

Diesel Exhaust Exposure Alters Microvascular Blood Flow and Wall Shear Rate

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Pulmonary exposure to particulate matter (PM) is a known cause of systemic cardiovascular dysfunction; however, the mechanism(s) of damage are not fully understood. While this laboratory has characterized microvascular dysfunction after exposure to PM, the specific hemodynamic adjustments that follow PM exposure are unknown. The purpose of this study was to determine the effects of pulmonary exposure to diesel exhaust particles (DEP) on peripheral microvascular function and hemodynamics. Rats were intratracheally instilled with SRM 1650b (NIST, 100 $\mu\text{g}/\text{rat}$). The spinotrapezius muscle was prepared for intravital microscopy 24 hr after exposure. Arteriolar reactivity was assessed by iontophoretic application of endothelial-dependent (acetylcholine, ACh, 0.025 M) and endothelial-independent (sodium nitroprusside, SNP, 0.05 M) vasodilators. To assess the contribution of nitric oxide (NO) in this process, ACh applications were repeated in the presence of the NO synthase inhibitor, NG-monomethyl-L-arginine (L-NMMA, 10⁻⁴ M). In all experiments, red cell velocity was measured to characterize the local hemodynamic consequences of DEP exposure. Plasma was sampled from each rat for multiplex analyses. Compared to controls, DEP exposure increased arteriolar flow (26 ± 5 vs 18 ± 3 nl/s) and decreased wall shear rate (3939 ± 415 vs 4840 ± 295 s⁻¹). Compared to controls, arteriolar responsiveness to ACh was enhanced by DEP exposure (80 ± 4 vs 93 ± 3 μm respectively). Furthermore, this response remained largely intact during L-NMMA superfusion in the DEP group ($90 \pm 10\%$ vs $56 \pm 13\%$ in controls). DEP exposure did not affect arteriolar responsiveness to SNP. Several inflammatory mediators were altered in the plasma of DEP exposed rats. These results suggest that arteriolar volume flow and wall shear rate are adversely affected by DEP exposure. Such alterations in microvascular hemodynamics may be indicative of upstream PM-dependent effects and appear to be linked to circulating inflammatory mediators. Support: NIH RO1-ES015022 and HEI#4730 (TRN).