone, suggesting that efforts

should be made to reduce greenhouse gas emissions and air pollution [15]. Diesel particles are composed of solid aggregates of non-toxic inorganic gases such as oxygen and nitrogen combined with carbon and metals. Diesel gas particles are known human carcinogens and have toxic effects on the lower respiratory tract by inducing oxidative stress. In an *in vivo* test using nasal challenge, Diaz-Sanchez *et al.* found that the addition of diesel particle challenge to ragweed and house dust mite stimuli had a synergistic effect on type 2 immune response [16].

2.2. Epidemiological studies on air pollution and allergic rhinitis

It is not possible to discuss the relationship between air pollutants and allergic rhinitis without discussing the epidemiological studies, which are mostly epidemiological.

First, there are epidemiological studies on the effects of air pollution or aeroallergens on respiratory diseases [17,18]. Heinrich *et al.* in Germany reported a decrease in non-allergic respiratory diseases in children after reunification in former East Germany due to a decrease in total suspended particulate matter and sulfur dioxide in the air [17]. Using subjective symptoms of rhinitis and respiratory disease, serological tests, and analysis of inflammatory cytokines in nasal lavage fluid, Wouters *et al.* found a greater frequency of upper respiratory tract infections and clinical findings such as rhinitis in a group of cleaning workers compared with normal controls, and this was associated with an increase in neutrophils [18]. Many epidemiological studies have investigated the role of air pollution in allergic rhinitis, as well as other non-allergic respiratory diseases. Epidemiological studies on air pollution in allergic rhinitis and respiratory diseases reported to date are shown in **Table 1**.

In airway immune diseases such as allergic rhinitis and asthma, increased levels of air pollution are associated with increased mucosal irritation by airborne allergens, which clinically increases the number of actual outpatient visits. Zhang *et al.* found that the frequency of outpatient visits for patients with allergic rhinitis increased with increasing concentrations of fine particulate matter, sulfur dioxide, and nitrogen dioxide in a time-lapse analysis in Beijing, China [19]. They also found that among carbon dioxide, nitrogen dioxide, fine particulate matter, ultrafine particulate matter, and sulfur dioxide, nitrogen dioxide, and sulfur dioxide concentrations caused the greatest change in the number of outpatient visits for allergic rhinitis [20]. Several domestic and international studies have shown that there are differences in indoor and outdoor air pollutant concentrations in different regions of the country, and corresponding differences in the clinical presentation, diagnosis, and treatment of allergic rhinitis and asthma [21,22]. In recent years, global warming since industrialization and urbanization has accelerated climate change, resulting in extreme weather events such as polar warming, prolonged rainy seasons, floods, and droughts. Indoors, the resulting insulation and increased humidity can lead to an increase in airborne allergens such as dust mites, mold, and cockroaches, as well as ultra-fine particulate matter and volatile organic compounds from pets such as dogs and cats. Outdoors, pollen, mold, diesel particles, fine particulate matter, nitrogen oxide, and ozone from car exhaust, heating, and fossil fuel-fueled factories contribute to a vicious circle of air pollution, which is then brought indoors and contributes to air pollution [23].

Long-term exposure to air pollutants increases not only the frequency but also the severity of allergic rhinitis. A study of 1,408 rhinitis patients in Europe reported that long-term exposure to fine particulate matter was associated with an adjusted odds ratio (OR) (95% confidential interval [CI]) of 1.20 (0.88–1.64) for mild, 1.53 (1.07–2.19) for moderate, and 1.72 (1.23–2.41) for severe allergic rhinitis, suggesting that long-term exposure to fine particulate matter has a significant impact on allergic rhinitis severity [24]. In children, meta-analyses have also confirmed an increased prevalence of allergic rhinitis with nitrogen

Table 1. Epidemiologic studies with regard to air pollution on respiratory diseases including allergic rhinitis and asthma

Study	Design	Air pollutants	Subjects	Description
Heinrich *et al.*, 2002 [17]	Prospective, cross-sectional survey	TSP, SO_2	7,632 children	The prevalence of non-allergic respiratory symptoms was decreased, along with improvements in air pollutants
Wouters *et al.*, 2002 [18]	Comparative, cross-sectional study	Organic dust	36 waste collectors and 11 controls	Waste collectors revealed increased upper airway inflammation and manifestations compared with controls.
Zhang *et al.*, 2011 [19]	Time-series study by biomedical big data analysis	PM_{10}, SO_2, NO_2	1,506 AR patients	There were strong associations between the daily concentration of air pollutants and the daily number of outpatients for AR.
Wang *et al.*, 2020 [20]	Time-series study by biomedical big data and 4 hospital data sets	$PM_{2.5}$, PM_{10}, SO_2, NO_2, O_3, CO	14,965 AR patients	Exposure to air pollutants was associated with increased AR risks and children might be more vulnerable.
Morand *et al.*, 2010 [21]	Objective, cross-sectional study	Benzene, VOC, SO_2, PM_{10}, NO_2, CO	4,907 children	There was an association between urban air pollution and childhood asthma and allergies.
Jeong *et al.*, 2011 [16]	Comparative, cross-sectional study	CO, CO_2, O_3, NO_2, PM_{10}, $PM_{2.5}$, formaldehyde, VOC, HDM, endotoxins	1,226 students from Incheon and 1,748 students from Jeju City	The children in Incheon, an industrialized area, had a high rate of AR and asthma symptoms compared to children in Jeju City, a non-industrialized area.
Burte *et al.*, 2020 [24]	Cross-sectional study from 2 European cohorts	NO_2, PM_{10}, $PM_{2.5}$, PMcoarse	1,408 adults with rhinitis	Rhinitis patients living in higher levels of pollution had more severe nasal symptoms.
Bedard *et al.*, 2020 [25]	Investigative study by using a mobile app	O_3, $PM_{2.5}$	36,440 VAS person-day (3,323 users)	There was a strong interaction between air pollutants and rhinitis symptoms during the grass pollen season.

Abbreviations: TSP, total suspended particulates; SO_2, sulfur dioxide; PM_{10}, particulate matter; NO_2, nitrogen dioxide; AR, allergic rhinitis; $PM_{2.5}$, fine particulate matter; O_3, ozone; CO, carbon monoxide; VOC, volatile organic compounds; HDM, house dust mite; VAS, visual analog scale.

dioxide, sulfur dioxide, fine particulate matter, and ultrafine particulate matter irritants, with regional differences in the association of sulfur dioxide and fine particulate matter in Asia compared to Europe [3]. This may be explained by the fact that allergic rhinitis is often comorbid with atopy and asthma, as well as host factors such as ethnicity and genetics, in addition to environmental factors.

A recent study on the relationship between air pollution and pollen season in allergic rhinitis was published using mobile application technology [25]. Using new mobile technology and computer learning techniques, the study analyzed different air pollutants and seasonal factors in terms of symptoms and quality of life and demonstrated a strong association between uncontrolled rhinitis and pollutants during the grass pollen season. There is also a large-scale project called POLLAR (Impact of air POLLution on sleep, Asthma, and Rhinitis) run by the European Institute of Innovation and Technology Health [26], which uses geographical information on air pollution in Europe to report on the relationship between air pollution, sleep, and allergic rhinitis using a mobile app and machine learning techniques. By combining air pollution, sleep, and allergy symptoms, new treatment guidelines can be proposed, cross-national networks can be established, and ultimately the interaction between air pollution and allergic rhinitis can be systematically evaluated. These studies suggest new directions for future research in allergic immune diseases such as asthma and atopy, including allergic rhinitis.

2.3. Traffic-related air pollution (TRAP) and allergic rhinitis

Poor air quality due to automobile exhaust can adversely affect allergic diseases such as allergic rhinitis, atopic dermatitis, and asthma. Min *et al.* statistically analyzed the risk of allergic rhinitis, atopic dermatitis, and asthma due to nitrogen dioxide, fine particulate matter, and ultrafine particulate matter irritation from automobile exhaust in 14,614 children living on the fourth floor or below, near major roads in Seoul [27]. Among them, the association of automobile exhaust with atopic dermatitis was high, and when examined by pollutant, nitrogen dioxide (OR, 1.07; 95% CI, 1.02–1.13) and fine particulate matter (OR, 1.08; 95% CI, 1.03–1.14) were statistically significant for atopic dermatitis symptoms and diagnosis, while ultrafine particulate matter (OR, 1.01; 95% CI, 0.95–1.07) was not statistically significant for atopic dermatitis. For allergic rhinitis, there was a marginal but not statistically significant association with fine particulate matter. Meanwhile, a multicenter study of 5,334 school-aged children in Korea found that air pollution near major roads was associated with higher diagnoses of asthma and allergic rhinitis, allergic sensitization, and lower lung function in school-aged children [28]. In particular, proximity to major roads was inversely associated with forced expiratory volume in 1 second (FEV1), FEV1/forced vital capacity, and FEF25%–75% (forced expiratory flow from 25% to 75% of the vital capacity) in lung function, confirming the role of motor vehicle exhaust-induced air pollution in pediatric lung function. In addition, a study of 484 children and adolescents aged 9–19 years with asthma and allergic rhinitis demonstrated an additive effect of fine particulate matter (OR, 1.83; 95% CI, 1.33–2.52) and black carbon (OR, 1.80; 95% CI, 1.22–2.66), the most common pollutant in vehicle exhaust, suggesting that the risk of allergic rhinitis increases with heavy traffic [29].

On the other hand, other studies have reported a lesser role for vehicle emissions in allergic rhinitis. A review of six cohort studies of motor vehicle exhaust-induced air pollution in pediatric allergic rhinitis found an odds ratio of 1.37 (95% CI, 1.01–1.86) for fine particulate matter. However, the role of motor vehicle exhaust in allergic rhinitis was minimal and did not increase prevalence, emphasizing host rather than environmental factors, as minor variants in genes involved in inflammation and oxidative stress metabolism are associated with a higher risk of allergic rhinitis [30]. In a study of the association between traffic congestion and allergic diseases in 2,000 adults in Sweden [31], higher exposure to vehicle exhaust was associated with a higher prevalence of allergic rhinitis and allergic asthma, but not with non-allergic rhinitis, suggesting that the role of exhaust exposure is not the same in all asthma and rhinitis.

3. How air pollutants worsen allergic rhinitis

Allergic rhinitis is a complex mechanism that is influenced not only by environmental factors such as air pollution and seasonal influences but also by epigenetics, with different transcriptomes expressed by different genotypes, resulting in different immune cell and mucosal immune responses. Recently, it has been hypothesized that air pollutants accumulate oxidative stress in tissues, triggers tissue inflammatory responses and apoptosis, and ultimately lead to the development of allergic rhinitis [8]. The non-IgE-mediated inflammatory response induced by air pollutants is first divided into a non-inflammatory phase and an inflammatory phase. In the non-inflammatory phase, reactive oxygen species are produced by air pollutants, which are metabolized and neutralized through redox reactions by the body's own antioxidant mechanisms (glutathione, superoxide dismutase). However, when the number of free radicals is increased and cannot be processed by its own sulfur oxidation mechanism, antioxidant enzymes such as heme oxygenase 1 (HO-

1) and glutathione S-transferase are newly produced. The antioxidant response element gene is involved, and transcription factors such as nuclear factor erythroid 2-related factor 2 (Nrf2), activator protein 1, and nuclear factor-kappa B are involved. Free radicals are neutralized by antioxidation, but when this threshold is exceeded, an inflammatory response is triggered by oxidative stress. Subsequently, inflammatory cells are recruited and the IgE-mediated immune response is activated, leading to exacerbation of allergic rhinitis. This immune response may vary depending on the air pollutant, but it is thought to involve more Th1/Th17 inflammatory responses than Th2 inflammatory responses. Gao *et al.* found decreased lung function and increased systemic inflammation in patients with chronic obstructive pulmonary disease (COPD) after stimulation with fine particulate matter, nitrogen dioxide, and carbon monoxide [32]. Serum levels of inflammatory factors after air pollutant stimulation were found to be elevated in the type 1 response factors interleukin (IL)-2, IL-12, interferon-γ (IFN-γ), and IL-17A, while the type 2 factors IL-4, IL-13, and eotaxin were not significantly changed. Eguiluz-Gracia *et al.* studied changes in mucosal innate and adaptive immunity after stimulation by cigarette smoke and air pollutants and demonstrated that cigarette smoke alters the mucosal microbiome, leading to biofilm formation by *Staphylococcus aureus* and worsening mucociliary transport [33]. Upon external stimulation by fine particulate matter, the airway mucosa expresses NLRP3 (nucleotide-biding domain, leucine-rich repeat protein 3), an inflammasome that secretes the CXCL1 chemokine to recruit neutrophils in the blood. Meanwhile, upon black carbon stimulation, IL-4 is produced via demethylation in the mucosa, which reacts with basophils and Th2 and B cells in the mucosa, resulting in increased local IgE production (**Figure 1**).

Hong *et al.* reported that *in vitro* experiments using human nasal epithelial cell lines confirmed that ultrafine particles induce oxidative stress and inflammatory responses, which may ultimately lead to intranasal inflammatory disease [34]. This suggests that ultrafine particles are cytotoxic by inhibiting cell growth and nasal epithelial barrier function, resulting in cellular injury. Cho *et al.* summarized the protective role of Nrf2 in diseases such as acute lung injury/acute respiratory distress syndrome, chronic

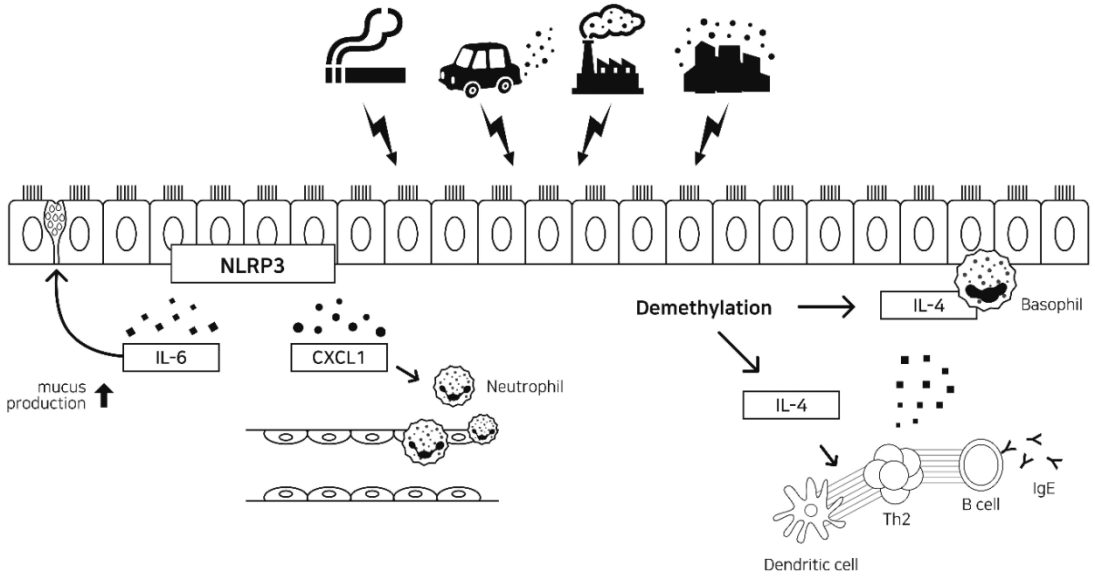

Figure 1. Innate and adaptive immune responses by outdoor air pollution on the respiratory epithelium. NLRP3, nucleotide-biding domain, leucine-rich repeat protein 3; IL, interleukin. Modified from Eguiluz-Gracia *et al.* Allergy 2020; 75: 2170–2184 [33], with permission of Wiley.

obstructive pulmonary disease, asthma, infection, and lung cancer using experimental models of oxidative stress and human studies [35]. On the other hand, pollen exposure has been shown to attenuate innate immunity against respiratory viruses, and Gilles *et al.* synthesized mouse models, cellular experiments, and big data cohort analyses to investigate changes following respiratory syncytial virus and birch pollen stimulation in allergic rhinitis [36]. In animal and *in vitro* studies, viral and pollen stimulation lowered IFN-γ and increased viral activity and a cohort analysis of 20,062 people confirmed a positive association between birch pollen and respiratory syncytial virus, suggesting that people at risk of allergic rhinitis should avoid outdoor activities during periods of coincident pollen and respiratory virus epidemics. In addition, studies have shown that nasal congestion to non-specific stimuli such as chlorine gas is relatively greater in patients with allergic rhinitis than in patients with non-allergic rhinitis [37], which is consistent with previous epidemiological studies showing that the response to air pollutants is relatively greater in allergic rhinitis. In addition, measurements of immune response factors in sputum from normal individuals and atopic asthmatics after ozone stimulation revealed a decreased ozone-induced response in normal individuals and an increased oxidative stress-induced immune factor response in asthmatics, suggesting a mechanism by which individuals with an allergic predisposition may be more sensitive to air pollutants [38].

4. Diagnosis and treatment

4.1. Diagnosis of allergic rhinitis

The diagnosis of allergic rhinitis is made by taking a history of allergic nasal and ocular symptoms, as well as a physical examination for comorbidities such as turbinate enlargement, septal curvature in adults, and adenoid hypertrophy in children. However, because allergic rhinitis symptoms are often non-specific, it is difficult to identify air pollution-induced allergic rhinitis based on history and physical examination alone [8]. Therefore, in addition to history and physical examination, objective confirmation of IgE-mediated hypersensitivity is required, which can be achieved by serological or skin prick testing. *In vitro* tests commonly performed in clinical practice include serum total IgE, radioallergosorbent test (RAST), multiple allergens simultaneous test (MAST), immunoCAP system and blood eosinophil and eosinophil cationic protein tests, and nasal cytology. *In vivo* tests can be broadly divided into skin prick tests and provocation tests. Among them, skin prick tests and intradermal tests are basic, economical, and highly diagnostic clinical tests that can identify the causative antigen, although they are invasive. However, there are no specific tests for air pollutants used in clinical practice to diagnose allergic rhinitis [8].

4.2. General treatment of allergic rhinitis

The general treatment of allergic rhinitis is based on the recommendations of the Allergic Rhinitis and its Impact on Asthma (ARIA) guideline, depending on severity and duration. The ARIA guidelines classify allergic rhinitis as intermittent or persistent based on the duration of asymptomatic symptoms and as mild or moderate-severe based on whether it interferes with sleep or daily activities [39]. The mainstay of pharmacological treatment in clinical practice for allergic rhinitis is topical steroids and oral antihistamines, supplemented by vasoconstrictors, anticholinergics, leukotriene modulators, mast cell stabilizers, and topical antihistamines. Topical steroids are the single agent with the least systemic absorption and the most effective symptom control with minimal side effects when used at appropriate doses. They work by inhibiting the recruitment of inflammatory cells such as eosinophils, neutrophils, and lymphocytes to the site of antigenic stimulation by modifying the genes for proinflammatory cytokines, which reduces the number of T-cells in the blood and inhibits their

activation but have the disadvantage of being slow acting [40]. Oral antihistamines control itching, sneezing, and rhinorrhea by inhibiting histamine secretion, thereby reducing vasodilation and permeability and reducing irritation to the nasal mucosal extremities. Vasoconstrictors work by acting on sympathetic nerve receptors to constrict nasal blood vessels to improve nasal congestion. Vasoconstrictors are classified as oral and topical agents, and while mucosal constriction is stronger with topical agents, prolonged use can lead to irreversible chronic rhinitis, including drug-induced rhinitis [41]. Anticholinergics bind to acetylcholine receptors and inhibit the action of acetylcholine, making them effective in reducing rhinorrhea, while leukotriene modulators inhibit leukotrienes, which are important inflammatory mediators in allergic inflammatory reactions and are metabolites of arachidonic acid. Leukotriene modulators are clinically effective in improving nasal congestion and are known to be helpful in cases of concomitant asthma [42]. Mast cell stabilizers stabilize the cell membrane of mast cells to inhibit the release of chemical mediators and are clinically used as prophylactic agents and can be used before allergic exposure to reduce allergy symptoms [43]. Topical antihistamines block histamine receptors in the nasal mucosa and are characterized by their anti-inflammatory properties and rapid clinical effect.

ARIA Pharmacy 2018 reviewed the role of self-care, over-the-counter medicines, pharmacies, and pharmacists in allergic rhinitis [44]. Although there are differences between countries, oral antihistamines and topical steroids are widely used as OTC medications, with oral antihistamines being more popular in terms of patient preference, but topical steroids being more popular in terms of overall effectiveness. If the visual analog scale (VAS) is 50 or less, oral antihistamines should be considered first, and if the VAS is 50 or more, topical steroids should be used, but if the VAS persists above 50 after 10 days of use, it is recommended to see a doctor.

4.3. Treatment of allergic rhinitis exacerbated by air pollution

For allergic rhinitis exacerbated by air pollution, personal avoidance of airborne allergens such as cigarette smoke, mold, carbon monoxide, nitrogen dioxide, sulfur dioxide, fine particulate matter, and diesel particles is the most important treatment [45]. During pollen season, it is recommended to close windows and avoid outdoor activities such as parks, and during rush hour, when heating and increased traffic increase the amount of fine particulate matter and worsen air quality. Reducing outdoor activity in the afternoons in summer, when ozone levels are at their highest, can help reduce irritation from air pollutants, and shift work, wearing personal protective equipment, or adjusting work hours can also be a way to avoid exposure. It is also recommended to avoid touching your eyes with your hands and wear glasses instead of contact lenses during periods of high particulate matter, as dry autumn and winter weather can irritate your eyes. On the other hand, indoor pollution can irritate the upper respiratory tract and increase airway hyperresponsiveness, causing asymptomatic symptoms, so it is important to reduce indoor pollutants as much as possible, ensure adequate ventilation, and ban indoor smoking. Whilst it is not practical to completely avoid exposure to indoor antigens, it can help to alleviate allergy symptoms and reduce the use of medication. However, there are no tests or specific treatments to distinguish allergic rhinitis exacerbated by air pollution, so patient and caregiver education on these avoidance strategies may be helpful. Specific avoidance techniques and tips for responding to air pollution are described in more detail in a later section (Tips for Responding to High Concentrations of Fine Particulate Matter or Air Pollution).

Nevertheless, there are not many studies on the effectiveness of specific medications in allergic rhinitis exacerbated by air pollution. One study reported the efficacy and safety of fexofenadine (Allegra), a second-generation antihistamine, in ragweed-induced allergic

rhinitis caused by diesel gas particles, and found that the degree of asymptomatic improvement after diesel gas particles and ragweed stimulation was superior in the fexofenadine-treated group compared with the placebo group [8]. Future studies should investigate the clinical implications of different air pollutants and exposure methods. For example, pollutants from different car engines produce different levels of particulate matter and gaseous components, each of which may have different clinical effects [46]. It would also be interesting to determine the severity of allergic rhinitis caused by individual pollutants, such as ozone, nitrogen dioxide, and diesel particles, using a chamber that simultaneously stimulates air pollutants and allergens. In addition, basic research is needed to determine how the increased oxidative stress in allergic rhinitis is changed by various drug treatments after stimulation with various air pollutants, and how this can be applied to clinical treatment.

5. Other measures

Disposable masks should be used as regular masks are less effective at filtering out fine particles and their effectiveness decreases when washed. Health masks that have been proven to be effective by the Korean Ministry of Food and Drug Safety (MFDS) should be used, with a KF of 80 or higher to block air allergens such as fine dust, and a KF of 94 or higher to block infectious diseases. According to data from the Korea Health Insurance Review and Assessment Service and the National Health Insurance Service, the medical environment has been changing since the early 2020s, when masks and handwashing were emphasized due to warnings about COVID-19 in Korea. In March-July 2020, the period of pollen dispersal, medical expenses decreased by 45.6% and 67.3% in otolaryngology and pediatrics, respectively, but increased by 12.9% in psychiatry, which deals with allergic diseases and upper respiratory tract infections, compared to the same period last year. By disease, allergic rhinitis decreased by 52.6% in March 2020 compared to March 2019 in terms of the number of patients, according to data from the Korea Health Insurance Review and Assessment Service. Influenza, acute upper respiratory tract infection, and pneumonia decreased by 98%, 50.4%, and 60.9%, respectively, but mood disorders such as depression increased by 7.1%. This suggests that wearing a mask and handwashing are important preventive measures for allergic rhinitis, upper respiratory tract infections, and respiratory illnesses. To avoid irritation from air pollutants, it is important to wear a mask correctly, which should be worn with the fixed part upwards to completely cover the nose and mouth, using both hands to press the clip so that the nose piece fits closely to the nose, and wrapping the entire mask to prevent air leakage.

Due to the harmful effects of air pollution, air purifiers have received increasing attention in recent years. Air purifiers are classified according to the size of dust that can be removed and the dust removal rate: semi-high-efficiency particulate air (semi-HEPA filter E10-12), high-efficiency particulate air (HEPA filter H13, 14), and ultra-low penetration air (ULPA filter U15-17), and the higher the number, the better the dust collection efficiency (**Table 2**). The HEPA filter blocks fine dust down to 0.3 μm, so it is widely used as an air filter in general air purifiers, vacuum cleaners, and air conditioners, while the ULPA filter is composed of more complex fibers and can filter out harmful substances down to 0.1 μm, and is mainly used in aseptic laboratories, hospital operating rooms, and semiconductor laboratories. Generally, filters above H13 have a dust collection efficiency of more than 99.95%, which can filter out automobile exhaust, bacteria, molds, viruses, and fine dust. Park *et al.* reported the role of indoor air purifiers in allergic rhinitis by confirming that the use of HEPA filters reduced medication uses in house dust mite-induced allergic rhinitis and significantly reduced particulate matter concentrations regardless of location in the room in a multi-center randomized double-blind study

Table 2. The classification for rating the efficiencies of HEPA and ULPA filters

Filter class	Filter type	Percentage (%) based on MPPS	
		Efficiency	Penetration
E10	Semi-HEPA	≥ 85	15
E11	Semi-HEPA	≥ 95	5
E12	Semi-HEPA	≥ 99.5	0.5
H13	HEPA	≥ 99.95	0.05
H14	HEPA	≥ 99.995	0.005
U15	ULPA	≥ 99.9995	0.0005
U16	ULPA	≥ 99.99995	0.00005
U17	ULPA	≥ 99.999995	0.000005

Abbreviations: HEPA, high-efficiency particulate air; ULPA, ultra-low penetration air; MPPS, most penetrating particle size.

[47]. A randomized, double-blind study of 90 patients with Artemisia pollen-induced allergic rhinitis found a significant improvement in allergy symptom scores after a room air purifier [48].

6. Tips for dealing with high concentrations of fine particulate matter or air pollution

(1) Avoid going outdoors as much as possible and minimize outdoor activities such as outdoor gatherings and sports activities;
(2) Wear a KFDA-certified face mask (KF 80 or higher) correctly when going out;
(3) Avoid areas with high air pollution and reduce your activity level when going out. Reduce delays at roadsides, construction sites, etc. with high concentrations of fine dust and reduce strenuous outdoor activities;
(4) Wash hands, feet, eyes, and nose thoroughly with running water and gargle after going outside;
(5) Maintain indoor air quality, including proper ventilation and water cleaning, and run air purifiers as needed. Check and replace air purifier filters regularly;
(6) Minimize activities that contribute to air pollution by using public transport instead of driving and avoiding open burning of waste.

7. Conclusion

Air pollutants affect the upper and lower respiratory tract and are a risk factor for allergic rhinitis. Immunologically, air pollutant-induced reactive oxygen species formation and associated oxidative stress, tissue inflammatory response, and cell death are important mechanisms in allergic rhinitis. The various epidemiological and clinical studies described in this review confirm that air pollutants exacerbate allergic rhinitis and airway disease. As a clinician, understanding these implications of air pollution for allergic rhinitis can be of practical help in implementing effective care at the point of care.

Disclosure statement

The authors declare no conflict of interest.

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