Relation between Doppler findings and perinatal outcomes in fetuses with intrauterine growth restriction

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Summary

Purpose of Investigation: To find the relationship between fetal Doppler findings and perinatal outcomes in intrauterine growth restriction. *Methods:* Eighty-two cases with a prenatal diagnosis of intrauterine growth restriction between November 2008 and July 2009 were included in this prospective study at Ege University School of Medicine. Fetuses were grouped according to Doppler parameters: those with normal Doppler findings (n = 43), and those with impaired arterial (n = 27) and venous systems (n = 12). *Results:* Out of 82 growth restricted cases, 43 (52.4%) had normal Doppler findings, while 27 (32.9%) displayed impaired arterial parameters and 12 (14.6%) had impaired venous parameters. The mean first minute Apgar scores were 7.57 ± 1.53 for the group with normal Doppler flows, 6.8 ± 2 for the group with an impaired arterial system, and 4 ± 1.94 for the group with an impaired venous system. Two cases from the normal Doppler flow group (n = 42), four cases from the impaired arterial flow group (n = 27), and 11 cases from the impaired venous flow group (n = 11) had fifth minute Apgar scores under 6. Evaluation of the umbilical artery blood gas revealed acidosis in two cases from the normal Doppler flow group (n = 42), three cases from the impaired arterial system group (n = 27), and five cases from the impaired venous system group (n = 11). *Conclusion:* A Doppler spectrum from normal to venous system impairment correlated with poor fetal outcomes including fetal acidosis, fetal mortality and morbidity, decreased Apgar scores at 1 and 5 min, and neonatal morbidity.

Key words: Fetal Doppler; IUGR, Perinatal morbidity.

Introduction

Normal fetal growth depends on genetic growth potential, along with maternal, fetal, placental and external factors. Defects in one or a combination of these factors affect fetal growth [1].

Intrauterine growth restriction (IUGR) is commonly characterized by birth weight below the 10th percentile. The American College of Obstetricians and Gynecologists (ACOG) describes IUGR as estimated fetal gestational age below the 10th percentile [2]. IUGR stands as one of the significant causes of perinatal mortality and morbidity in modern obstetric practice. Cooperation of an obstetrician and neonatologist in the management of fetuses with IUGR is essential. Mortality and morbidity rates can be decreased with correct diagnosis, suitable care and timely intervention. Timing of birth is very essential in antenatal management as there is no currently available successful intrauterine therapy. Maximum gestational age and minimum risk for intrauterine life should be aimed in timing of birth [3]. Neonatal consequences of IUGR comprise perinatal asphyxia and neonatal adaptive problems, and short- and long-term sequelae. Perinatal mortality rate increases by 10-20 times in infants with IUGR compared to normal fetuses [4].

Presence and severity of fetal hypoxemia and its prenatal consequences can be correctly determined by Doppler ultrasound (US). Doppler US can noninvasively detect blood flow in uteroplacental circulation. It has been more commonly used in recent years due to its noninvasive and easy to use nature, and the fact that it provides reproducible results. Doppler US provides correct antenatal detection of IUGR, on-time intervention, and decrease in mortality and morbidity rates [5].

The relation between fetal venous and arterial Doppler findings and perinatal outcomes were correlated in a cohort of IUGR fetuses.

Materials and Methods

Eighty-two cases hospitalized in Ege University Faculty of Medicine, Obstetrics and Gynecology Clinic with a prediagnosis of IUGR between November 2008 and July 2009 were included in this study prospectively. The study was conducted in accordance with the guidelines, and approval was given by the Ethical Committee of the Ege University Hospital. Demographic and US data and Doppler parameters of all the patients and fetuses were recorded and prospectively evaluated. Patients were grouped according to Doppler parameters: those with normal Doppler findings (n = 43), and those with impaired arterial (n = 27) and venous systems (n = 12). Fetal or chromosomal anomalies, fetal infections, multiple pregnancies, premature membrane rupture and birth weight above the 10th percentile were criteria for exclusion from the study.

Gestational weeks were determined according to the date of last menstrual period, and confirmed by early US measurements. In patients who were not sure of the date of the last menstrual cycle, gestational weeks were calculated by first trimester crown-rump length (CRL) measurement. CRL was taken as a reference when a difference more than five days was present between the calculation based on the last menstrual date and CRL.

Fetal weight was calculated in all the cases by US measurements of biparietal diameter, head circumference, femur length,

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humerus length, and abdominal circumference. Intrauterine growth restriction diagnosis was confirmed when the birth weight was under the 10th percentile.

All US examinations and measurements were performed by a single operator with Voluson 730 Expert Ultrasound Color Doppler equipment. A 4-MHz convex probe was used in these procedures. The umbilical artery, bilateral uterine arteries, middle cerebral arteries, umbilical vein and ductus venosus parameters were assessed.

Umbilical artery Doppler measurements were performed at the free segment of the umbilical cord, distant from the fetus and the placenta. Following the observation that the acquired waveforms stayed stable for at least five cardiac cycles, measurements were performed on three different cycles and the results were averaged.

In the fetal middle cerebral artery (MCA) measurements, following detection of the vascular structures of the Willis polygon by color mode, Doppler indexes were measured at 0 degree angle from the MCA closest to the probe.

Absent diastolic flow or reverse flow in the umbilical artery, or an MCA PI less than the 5th percentile was evaluated as a sign of an impaired arterial system. The venous system was considered impaired in case of pulsation in the umbilical vein, and A wave absence or reversal in ductus venosus.

Birth was performed in at most 24 hours following Doppler US measurement. Right after the infant was born, the cord was clamped before the first respiration, and 2 to 3 cc blood was collected with a heparin-coated needle from the umbilical artery prior to placenta separation. The blood was examined within at most 10 min with a Nova Biomedical blood gas analyzer. Umbilical artery pH values under 7.20 were considered as acidosis.

The clinical parameters compared were maternal age, gestational week, birth weight, Apgar score at 1 and 5 min, umbilical artery blood gas, intrauterine death, neonatal death, and neonatal morbidity.

To evaluate the findings of the study, SPSS 13.0 (Statistical Package for Social Sciences) software was used for statistical analysis. Comparison of the significance of quantitative data between the groups was performed by the variance analysis test, while the chi-square test was used to assess the significance of the differences between the qualitative data obtained. Relations between the parameters were examined by the Pearson correlation test. The results were evaluated in mean ± standard deviation, 95% confidence interval, and $p < 0.05$ significance level.

Results

Out of 82 IUGR cases, 43 (52.4%) had normal Doppler findings, while 27 (32.9%) displayed impaired arterial parameters and 12 (14.6%) had impaired venous parameters.

Mean age was 29.04 ± 5.49 years in the group with normal Doppler flows, 30.5 ± 5.7 years in the group with impaired arterial system, and 28.5 ± 4.94 in the group with impaired venous system. There was no statistically significant difference between the groups in terms of maternal age.

In the group with normal Doppler flow, mean gestational age was 258.6 ± 19.1 days and mean birth weight was 1968.8 ± 471 g; while mean gestational age was 231.2 ± 17 days and mean birth weight was 1233.7 ± 381 g in the group with an impaired arterial system; and these figures were 222.7 ± 23.7 days and 991.2 ± 564 g, respectively, for the group with an impaired venous system. While there were no statistically significant differences in terms of gestational age between the groups with impaired arterial and venous systems, a statistically significant difference was apparent between the group with normal Doppler flows and the other two groups ($p < 0.05$). No significant difference was detected in terms of birth weights between the group with an impaired arterial system and that with an impaired venous system, yet a significant difference was found between the groups with impaired arterial and venous systems and the group with normal Doppler flows ($p < 0.05$).

Mean first minute Apgar scores were 7.57 ± 1.53 for the group with normal Doppler flows, 6.8 ± 2 for the group with an impaired arterial system, and 4 ± 1.94 for the group with an impaired venous system. While there was no statistically significant difference between groups with normal Doppler flows and impaired arterial system in terms of the first minute Apgar scores, the difference detected between the group with an impaired venous system and the other two groups was statistically significant ($p < 0.05$).

Two cases from the normal Doppler flow group (n = 42), four cases from the impaired arterial flow group (n = 27), and 11 cases from impaired venous flow group (n = 11) had fifth minute Apgar scores under 6. In terms of the fifth minute Apgar scores, there was no statistically significant difference between groups with normal Doppler flows and impaired arterial systems, and the difference detected between the group with impaired venous systems and the other two groups was significant ($p < 0.05$).

Evaluation of the umbilical artery blood gas revealed acidosis in two cases from the normal Doppler flow group (n = 42), three cases from the impaired arterial system group (n = 27), and five cases from the impaired venous system group (n = 11). While the group with normal Doppler findings and that with an impaired arterial system had no significant difference between them in terms of umbilical artery blood gas values, a significant difference was observed between the group with an impaired venous system and the other two groups ($p < 0.05$).

Two postnatal death cases occurred in the group with normal Doppler flows (n = 43), while this rate was four for the group with an impaired arterial system (n = 27), and five for the group with an impaired venous system (n = 12). There was one fetal death case in utero in each one of the groups with normal Doppler findings and impaired venous systems. The groups with impaired arterial systems and normal Doppler flow had no statistically significant difference between them in terms of mortality rates, while there was a significant difference between the impaired venous system group and the other two groups ($p < 0.05$).

There was a significant difference between the three groups in terms of intubation status and respiratory distress syndrome (RDS) ($p < 0.05$), however there was no significant difference in terms of intraventricular hemorrhage (IVH) (Table 1).

Table 1. — *Neonatal morbidity status*.

	Normal Doppler (n = 42)	Abnormal Arterial (n = 27)	Abnormal Venous (n = 11)	
RDS	4 (%9)	9 (%33)	10 (%91)	$p < 0.05$
IVH	1 (%2)	1 (%3.7)	1 (%9)	n.s.
Intubation	3 (%7)	9 (%33)	10 (%91)	$p < 0.05$

RDS: Respiratory distress syndrome; IVH: Intraventricular hemorrhage; ns: non significant; $p < 0.05$: statistically significant.

Discussion

Fetuses with IUGR are at higher risk for poor perinatal and long-term consequences compared to the fetuses with normal growth patterns. Perinatal mortality increases 8-fold when fetal weight is under the 10th percentile, and by 20-fold when the fetal weight is under the 3rd percentile [6]. Combined use of fetal biometry, biophysics profile (BPP), NST, and arterial and venous Doppler US provides the best results in the management of these fetuses. When used alone, these tests have a limited value in IUGR management. Timing of birth is very critical in preterm fetuses with IUGR, and gestational age is the factor that contributes the most to poor outcomes [7, 8]. Bilardo *et al*. [9] found poor perinatal outcomes to be 45% and perinatal mortality rate to be 36% under 30 weeks gestation in a severely premature IUGR group (n = 33).

Birth weight is one of the most significant findings affecting perinatal morbidity and mortality. Risk for poor perinatal consequences increases by 5-30 times for infants born with a birth weight of 1500-2500 g (< 10th percentile) at term compared to infants born at 10th-90th percentile, while this risk is increased by 70-100 times for infants with a birth weight of 1500 g or less (3rd percentile) [10]. In our study, mean birth weight was 991 ± 564 g in the group with an impaired venous system, 1,233 ± 381 g in the impaired arterial system group, and 1,968 ± 471 g in the normal Doppler flow group.

The relation between venous Doppler anomalies and perinatal consequences is very significant for clinical management. A progressive rise in venous Doppler indexes reflects impairment in cardiac function. This impairment indicates progress from fetal hypoxemia to acidosis and intrauterine death if birth does not occur. In case of increase or abnormality in venous system Doppler indexes, sensitivity for fetal acidemia is 70-90%, and specificity is 70-80% [11]. In our study, we detected acidemia (umbilical artery pH < 7.2) in 45% (5/11) of the group with an impaired venous system, in 11% (3/27) of the group with an impaired arterial system, and in 4.7% (2/42) of the normal Doppler flow group. As a result, Doppler US is useful in the evaluation of fetal oxygenation and acid-base status.

Fetuses with IUGR are also prone to multiorgan failure, RDS, IVH, NEC, bronchopulmonary dysplasia, and hemorrhage disorders [12,13]. In a study which included 300 fetuses with IUGR, cases were separated into 2 groups [14]. Group 1 (n = 137) consisted of fetuses with end-diastolic flow in the umbilical artery, while group two (n = 163) consisted of those with absence of diastolic flow or reverse flow in umbilical artery. Rate of RDS, sepsis, perinatal mortality and morbidity, and need for a neonatal unit was higher in Group 2. Also in a study where 404 pregnant women with IUGR fetuses were examined, 39 (9.7%) of the fetuses developed NEC [15]. NEC incidence has been observed to increase in particular with change in the venous parameters from normal to abnormal in Doppler ultrasound.

Conclusion

IUGR stands as one of the significant causes of perinatal mortality and morbidity in modern obstetric practice. Mortality and morbidity rates can be decreased with a correct diagnosis, suitable care and on-time intervention. Time of birth is very essential in antenatal management, as there is no currently available successful intrauterine therapy. In our study, gestational age at delivery and birth weight decreased, acidosis in umbilical artery blood gas and mortality increased, first and fifth minute apgar scores decreased, and the neonatal morbidity rate was elevated from normal to impaired venous system findings in Doppler.

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