Journal of
Pulmonary & Respiratory Medicine

Wang, et al., J Pulm Respir Med 2018, 8:4
DOI: 10.4172/2161-105X.1000465

Review Article Open Access

Particulate Matter and Respiratory Diseases: How Far Have We Gone?

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Abstract

Air pollution is a potential threat to public health worldwide, especially in South Asia. The Global Burden of Diseases, Injuries, and Risk Factors Study 2016 (GBD 2016) reported that most of global deaths attributable to ambient particulate matter occurred in China and India. Particulate matter (PM), as the main air pollutant, is receiving increasing attention due to its specific biological properties. PM is a complicated mixture and varies in sizes, compositions and sources. Increasing epidemiological studies have shown that both short- and long-term PM exposure are associated with the morbidity and mortality of respiratory diseases, including chronic obstructive pulmonary disease (COPD), asthma, lung cancer, and pneumonia, especially in the elderly and children. Several potential biological mechanisms have been proposed to explain the adverse effect of PM on the respiratory diseases, including oxidant stress, pro-inflammation, epigenetic modifications, DNA damage and carcinogenesis. However, there are still some contradictions with regard to the role of PM in the development of these respiratory diseases. Thus, this review made a summary of results from epidemiological studies about the association between PM and COPD, asthma, lung cancer, and pneumonia, and elucidated its potential biological mechanisms.

Keywords: Particulate matter; Respiratory diseases; Adverse effect; Epidemiology

Abbreviations: PM: Particulate Matter; ED: Emergency Department; HAs: Hospital Admissions; RR: Risk Ratio; OR: Odds Ratio; CI: Confident Interval.

Background

Particulate matter (PM) is a key component of air pollution, which causes a public health challenge around the world, especially in developing countries. It has been estimated that 92% of the world's population live in places where the World Health Organization (WHO) air quality guidelines levels are not met for PM2.5 [1]. The Global Burden of Diseases, Injuries, and Risk Factors Study 2016 (GBD 2016) showed that PM had increased to the sixth with 105.7 million global disability-adjusted life-years (DALYs) in overall ranking and contributed to approximately 4.1 million deaths worldwide in 2016. Of these, most of PM-related DALYs and deaths occurred in the South Asia, especially in China and India [2]. It was estimated that PM caused about 1.1 million deaths in China in 2016 [3]. However, a national study in China showed that PM2.5 exposure contributed to 1.5 million total deaths, which was higher than that was estimated by GBD 2016 [4]. Therefore, the current health burden attributable to PM exposure is heavier than we considered.

Recently, several epidemiological and experimental studies have demonstrated that PM exposure is associated with the morbidity and mortality of cardiopulmonary diseases, such as chronic obstructive pulmonary disease (COPD), asthma, lung cancer, pneumonia, ischemic heart disease, and stroke [5,6]. It is estimated that air pollution contributes to 5% of all cardiopulmonary deaths worldwide [7]. Besides, PM contributes to diabetes and premature birth [8,9]. As airways and lungs are the first affected targets of air pollutants, PM deposits can cause a series of biological responses in lung cells, including oxidant stress, pro-inflammation, cytotoxicity, epigenetic changes and carcinogenesis [10]. Thus, the review focused on the results from meta-analysis and several multicentre studies to analyze the associations between PM exposure and the morbidity and mortality of respiratory diseases, including COPD, asthma, lung cancer and pneumonia. The potential biological mechanisms were elucidated to provide a brief overview of health effects of PM exposure on respiratory system.

The Definition of PM

PM is a complicated mixture with different sizes and chemical components. According to their aerodynamic diameters, PM is divided into coarse (≤ 10 μm and >2.5 μm; PM10), fine (≤ 2.5 μm and >0.1 μm; PM2.5) and ultrafine (≤ 0.1 μm; PM0.1) particles [6]. PM10 is usually deposited in the nasal cavity and upper airways because of the respiratory barrier. However, PM2.5 and PM0.1 can escape from these barriers and directly enter the lower airways through breathing, and can even penetrate into the circulation system through lung gas-blood exchange regions and cause damage to the entire body [10]. Approximately 60% and 20% of total PM depositions in the lung are found to be ultrafine and fine particles, respectively [6]. Moreover, PM2.5 makes up 96% of particles retained in the lung parenchyma [11]. Thus, PM2.5 and PM0.1 have more destructive effects on the lung. Besides, the components of PM are also complicated and diverse in different areas and seasons. Generally, PM is composed of inorganic matter (including sulfates, nitrates, ammonium, acids, heavy metals, polycyclic aromatic hydrocarbons, and crustal material) and biological materials (including allergens and microbial compounds) [12].

PM is usually made up of primary and secondary PM from both anthropogenic and natural sources. Primary PM is directly emitted from different sources, including agricultural activities, industrial

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Received July 18, 2018; **Accepted** August 01, 2018; **Published** August 07, 2018

Citation: Wang J, Chen S, Zhu M, Miao C, Song Y, et al. (2018) Particulate Matter and Respiratory Diseases: How Far Have We Gone?. J Pulm Respir Med 8: 465. doi: 10.4172/2161-105X.1000465

processes, the transportation sector, construction sites and forest fires [13]. Secondary PM is derived from complex chemical reactions of gases in the atmosphere. For example, sulfur dioxide and nitrogen oxides can be converted into sulfate and nitrate particles to form the main components of fine particles [14]. The latest update of air quality guidelines (AQG) for PM from the WHO in 2005 showed that the PM10 values were limited to an annual mean of 20 μg/m^3 and a 24-hour mean of 50 μg/m^3, while the values of PM2.5 were limited to an annual mean of 10 μg/m^3 and a 24-hour mean of 25 μg/m^3 (not to be exceeded for more than 3 days/year) [15].

The Effect of PM Exposure on Respiratory Diseases

Epidemiological evidences show that both short- and long-term PM exposure have a close association with the development of respiratory diseases, such as COPD, asthma, lung cancer and pneumonia [16,17]. Moreover, strong evidences have demonstrated that PM exposure increases the mortality of patients with respiratory diseases [18-20]. In China, a nationwide analysis showed that the mortality from respiratory diseases increased 0.29% with a 10 μg/m^3 increment in PM2.5 every 2 days [21]. Additionally, PM exposure increases respiratory symptoms and medication use, and decreases pulmonary function [7]. All populations are threatened by PM exposure, but the elderly and children are the most susceptible. Now, numerous studies, especially the meta-analysis studies, have evaluated the health risk values of PM for different respiratory diseases (Table 1).

PM and COPD

COPD is a common pulmonary disease, mainly characterized by irreversible airway flow limitations [22]. The GBD 2016 showed that there were approximately 251.6 million patients suffering from COPD thus far, and COPD has become one of the leading causes of global deaths [23]. With increasing evidences to support the adverse effect of PM10 or PM2.5 on the patients with COPD, PM is considered to be an important risk factor for COPD. Now, short-term (hours, days) or long-term (months, years) exposure to PM are the two different exposure metrics to evaluate the health effect of PM on the patients with COPD.

The short-term exposure to PM could exacerbate the disease process of COPD. Several meta-analysis have confirmed that PM10 or PM2.5 with a 10 μg/m^3 increase in concentration could lead to a decrease in forced vital capacity (FVC), forced expiratory volume during the first second (FEV_1), FEV_1/FVC ratio and peak expiratory flow (PEF) [24,25]. PM2.5 even showed a stronger harm on the lung function of COPD patients than PM10. One possible reason is that the PM2.5 with smaller size are easier to be inhaled into the small airways and the alveoli of the lung. Two successive meta-analysis studies showed that a 10 μg/m^3 increase in PM2.5 could contribute to a 3.1% (95% CI: 1.6% to 4.6%) increase in COPD-related HAs and a 2.5% (95% CI: 1.5% to 3.5%) increase in COPD mortality, and a 2.5% (95% CI: 1.6% to 3.4%) increase in the risk of COPD-related ED visits and HAs [26,27]. As for PM10, Zhu et al. showed that a 10 μg/m^3 increase in PM10 was associated with a 2.7% (95% CI: 1.9% to 3.6%) increase in COPD-related HAs and a 1.1% (95% CI: 0.8% to 1.4%) increase in COPD mortality [28].

However, evidences about association between long-term PM exposure and patients with COPD were limited. Four cohorts from the European Study of Cohorts for Air Pollution Effects (ESCAPE) were included to assess the impact of PM on the prevalence and incidence of COPD which was defined according to FEV_1/FVC and the GOLD criterion, but no statistically significant associations between PM and COPD morbidity were defined [29]. Similar results were acquired according to the data from a nationally representative cohort in England [30]. These inconclusive results might be due to differences in

Disease	Age	PM (μg/m^3)	Exposure time	Evaluation index	RR/OR (95% CI)	Reference
COPD	—	PM2.5 (10 μg/m^3)	multi-day averages	ED visits and HAs	1.03 (95% CI 1.02-1.03)	DeVries et al. [26]
			single-day lags		1.01 (95% CI 1.01–1.02)	
COPD	—	PM2.5 (10 μg/m^3)	lag days 0-7	HAs	1.03 (95% CI 1.02-1.05)	Li et al. [27]
				mortality	1.03 (95% CI 1.02 –1.04)	
COPD	—	PM10 (10 μg/m^3)	lag days 0-7	HAs	1.03 (95% CI 1.02–1.04)	Zhu et al. [28]
				mortality	1.01 (95% CI 1.01 –1.01).	
Asthma	under 18 years old	PM2.5 (1 μg/m^3)	—	incidence	1.03 (95% CI 1.01-1.05)	Khreis et al. [34]
		PM10 (2 μg/m^3)			1.05 (95% CI 1.02-1.08)	
Asthma	under 20 years old	PM2.5 (10 μg/m^3)	short-term	ED visits and HAs	1.05 (95% CI 1.03-1.07)	Lim et al. [37]
Asthma	—	PM2.5 (10 μg/m^3)	short-term	ED visits	1.02 (95% CI 1.02-1.02)	Fan et al. [39]
Asthma	—	PM2.5 (10 μg/m^3)	lag day 1	ED visits and HAs	1.02 (95% CI 1.02-1.03)	Zheng et al. [38]
		PM10 (10 μg/m^3)			1.01 (95% CI 1.01-1.01)	
Lung cancer	—	PM2.5 (10 μg/m^3)	—	incidence	1.03 (95% CI 0.48–1.58)	Cui et al. [43]
				mortality	1.09 (95% CI 1.06–1.11)	
		PM10 (10 μg/m^3)		incidence	1.45 (95% CI 0.87–2.03)	
				mortality	1.05 (95% CI 1.03–1.07)	
Lung cancer	—	PM2.5 (10 μg/m^3)	—	incidence and mortality	1.09 (95% CI 1.04-1.14)	Hamra et al. [46]
		PM10 (10 μg/m^3)			1.08 (95% CI 1.00-1.17)	
Lung cancer	—	PM2.5 (10 μg/m^3)	—	incidence	1.11(95% CI 1.00-1.22)	Chen et al. [85]
Pneumonia	under 18 years old	PM2.5 (10 μg/m^3)	short-term	ED visits	1.02 (95% CI 1.01-1.03)	Nhung et al. [56]
		PM10 (10 μg/m^3)			1.02 (95% CI 1.01-1.02)	

Table 1: A summary of meta-analysis on the association between PM exposure and respiratory diseases (COPD, asthma, lung cancer and pneumonia).

study design, definition of COPD, exposure assessment and statistical methods. However, significant association of chronic PM exposure with COPD was identified in some specific subgroups. For example, Kariisa et al. found that long-term PM2.5 exposure significantly decreased lung function and increased respiratory symptoms in 1218 severe COPD patients [31]. Pun et al. showed that long-term PM2.5 exposure could lead to a 10% increased risks of COPD mortality in older US adults [20].

PM and Asthma

It is estimated that asthma affects more than 300 million people around the world. In 2010, it ranked as the 28th highest cause of disability-adjusted life years worldwide [32,33]. Asthma can appear at any age and has the highest prevalence in children and young adults [32]. As for the immature defense function of respiratory system, children exposed to PM are more likely to develop asthma. A recent meta-analysis reviewed 41 epidemiological studies about the association between PM exposure and the risk of asthma incidence or lifetime prevalence in childhood aged from 1 to 18 years, and found that PM10 or PM2.5 exposure was a risk factor for the development of asthma in children. The overall random-effects risk estimates for asthma development were 1.05 (95% CI: 1.02 to 1.08) per 2 μg/m^3 PM10 and 1.03 (95% CI: 1.01 to 1.05) per 1 μg/m^3 PM2.5, respectively [34]. Further, another meta-analysis showed that prenatal exposure to PM10 could increase the risk of wheezing and asthma development in childhood aged 0 to 10 years (OR=1.08; 95% CI: 1.05 to 1.12), but non-significant effect of prenatal PM2.5 exposure on children asthma (OR=1.4; 95% CI: 0.97 to 2.03) [35]. However, the effect of PM on incidence of asthma remains elusive in adults. PM 10 and PM2.5 showed a positive, but not significant, association with the incidence of adult asthma in six European cohorts [36]. The diagnosis bias, population heterogeneity and exposure assessment limited this result, and further studies were needed to elucidate the association between PM and adult asthma incidence.

Recently, the effect of PM on the exacerbation of asthma, including ED visits and HAs, was well-defined in both children and adults. For children, a recent meta-analysis showed that a short-term 10 μg/m^3 increase in PM2.5 increased children's ED visits and HAs due to asthma (RR=1.048; 95% CI: 1.028 to 1.067) [37]. In another meta-analysis, a positive association between asthma-related ED visits and HAs and exposure to PM10 (RR=1.010; 95% CI: 1.008 to 1.013 per 10 μg/m^3) or PM2.5 (RR=1.023; 95% CI: 1.015 to 1.031 per 10 μg/m^3) was defined in children and adults. Further, the subgroup analysis found that three factors (male, children and warm season) could make association stronger [38]. Similar conclusions were drawn in a meta-analysis that evaluated the asthma-related ED visits and PM2.5 exposure in children and adults [39]. Thus, PM exposure led to an adverse impact on the exacerbation of asthma, especially in children and in warm season.

PM and Lung Cancer

Lung cancer is a multi-factorial cancer with poor prognosis and causes large disease burden worldwide. In 2015, it was estimated that the global morbidity and mortality of lung cancer were 2 million and 1.7 million, respectively [40]. The International Agency for Research on Cancer (IARC) has classified outdoor air pollution and PM as proven carcinogens for humans [41]. The effect of long-term PM exposure on lung cancer focused on incidence and mortality of lung cancer.

There were still some conflicts about the association between PM and the incidence of lung cancer. In one meta-analysis reviewing six studies, PM2.5 in traffic-related air pollution showed positive association with the lung cancer incidence (OR=1.11; 95% CI: 1.00 to 1.22 per 10 μg/m^3) [42]. Paradoxically, no significant association between PM and lung cancer incidence was identified in another meta-analysis, which only included three studies for PM10 and two studies for PM2.5 [43]. The limited number of studies for meta-analysis and the different selection criteria make these results inconsistent, and thus more studies are needed to address the association between PM and lung cancer incidence. However, the ESCAPE conducted a subgroup analysis according to histological cancer subtype and found that both PM10 and PM2.5 significantly contributed to adenocarcinomas of the lung [44]. Further, the effect of PM components on lung cancer incidence was identified in a European study. They compared eight elements (copper (Cu), iron (Fe), potassium (K), nickel (Ni), sulfur (S), silicon (Si), vanadium (V) and zinc (Zn)) in PM10 and PM2.5, and found that Cu from PM2.5 and Zn, S, Ni and K from PM10 had positive associations with the incidence of lung cancer [45].

However, the effect of PM on the lung cancer mortality is well defined. Recently, several meta-analysis have demonstrated that both PM2.5 and PM10 contributed to increasing lung cancer mortality [43,46,47]. The relative risk for lung cancer mortality were 1.09 (95% CI: 1.06 to 1.11) for PM2.5 per 10 μg/m^3, and 1.05 (95% CI: 1.03 to 1.07) for PM10 per 10 μg/m^3 [43]. Smoking is an important risk factor for lung cancer and is considered to confound the estimates for associations between PM and lung cancer mortality. One subgroup analysis according to smoking status found that former smokers had the greatest lung cancer risk associated with PM2.5, followed by never-smokers and current smokers [46]. Besides, the adverse effect of PM10 on lung cancer mortality strengthened in second-hand smokers, compared with never smokers [48]. Thus, smoking status should be included to analyse the association between PM and lung cancer in further studies.

PM and Pneumonia

Pneumonia is a common respiratory disease that can be caused by bacteria, viruses, or fungi. The morbidity and mortality of pneumonia vary with age, geographic region, and population at risk among other factors [49]. Recently, most of epidemiological studies have supported the evidence that PM had a positive association with morbidity (ED visits and HAs) and motility of pneumonia. The study from Atlanta showed that a short-term PM10 and PM2.5 exposure were associated with 1%-3% increase in ED visits due to upper respiratory infection and pneumonia [50]. Moreover, another two studies from different countries have demonstrated an increase in HAs for pneumonia with PM10 levels [51,52]. Further, PM10 had a more marked effect with an increase of 1.47% (95% CI: 0.93% to 2.01%) in pneumonia-related HA during the warm season [52]. Besides, in a study from Hong Kong, PM2.5 caused a 0.67% (95% CI: 0.14% to 1.21% per 10 μg/m^3) increase in mortality due to pneumonia in daily mean concentration at lag 2 day [53]. However, the study from a Chinese city showed that there was no significant effect of PM on the morbidity of pneumonia [54]. Thus, further studies should cover more different areas, make exposure assessment harmonization and include confounding factors to make the results consistent.

The elderly, children under five years of age, and those with special comorbidities are more susceptible to pneumonia [55]. The adverse effect of PM on pneumonia incidence and pneumonia-related ED visits and HAs among these special individuals was analyzed. A latest meta-analysis showed that short-term PM10 and PM2.5 exposure increased the ED visits in children under five years old (1.5% (95% CI: 0.6% to 2.4%) for PM10 per 10 μg/m^3 and 1.8% (95% CI: 0.5% to 3.1%) for PM2.5 per 10 μg/m^3) [56]. The positive association between

PM exposure and pneumonia-related HAs was also identified in older adults or children [57,58]. However, the ESCAPE Project showed that PM10, but not PM2.5, had a statistically significant association with pneumonia incidence in early children (OR=1.76; 95% CI: 1.00 to 3.09 per 10 μg/m^3) [59]. More interesting, only Zn from PM10 was independently associated with the early-life pneumonia incidence in children [60].

The Potential Biological Mechanism

The toxic effect of PM is complicated and different mechanisms have been proposed to explain the adverse effect of PM on respiratory diseases, such as COPD, asthma, lung cancer and pneumonia. The PM enters and deposits in the lung with breathing to directly or indirectly cause the oxidant stress, pro-inflammation, epigenetic modifications, apoptosis, DNA damage and even carcinogenesis in the lung cells. These biological dysfunctions contribute to the increasing morbidity and mortality of respiratory diseases (Figure 1).

Oxidant Stress and Pro-Inflammation

The cellular redox equilibrium is essential in maintaining normal biological process. Under physical condition, cells produce a variety of antioxidants to neutralize the reactive oxygen species (ROS) and oxygen radicals [61]. However, exogenous and endogenous stimuli often disturb the balance between oxidation and anti-oxidation and make excessive ROS accumulation to form oxidant stress. Oxidant stress has been demonstrated as an important mechanism in PM-induced respiratory diseases and excessive ROS acts as a key mediator to initiate pro-inflammation, physical barrier disruption, cell death and carcinogensis [62]. There is accumulating evidence that PM can induce the ROS generation *in vitro* and *in vivo*. Bronchial epithelial cells, macrophages and neutrophils, as the main targets of PM in the lung, can generate ROS with the stimulation of PM *in vitro* [63-65]. Our study also found that urban dust 1649b could increase the generation of ROS in a time- and dose-dependent manner significantly [66]. Li et al. compared the oxidant stress responses for particles in different cells and found that bronchial epithelial cells generated more superoxide radicals and were more susceptible to cytotoxic effects than macrophages [67]. The animal studies also showed that intratracheal administration of PM could markedly elevate the ROS levels in the lung tissue. The high level of ROS could increase neutrophils infiltration in the lung tissue and activate neutrophils to produce more ROS. In addition, pretreatment with antioxidant N-acetylcysteine could attenuate the PM-induced lung inflammation [68-70]. However, no direct evidences have been found that PM could increase the ROS production in human lung tissue.

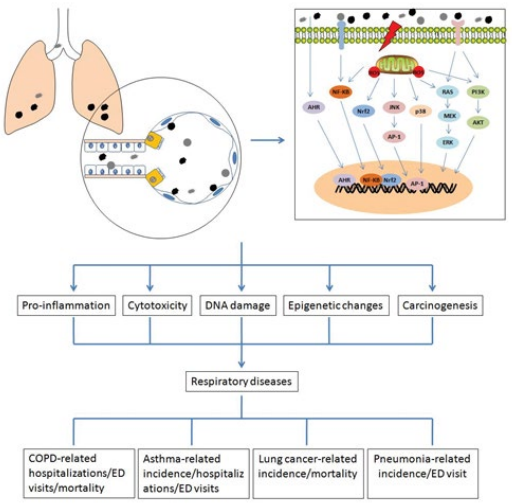

Figure 1: The potential mechanism for the effect of PM on the morbidity and mortality of respiratory diseases.

Inflammatory responses for PM are a universal biological process in different lung cells. Numerous studies have showed that oxidant stress could activate intracellular different signaling pathways to promote PM-induced inflammatory pathogenesis *in vitro* and *in vivo* [71]. The transcriptional activation of cytokines, chemokines and adhesion molecules played an important role in PM-induced lung inflammation. Our study found that urban dust 1649b could induce the expression of pro-inflammatory mediators IL-1β, IL-6, IL-8, MMP-9 and COX-2 *via* ROS-MAPK-NF-κB signaling pathway in bronchial epithelial cells [66]. However, the compositions of PM determine differential inflammatory responses in the lung. Jeong et al. used two different methods to obtain water-soluble (W-PM2.5) and organic-soluble (O-PM2.5) from PM2.5 samples and the cytokine antibody array revealed differential cytokines expression in human alveolar epithelial cells with exposure to W-PM2.5 or O-PM2.5, respectively [72]. The animal models also showed a different response to W-PM2.5 or O-PM2.5, especially with regard to IL-8 expression. In an asthmatic mice study, acute exposure of PM2.5 greatly increased the expression of pro-inflammatory cytokines and Th2-related cytokines, and aggravated the severity of asthma [73]. Similarly, PM2.5 exposure promoted the production of pro-inflammatory cytokines (IL-6, IL-8 and TNF-α) and aggravated lung tissue damage in COPD mice model [74]. In addition, inflammatory responses disturb the microenvironmental homeostasis to promote the development and progression of lung cancer.

Cytotoxicity and Carcinogenesis

Cell death is another mechanism for PM-induced respiratory diseases. The oxidative stress, inflammation-related cascades and DNA damage are considered to participate into PM-induced cell death [75]. Recently, different cell death types (apoptosis, autophagy and necrosis) have been demonstrated to be associated with PM exposure in lung cells. Deng et al. found that PM2.5 could activate extrinsic and intrinsic apoptosis pathway and increase autophagy in A549 cells [76]. p53, as an important tumor suppressor, was activated by PM to mediate mitochondrial dysfunction, which was the result of regulating Bcl-2/Bax ratio, to induce PM-induced apoptosis [77]. In addition, Zhou et al. showed that high dose of PM2.5 exposure contributed to cell necrosis and autophagy [78]. The components of PM often affect the cytotoxicity of PM. Schilirò et al. showed that water-soluble PM inhibited cell proliferation more strongly than organic-soluble PM [79]. The polycyclic aromatic hydrocarbons (PAHs) in organic-soluble PM are apt to permeate into cells and disrupt the structure of DNA to cause DNA damage [75]. However, some studies showed that PM had no pro-apoptotic effect on lung cells. The aryl hydrocarbon receptor (AHR)-related pathway was activated by PAHs in PM to induce the expression of anti-apoptotic genes Bcl-2 and Bcl-2L1 [80].

PM could promote the carcinogenesis by inducing DNA damage and genomic instability. Hornberg et al. found that sister chromatid exchange was induced in bronchial epithelial cells when exposed to PM10 and PM2.5 [81]. The PAHs in PM could directly act on the DNA to form DNA adduct and abasic sites [82]. Yu et al. found that PM exposure contributed to somatic mutations in lung cancer and several gene mutations had a positive association with benzo[a]pyrene (BaP) exposure [83]. In addition, PM-induced oxidant stress, DNA damage and gene expression alternation for cell-cycle checkpoint disturbed cell-

cycle progression at different phages to induce genetic instability [80]. Cancer is multi-factorial disease and the mechanism of PM-induced carcinogenesis also remains unclear.

Epigenetic Changes

The PM-induced epigenetic changes focus on DNA methylation and histone modification [70]. Baccarelli et al. found that PM exposure caused a decrease in repeated-element methylation [84]. Chen et al. showed that PM2.5 exposure decreased the NOS2A DNA methylation and increased FeNO in COPD patients [85]. Several studies also showed that PM could affect histone modification. The effect of different exposure level of PM2.5 on histone 3 lysine 27 acetylation (H3K27ac) was revealed by using the genome-wide chromatin immunoprecipitation sequencing (ChIP-Seq) and there was a global elevation of the enhancer-associated H3K27ac markers in individuals exposed to high level of PM2.5 [86]. Besides, the H3K9 acetylation was found to increase in both peripheral blood mononuclear cells (PBMCs) and lung tissues of rat with PM2.5 or PM10 exposure [87].

Conclusion

There are strong epidemiological evidences to support the adverse effect of PM exposure on the morbidity and mortality of respiratory diseases, including COPD, asthma, lung cancer and pneumonia. Thus, effective interventions to reduce PM exposure can help to decrease the risk of respiratory diseases. Guan et al. proposed several substantial measures including novel medications, industrial upgrading, renovation of vehicle fuel and public transportation, incorporation of PM2.5 levels in weather forecasts, improving cooking fuel and ventilation, implementing environmental policies and building up healthy cities [88]. At a personal level, wearing face masks outdoors, using air filters indoors and smoking cessation are efficient methods to reduce PM exposure and decrease PM-related respiratory diseases in the public [88,89]. With the increasing understanding of PM on respiratory diseases, there will be more efficient interventions to alleviate the PM-induced health burden.

Acknowledgement

This research was supported by the State Key Basic Research Program (973) project (2015CB553404), Doctoral Fund of Ministry of Education of China (20130071110044), Shanghai Science and Technology Committee (15DZ1930600/15DZ1930602), Shanghai Municipal Commission of Health and Family Planning (201540370), the National Natural Science Foundation of China (81490533, 81500026, 81630001 and 81770055).

Competing Interest

The authors declare that they have no competing interests. Wang J and Chen S have contributed equally to this work.

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