THE UNIVERSITY OF MEDICINE AND PHARMACY
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THE STUDY OF PLACENTAL CIRCULATION IN FETAL GROWTH RESTRICTION

- DOCTORAL THESIS -

ABSTRACT

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2011
Intrauterine/Fetal growth restriction (IUGR/FGR) is the most important cause of perinatal morbidity and mortality affecting normal pregnancies in approximately 7-15% or pregnancies complicated with hypertension in up to 30% of the cases.

Although "small" fetuses with intrauterine growth restriction are described in many ways, the specialty literature defines it most commonly as a fetus with estimated weight below the 10th percentile for its gestational age.

Recently fetuses with IUGR are evaluated from the metabolic and vascular point of view, demonstrating that metabolic and transport alterations occur in these fetuses even when umbilical blood flow and fetal heart rate are normal.

This thesis aims to identify fetuses which are small for their gestational age based on specific local population growth curves and also aims to differentiate fetuses with real IUGR from those which are "small" but healthy based on the Doppler assessment of uterine blood flow, umbilical and especially fetal changes.

The theoretical part presents an outline of the concept and ultrasound diagnosis of IUGR, the most important arterial and venous vessels investigated with Doppler in fetal growth restriction, normal and pathological aspects of the development of placental circulation and possible perinatal complications in pregnancies with IUGR.

The special part, after describing research methodology, includes several chapters. The first one is based on the elaboration of fetal growth curves of newborns from the Obstetrics and Gynecology II Clinic, Tg. Mureș during the studied period (2008-2011) based on birth weight and gestational age. The following chapters include Doppler parameter studies of placental and fetal circulation in normotensive and hypertensive pregnancies with SGA (small for gestational age) fetuses and with growth restriction compared to fetuses with normal weight at birth (appropriate for gestational age - AGA) and the velocimetry indices correlated with perinatal outcomes. Another chapter analyzes the correlations between fetal and utero-placental Doppler parameters and fetal erythropoietin value (determined from the umbilical cord immediately after birth - before the first breath) as a marker of intrauterine fetal hypoxia.

Maternal-fetal arterial Doppler ultrasound investigations enabled us to diagnose pregnancies with real fetal growth restriction in both normotensive and hypertensive pregnancies as well as in pregnancies without a clear etiologic factor for IUGR, distinguishing them from those with SGA but healthy fetuses.

Placental vascularization assessed by color Doppler and 2D power Doppler technique was statistically significant in a lower rate in the SGA group than in the AGA group in all performed studies.
The frequency of Doppler changes (uterine and umbilical RI above the 95th percentile, cerebral (MCA) RI below the 5th percentile according to the reference values of the gestational age and CPR under 1.08) was obviously higher in SGA fetuses with statistically significant but different values than in AGA fetuses in both normotensive (with mild and progressive placental dysfunction) and hypertensive pregnancies (with progressive and severe placental dysfunction), the intensity of Doppler changes being higher in hypertensive pregnancies.

In case of hypertensive pregnancies, the rate of premature birth under 37 weeks was found to be 3 times higher in SGA than in AGA fetuses and births less than 34 weeks of gestation were found only in the group of SGA fetuses, the best predictor of prematurity in hypertensive pregnancies being the RI of the umbilical artery over the 95th percentile.

The onset of centralization of fetal circulation, especially before 34 weeks of pregnancy with IUGR and preeclampsia by real-time assessment of fetal Doppler changes was essential for proper and individualized monitoring of each pregnancy in order to be able to determine the optimal timing for delivery.

The most effective parameter in the study of normotensive and mainly hypertensive pregnancies proved to be CPR below 1.08. This parameter had a Se, PPV, Sp, NPV superior to other RI evaluated separately regarding the diagnosis of SGA, birth by caesarean section, admission to the newborn intensive care unit (NICU) and neonatal respiratory complications. The CPR subunit also played an important role in taking decisions in case of delivery in hypertensive pregnancies.

Neonatal evolution on admission to NICU, respiratory complications, oxygen dependency and the number of hospitalization days presented better statistically significant values for AGA fetuses compared to SGA fetuses.

Fetal venous velocimetry presenting isolated and minor changes was not important in taking decisions regarding delivery in pregnancies with IUGR, but was useful in monitoring pregnancies with preeclampsia where the phenomenon of centralization of circulation was confirmed.

The EcoDoppler examination performed in all studies also allowed the identification of fetuses with IUGR and the "brain sparing" phenomenon but with normal umbilical Doppler, requiring closer monitoring of these cases.

The more advanced the adaptive hemodynamic fetal changes were the higher the fetal erythropoietin (EPO) values determined at birth were and it was best correlated with the RI of the MCA. EPO is a marker of hypoxia at birth in pregnancies with IUGR and
preeclampsia, its values being also high in pregnancies where the placental insufficiency was not revealed during the umbilical artery Doppler ultrasound.

Doppler ultrasound remains extremely useful for the obstetrician for screening tests and monitoring high risk pregnancies (PE and IUGR), at the same time being accessible, affordable, accepted by patients, with reproducible results and less expensive than other methods.

The clinical use of serum measurements of fetal EPO in the management of high risk pregnancies and treatment using EPO in case of fetuses coming from premature births for normal neurological development are promising.