Impact of Pregestational Type-2 Diabetes Mellitus on Fetal Growth and Endothelial Function of Uteroplacental Radial Arteries in Rat Pregnancy

Abstract

Significant remodeling of the maternal uterine vascular system occurs during mammalian pregnancy. Under normal conditions, both anatomical and physiological changes allow arteries to supply adequate blood flow and bring necessary nutrients to the developing fetuses. Small radial uteroplacental arteries are fundamental in this process by controlling vascular resistance and regulating maternal uterine blood flow from placenta to fetus. In this study, the impact of pregestational type-2 diabetes on fetal growth outcome and endothelial function of uteroplacental radial arteries during rat pregnancy was investigated. On the 20th day of pregnancy, second order uteroplacental radial arteries feeding the placenta from Wistar (non-diabetic control model) and Goto-Kazaki (type 2 diabetic model) rats were dissected, cannulated, and pressurized to 50 mmHg. Phenylephrine was used to pre-constrict the arteries, followed by testing of acetylcholine, a vasodilator, in increasing concentrations (0.01 - 10μM). Parallel arteries were tested with phenylephrine and acetylcholine in the same manner but in the presence of L-NNA (200 μM) and indomethacin (10 μM) to inhibit the production of NO and prostacyclin. The Goto-Kazaki rat arteries showed reduced NO- and prostacyclin independent vasodilation and impaired acetylcholine-induced vasodilation. There was a significant reduction in number of fetuses and a marked increase of fetal resorption, likely due to endothelium-mediated vasodilatory dysfunction of resistance arteries.