

The clinical significance of antenatal pathological Doppler findings in the fetal middle cerebral artery in cases with peripheral reduced diastolic Doppler flow but no absence of end-diastolic flow in the umbilical artery or fetal aorta

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Summary

Purpose: The effects of antepartum pathological Doppler findings in the fetal middle cerebral artery in cases with simultaneously peripheral reduced diastolic Doppler flow on perinatal outcome and the odds ratio of perinatal risks were studied.

Methods: 214 patients were examined by color Doppler ultrasound in relationship to complications in gestation and labor and fetal outcome. One thousand and seventy Doppler flow measurements of the middle cerebral artery, the umbilical artery and the fetal aorta between 28 and 40 weeks of gestation were performed. Sensitivity and odds ratio of synchronous cerebral pathological and peripheral pathological Doppler blood flow with regard to the prediction of intrauterine growth retardation, rate of cesarean section, preterm delivery and newborn depression was calculated. In all Doppler measurements there were no cases with absence of end-diastolic flow.

Results: Preterm delivery rate and intrauterine growth retardation rate were significantly higher in cases of synchronous cerebral pathological and peripheral pathological Doppler blood flow as in cases of isolated reduced peripheral blood flow ($p < 0.001$; odds ratio 13.2 and 16.6).

Conclusion: Pregnancies with no absence of end-diastolic flow in the fetal aorta or umbilical artery, but with reduced diastolic flow in these vessels and simultaneous pathological Doppler findings in the fetal middle cerebral artery are high risk pregnancies, above all in respect to intrauterine growth retardation, preterm delivery and newborn depression. Surveillance of pregnant women should be performed in a perinatal centre.

Key words: Doppler flow measurements; Fetal middle cerebral artery; Pregnancy.

Introduction

By allowing noninvasive assessment of fetal and maternal circulation, development of Doppler sonography plays an important role in prenatal diagnosis. Doppler sonographic measurement has allowed insights into the pathophysiology of human fetal response to in utero stress [1]. This ushered in the possibility of using it for antepartum fetal surveillance, so that timely recognition of fetal compromise and appropriate intervention could improve perinatal outcome [2-5].

The objective of fetal Doppler is to detect at an early stage any hemodynamic changes that allow us to identify and quantify any placental dysfunction with associated fetal distress. Cerebral blood flow changes in relation to hypoxia and fetal distress continue to be one of the most interesting areas of investigation. If peripheral vascular resistance increases there is reduced diastolic flow until the absence of end-diastolic velocity. Simultaneously the reduced flow in the cerebral vessels develops progressively, called centralisation of the circulation or brain-sparing effect [6].

Many studies have demonstrated positive correlations between cerebral Doppler data and fetal hypoxia or fetal well-being in cases with absence of end-diastolic flow in the fetal aorta or umbilical artery [2, 4, 7-9].

The purpose of this paper was to examine the clinical significance of antenatal pathological Doppler findings in the fetal middle cerebral artery in cases of pathological Doppler velocity waveforms at the peripheral vessels but no absence of end-diastolic flow in the umbilical artery or the fetal aorta.

Methods

Two hundred and fourteen patients between 28 weeks and 40 weeks of gestation were examined by Doppler ultrasound in relationship to complications in gestation, labor, and fetal outcome. One thousand and seventy Doppler blood flow velocity waveforms in the middle cerebral artery, the umbilical artery and the fetal aorta were recorded. S/D ratio below the 10th percentile of our own reference ranges [10] were defined as pathological in the middle cerebral artery. A 3,5-Mhz pulsed waved duplex color Doppler ultrasound instrument was used (Combison 530, Kretz Technic).

Three groups were compared: 118 patients with normal velocity waveforms in all arteries (group I), 57 patients with pathological Doppler blood flow velocity waveforms in the umbilical artery and in the fetal aorta (group II), 39 patients with pathological measurements in all three vessels (group III).

Sensitivity with regard to the prediction of intrauterine growth retardation, rate of cesarean section, preterm delivery and newborn depression was calculated and compared. Odds ratio was also calculated.

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Results

In group III, 82% of the patients were delivered by cesarean section in case of pathological fetal heart rate (54% in group II; $p < 0.01$), all newborns showed a birthweight below the 10th percentile, 51% weighed less than the 5th percentile (56% and 28% in group II; $p < 0.001$). The average birthweight was 1,723g, 21% below 2,000g (7% in group II). In group III, 100% of the babies were premature (58% in group II, $p < 0.001$). In group III, an arterial umbilical-cord-pH < 7.2 and/or Apgar-score after one minute < 7 were diagnosed in 58% of the newborn babies (25% in group II; $p < 0.05$).

The highest sensitivity of the Doppler flow method was found in group III. Diagnostic capacity with regard to the prediction of preterm delivery was 72%, specificity and positive predictive value 100% (69%, 81% and 58% in group II). Sensitivity with regard to the prediction of birthweight below the 5th percentile was 64%, specificity and positive predictive value 100% (59%, 79% and 56% in group II). The diagnostic capacity is shown in Table 1. Fetal outcomes of the groups with the statistical significance are shown in Table 2.

Table 1. — *Diagnostic efficacy of pathological Doppler findings: Group II: reduced diastolic flow in the umbilical artery and/or the fetal aorta (n=57). Group III: reduced diastolic flow in the umbilical artery and/or the fetal aorta and simultaneously increased diastolic flow in the fetal middle cerebral artery (n=39).*

Regarding the prediction of	Sens (%)	Spec (%)	PPV (%)	NPV (%)
Preterm delivery (< 37 wks)	69/72	81/100	58/100	87/88
Cesarean section	63/64	79/93	54/82	85/87
Birth weight $< 10^{\text{th}}$ percentile	59/64	79/100	56/100	81/83
Umbilical arterial pH < 7.20 and Apgar 1 min < 7	61/72	72/87	25/59	92/94

Sens = sensitivity; Spec = specificity; PPV = positive predictive value; NPV = negative predictive value (group II/group III).

Table 2. — *Fetal outcome with statistical significance (group II vs group III) and odds ratio.*

	Group II	Odds ratio	Group III	Odds ratio	p
Preterm delivery	58%	12.5	100%	16.6	< 0.001
Cesarean section	54%	2.0	82%	2.2	< 0.01
Birth weight $< 5^{\text{th}}$ percentile	28%	5.5	51%	13.2	< 0.001
Birth weight < 2000 g	7%	3.3	21%	5.3	< 0.01
Umbilical arterial pH < 7.20 and/or Apgar 1 min < 7	25%	3.2	58%	5.2	< 0.05

Discussion

The efficacy of fetal Doppler investigations for predicting adverse perinatal outcome in complicated pregnancies has been widely investigated [9, 11, 12]. Most studies indicated that the Doppler results were efficacious for identifying the fetus at risk in complicated pregnancies or in pregnancies with absence of end-diastolic flow in the fetal aorta or umbilical artery [13-16]. There are, however, wide variations in the performance of the technique, with the sensitivity ranging from 20% to more than 90% and the specificity from 60% to 97% [17]. The

studies were heterogeneous in several ways, including the population selection criteria, the method of using Doppler surveillance, the diagnostic vessels, and the outcome parameters. The purpose of this paper was to examine the clinical significance of antenatal pathological Doppler measurements in the fetal middle cerebral artery (MCA) in cases with reduced diastolic flow in the umbilical artery and/or fetal aorta, but no absence of end-diastolic flow in these vessels.

In cases of reduced diastolic flow in the umbilical artery or the fetal aorta, 56% of the newborn babies showed a birthweight below the 10th percentile and 58% were delivered prior to 37 weeks of gestation. Trudinger *et al.* studied 2,178 high risk pregnancies. The incidence of abnormal umbilical artery velocimetry was 24%. Among pregnancies requiring premature delivery, the incidence was significantly higher, 33% for those who delivered at 34-36 weeks of gestation. The ability to identify the fetus below the 10th percentile was 51%, compared with 78% for those who delivered prior to 37 weeks of gestation [18]. In a study by Devoe *et al.* 74 of 352 pregnant women with increasing umbilical artery systolic-diastolic ratios had a significantly higher perinatal morbidity than the rest of the group: cesarean section for fetal distress 40% versus 6% (54% versus 15% in our study), low 5-minute Apgar scores 5% versus 2% (14% versus 5% in our study) and acidosis 19% versus 3.3% (10% versus 3% in our study) [19].

The Doppler measurements of the fetal middle cerebral artery are sensitive to any vasoconstriction or vasodilatation of the brain vessels [20]. An increase in diastolic cerebral flow is interpreted as a vasodilatation to hypoxia [21]. Comparisons between the cerebral Doppler index and the measurement of PO_2 , PCO_2 , pH, and O_2 content by cordocentesis have demonstrated a good correlation between blood gas values and the cerebral Doppler index in cases of severe hypoxia [22, 23]. In our study the PCO_2 measured in the umbilical cord after delivery was significantly higher in the group with pathological Doppler blood flow velocity waveforms in the middle cerebral artery ($p < 0.05$). A fetal blood distribution beyond physiological range – for example in case of centralisation – is associated with Doppler flow indices out of normal range [24].

Kjellmer *et al.* demonstrated in animals that IUGR is generally associated with cerebral metabolic disturbances and delayed development of the brain [25]. Gramellini *et al.* studied 45 growth-retarded fetuses and found a sensitivity of 90% for the cerebral placental ratio when it was used as a predictor of poor perinatal outcome [26]. The sensitivity of other indices was 78% for the middle cerebral artery and 83% for the umbilical artery. In their study the parameters taken into account to evaluate fetal well-being were the fetal heart rate, gestational age, birth weight, cesarean section rate, umbilical vein pH, 5-minute Apgar score, incidence of admission to the neonatal intensive care unit, and neonatal complications.

In conclusion this study shows a benefit in measurements of Doppler velocity waveforms in the fetal middle

cerebral artery in clinical routine in patients with peripheral reduced diastolic flow. The efficacy of cerebral Doppler investigation in such cases is to type the risk category of the study population. The Doppler blood measurements of the fetal middle cerebral artery in cases of reduced diastolic flow in the fetal aorta and the umbilical artery increase the diagnostic value of the Doppler flow method. The clinical important positive predictive value in respect to intrauterine growth retardation and preterm delivery go up to 100%. Pregnancies with these Doppler velocity waveforms are high risk pregnancies, above all in respect to intrauterine growth retardation, preterm delivery and newborn depression. The surveillance of the pregnant women and the newborn infants should be performed in a perinatal centre.

It would be interesting to know whether there are additional parameters of fetal Doppler flow measurements to find the most favorable time for delivery. A study with measurements of the absolute flow-velocity in the fetal middle cerebral artery is currently in progress.

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