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Cardiac and mitochondrial function in HIV-uninfected fetuses exposed to antiretroviral treatment

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Objective

HIV-exposed but uninfected (HEU) children are generally considered healthy. However, several studies have reported changes in cardiac structure and function. The underlying mechanism of these cardiac changes remains to be elucidated, but mitochondrial toxicity secondary to combined antiretroviral therapy (cART) exposure during fetal life is suggested as a pathogenic pathway. Our objective was to evaluate fetal cardiovascular and mitochondrial biomarkers in HIV pregnancies.

Methods

A prospective cohort study including 47 non-infected fetuses from HIV pregnant women on cART and 47 fetuses from non HIV-infected women. Fetal echocardiography was performed at 26-32 weeks of pregnancy. Umbilical cord blood and placental tissue were collected at delivery to study mitochondrial parameters including mitochondrial DNA content (mtDNA) (ratio 12SrRNA/RNAseP) by rtPCR and mitochondrial function (cytochrome c oxidase, COX, enzymatic activity) normalized by mitochondrial content (citrate synthase, CS), by spectrophotometry.

Results

HEU fetuses presented larger and hypertrophic hearts (cardiothoracic ratio: HIV mean 3. 21 mm (SD 0. 81) vs. non-HIV 2. 72 (0. 42), p=0. 012) and mild pericardial effusion together with signs of systolic and diastolic dysfunction (isovolumic relaxation time: HIV 52. 2 ms (8. 85) vs. non-HIV 42. 5 ms (7. 30); p<0. 001). Cord blood mitochondrial content was significantly increased in HIV-exposed fetuses (CS activity: HIV 82. 9 nmol/min. mg of protein (SD 40. 5) vs. non-HIV 56. 7 nmol/min. mg of protein (28. 4); p=0. 007), with no differences in mtDNA content and COX activity. Myocardial and mitochondrial mass parameters were both significantly associated with zidovudine exposure.

Conclusion

HEU fetuses exposed to maternal cART presented signs of increased myocardial and mitochondrial mass associated with maternal zidovudine treatment, suggesting a fetal adaptative response to cART toxicity. Future studies are warranted to evaluate the toxicity of different cART combinations on the fetal heart in order to identify the safest options to be incorporated in the clinical management of these pregnancies.