Doppler examination in the evaluation of outcomes in pregnancies complicated by gestational hypertension and fetal intrauterine growth retardation - is it enough?

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Summary

Aim: The relations between abnormal umbilical and cerebral Doppler, cerebral-umbilical (C/U) ratio, and outcomes in pregnancies complicated by gestational hypertension and fetal intrauterine growth retardation were evaluated. *Materials and Methods:* A retrospective study of 53 monofetal pregnancies in 2010 was conducted at the Institute of Gynecology and Obstetrics, Belgrade. Statistical analysis: chi-square likelihood ratio test, Student's t-test and Spearman's coefficient correlation. *Results:* There was not a significant correlation between the timing of registration of abnormal umbilical Doppler to delivery and outcomes of high-risk pregnancies. There was a significant correlation between C/U ratio and APGAR-5 ($p = 0.003$). We found a significant correlation between neonatal birth weight and APGAR-5 ($p = 0.000$), neonatal asphyxia ($p = 0.000$), intracranial hemorrhage ($p = 0.000$) and respiratory distress syndrome ($p = 0.000$). *Conclusion:* Umbilical and cerebral artery Doppler is a relatively poor predictor of neonatal outcome. It seems that neonatal birth weight is the best predictor of neonatal outcome in high-risk pregnancies.

Key words: Gestational hypertension; Intrauterine growth retardation; Doppler; Fetus; Umbilical and cerebral velocimetry; Neonatal outcome.

Introduction

In 2008, The Society of Obstetricians and Gynecologists of Canada (SOGC) revised guidelines that simplified the classification of hypertension in pregnancy into two categories, preexisting or gestational, with the option of adding "with preeclampsia" to either category if additional maternal or fetal symptoms, signs or test results support this. It occurred in about 5-8% of all pregnancies in Canada [1] and in about 7% of all pregnancies in Yugoslavia in 1996 [2]. Intrauterine growth restriction (IUGR) fetuses have low growth potential, either as a result of genetic disease or environmental damage, or due to reduced placental perfusion and utero-placental insufficiency, and they are at increased risk of perinatal morbidity and mortality and will require close fetomaternal monitoring and probably earlier intervention. IUGR occurs when gas exchange and nutrient delivery to the fetus are not sufficient to allow it to thrive in utero. This process can occur primarily because of maternal disease causing decreased oxygen-carrying capacity (e.g., cyanotic heart disease, smoking, etc.), a dysfunctional oxygen delivery system secondary to maternal vascular disease (e.g., diabetes with vascular disease, hypertension, etc.), or placental damage resulting from maternal disease (e.g. thrombophilia, various autoimmune diseases). In pregnancies complicated by placental dysfunction, there may be a reduction in the number of functional villi and/or small blood vessels with resulting increased impedance, mainly reflected by decrease in end-diastolic velocity. When the resistance increases even more, there is no diastolic forward velocity (absent end-diastolic velocity - AEDV). Further increase in the resistance causes reversed end-diastolic velocity - REDV and middle cerebral centralization, a late step in the cascade of events leading to poor perinatal outcome [3].

The aim of the study was to assess the accuracy of pathological antepartum Doppler velocimetry AEDV, REDV and middle cerebral artery centralization on prediction of poor perinatal outcome in pregnancies complicated by hypertensive disorders.

Materials and Methods

Fifty-three pregnancies in and after the 28th to 39th gestational week complicated with gestational hypertension and IUGR (below the 10th percentile for estimated gestational age), and treated at the Institute of Obstetrics and Gynecology, Clinical Center of Serbia, in 2010, were retrospectively included in the study. Gestational age was calculated according to date of the last menstrual period and confirmed by first trimester ultrasonography. If there was a discrepancy (> 5 days), ultrasound (US) examination was used to determine gestational age. According to the criteria of Xiong and Fraser [4] gestational hypertension was defined as a blood pressure equal to or greater than 130/90 mmHg on more than two occasions more than six hours apart without proteinuria after 21 weeks of gestation in 40 (75.48%) out of 53 patients. Preeclampsia was diagnosed as hypertension of equal or greater than 130/90 mmHg but less than 160/110 mmHg with proteinuria of 1+ or 2+ on dipstick in two samples six hours apart or more than 0.3 g in a 24-hour urine collection in 24.52% of patients (13/53) but severe preeclampsia was diagnosed when preeclampsia was complicated by a systolic pressure of ≥ 160 mmHg or diastolic pres-

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sure ≥ 110 mmHg and/or if proteinuria was more than 2+ on dipstick or 5 g in 24-hour urine collection in 46.1% (6/13) of patients. US measurements of fetal biometry were obtained every two weeks. IUGR was based on: 1) US biometry of the fetus, combination of biparietal diameter (BPD), abdominal circumference (AC), femer length (FL) and head circumference (HC) - 96.2% (51/55); 2) US estimated fetal weight (Hadlock formula, based on measurements of the fetal head, body and femur) - 90.1% (48/53); and 3) US Doppler flow umbilical and cerebral velocimetry and cerebral-umbilical (C/U) ratio 100% (53/53). The fetal biophysical profile was performed in 20 min and Doppler velocimetry studies of fetal umbilical artery (UA), and middle cerebral artery (MCA) activity were performed at least every two weeks. The frequency of testing was increased if the results were abnormal or borderline. The last Doppler examination was performed approximately 24 hours before delivery. A combined real-time pulsed Doppler system fitted with 3.75 MHz curvilinear probe (Toshiba) was used. The spatial peak temporal average power did not exceed 87 mW/cm. The Doppler angle of insonation was less than 30; the sweep speed was 2.5 cm/sec. The women rested in a semi-recumbent position during Doppler examination. All measurements were performed by the same physician during fetal apnea. Blood velocity waveforms were obtained from both UA and fetal MCA. The UA was insonated close to its placental insertions and the MCA about 1 cm distal to its origin from the internal carotid artery. The resistance index was calculated for each vessel by averaging the first two good quality resistance indexes obtained from two consecutive waveforms.

Continuous variables are presented as mean (standard deviation as 95% confidence interval/CI) assessed for normality or not, and comparisons were made using the chi-square likelihood ratio test to estimate the difference between resistance indexes in the UA resistance index (RI - REDV AEDV), MCA RI and C/U ratio and perinatal outcomes of pregnancy (Apgar/5 min, neonatal asphyxia, intracerebral hemorrhage (ICH) and respiratory distress syndrome (RDS). Spearman's test was used to estimate significance of correlation between abnormal umbilical and cerebral Doppler and perinatal outcomes as well as neonatal birth weight and perinatal outcome.

Multifetal pregnancies, suspected fetal congenital malformations, and maternal Rh isoimmunization were excluded from the study.

Results

The mean age of all women participating in our study was 28.26 ± 6.1 years. Of the women, 18.8% were older than 35 years and 24.5% were younger than 25 years. Most of them were nulliparous - 71.7%. Recurrent IUGR was found in two cases. The majority of women had had adequate prenatal care during their pregnancy (94.3%). The most common cause of fetal IUGR might be attributable to pregnancy induced hypertension (PIH), accounting for 62.2% (33/53), preeclampsia - 26.4% (14/53), and severe preeclampsia 11.4% (6/53). IUGR was diagnosed before 24 gestational weeks in 37.7% (20/53) of fetuses. The biophysical profile score (BPP) was 6 in 15 (28.30%) while BPP score was 4 in ten (18.9%) fetuses. In two fetuses BPP score was 2. Fifteen fetuses had an increased resistance index in UA, but 11.3% fetuses had no structural and chromosomal abnormalities in which the development of AEDV was evidenced by Doppler imaging. RDEV was

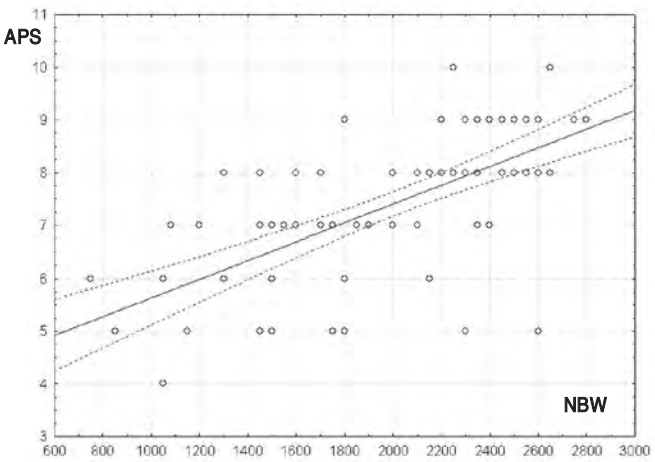

Figure 1. — Neonatal birth weight (NBW) significantly correlated with Apgar score (APS) - 5 min (p = 0.000).

diagnosed in six and cerebral centralization in six fetuses. In our study, the time interval between incidence of AEDV in the umbilical artery and delivery was 48 hours as documented by obstetric history.

The mean gestational week at presentation was 35.6 ± 2. Urgent cesarean section was performed in 58.5% (31/53) and elective cesarean section was performed in 41.5% (22/53) of cases. Six patients delivered before 32 gestational weeks and four patients delivered before 37 gestational weeks. Mean neonatal weight was 1,925.5 ± 524 g (med 1,850; IQR 1700) Incidence of low birth weight (LBW) neonates under 2,500 g was 15.1% (8/53). Apgar score - 5 min and less than 7 - was found in 28.0% (15/53). C/U ratio < 1 and Apgar score - 5 min were significantly correlated (p = 0.003), but the time interval between abnormal UA and cerebral Doppler and gestational week at presentation were not significantly correlated. There was a significant correlation between neonatal birth weight and perinatal asphyxia, (p = 0.000), IVH (p = 0.000), RDS (p = 0.000) as well as between Apgar score - 5 min and neonatal birth weight (p = 0.000) (Figure 1).

Discussion

Of the women, 24.5% were younger than 25 years and most were nulliparous (71.7%). PIH and preeclampsia occurs most often in young nulliparous women as documented in studies. Our study showed that gestational hypertension was the most frequent complication of the pregnancies. PIH, preeclampsia and IUGR might have similar determinants and consequences. Attempting to identify the cause of fetal growth restriction is important because it may have an influence on estimating recurrence and future pre-conception counseling, pregnancy management, prenatal diagnostic procedures and neonatal management [5].The majority of women (94.3%), had had adequate prenatal care during pregnancy.

When primary surveillance with UA Doppler is found to be abnormal, the biophysical profile is likely to be use-

ful given its good negative predictive value in high-risk populations [6]. The combination of small abdominal circumference, normal anatomy, low BPP score values and abnormal UA Doppler recording is strongly suggestive of fetal IUGR due to placental insufficiency [7]. Kurkinen-Rati *et al*. [8] concluded in their study that early AEDV or REDV (before 34th gestational week.) in the UA was a serious warning signal of probable fetal distress. In such cases, the rates of perinatal morbidity and mortality are very high, which is a reflection of the severity of the condition. Six fetuses had no structural and chromosomal abnormalities in which the development of AEDV was evidenced by Doppler imaging. Sallout *et al*. evaluated the time interval between incidence of AEDV in the umbilical artery and either the development of abnormal fetal heart-rate patterns or delivery. The median time interval between AEDV and the onset of late decelerations was 12 days (range 0-49 days) [7]. In our study, this time interval was approximately 48 hours. The study revealed a significant reduction in elective cesarean section for fetal distress and most deliveries were performed before 37 gestational weeks. In the management of the preterm (before 32 gw) IUGR fetuses there is uncertainty whether iatrogenic preterm delivery should be undertaken before the development of signs of severe hypoxemia, with a consequent risk of prematurity-related neonatal complications, or whether delivery should be delayed - but with the risks of prolonged exposure to hypoxia. An Apgar score - 5 min and less than 7 found in 28.0% C/U ratio < 1 and Apgar score - 5 min were significantly correlated ($p = 0.003$). The last calculated C/U ratio could not predict the development of brain lesions and only repeated measurements of fetal Doppler indices over a longer period before delivery could be useful [9]. Resnik and Creasy [10] reported that birth weight after 29 weeks appeared to be a better predictor of survival than Doppler, as documented in our study as well (Figure 1).

Conclusion

A weekly biophysical profile or fetal heart rate testing as well as umbilical and cerebral artery Doppler is a relatively poor predictor of neonatal outcome (especially brain damage) due to placental dysfunction. It seems that neonatal birth weight is the best predictor of neonatal outcomes in pregnancy complicated by hypertension and fetal IUGR.

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