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Involvement of Heme Oxygenase system in airborne particulate matter-mediated alteration of NO responsiveness in rat intrapulmonary arteries

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Background and Objectives. Particulate air pollution exerts deleterious effects on cardiovascular and pulmonary systems. We previously described that exposure to urban particulate matter (SRM1648) impairs NO responsiveness in rat intrapulmonary arteries. Heme Oxygenase-1 (HO-1) system, which may be induced by particulate matter, is known to alter NO dependent relaxation. Therefore, this study was designed to characterize whether HO-1 is involved in SRM1648-induced alteration of NO responsiveness in rat intrapulmonary arteries.

Methods. Intrapulmonary arteries isolated from Wistar rats were prepared with or without endothelium. They were exposed to SRM1648 (200 µg/ml) in culture medium, in absence or presence of Chromium MesoPorphyrine (HO-1 inhibitor, CrMP), or Cobalt Protoporphyrine (HO-1 inductor, CoPP). After 24h, NO-dependent relaxation was assessed with DEA-NOnoate (NO-donor, 3.10^{-9} to 3.10^{-5}M) in endothelium intact or endothelium denuded vessels pre-contracted with $PGF_{2\alpha}$. HO-1 and soluble guanylate cyclase (sGC) expressions were assessed by Western blotting in endothelium intact arteries.

Results. After 24h, SRM1648 and CoPP induced HO-1 expression, and decreased DEA-NOnoate mediated relaxation in endothelium-intact rat intrapulmonary arteries. However,

none of these treatments altered sGC expression. Co-treatment with CrMP for 24h prevented the SRM1648-mediated induction of HO-1 and partially restored NO-dependent relaxation. In addition, when CrMP co-treatment was added continuously in organ bathes during the experiments, SRM1648 induced-alteration of NO responsiveness was totally reversed. However, after 24h, SRM1648 failed to alter NO-dependent relaxation in endothelium free arteries.

Conclusion. These data provide evidence of HO-1 implication in particulate matter-mediated alteration of NO responsiveness in rat intrapulmonary arteries. These alterations probably initiate from endothelium and disrupt the NO-dependent activation of soluble guanylate cyclase and subsequent relaxation.