ABSTRACT

Intrauterine growth restriction (IUGR) refers to a condition in which a fetus is unable to achieve its genetically determined intrinsic growth potential. IUGR pathology is mainly attributed to limited maternal oxygen and nutrient supply to the fetus and is associated with increased perinatal morbidity and mortality, as well as long term complications during childhood and adult life.

In the present study, metabolomics was applied in order to identify secondary metabolites that characterize IUGR pathology. Nuclear magnetic resonance (NMR) metabolomics was implemented in umbilical cord blood and maternal blood samples. The study comprised 84 parturients giving birth to 48 IUGR and 36 appropriate for gestational age (AGA) infants. Supervised and unsupervised multivariate statistical analysis discriminated IUGR and AGA umbilical cord blood and maternal blood samples.

A clear association between maternal and umbilical cord blood altered metabolomic profile was evidenced in IUGR pregnancies. A total of 56 metabolites were identified in the NMR spectra, with 7 metabolites being equally connected to IUGR-AGA discrimination in both umbilical cord and maternal blood samples. This correlation probably suggests common mechanisms that differentiate the metabolic imprint between IGUR fetuses and their mothers. This conclusion, which needs further confirmation by additional studies, could lead to the use of biomarkers in the blood of pregnant women in order to develop new diagnostic tools for IUGR. The emergence of potential biomarkers at an early stage of pregnancy could help halt the negative effects of IUGR either through medication or nutritional intervention for the mother.

In particular, the enhancement of gluconeogenesis and the suppression of glyceroneogenesis in the neonatal IUGR group is probably attributed to the association of IUGR pathology with insulin resistance.

Moreover, the increase in BCAAs and consequently 3-methyl-2-oxovaleric acid in the IUGR groups may be related to the deficiency or dysfunction of the Branched Chain α-Keto acid Dehydrogenase (BCKD) complex.

Finally, the decrease in tryptophan in IUGR neonates seems to be related to the adaptation mechanisms in order to meet its increased serotonin needs.

The results of the present dissertation confirm previous ambiguous results related to the complex pathology of intrauterine growth restriction, and offer new data on potential biomarkers for future application in early diagnosis.