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The Impact of Air Pollution on Atopic Dermatitis. Literature review

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Abstract

Introduction and purpose

The rising level of air pollution is currently a serious worldwide problem. Airborne pollutants, such as PM, O3, CO, NOx, SO_2, and heavy metals, negatively impact the entire body, contributing to the dysfunction of many systems. The aim of this study was to review the literature on the impact of selected air pollutants on the development or exacerbation of atopic dermatitis, and to elucidate the mechanisms responsible for this.

Materials and methods

The literature available in PubMed and Google Scholar databases was reviewed using the keywords: “air pollution”, “atopic dermatitis”, “skin lesions”.

Description of the state of knowledge

Available studies have provided information on the significant impact of air pollution on the development and exacerbation of atopic dermatitis. Air pollutants can induce skin changes through various mechanisms, such as damage to the epidermal barrier, disruption of skin microflora, oxidative stress, initiation of inflammatory responses, or activation of the aryl hydrocarbon receptor pathway.

Conclusions

Reducing air pollution is crucial for improving overall public health and decreasing the incidence of many diseases, including atopic dermatitis. Further research is needed to deepen the understanding of the relationship between air pollution and atopic dermatitis, as well as the mechanisms responsible for it, and to develop effective strategies for protecting the skin from pollutants.

Keywords: “air pollution”, “atopic dermatitis”, “skin lesions”

INTRODUCTION AND OBJECTIVE

Air pollution has been recognized by WHO as the largest environmental health threat in Europe. [1,2] The increasing presence of particulate matter, nitrogen dioxide, carbon monoxide, and sulfur dioxide, as well as ozone in the air, is causing higher morbidity rates, particularly in cardiovascular and respiratory diseases, and contributes to the premature death of many people worldwide. These compounds also contribute to the development and exacerbate the course of many skin diseases. [3,4] In recent years, a link between air pollution and the occurrence of acne, atopic dermatitis, or psoriasis has been demonstrated. [5,6] Atopic dermatitis is the most common chronic inflammatory skin disease with a recurrent course, characterized by the presence of typical eczema-like skin lesions and intense itching.[7] The rising level of air pollution, as well as the increasing number of patients struggling with atopic dermatitis [8,9,10] have contributed to the conduct of numerous studies in recent years. Therefore, due to the current relevance and prevalence of the problem, the aim of this study was to review the available literature indicating the existence of a relationship between environmental pollution and the occurrence or exacerbation of atopic dermatitis, and to elucidate the mechanisms

underlying this process.

DESCRIPTION OF THE STATE OF KNOWLEDGE

Atopic dermatitis is one of the most common skin diseases characterized by recurrent skin lesions in typical locations with accompanying itching. This dermatosis is most commonly diagnosed in childhood, and predisposing factors include genetic factors, dysfunction of the epidermal barrier, changes in the microbiome, immune system dysregulation, and environmental factors. [7,11] Increasing research indicates a significant role of air pollution in the development and exacerbation of atopic dermatitis in both children and adults.

A study conducted in Chongqing, which collected data on 214,747 children with atopic dermatitis from January 1, 2015, to December 31, 2019, showed that an increase in PM2.5, PM10, SO2, NO2, and CO concentrations contributed to an increase in outpatient consultations among children with atopic dermatitis. Additionally, the relationship between air pollution and atopic dermatitis was stronger in the autumn-winter period and in the age group of 0-3 years.[12] Similar conclusions were reached by researchers from Guangzhou, China, who assessed the short-term impact of air pollution on daily hospital visits due to atopic dermatitis. [13]

A cohort study based on data from the UK Biobank, focusing on the analysis of the relationship between air pollution and genetic risk with the occurrence of atopic dermatitis in older adults aged 40-70, showed that exposure to air pollution had a more significant impact on the development of atopic dermatitis than genetic factors and that air pollution affects the development of atopic dermatitis in older adults regardless of genetic susceptibility. Additionally, the effects of exposure were stronger in women than in men. [14]

Data from a study conducted in Shanghai from January 2013 to December 2018, which included 34,633 patients, revealed that increased concentrations of air pollutants, except ozone (O3), contribute to an increased risk of atopic dermatitis. An increase in sulfur dioxide (SO2) and nitrogen dioxide (NO2) concentrations by 10 μg/m3 was associated with an increase in outpatient visits by 6.03% and 1.96%, respectively. Moreover, researchers showed that patients aged 0 to 7 years were most susceptible to the development of atopic dermatitis in the course of air pollution. It was also found that women are more susceptible to air pollution and that the adverse effects of SO2 and NO2 on the development of atopic dermatitis can be significantly enhanced by warm weather or other pollutants. [15]

The skin, being the largest organ of the human body, plays a crucial role as a protective barrier against harmful external factors. However, prolonged exposure to environmental pollutants can cause dysfunction of this organ and lead to the development of many skin diseases. Several mechanisms have been identified through which environmental pollution can contribute to the development and exacerbation of atopic dermatitis, including damage to the epidermal barrier, disruption of skin microflora, oxidative stress, initiation of inflammatory responses, and activation of the aryl hydrocarbon receptor pathway.

The skin serves as the first line of defense against air pollution, and changes in its microflora can cause increased susceptibility to allergies, promoting the development of atopic dermatitis. [16] A study conducted in Shanghai (China) showed that air pollutants from heavy traffic can weaken the physical properties and antioxidant barrier of the skin and contribute to the development of skin dysbiosis. Additionally, it was shown that smoking further enhances the harmful effects of air pollution on the microbiome and skin. [17,18] Another study

investigating the harmful effects of NO2 on selected commensal bacterial strains of the skin showed that exposure to NO2 can contribute to the development of dysbiosis.
It was noted that the effects of the substance vary depending on the bacterial species and NO2 concentration. Very harmful effects of NO2 were observed, particularly in the case of S. capitis MFP08 and C. tuberculostearicum CIP102622, while S. aureus MFP03 appeared to be a less sensitive strain. [19] Prolonged exposure to polycyclic aromatic hydrocarbons (PAHs) can also have a negative impact on skin microflora. [20]
An intact epidermal barrier plays a key role in limiting the penetration of allergens and infectious agents and preventing transepidermal water loss (TEWL). [21] Assessment of the epidermal barrier includes measuring TEWL, thus providing information about its permeability under various conditions. When the epidermal barrier is intact, the TEWL level is low, while in the case of its damage, the TEWL value is significantly elevated, as observed in patients exposed to acute contact with surrounding NO2 and formaldehyde.[7, 22,23]
It has also been observed that exposure to particulate matter contained in air pollution impairs the protective function of the skin by reducing the expression of E-cadherin, which plays an important role in epithelial cell adhesion, as well as other structural proteins found in the stratum corneum, such as cytokeratin and filaggrin.[24] Furthermore, oxidative stress can damage the epidermal barrier, promoting the colonization of the skin by microorganisms. Microbial colonization facilitates the penetration of microbial agents through the skin, leading to subsequent IgE sensitization, as demonstrated in a study comparing TEWL among patients infected with S. aureus and patients with atopic dermatitis without the presence of S. aureus. The results showed that TEWL was significantly higher among patients infected with S. aureus and that TEWL increased with bacterial load.[25] Considering the crucial role of an intact epidermal barrier, it seems important to strengthen its function through moisturizing the skin and using emollients, which currently form the basis of atopic dermatitis therapy.[26,27]
Similar to other chronic inflammatory diseases, oxidative stress plays an important pathogenic role in the development of atopic dermatitis (AD). [10] Many compounds present in air pollutants, such as nitrogen oxides, O3, and polycyclic aromatic hydrocarbons (PAHs), exhibit pro-oxidative effects. The resulting free radicals induce oxidative damage to proteins in the stratum corneum, leading to a disruption of barrier functions and exacerbation of AD. Oxidative stress can be measured by assessing biomarkers such as malondialdehyde (MDA), 8-hydroxydeoxyguanosine (8-OHdG), nitrites/nitrates, and selenium in urine and serum. Numerous studies have shown that these markers positively correlate with the severity of skin symptoms. Additionally, lower levels of antioxidant vitamins A, C, and E have been observed in the serum of patients with eczema. [28,43,44] It has also been found that the skin of patients with AD is more susceptible to damage caused by reactive oxygen species compared to a control group with intact epidermal barriers. [29,30] Inflammation and oxidative stress are interrelated. In response to pro-oxidative compounds found in polluted air, lipid peroxidation in the skin occurs, which in turn induces the release of pro-inflammatory mediators, including IL-33, IL-6, and IL-8, and stimulates the inflammatory response through the activation of various pathways, such as the NF-κB pathway and the NOD-like receptor protein 3 (NLRP3) inflammasome, contributing to the development of skin inflammation. [28] NF-κB also plays a key role in the activation and differentiation of innate immune cells and T lymphocytes. [21,

31]

Furthermore, exposure to particulate matter PM 2.5 has been shown to significantly increase the expression of genes related to Th1, Th2, Th17, and Th22 cells, as well as the aryl hydrocarbon receptor (AhR) pathway and genes related to the epidermal barrier (e.g., SPRR2A and KRT71). [32]

In recent years, increasing attention has been given to the impact of environmental pollutants on the signaling system of the nuclear translocator of the aryl hydrocarbon receptor. PAHs, which are significant components of exhaust fumes, can diffuse through the stratum corneum and activate the AhR receptor [24], influencing the transcription of CYP1A1, whose increased expression enhances the production of ROS, pro-inflammatory cytokines such as interleukin (IL)-1, IL-6, and IL-8, and causes various genetic material damage. [11, 33,34] Studies also indicate an important role of the receptor in immune mechanisms, particularly in the maturation of Th17/22 and Treg cells. [34] Growing knowledge about the molecular mechanisms underlying AD has enabled the development of new treatment strategies. Recent studies have demonstrated the therapeutic benefits of topical Tapinarof in the treatment of AD. Tapinarof is a selective AhR agonist, which, due to its ROS-scavenging structure, exhibits strong antioxidant effects. Moreover, it induces gene expression that leads to reduced skin inflammation and participates in the normalization of the epidermal barrier by increasing the expression of proteins such as filaggrin, loricrin, and involucrin. [28,34,35,36]

Tobacco smoke and heavy metals can also increase the risk of developing AD. [45, 46,47] The Children's Health and Environment Research study conducted among 7,030 children aged 6-13 years in Korea revealed a strong correlation between the risk of developing AD and the presence of tobacco smoke, especially among children whose mothers smoked during pregnancy and/or in the first year after birth. [37] Another study conducted in Germany, which analyzed the expression of different numbers of T-reg cells and miRNAs in maternal and umbilical cord blood during pregnancy, found that maternal smoking during pregnancy was associated with higher expression of miR-233 and fewer regulatory T lymphocytes in maternal and umbilical cord blood, and children with fewer T-reg cells were more likely to develop AD within the first three years of life. [38] The exact mechanism explaining the relationship between smoking and increased susceptibility to atopic dermatitis remains unclear. It has been shown that cigarette smoke increases the production of numerous pro-inflammatory cytokines, such as IL-1, IL-6, IL-8, and GM-CSF, while reducing the levels of anti-inflammatory cytokines, such as IL-10. [48] Furthermore, significant increases in the synthesis and release of TNF-α have been observed following exposure to tobacco smoke. [49] The overproduction of TNF-α impairs the skin barrier function and leads to the development of inflammatory skin diseases by modulating the skin's lipid properties, reducing saturated free fatty acids ≥ C20:0, and decreasing the expression of the ELOVL1 protein. [45] Additionally, it has been demonstrated that serum IgE levels are significantly higher in smokers than in non-smokers. [48,50] A study examining the relationship between heavy metal concentrations and AD symptoms in children aged 4 to 13 years showed that airborne lead could be associated with AD symptoms even if recorded lead concentrations in the air were below the reference level suggested in guidelines. [39] Another

study, which evaluated the concentration of heavy metals in mothers' blood and in umbilical cord blood, confirmed the hypothesis that exposure to cadmium or manganese may affect the development of eczema, as well as other atopic diseases, such as asthma or food allergies. [40]

It has been shown that skin exposure to nickel can influence local immune activity by stimulating both Th1 and Th2 cytokine responses. [41] Additionally, exposure to nickel can contribute to the degradation of filaggrin, a principal epidermal barrier protein. One study confirmed the susceptibility of filaggrin peptides to hydrolysis and pH-dependent cleavage facilitated by Ni 2+, which may be associated with multiple allergic manifestations, including atopic dermatitis and contact allergy to nickel. [42]

SUMMARY

Air pollution is currently a significant public health issue, causing negative effects on the human body. Clinical studies confirm a positive correlation between exposure to atmospheric air pollutants and the occurrence or exacerbation of AD, and the continuous increase in the incidence of this dermatosis underscores the important role of environmental factors in its pathogenesis. Further research focusing on understanding the exact pathomechanisms, such as AhR pathway activation, promotion of oxidative stress, skin barrier damage, and initiation of the pro-inflammatory response, is essential for developing effective treatment strategies. However, it is undeniable that the most effective way to improve overall public health would be to reduce air pollution through coordinated global actions.

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The data presented in this study is available upon request from the corresponding author.

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Conflict of Interest Statement
All authors declare that they have no conflicts of interest.

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