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Influence of intrauterine growth restriction on postnatal osteoprotegerin concentrations and aortic intima-media thickness

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Introduction: Intrauterine growth restriction (IUGR) is considered a risk factor for atherosclerosis and coronary artery disease in adulthood. Understanding the pathophysiology of cardiovascular disease involves the identification of novel risk factors and biomarkers. There is emerging evidence that osteoprotegerin (OPG), a member of the tumor necrosis factor-receptor superfamily, participates in the pathogenesis of atherosclerosis by amplifying the effects of inflammation and traditional risk factors. In this case-control study we investigated whether IUGR affects postnatal OPG concentrations and the possible association between OPG levels and aortic intima-media thickness (aIMT), an index of preclinical atherosclerosis.
Methods: We studied 30 IUGR and 30 appropriate for gestational age (AGA) neonates matched for gestational age and gender. Quantitative determination of plasma OPG was performed with enzyme immunoassay on the second (DOL2) and fifth day of life (DOL5). Aortic intima-media thickness (aIMT) was measured in the distal abdominal aorta using a linear array probe, and adjusted for aortic lumen diameter.
Results: Neonates with IUGR had significantly higher OPG levels on both DOL2 and DOL5 as compared to controls (DOL2: 5.4±1.0 mmol/L vs. 4.6±1.0 mmol/L, p=0.002 and DOL5: 5.1±0.8 mmol/L vs. 3.9±0.7 mmol/L, p<0.001). Between DOL2 and DOL5, OPG concentrations did not change significantly in neonates with IUGR (p=0.087), but decreased slightly in controls (p=0.003). IUGR was also associated with increased aIMT (0.11±0.03 vs. 0.06±0.02, p<0.001). There was a positive correlation between OPG and aIMT on DOL2 (r =0.494, p<0.001), which became stronger on DOL5 (r=0.791, p<0.001; Figure).
Conclusion: We report significantly increased concentrations of OPG in IUGR neonates and a positive correlation with aIMT. The dynamics of OPG concentrations during the transitional period support the fetal origin of the cytokine. Follow-up studies with repeat OPG and aIMT measurements may be indicated to evaluate whether these findings represent a permanent effect of IUGR on the offspring.