Poor Placental Perfusion is Associated with Placental Endothelial Dysfunction in the First trimester

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BACKGROUND

Failure of the placental capillary network to develop normally has been associated with common pregnancy disorders including fetal growth restriction (FGR) and pre-eclampsia (PE). Although the effects are observed at term the problem begins early in gestation. Investigation of this at a relevant stage have been hindered by difficulties in identifying pregnancies in the 1st trimester that are affected as well as the capacity to isolate placental endothelial cells (PEC) at this time. We have used uterine artery Doppler ultrasound (UtAD) as a proxy measure of poor placental perfusion and our studies have established a correlation between high resistance indices (hRI) in 1st trimester uterine arteries and birth weight due to placental insufficiency. Using this technique we have isolated PEC from tissue obtained from terminations of first trimester normal pregnancies (nRI) and those at increased risk of developing FGR and subjected them to a number of comparisons.

HYPOTHESIS

We hypothesise that the behaviour of 1st trimester PEC isolated from pregnancies with hRI, and at increased risk of developing FGR, are compromised leading to the poorly developed vascular network seen at term.

METHODS

UtAD was performed on women undergoing surgical termination of pregnancy in the late 1st trimester. Inclusion criteria were: singleton pregnancy, gestational age 10-14 weeks, normal fetal anatomy and nuchal translucency thickness with no known maternal medical condition or history of recurrent miscarriage. PEC were isolated by enzymatic digestion and selection using CD31-coated magnetic beads. Cell proliferation, apoptosis and cell motility were assessed by time-lapse microscopy. Apoptosis was induced with 30ng/ml TNFα. The study had local Ethics Committee approval and patients gave full informed consent.

RESULTS

PEC isolated from 1st trimester pregnancies with a hRI divide more slowly in culture. The basal rate of apoptosis in these cells was also significantly greater than that seen in the nRI group. The pro-apoptotic stimulus, TNFα, induced significant levels of apoptosis in the hRI PEC but not nRI PEC. Inhibition of nitric oxide (NO) production by the NO synthase inhibitor, L-NAME, significantly increased the sensitivity of cells to apoptotic stimuli from the nRI group but not the hRI group. There was a small decrease in the motility of PEC isolated from hRI compared to nRI cells but this did not reach statistical significance.

CONCLUSION:

PEC from hRI 1st trimester pregnancies are inherently different to PEC from a nRI pregnancies and this may contribute to poor placental vascular development seen in FGR.

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