THE ECODOPPLER EXAMINATION VALUE IN MONITORING THE FETAL GROWTH RESTRICTION (FGR) IN PREGNANCIES WITH HYPERTENSION

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Keywords: *velocimetry, eco Doppler, preeclampsia, FGR*

Abstract: *The characteristics of the cardiovascular manifestations in FGR are determined by the gestational age at onset and the severity of placental dysfunction, identified by the umbilical artery Doppler. The RI analysis of umbilical artery in our study showed: Se 80%, Sp 100%, PPV 100% and NPV of 75% for FGR because of HT at the age group of 32-36 weeks; serial observations of UA Doppler status remain a cornerstone for determining monitoring intervals in FGR.The assessing in real-time of the maternal-fetal Doppler changes and selective monitoring in order to surprise the onset of the "brain sparing" phenomenon especially before 34 weeks are essential in risk pregnancies (PE and FGR) to decide the best time of birth and to reduce as much as possible perinatal morbidity and mortality.*

Cuvinte cheie: *velocimetrie, eco Doppler, preeclampsie, RCIU*

Rezumat: *Caracteristicile manifestărilor cardio-vasculare în RCIU sunt determinate de vârsta gestaţională la debut şi de severitatea disfuncţiei placentare identificată prin velocimetria arterei ombilicale. Analiza IR al arterei ombilicale în studiul nostru a arătat o Se de 80%, Sp 100%, VPP de 100% şi o VPN de 75% pentru RCIU datorită HTA la grupa de vârstă 32-36 săptămâni, observaţiile seriate eco Doppler ombilicale rămânând fundamentale în stabilirea intervalului monitorizării în RCIU. Aprecierea modificărilor Doppler materno-fetale în timp real şi monitorizarea selectivă pentru surprinderea debutului centralizării circulaţiei fetale mai ales înainte de 34 de săptămâni sunt esenţiale în sarcinile cu risc (PE şi RCIU) pentru a decide optim momentul naşterii cu reducerea cât mai mult posibil a morbidităţii şi mortalităţii perinatale.*

INTRODUCTION

Pre-eclampsia (PE) and intrauterine fetal growth restriction (FGR) represent important causes of maternal and perinatal morbidity and mortality. These 2 conditions are felt to be the result of abnormal placenta formation involving abnormal trophoblast invasion of spiral arteries with the modification of the blood flow in the uteroplacental circulation.(1,2)

The arterial and venous Doppler ultrasound performed in maternal-fetal risk pregnancies is particularly useful for both predictive value of perinatal complications and for FGR fetuses monitoring to improve prognosis at birth**.**

THE AIM OF THE STUDY

The aim in our study was to evaluate the intrauterine functional status of fetuses in which growth restriction was found because of maternal hypertension (HT), by assessing the maternal-fetal ecoDoppler changes in dynamic and to choose the best time to birth.

MATERIAL AND METHODS

We performed a prospective study between 2008-2011 in Obstetrics-Gynecology Clinic of Tg. Mureş District Hospital, being examined (clinical, by laboratory and ultrasound) a more than 80 pregnant women from the first trimester until the postnatal period and who had hypertension. Among these we selected a total of 52 pregnant women with HT hospitalized in the third trimester of pregnancy and to whom we could follow in dynamic both the intrauterine fetal development by repeated biometric ultrasound examination and serial arterial and venous eco Doppler changes at a variable interval depending on the particularities of each pregnancy. Exclusion criteria included: multiple pregnancies, maternal diseases, fetal malformations and other causes of FGR.

Ultrasound examinations were performed with the device Logiq S6 produced by General Electric HealthCare (2006) and purchased by our clinic in 2008. Database included:

- Pesonal details - age of pregnant women, the environment of origin, socio-economic conditions, education, body mass index.
- Fetal biometry - biparietal diameter (BPD), head circumference (HC), abdominal circumference (AC), femur length (FL), reports: FL/HC, FL/AC, HC/AC, estimated fetal weight (EFW).
- Doppler velocimetry - resistance index (RI), pulsatility index (PI), systolic-diastolic index (S/D) for placental uterine arteries (PUA) and non-placental uterine arteries (NPUA), umbilical artery (UA) middle cerebral artery (MCA), cerebral-placental ratio (CPR=RIcer/RIumb) and umbilical-placental ratio (PIumb/PIcer). Venous Doppler (where appropriate) was performed in the inferior vena cava (IVC), venous duct (VD) and umbilical vein (UV). • Non-stress test (NST)
- Data regarding birth: gestational age, modality of delivery (spontaneous, oxytocin perfusion or by caesarean section),

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Apgar score at 1' and 5', weight, days of hospitalization.

The 52 pregnancies included in the study were divided into 2 groups: one consisting of 16 pregnancies with HT and FGR and the second group consisting of 36 pregnancies with HT but without FGR. The FGR diagnosis was established by most accepted criteria (2, 3) and adapted to our population and also confirmed after birth.

Doppler examinations were performed after 28 weeks of amenorrhea for the 52 pregnancies and velocimetric measurements taken in the statistical calculation were those made before birth.

Statistical analysis of obtained data was performed by processing in the "Microsoft Excel" and "Graphpad Prisma" programs. We followed parameters in the descriptive statistics, it was applied Student test, based on contingency table 2 × 2 it was applied Chi square test and Fisher test when we need. P-value less than 0.05 was considered statistically significant. We used tables and graphs for nominal and ordinal data.

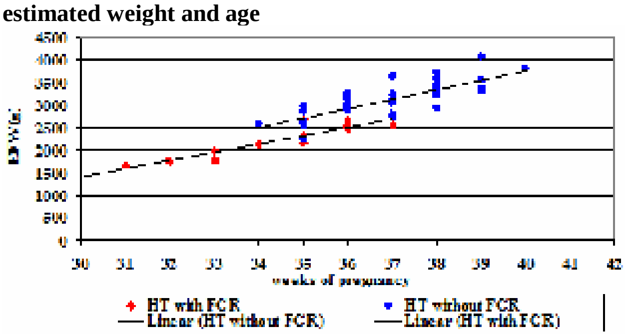
For establishing the Doppler criteria in FGR diagnosis in pregnancies with HT we set 4 gestational age groups for each of the two lots. According to charts based on studies much more complex we considered the maximum value of uterine, umbilical and middle cerebral artery RI for the different ages of pregnancy and to these values we have appreciated RI of the arteries examined in our study. The assessing of diagnostic test accuracy with known parameters: sensitivity (Se), specificity (Sp), positive predictive value (PPV) and negative predictive value (NPV), was achieved by a model based on standard threshold of artery resistance index as we stated above.

RESULTS

Between the two groups there were no statistically significant differences regarding: age, area of origin, education and body mass index, the value of p being >0.05.

Following the application of student test we found a statistically significant difference ($p<0.0001$) between the 2 groups for all ultrasound measured fetal biometric parameters (BPD, HC, AC, FL, FL/HC, FL/AC, HC/AC). Similarly, there was a statistically significant difference both on the ultrasound estimated fetal weight and the weight at birth between the two groups ($p<0.0001$). The distribution of fetuses based on ultrasound estimated weight and age and the distribution of fetuses according to weight and age at birth are shown in Figures 1 and 2.

Figure no. 1. Distribution of the fetuses based on ultrasound estimated weight and age



Analyzing types of hypertension in the two groups it was found the presence of severe PE in 25% in the group with FGR compared to 2.8% in the group without FGR as can be seen in Figure 3.Mean and standard deviation of the velocimetric indices and ratios in the 2 groups with the value of p we have shown in Table 1.

Applying a Fisher test for the bilateral notch presence in the uterine arteries it is obtaining a statistically significant p of 0.0016, a relative risk RR of 3.72 with confidence interval CI: 1.815 to 7.654, so a risk of 3.72 higher occurrence of FGR if the notch is present bilaterally. Graphical representation between the two groups is shown in Figure 4. PPV is 72.73%.

Figure no. 2. Distribution of fetuses according to weight and age at birth

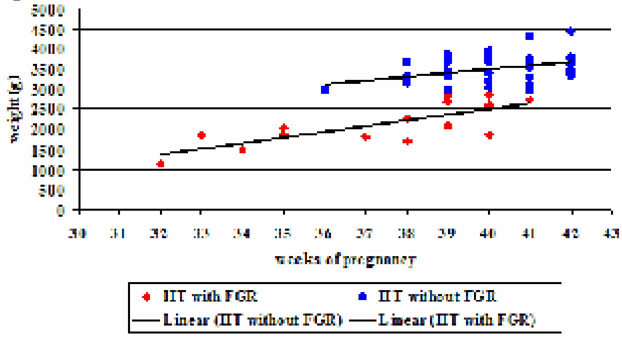


Figure no. 3. Graphical representation of types of HT in the 2 pregnancy groups

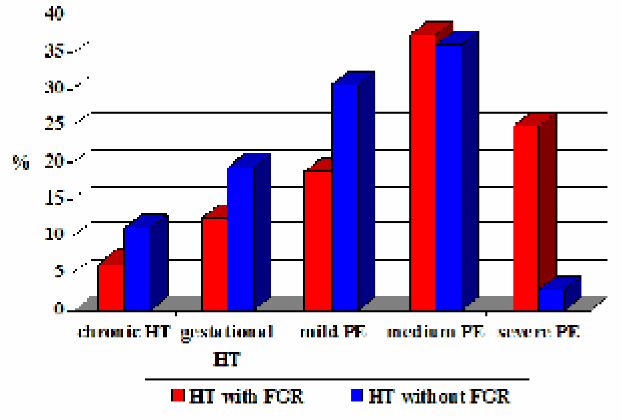


Table no. 1. Descriptive study of the velocimetric indices in the 2 groups

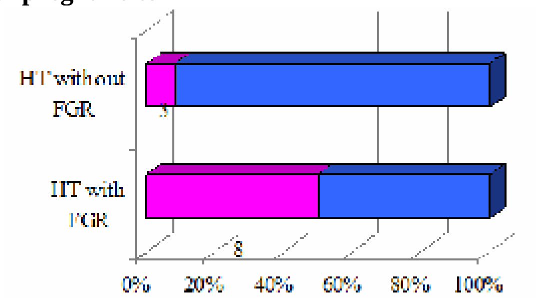
Artery	Velocimetric indices	Mean		Std. Deviation		Mean
Placental uterine (PUA)	IR	0.57	0.14	0.46	0.07	**0.0004**
Non-placental uterine (NPUA)	IP	1.08	0.48	0.68	0.16	**<0.0001**
	S/D	2.65	0.93	1.88	0.26	**<0.0001**
	IR	0.67	0.12	0.53	0.09	**<0.0001**
Umbilical (UA)	IP	1.46	0.61	0.88	0.30	**<0.0001**
	S/D	3.56	1.55	2.24	0.56	**<0.0001**
	IR	0.68	0.15	0.54	0.07	**<0.0001**
Middle cerebral (MCA)	IP	1.29	1.07	0.80	0.16	**0.0096**
	S/D	3.14	0.89	2.25	0.41	**<0.0001**
	IR	0.69	0.09	0.69	0.07	0.7359
Ratio	IP	1.27	0.35	1.26	0.28	0.9190
	S/D	3.62	1.28	3.68	1.63	0.9124
	CPR (Arbeille I.)	1.05	0.27	1.30	0.22	**0.0010**
	Umb PI /Cer PI	1.15	1.23	0.66	0.22	**0.0217**
Artery	Velocimetric indices	Mean	Std. Deviation	Mean	Std. Deviation	P value

The study by age groups of velocimetry in examined arteries for FGR we summarized in Table 2. It is seen for umbilical artery a Se of 80% between 32-36 weeks and 77.8% between 36-40 weeks and a PPV of 100% and 77.8% respectively. For age groups between 28-32 weeks and over 40 weeks we found little value in order to make an objective analysis.

Table no. 2. Arteries velocimetric study in the age groups

Artery	NPUA		PUA		UA		MCA	
Chronol. age	32-36 weeks	36-40 weeks	32-36 weeks	36-40 weeks	32-36 weeks	36-40 weeks	32-36 weeks	36-40 weeks
Se	40%	66,6%	60%	66,6%	80%	77,8%	40%	77,7%
Sp	100%	72,7%	33,33%	90,0%	100%	90,9%	33,3%	22,7%
PPV	100%	50%	60%	75%	100%	77,8%	50%	29,2%
NPV	50%	84,2%	33,3%	86,9%	75%	90,9%	25%	71,4%

Figure no. 4. The presence of bilateral "notch" in the 2 groups of pregnancies



The decision for delivery was made taking into account the mother condition, BP values, gestational age, fetal weight and eco Doppler changes for each pregnancy.

Proportion of births by caesarean section was higher in pregnancies with FGR ie 68.8% compared to pregnancies without FGR (47.2%) but not significant p (p = 0.46); births directed by oxytocin perfusion were close numerical (p = 0.39); the proportion of spontaneous births of fetuses without FGR was over four times greater (27.8%) than in group 1 (6.3%) (however, p = 0.46); videx application at birth to one case in each group generated a statistically significant difference (p = 0.001) between the two groups. Applying student test between Apgar score at 1 minute averages of the two groups we have obtained a value of p close to significance (p = 0.0625) and between Apgar score at 5 minutes averages of the two groups it was found a statistically significant difference (p = 0.0012).

Duration of hospitalization of new-born babies with FGR was almost double compared with those with normal weight at birth: 13.94 days SD 9,334 from 6.94 days SD 1,655 (p = 0.0023).

DISCUSSIONS

The hypertension action and especially PE on the second half of pregnancy influenced fetal growth potential resulting in the development of an asymmetric hypotrophy of fetuses in our study, the FL/AC ratio being >0.24 in the first group; the influence on fetal growth and development was more powerful and evident by biometry when hypertension was present early in pregnancy. (4)

As shown in Figures 1 and 2, a much smaller proportion of the pregnancies from the first group developed until term, the decision for delivery being influenced by several factors. Respecting the classification of hypertension in pregnancy as reference books (4.5) and updated clinical guide (6) we set the proportion of each type of hypertension in the 2 groups as shown in Figure 3. The presence of a greater proportion of medium and severe PE in the first group also explains the more obvious velocimetric changes in this group (Table 1); fetal monitoring in this group was more common (at 2-5 days) or even daily after some recommendations from the literature (7) in the situation of an absent or reversed diastolic flow in the umbilical artery as we have done in one case from the first group.

Uterine artery Doppler study showed a 100% PPV of IR in NPUA and 60% PPV of the IR in the PUA between 32-36 weeks for FGR, the predictive value increased to 75% between 36-40 weeks. These results are supported by some authors (8,9) but other more complex studies (1) believe that changes in uterine velocimetry have predictive value for PE more than for FGR. Doppler ultrasound significance of the uterine arteries increases when taking into account both the values of velocimetric indices and the presence of "notch" (8) especially bilateral (8,10) as shown in our study (Figure 4).

Umbilical artery flow monitoring in our study allowed assessing placental function reserve in dynamic, knowing that the progression of vascular lesions with progressive worsening of placental dysfunction induces abnormal umbilical Doppler aspects from reduced diastolic flow to reverse it. (11)

Umbilical artery flow appreciation by determining velocimetric indices (especially the S/D ratio) can predict the likelihood of perinatal consequences of fetuses with RCIU, as an independent factor with significant predictive value. (12)

RI analysis of umbilical artery in our study showed a high Se (80%), 100% Sp, 100% PPV and NPV of 75% for RCIU in the age group of 32-36 weeks, these indicators having lower values in pregnancies between 36-40 weeks. The time from one to another Doppler abnormality was found to be much lower as the age of pregnancy at which the first Doppler changes were observed was lower (11) in our study before 30 weeks. If the Doppler changes occur later, by increasing BP values after 33-34 weeks then fetal growth potential is less influenced and the time from one Doppler change to another is higher (11) as we observed in our study.

Analysis of MCA indices does not show a statistically significant difference between the two groups (Table 1) and the value of indicators is higher in the age group of 36-40 weeks, Se is 77.7% and NPV is 71.4% (Table 2).

CPR increases the sensitivity of velocimetric exploration considering both placental vascular abnormalities responsible for impaired maternal-fetal exchange and fetal cerebral hemodynamics response to the occurrence of hypoxia. (8) Concerning CPR the difference was statistically significant between the 2 groups.

Venous Doppler changes were recorded in the venous duct by decreasing atrial contraction wave (a) observed in one case with reversed diastolic flow in umbilical artery.

Even if we failed to statistically analyze the progression of Doppler abnormalities in FGR as shown in some studies more complex (11), we observed that the time from the phenomenon of centralization of fetal circulation ("brain sparing") with a clear cerebral vasodilatation (low RI in MCA) and CPR subunit until the birth was between several hours and 7 days. The decision for delivery was made taking into account the mother condition, BP values, gestational age and fetal weight. NST changes were observed in 4 cases in the first group.

Extension of the hospitalization was explained by the addition of prematurity to 4 fetuses with FGR in the first group. Some authors (13) supported and demonstrated the importance of evaluation of the report umbilical PI/cerebral PI (in our study this ratio was statistically significantly different between the 2 groups), showing direct correlation with FGR and the predictive value of this report for non-reactive fetal cardiotocographical tests and for the period of hospitalization. A ratio above 1.26 predicts a period of hospitalization of the newborn more than 15 days. Among fetuses with FGR in our study in one case we found an umbilical PI/cerebral PI report of 5.61 and for this newborn the period of hospitalization was 40 days. Postnatal evolution was favorable except one neonatal death in a pregnancy from the first group that there was a hematoma retroplacental, death occurred at 5 days postpartum.

CONCLUSIONS

The best screening and monitoring tests in high risk pregnancies such as PE and FGR have to be accessible, available and relatively inexpensive. They must also provide reproducible results and be acceptable to patients. Maternal-fetal arterial and venous Doppler ultrasonography fulfills these criteria and is relatively easy to perform with training and experience. From our case studies shows the importance of the assessments in real-time of the maternal-fetal Doppler changes and of selective monitoring in order to surprise the onset of fetal circulation centralization (“brain sparing”) especially before 34 weeks to decide the best time of birth as much as possible to reduce perinatal morbidity and mortality.

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