Editorial Comment

Air Pollution Particular Matter and Atherosclerosis

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In recent years, air-pollution in China attracted attention from the social communities and politic governments. The potentially tremendous impact of air pollution on human health has been noticed since 1952 when Great Smog shaded the winter sun in London city.[1] Increasing evidence has linked the exposure of ambient particular matter (PM) air pollutants to increased cardiovascular morbidities and mortalities.[2-4] PM is heterogeneous materials suspended in the air, of varying sizes, number, surface areas, concentrations, and chemical compositions[3] (also see website of United States Environmental Protection Agency. https://www.epa.gov/clean-air-act-overview). Based on aerodynamic diameters, PMs are classified into thoracic particles (PM > 10 μm), coarse particles (PM2.5-10 μm), fine particles (PM < 2.5 μm), and ultrafine particles (PM < 0.1 μm).[5]

The PM2.5 and ultrafine particles are able to reach the smallest airways and alveoli, where can spread into the blood circulation through the alveolar-capillary membrane.[6] PM2.5 particles are mainly derived from the burning of fossil fuels from traffic and industry, and the composition includes sulfates, nitrates, and elemental and organic carbon.[5,7] PM2.5 has been considered as the culprit of the deleterious effects of PM air pollution on coronary atherosclerosis and events.[4,8,9] Metal fume PM2.5 has been implicated as an additional causative factor for coronary atherosclerosis with decreased cell viability and increased levels of 8-hydroxy-2'-deoxyguanosine (8-OHdG), interleukin (IL)-6, nitric oxide (NO) in human coronary artery epithelial cells.[10] PM2.5 also disturbed gene expression on immune and cellular responses in human umbilical vein endothelial cells.[11]

The first epidemiologic evidence of an association between atherosclerosis and ambient air pollution PM2.5 in human subjects was performed in Los Angeles.[12] This cross-sectional study estimated a 5.9% increase in carotid intima-medial thickness for every 10 μg/m^3 rise in PM2.5 levels. Likewise, PM2.5 was also found to accelerate progression of coronary atherosclerosis as assessed by coronary artery calcification scores in a prospective German cohort study.[13] In subjects with coronary artery disease and myocardial infarction, PM2.5 was determined with correlation to circulatory inflammation biomarkers such as C-reactive protein (CRP), IL-6, soluble tumor necrosis factor (TNF) receptor II and fibrinogen.[14,15]

Studies in animal models of PM support its causal association with atherosclerosis. Most models applied long-term exposures to concentrated ambient particles to study the effects of inhaled PM2.5 on aortic atherosclerosis on apoE null mice.[5] In the present issue, Hongmei Yao et al. use a rat model in which high cholesterol, salt and vitamin D3 were given to enhance development of aortic and coronary atherosclerosis.[16] They used intravenous injection of PM2.5 suspension to study PM2.5 effect on progression of atherosclerosis. They claimed that this approach is lossless and time-saving compared with aerosol inhalation. After only 24 hours, PM2.5 injection changed plasma lipid profile, with reduction in triglyceride and HDL-cholesterol, and increase in total cholesterol and LDL-cholesterol. These changes were associated with reduction of superoxide dismutase (SOD) and increase of malondialdehyde (MDA), TNF-α and high sensitive-CRP. The PM2.5-induced adverse effects were partially corrected by atorvastatin treatment, which has well-known anti-inflammatory and anti-oxidative pleiotropic effects other than cholesterol-lowering efficacy.[17] In their morphological study, although not sharply illustrated, damaged endothelial cell, abundant lipid droplets, thinned tunica media, and irregular smooth muscle cell and lumen were described. In their immuno-

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histochemistry and electrophoretic mobility shift assay (EMSA) experiments, enhanced nuclear factor-kappa B (NF-κB) transcriptional activity by PM2.5 which was suggested as the possible mechanism, was also partially corrected by atorvastatin. Noteworthy, atorvastatin had been administered concurrently with the "atherosclerosis-facilitated" treatment for 12 weeks before PM2.5 exposure in their rat model.

If pharmacological treatment with statin is able to improve PM2.5-induced progression of atherosclerosis, this would bring several questions unanswered. First, whether the atorvastatin protection is from cholesterol-lowering or from SOD-elevation? Will statin also be beneficial for high PM2.5 exposure individuals who have normal cholesterol metabolism and plasma levels? Second, is atorvastatin able to treat PM2.5 induced inflammation when administered after PM2.5 exposure? Third, if the protective effect of atorvastatin is dose-dependent? Forth, if the protective effect to prevent PM2.5-induced progression of atherosclerosis is a class effect? Will other statins exert the same or similar protection for PM2.5? And finally, before a significant PM2.5 reduction can be achieved in our living ambient, it is probably mandatory to seek a biomarker to quantify the burden of PM2.5-induced inflammation for high risk atherosclerotic patients, for whom an adjunctive anti-inflammatory therapy may be needed to prevent acute events during the foggy days.

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