



Review

Impact on Eye Health Regarding Gaseous and Particulate Pollutants

Chia-Jen Chang^{1,2}, Hsi-Hsien Yang^{3*}

¹ Department of Ophthalmology, Taichung Veterans General Hospital, Taichung 40705, Taiwan

² Department of Optometry, Central Taiwan University of Science and Technology, Taichung 40601, Taiwan

³ Department of Environmental Engineering and Management, Chaoyang University of Technology, Taichung 413310, Taiwan

ABSTRACT

Air pollutants are a mixture of thousands of compounds, including ozone (O₃), carbon monoxide (CO), sulfur dioxide (SO₂), nitrogen oxides (NO_x), volatile organic compounds (VOCs), and particulate matter (PM), all of which are considered to be the most significant compounds from a health provider's viewpoint. The association between air pollutants and human health has been investigated for many decades. These adverse health effects on mankind include acute and chronic impacts. Nearly all the systems of the human body can be affected. There had been substantial evidence pointing out that air pollutants are able to cause serious consequences in human's respiratory and neurological health system (Mannucci *et al.*, 2015; Mannucci and Franchini, 2017; Chen *et al.*, 2020). The retinal tissue and optic nerve are regarded as part of the central nervous system (CNS), because their development are protuberances of an embryological brain (Sebastian, 2010). However, the eyes are often a neglected organ in the area of environmental medicine. Most people anticipate air pollutants' health impacts on the eyes are limited to the eye surface, and simple eye irritation; in fact, air pollutants have a much greater impact on the eyes than we think. In this article, the authors reviewed all the acute and chronic health effects of gaseous and particulate air pollutants on the eyes to highlight the complexity of the relationship of air pollutants and eye health.

ACUTE IMPACTS

Ocular Surface Disorders

Gaseous and PM

It's well known air pollutants can lead to significant eye irritation and discomfort due to their having direct contact with the ocular surface. People who exposed to higher level of air pollutants were supposed to have significantly worse performance in tear break-up time (TBT) and Schirmer's test. Approximate a half of these air pollutants exposed people complained of both eye redness and irritation, compared to one fifth in less exposed ones (Saxena *et al.*, 2003). The subjective ocular surface symptoms, as well as those of respiratory tract, were not compatible with the objective test values. Sometimes, air pollutants caused more severe symptoms than test measurements, especially for certain gaseous pollutants (Lang *et al.*, 2008). Furthermore, air pollutants lead to ocular surface irritation and disorders not only in ambient air, but also in an indoor air environment. For those workers in buildings, indoor air pollutants, both gaseous and particulate

pollutants, were proved to be one reason of their symptoms of sick building syndrome (Chang *et al.*, 2015).

To study the association between gaseous and particulate pollutants and the incidence of dry eye disease, a case-crossover study included more than five thousand subjects. The results showed air pollutants indeed had significant effects on incidence of dry eye disease without lag effects (Mo *et al.*, 2019). In Japan, this significant association between allergic conjunctivitis and PM was also been revealed. And the effects showed no lag effects as well (Mimura *et al.*, 2014). Additionally, not only for allergic conjunctivitis, similar results regarding nonspecific conjunctivitis had been reported in a study from Taiwan. In that study, Gaseous and particulate air pollutants increased the chance of nonspecific conjunctivitis. Once again, these effects have no time lag (Chang *et al.*, 2012). The no lag effect seen in all the above studies was compatible with the data from Paris, which suggested that quantities of air pollution were linked to increases of emergency room visits for ophthalmological reasons (Bourcier *et al.*, 2003). These many population-based researches supported the belief that air pollution related ocular surface impact is acute and has nearly no time lag effects.

The following are possible mechanisms of ocular surface disorders. As the outermost layer of the ocular surface, tear film plays a critical role in both the irritation and discomfort of the eyes. For people with increased air pollutants exposure,

* Corresponding author.

Tel.: 886-4-2332-3000 ext. 4451; Fax: 886-4-2374-2365

E-mail address: hhyang@cyut.edu.tw

tear evaporation rate, TBT, and corneal staining scores could be significantly worsened. The alternation of tear cytokine and ocular surface microstructure led to possible reasons regarding tear film problems. Tear chemical concentration's increase explained functional changes in the tear lipids and its spread (Rummenie *et al.*, 2008). In addition to tear physiology, an increase of lots sorts of inflammatory related chemical factors in ocular surface after exposure to air pollutants, confirmed that air pollution exposure enhanced inflammatory level in people's conjunctiva (Fujishima *et al.*, 2013). A higher goblet cell density, along with strong eosinophil infiltration in conjunctiva was noticed in an animal study performed to investigate PM induced conjunctivitis showed. This provided tissue proof of conjunctival tissue structure change after exposure to PM (Tang *et al.*, 2019). In recent years, there also was molecular biological level evidence suggested particles in the air may induce cell death in human corneal epithelial (Park *et al.*, 2017).

Blepharitis

Gaseous and PM

Besides alternations in the corneal epithelium, conjunctiva and tear film, which in turn could lead to irritation, red eyes and discomfort, air pollutant exposure is known to be connected with blepharitis, which is associated with acute symptoms and signs of ocular surface disorder as well. Increases in the concentration of PM, and CO were correlated to increases in incidence of blepharitis without lag effects (Malerbi *et al.*, 2012). However, the mechanism of this impact was not clearly known.

Retinal Vessel Narrowing

PM

Both adults and children are susceptible to this health impact. The impact of air pollutants on retina is on the microvascular structure. Increases of monitoring data on PM₁₀ was associated with a decrease in Central Retinal Arteriolar Equivalent (CRAE), and Central Retinal Venular Equivalent (CRVE). The impact can be noted after days of exposure (Louwies *et al.*, 2013). Retinal microvascular narrowing effects were also found in children with regards to smaller particulate matter, PM_{2.5}. A study was performed involving the repeated retinal microvascular measurements in children, with the results revealing that increase in same-day exposure to PM_{2.5} measured was associated with narrower retinal arteriolar/venular structures (Provost *et al.*, 2017). Some mechanisms were proposed. The first is that air pollution causes systemic inflammation. In the study conducted by Louwies *et al.* (2016), PM was suggested to affect miRNAs and miRNA further led to inflammation and oxidative stress. This inflammatory condition initiated vessel endothelium dysfunction. The second possible mechanism is that air pollution triggers sympathetic nerve activity and then causes vessel smooth muscle constriction as a result (Provost *et al.*, 2017).

CHRONIC IMPACTS

Blepharitis

Gaseous

Air pollutant exposure is suggested to be an acute risk

factors of blepharitis. This impact can also be noted after a 1-week lag exposure. Mean levels of NO₂ exposure for 7 days have impact on incidence of blepharitis. The association between NO₂ quartiles and reported ocular discomforts was significant, as well as a significant negative association between TBT and mean levels of NO₂ (Novaes *et al.*, 2010). Sulfur was one of the most copious component in the PM from traffic emissions in China. Besides NO₂, S was also suggested to play an important role in the mechanism of blepharitis (Hao *et al.*, 2019).

Retinal Vessels Narrowing and Occlusion

Gaseous and PM

In 2004, the earliest field study which connected air pollutants and retinal microvascular changes reported that chronic exposure to carbon disulfide leads retinal venous diameters to become significantly smaller, while also causing retinopathy (Remky *et al.*, 2004). After Remky's study, a population-based study investigated the association between short- and long-term levels of air pollutants and microvascular characteristics, using the arteriolar vessel width as measured by color pictures of retina. These correlations were noticed in a joint exposure model with decreases in the CRAE in long- and short-term PM_{2.5} levels, respectively (Adar *et al.*, 2010). Air pollutants seem to have chronic retinal vessel changing effects not only on adults but also on children. Measuring recent (same and previous day), and chronic (yearly mean) air pollutant exposure, the results revealed that there were both significant acute and chronic effects on children living closer to a main road, with the children experiencing narrower arterioles (Provost *et al.*, 2017).

The narrowing of retinal vessels, both arterioles and venules, could be even worse in other circumstances and eventually become retinal vessel occlusion. That was proved by various population-based studies. The risk of central retinal artery occlusion (CRAO) onset significantly increased during a period less than 1 week, following a 1 PPM increase in NO₂ levels. However, particulate matter and O₃ did not show significance in this study which was conducted in Taiwan (Cheng *et al.*, 2016). Besides CRAO, components of air pollutants lead to central retinal vein occlusion (CRVO) as well. Long-term exposure to total hydrocarbons and nonmethane hydrocarbons increased the incidence of developing CRVO. The possible mechanism of chronic air pollution exposure on retinal vessels is due systemic inflammation which may cause endothelial dysfunction. Systemic inflammation also induces hypercoagulability. Inflammatory cytokines including interleukin-1 beta, tumor necrosis factor-alpha, and interleukin-6 activate the extrinsic coagulation. They also down regulate tissue-type plasminogen activators and disrupt fibrinolysis (Zhang *et al.*, 2019).

Myopia

Gaseous and PM

Causes of myopia are various, including genetic and environmental factors. In recent years, there were population-based studies suggested links between air pollutants and the progression of myopia. The possibility of myopia increased with exposure to higher level of PM_{2.5} and

NO_x concentrations. The mechanism for the association was particulate matter enhanced inflammation and then further induced progression of myopia, which was conclude form evidence of animal experiments (Wei *et al.*, 2019). Another study which focused on myopia in the elderly aged 50 years and above suggested that particulate matter and O₃ were associated with a more than ten percent increase in myopia prevalence (Ruan *et al.*, 2019). In a population-based study which investigated the relationship between traffic air pollutants and children, oxidative stress and systemic or local inflammation were suggested to be the possible mechanism how air pollutants led to the occurrence and progress of myopia. Nitrogen dioxide and PM were significantly associated with the occurrence of myopia (Dadvand *et al.*, 2017).

Color Vision

Gaseous

Color vision function shows considerable sensitivity to numerous different chemical agents. These effects, which are often dose-dependent and in the blue–yellow axis have been reported to follow chronic industrial and environmental exposure to chemical mixtures (Iregren *et al.*, 2002).

Glaucoma

Gaseous and PM

Carbon monoxide had been suggested to be related with glaucoma control by affecting the intraocular pressure (Bucolo and Drago, 2011). Other than intraocular pressure, air pollutants can impact glaucoma control by different ways. Ozone, NO, and PM were proved associated with the Endothelin-1 (ET-1) system regulation. The increased ET-1 which can lead to vascular dysfunction was the suggested reason making primary open angle glaucoma progressive (Cellini *et al.*, 2012; Finch and Conklin, 2016). A greater exposure to PM_{2.5} was correlated with glaucoma and adverse structural change of this disease. The absence of a correlation between PM_{2.5} and intraocular pressure suggested that the relationship may take place through the non–pressure-dependent mechanism, possibly neurotoxic and/or vascular effects (Chua *et al.*, 2019). For children, particulate matter also had been proven to increase the incidence of child hood glaucoma in a cohort study including near ten thousand subjects. However, the possible mechanism was not proposed (Min and Min, 2020).

Age-related Macular Degeneration

Gaseous

To investigate whether air pollutants increase the risk for Age-related Macular Degeneration (ARMD), one population-based research which included near forty thousand subjects with follow-up time for more than ten years was conducted in Taiwan. The study included people aged 50 years and older. This study suggested that chronic exposure to NO₂ and CO had significant impact on the incidence for ARMD (Chang *et al.*, 2019). The mechanism how air pollution led to ARMD was not mentioned. This is an observational study, and the authors didn't propose possible mechanism.

Cataract

Gaseous

As early as 1999, a rural population-based study in India suggested that the duration of exposure to air pollutants was associated with age-related cataract (Sreenivas *et al.*, 1999). For those who use biomass fuels in daily cooking, the connection between exposure to the emission and development of cataract had been established. Of the included subjects (both men and women), the incidence of nuclear cataract became higher with increase biomass fuel use (Ravilla *et al.*, 2016). Interestingly, air pollutants included in a study from Korea involving PM₁₀, O₃, NO₂, and SO₂, offered no potential to aggravate cataract. Moreover, O₃ and NO₂ levels revealed negative associations with all types of cataract which suggested a protective effect. There are many factors, including subject's age, diabetes mellitus, blood pressure, medications, and nutrition being considered which could be related to cataract formation. Oxidative stress from reactive oxygen and nitrogen species has been taken as one of the main mechanisms to cataract formation. Ultraviolet light exposure is one of the main sources in oxidative stress. The possible mechanism of the protective effect could be that increasing levels of tropospheric O₃ may shield the lens from ultraviolet light exposure (Choi *et al.*, 2018). However, there is another possible reason for cataract formation in people who have household fuel air pollutants exposure, which is high temperature of the working environment. The relationship between high temperature exposure and cataract formation has been established for decades (Okuno, 1991). It's difficult to know if this health impact was caused by heat, air pollutants or both of the two factors.

CONCLUSIONS

Although eye diseases do not decrease life expectancy directly, they nevertheless do cause a significant decrease in human life quality. Plentiful evidence originating from cell studies, animal research, case cross over studies, cohort studies, and population-based studies has shown that acute and chronic exposure to high levels of air pollutants will cause many different eye diseases, including dry eye syndrome, conjunctivitis, and retinal vessels occlusion along with others. Environmental factors such as humidity and temperature should be taken into consideration when discussing impacts of air pollutants on eyes. However, they were not studied in these literatures. We will have a clearer view with regards to the health impact of air pollutants on eyes, as soon as additional studies are performed to determine the mechanisms involved, while examining the role each specific component plays in the myriad of air pollutants.

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