Proportional Impact of Inhibitors on Vascular Reactivity - Unraveling the Effects of Titanium Dioxide on Endothelium-Dependent Relaxation

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Nano-titanium dioxide (nTiO2), an engineered nanoparticle extensively used in consumer products. Exposure to nanosized particles during pregnancy has been shown to impair maternal health and fetal growth. We have previously identified that maternal inhalation of aerosolized nTiO2 during gestation can impair uterine arterial relaxation, limiting blood delivery to the feto-placental unit, a process that can have dangerous implications for fetal health. The purpose of this study was to identify the mechanism of nTiO2-induced vaso-impairment. We hypothesized that maternal nTiO2 inhalation will impair endothelium-dependent dilation due to reduced nitric oxide (NO) bioavailability. Pregnant rats were exposed to aerosolized nTiO2 nanoparticles (9.48 µg/m3 ± 0.11) from gestational day (GD) 5 to 19. Particle aerodynamic diameter was measured in real-time using a scanning mobility particle sizer (SMPS) (125.26 nm ± 1.82). On GD 20, maternal aorta and uterine artery were isolated, excised, and threaded onto metal wires to evaluate vasoactive responses to increased concentrations (10-9M – 10-4M) methacholine (an endothelium-dependent dilator). These measures were repeated in the presence of N(gamma)-nitro-L-arginine methyl ester (L-NAME; 10-4M), an endothelial nitric oxide synthase inhibitor. Although L-NAME successfully inhibited vasorelaxation, there were no significant differences between the vascular reactivity of control and exposed animals (82.0 ± 7.2 vs 74.8 ± 12.3 percent maximum tension in uterine arteries). By understanding the effects exerted by nTiO2 exposure during pregnancy, we can formulate targeted preventive strategies aimed at preserving maternal and fetal health while mitigating the potential risks associated with nTiO2 exposure during gestation. Supported by NIH R01ES031285 and NIH R25ES020721.