Study of CYP17 Gene Polymorphism in Fetal Growth Restriction with Reference to Organochlorine Pesticide Levels

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Background

The cytochrome P-450c17alpha enzyme encoded by the P-450c17alpha (CYP17) gene functions in the key steps of the estrogen synthesis pathway. The genetic variation in the maternal CYP17 gene leads to differences in estrogen level which affects fetal growth and causes fetal growth restriction (FGR). Organochlorine pesticides (OCPs) are endocrine disruptors which alter the normal estrogen-progesterone balance and are reported to be associated with adverse reproductive outcomes.

Aims & Objectives

To investigate the gene-environmental interaction between maternal and cord OCPs level, and maternal CYP17 gene polymorphism with the risk of FGR.

Material & Methods

Maternal and cord blood samples of 50 term FGR cases (birth weight <10th percentile for gestational age as per Lubchenco's growth chart) and of equal number of normal pregnancies were collected. Women with occupational exposure to OCPs, anemia, hypertension, antiphospholipid antibody syndrome, medical disease, parity more than four, history of smoking, alcohol consumption or chronic drug intake were excluded from both the groups. The samples were collected at the time of delivery/after delivery and were analyzed for OCPs levels by Gas chromatography system equipped with electron capture detector and for polymorphic analysis of CYP17 gene using PCR-RFLP.

Results

Significantly higher levels of á-HCH, â-HCH, and ã-HCH were found in maternal blood and cord blood samples of FGR cases as compared to controls. The frequency of A1A2/A2A2 genotype was significantly lower (p=0.041, OR=0.421, 95% CI=0.184-0.966) in FGR cases as compared to controls. When gene environmental interaction between the CYP17 gene polymorphism and OCPs level was considered, significant (p=0.004) association was seen between endosulfan and CYP17 A1A1 genotype with an estimated reduction in birth weight of 315g.

Conclusions

Higher levels of OCPs and CYP17 homozygous A1/A1 in pregnant women may be considered as an important etiological factor in 'idiopathic' FGR. The present study provides evidence that genetic variation and its interaction with the environmental exposure may increase the risk of FGR. Further studies are needed with larger sample size, incorporating other gene polymorphism and environmental exposures to strengthen the observations obtained in the present study.