Early Life Exposure to Hypoxia: A Developmental Insult Critical to the Programming of Cardiovascular Risk

Barbara T. Alexander

Genetics and environmental factors are known contributors to hypertension, a risk factor for cardiovascular disease. Intrauterine growth restriction (IUGR) as evidenced by low birth weight (LBW) is associated with elevated blood pressure indicating a critical role for adverse influences during early life on later cardiovascular health. Placental insufficiency is a major cause of IUGR, and nutrient and oxygen supply are components of the intrauterine environment that limit fetal growth resulting in LBW. In rodent models of placental insufficiency or maternal undernutrition during gestation, marked increases in systolic blood pressure (SBP) are observed in LBW offspring. However, the importance of hypoxia per se during early life on later increases in SBP has not been clearly elucidated.

Recent studies indicate that the period of developmental plasticity may extend beyond birth to include early postnatal life. SBP, blood pressure variability, and aortic pulse wave velocity are predictors of cardiovascular mortality. In this issue of the American Journal of Hypertension, Ross and colleagues demonstrated using the gold standard method of radiotelemetry that SBP was elevated in offspring exposed to hypoxia during the first 10 days of postnatal life. Blood pressure variability and aortic pulse wave velocity were also increased. Therefore, these findings indicate a critical role for postnatal hypoxia in the developmental programming of cardiovascular risk.

The effects of hypoxia on the programming of cardiovascular risk can be confounded by weight loss indicating undernutrition as a potential contributor. This study diminished the causative effect of undernutrition on SBP by comparing pups exposed to postnatal hypoxia to pups exposed to maternal nutrient restriction during the same period of development. Although pup weight was reduced to a similar degree in nutrient-restricted pups relative to hypoxic pups, SBP was not elevated in the nutrient-restricted pups indicating that moderate undernutrition during postnatal life alone is not sufficient to alter blood pressure in later life. However, the direct effect of postnatal undernutrition on adult blood pressure variability and adult aortic pulse wave velocity were not reported in this study. Differential and time-dependent changes in cardiovascular structure and function are observed in offspring programmed by exposure to prenatal hypoxia compared to offspring directly programmed by prenatal undernutrition. Whether postnatal undernutrition per se increased other predictors linked to cardiovascular risk is not yet known; thus, the exact role of moderate postnatal undernutrition as a developmental insult on later cardiovascular risk remains unclear.

Importantly, this study demonstrated that postnatal hypoxia is associated with elevated SBP in later life; yet the mechanism(s) is not known. The kidneys play a major role in the long-term regulation of arterial pressure and the kidney is sensitive to adverse influences during fetal and early postnatal life. Adverse postnatal influences that alter renal development in the rat lead to increased SBP. Moreover, developmental insults such as placental insufficiency and undernutrition alter renal mechanisms that are intrinsic to arterial pressure regulation including the renin–angiotensin system and the renal sympathetic nervous system. The importance of these factors in mediating hypertension in adult offspring exposed to hypoxia during early postnatal life warrants further investigation.

Disclosure: The author declared no conflict of interest.