Is fetal hypoxia a precursor of neonatal white matter changes in congenital heart disease?

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Target Audience

Neonatologists, pediatric cardiologists and neurologists involved in the care of newborn babies with congenital heart disease. Future therapeutic implications are also in the fields of obstetrics and fetal medicine.

Purpose

Congenital heart disease (CHD) is associated with brain dysmaturation, increased risk of perioperative white matter (WM) injury and neurodevelopmental delay (1). Fetal Doppler studies have shown altered cerebrovascular flow dynamics in CHD, suggesting 'brain-sparing physiology'. We sought to determine whether postnatal cerebral WM microstructural abnormality relates to abnormal fetal hemodynamics.

Methods

This prospective IRB approved study included 15 fetuses with CHD and 25 normal fetuses at 36 gestational weeks, who underwent phase-contrast MRI using metric optimized gating and T2-mapping for MR oximetry in the major vessels, according to our previously published technique (2,3). Neonatal MRI was performed at 5 days (SD 5 days) including diffusion tensor imaging and axial T2W-FSE. Both fetal and neonatal MRI studies were performed on the same 1.5T magnet (Siemens Avanto, Siemens, Erlangen, Germany). Apparent diffusion coefficient (ADC) values were measured in the centrum semiovale (CSO), frontal and parietal deep WM, and mean cerebral WM-ADC was calculated. Visual scoring of WM was performed using a 0 – 6 scale (number of T2-hyperintense regions). T-tests were used to compare the means of measured flow and WM values between the two groups, and Pearson's coefficient was calculated for correlation between fetal flows and WM parameters. GraphPad Prism 6 was used for statistical analysis, and a p-value of < 0.05 was considered statistically significant.

Results

Ascending aortic oxygen saturation ($AAoSO_2$), fetal oxygen consumption (VO_2) and cerebral VO_2 were significantly lower in the CHD group (49% vs. 58%, p = 0.02; 5.03 ml/min/kg vs. 7.12 ml/min/kg, p= 0.02 and 2.98 ml/min/kg vs. 4.23 ml/min/kg, p= 0.03, respectively). Although mean superior vena caval (SVC) flow (a surrogate for cerebral flow) was higher in CHD fetuses, the difference was not statistically significant. However, there was a moderately strong correlation between SVC flow and mean cerebral WM-ADC (Pearson's r = 0.38, p= 0.012) (Figure 1a). ADC was higher in CHD neonates in the frontal WM (by 6.9 %, p= 0.008), parietal WM (by 5.9 %, p= 0.02), and CSO (by 2.3 %, NS). Visual T2-score was significantly higher in CHD neonates (3.08 vs. 1.16, p= 0.002), with a negative correlation with $AAoSO_2$ (r = -0.33, p= 0.04) and VO_2 (r= -0.47, p= 0.005) (Figure 1b and 1c).

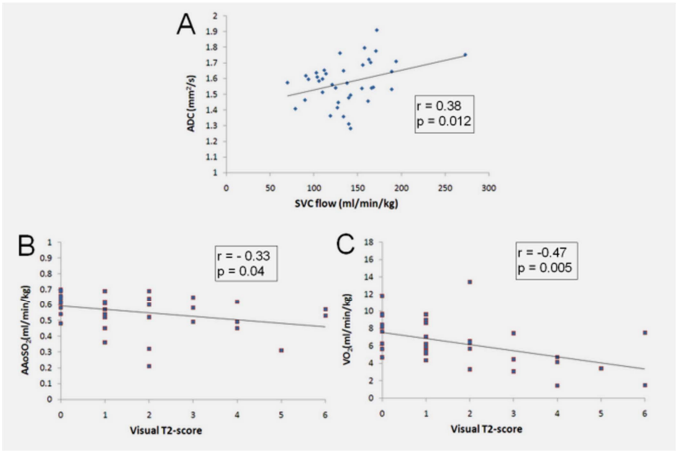

Figure 1. A) Positive correlation between fetal SVC flow and neonatal WM ADC. B) Negative correlation between fetal $AAoSO_2$ and neonatal WM T2-score. C) Negative correlation between fetal oxygen consumption and neonatal WM T2-score. Pearson's r and p-values are in accompanying boxes.

Conclusions

We conclude that neonatal WM abnormalities in CHD could be the result of reduced fetal oxygenation. The correlation between more severe WM abnormality and elevated SVC flow, a known marker of acute fetal hypoxia (the "brain sparing" response) is further evidence that WM changes are driven by reduced cerebral oxygenation in utero.

References

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