

Fetal programming: Increased Neurofilament and MR-proANP levels in umbilical cord blood by fetal growth restriction as a sign of neuronal injury and heart failure

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Objective

The impact of fetal growth restriction on cardiovascular and brain function in the infancy is already well established. There are already some biophysical, but till now no biochemical markers that can be assessed prenatally, that prove fetal remodeling. Neurofilaments (NFL) are proteins which are involved in axonal transport. There is also a correlation between the NFL levels and the degree of disability and brain atrophy rate. Mid-regional pro-atrial natriuretic peptide (MR-proANP) is a peptide which can help in the assessment of heart failure. The aim of this study was to correlate the levels of NFL and MR-proANP in umbilical cord blood in pregnancies complicated with fetal growth restriction (FGR) to prove the neuronal and cardiac fetal programming.

Methods

This prospective case-control study enrolled 87 pregnant women, who delivered between 2020 and 2021 at the University Hospital of Dresden, Germany. FGR group (N=29) was defined according to the latest classification criteria of International Society of Ultrasound in Medicine: estimated fetal weight and birth weight below 10th centile combined with pulsatility indices of umbilical artery above 95th centile. The control group (N=58) was defined by patients having neither FGR nor other fetal or obstetrical pathologies. NFL and MR-proANP levels were measured in umbilical cord arterial blood after the delivery.

Results

The median levels of NFL and MR-proANP were significantly higher in FGR group (14.3 (9.7 - 25.1 IQR) ($p=0.014$) for NFL and 487.2 (218-708.8 IQR) ($p<0.0001$) for MR-proANP) compared to the controls (11.6 (8.2 - 15.9 IQR) for NFL and 170.4 (142.9-211.5 IQR) for MR-proANP). When the FGR group is divided into "early onset" FGR (N=11) and "late onset" FGR (N=18) groups, the median levels of NFL and MR-proANP were significantly higher in "early onset" FGR group (29.8 (24.5 - 34.8 IQR) ($p<0.0001$) for NFL and 764.4 (503.7-929.1 IQR) ($p<0.0001$) for MR-proANP) compared to the controls. There was no significant difference in median NFL and MR-proANP levels between "late onset" FGR group (11.3 (9.2 - 14.3 IQR) ($p=0.8915$) for NFL and 221 (150.8-454.4 IQR) ($p=0.0608$) for MR-proANP) and controls.

Conclusion

The significant increase in NFL and MR-proANP levels in cord blood in pregnancies complicated with FGR could be a sign of fetal programming, deteriorated brain development and heart failure of the fetuses and therefore interesting markers to predict the further neurological development and heart function.