CEO Clinical and Experimental Otorhinolaryngology Vol. 14, No. 4: 365-366, November 2021 https://doi.org/10.21053/ceo.2021.02054
pISSN 1976-8710 eISSN 2005-0720

Editorial

Does Particulate Matter Really Affect Sinusitis?

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Sinusitis is caused by many risk factors, such as smoking, colds, age, allergens, and air pollutants. Mortality from chronic respiratory diseases has increased from 1990 to 2017; this change is closely correlated with industrialization and urbanization [1], which are social changes that have resulted in outdoor and indoor air pollution. According to the U.S. Environmental Protection Agency, the most common and hazardous air pollutants are particulate matter (PM), ozone, sulfur dioxide, nitrogen dioxide, lead, and carbon monoxide. In particular, PM contributes to several major diseases, such as cardiovascular and circulatory diseases, chronic respiratory diseases, and cancer [2].

It is well known that PM affects the lower respiratory tract. Short-term exposure to PM is highly associated with increased hospitalizations for chronic obstructive pulmonary disease, asthma, and pneumonia [3]. *In vitro* studies have reported that exposure to PM induced interleukin (IL)-6 production by alveolar macrophages and tumor necrosis factor-alpha, IL-1β, granulocyte-macrophage colony-stimulating factor, and IL-8 by bronchial epithelial cells [4,5]. Several *in vivo* studies have also demonstrated the effect of PM on the lungs. For example, Brandt et al. [6] exposed mice to diesel exhaust particles (DEPs) with house dust mites (HDM) for 3 weeks. DEPs with HDM caused T_H2/T_H17 responses, eosinophil and neutrophil infiltration, mucus hypersecretion, and airway hyperresponsiveness, which are characteristics of severe asthma.

• Received November 3, 2021
Accepted November 4, 2021

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The impact of PM on the upper airway is similar to its impact on the lower airway. Although some epidemiological studies have reported inconsistent findings regarding correlations between PM and sinusitis [7], a recent case-control study demonstrated that $PM_{2.5}$ exposure showed a significant association with chronic rhinosinusitis (CRS) diagnosis. The authors in this study investigated 2,034 non-allergic CRS patients and 4,068 controls and recorded exposure levels up to 60 months before the date of diagnosis [8]. They divided the patients into maxillary, frontal, ethmoidal, sphenoidal, and severe (presence in all four sinuses) sinusitis. The odds ratio (OR) was particularly high for ethmoidal sinusitis, as the ethmoid sinuses have the widest area for contact with air. The OR for severe sinusitis progressively increased and peaked at 36 months (OR, 7.91) [8]. These results furnish strong evidence that long-term exposure to PM affects the likelihood of being diagnosed with CRS.

PM induces epithelial barrier dysfunction, leading to the pathogenesis of CRS. PM exposure in human nasal epithelial cells reduced transepithelial electrical resistance and the expression of tight junction proteins. Because many air pollutants produce reactive oxygen species, the authors activated an antioxidant transcription factor, nuclear factor-E2 p45-related factor 2 (Nrf2). Nrf2 effectively restored epithelial barrier function [9]. Furthermore, DEPs induce the epithelial-to-mesenchymal transition (EMT), which is a process involving the loss of epithelial polarity and junctional proteins [10]. PM-induced EMT could even influence the development of nasal polyps, the most severe type of CRS. In mice exposed to DEPs and HDM intranasally or through a nose-only inhalation system for 8 weeks (before that, HDM was administrated for sensitization and maintenance of inflammation), it was found that DEPs with HDM significantly increased nasal polyp numbers and epithelial disruption. The authors found the zinc finger E-box-binding homeobox 2

(ZEB2) protein is the key factor in DEP-mediated EMT [10]. This study demonstrated that PM participates in nasal polyp formation by inducing the EMT.

Air pollution is a mixture of thousands of components, and exposure is often unclear in terms of time and concentration. Thus, it is difficult to determine causality. Nevertheless, many researchers have shown that air pollution, especially PM, can cause and exacerbate sinusitis. These studies demonstrate the importance of environmental factors in sinusitis. However, further studies are needed to fully elucidate the role of PM. For example, PM exposure in childhood and adolescence could substantially affect the development of sinusitis. Therefore, recording PM exposure from infancy to adulthood might be important. In addition, when epithelial disruption by EMT occurs, PM can easily penetrate the nasal tissue. PM can influence neutrophils, eosinophils, macrophages, or fibroblasts, particularly if the EMT takes place. There is also a need for research to clarify the main component of PM that causes sinusitis and/or the implication of PM in endotypes of CRS.

CONFLICT OF INTEREST

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

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ACKNOWLEDGMENTS

This work was supported by the Education and Research Encouragement Fund of Seoul National University Hospital (2021).

AUTHOR CONTRIBUTIONS

Conceptualization: all authors. Data curation: all authors. Writing–original draft: SL. Writing–review & editing: HWS.

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