OBSTETRICS

The prognostic role of uterine artery Doppler investigation in patients with severe early-onset preeclampsia

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OBJECTIVE: The purpose of this study was to evaluate the prediction capacity of uterine artery Doppler investigation for maternal and neonatal complications in women who are admitted with severe early-onset preeclampsia.

STUDY DESIGN: A uterine artery Doppler examination was performed at admission for patients with severe early-onset (<34 weeks of gestation) preeclampsia. The maternal and neonatal outcome of women with abnormal uterine Doppler results was compared with those with normal Doppler results.

RESULTS: One hundred twenty patients were included. In 53% of them, uterine Doppler results were abnormal. This group had a lower gestational age at delivery (30.2 vs 32.7 weeks; $P < .001$) and a higher proportion of small-for-gestational age infants (87.5% vs 67.9%; $P = .009$). Neonatal (40.6% vs 14.3%; $P = .01$) and maternal (28.1% vs 5.4%; $P = .001$) complications were more common in the abnormal uterine Doppler group.

CONCLUSION: Women with severe early-onset preeclampsia are at higher risk of maternal and neonatal complications if abnormal uterine blood flow is present.

Key words: early-onset preeclampsia, uterine artery Doppler investigation

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Preeclampsia affects approximately 2-3% of pregnancies and is a major contributor to maternal death, with an estimate of 50,000 deaths a year worldwide.[1] In developing countries, preeclampsia is the second most common cause of maternal death[2] and the first cause of maternal admission to intensive care units.[3]

We and others have shown that early (developing at <34 weeks of gestation) and late-onset preeclampsia are associated with different biochemical and clinical features.[4,5] Although the early-onset form is almost invariably associated with placental insufficiency and growth restriction because of defective trophoblastic invasion, the late-onset form is more prevalent; in general, placental involvement is minimally present. In patients with early-onset preeclampsia, expectant management improves neonatal outcome in selected cases and decreases neonatal care intensive unit admittance and neonatal respiratory distress.[6,7]

Uterine artery Doppler evaluation has been studied extensively for the prediction of preeclampsia and intrauterine growth restriction that reflects the involvement of a defective trophoblastic invasion. However, it has scarcely been evaluated as a prognostic tool at the onset of preeclampsia.[8,9] Only recently has it been reported that women with late-onset preeclampsia show a higher risk of perinatal complications when the uterine blood flow is abnormal.[10] The role of uterine artery Doppler evaluation in the identification of pregnancies that are at risk of maternal or fetal morbidity with early-onset preeclampsia has not been investigated.

This study was aimed to evaluate the prediction capacity of uterine artery Doppler investigation for maternal and neonatal complications in women who are admitted with severe early-onset preeclampsia.

Materials and Methods

Population

Between January 2002 and December 2008, a cohort was created of singleton pregnancies with severe preeclampsia at <34 weeks of gestation that were admitted consecutively to a referral hospital (Barcelona, Spain). Exclusion criteria included threatened preterm labor, premature rupture of membranes, congenital malformations, and the presence of intrauterine fetal death at admission. The study protocol was approved by the Ethics Committee, and participants provided their written informed consent.

Measurements

At admission all women underwent a blood and urine work-up according to standard recommendations.[11] In addition, a Doppler examination was also performed on admission with a Voluson 730 Pro or Voluson 730 Expert (GE Medical Systems, Milwaukee, WI) equipment. All

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TABLE 1
Clinical characteristics of the study population according to uterine artery Doppler investigation at admission

Variable	Normal Doppler (n = 56)	Abnormal Doppler (n = 64)	*P* value
Maternal age, y[a]	31.8 ± 5	31.4 ± 5.1	.6[b]
Primiparity, n (%)	33 (58.9)	42 (65.6)	.45[c]
Body mass index >30 kg/m^2, n (%)	12 (21.4)	10 (15.6)	.41[c]
Previous preeclampsia, n (%)	4 (7.1)	7 (10.9)	.47[c]
Diabetes mellitus, n (%)	3 (5.4)	1 (1.6)	.34[d]
Autoimmune disease, n (%)	2 (3.6)	3 (4.7)	1.0[d]
Thrombophilia, n (%)	3 (5.4)	4 (6.3)	1.0[d]
Gestational age at onset, wk[a]	31 ± 2.4	29.6±2.7	< .00[b]
Mean blood pressure, mm Hg[a]	128.5 ± 11	129.7 ± 12.5	.58[b]
24-hour proteinuria, g[a]	2.9 ± 2.5	3.1 ± 2.8	.78[b]

[a] Data expressed as mean ± SD; [b] Student *t* test; [c] χ^2 test; [d] Fisher's exact test.

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scans were performed by 1 of 5 experienced observers. Uterine artery Doppler examination identified the vessel in an oblique plane, with the sample volume placed distal to the anatomic crossing with the external iliac artery. The pulsed Doppler gate was placed over the whole width of the vessel once it had been ensured that the angle was <30 degrees. Angle correction was then applied, and the signal was updated until 3 similar consecutive waveforms were obtained. Pulsatility indexes of the left and right arteries were measured, and the mean was calculated. Gestational age was calculated according to the crown-rump length at the first-trimester ultrasound examination.[12]

Definitions

Preeclampsia was defined according to the International Society Study of Hypertension in Pregnancy as resting blood pressure ≥140/90 mm Hg on 2 occasions at least 4 hours apart and the presence of proteinuria ≥0.3 g/dL after the 20th week of gestation in previously normotensive women. *Severe preeclampsia* was defined as blood pressure ≥160/110 mm Hg in ≥2 determinations, proteinuria ≥5 g/24 hours, or the presence of maternal complications that included (1) eclampsia and other neurologic manifestations (visual disturbances or severe headache that persisted >24 hours), (2) HELLP (hemolysis, elevated liver enzymes, and low platelet count) syndrome (lactate dehydrogenase, >600 IU/L; aspartate transaminase, >62 IU/L; platelet count [10^9/L], <100,000), (3) *acute renal failure* defined as creatinine >1.2 g/dL, (4) subcapsular hepatic hematoma, (5) pulmonary edema, and (6) the presence of disseminated intravascular disease.

Small-for-gestational age was defined as birthweight <10th percentile according to local standards.[13] *Adverse neonatal outcome* was defined by the presence of any of the following criteria: (1) fetal or neonatal death, (2) acidosis at birth (umbilical artery pH at birth <7.10 and base excess >12 mEq/L), (3) 5-minute Apgar score <7, or (4) significant neonatal morbidity: seizures, intraventricular hemorrhage grade III or less, periventricular leukomalacia, hypoxic-ischemic encephalopathy, necrotizing enterocolitis, acute renal failure (serum creatinine >1.5 mg/dL), or cardiac failure that required ionotropic agents.

Management

Magnesium sulfate seizure prophylaxis was administered to all women; first- and second-line antihypertensive therapy was labetalol and hydralazine, respectively, when blood pressure was persistently ≥160/110 mm Hg. Corticosteroid therapy for fetal lung maturity was also administered at admission. Maternal blood pressure was recorded several times per day, and laboratory testing was performed at least twice a week. Fetal assessment was performed by daily cardiotocography and Doppler examination at least every 3 days. Indications for delivery were uncontrollable blood pressure, maternal complications (defined earlier), placental abruption, or cardiotocographic decelerations (>5 decelerations of >30 beats/minute from basal line in 30 minutes). Beyond 28 weeks, indications for delivery also included umbilical artery Doppler examination with reversed end-diastolic velocities or persistent (>12 hours apart) ductus venosus Doppler examination with reversed end-diastolic velocity. Elective delivery was performed at >32 weeks of gestation after completion of pulmonary maturation.

Analysis

Doppler parameters were transformed into z-values for gestational age[14,15] and were considered abnormal if they were >2 SDs. Variables were checked for normal distribution with the Kolmogorov-Smirnov test. Comparisons between groups were performed by Student *t*, χ^2, or Fisher's exact tests. From 2 × 2 tables, odds ratios (with 95% confidence intervals [CIs]) for both maternal and neonatal complications were calculated. The association between abnormal uterine Doppler results and neonatal complications was further adjusted for gestational age at delivery by logistic regression. Likewise, the association between abnormal uterine Doppler results and maternal complications was adjusted for gestational age at admission.

RESULTS

Overall, 129 women fulfilled the inclusion criteria. A total of 9 women (2 of whom met >1 criteria) were excluded because of congenital malformation (n = 1), premature rupture of membranes (n = 2), preterm labor (n = 5), or intrauterine fetal death at admission (n = 3), which left a study population of 120 pregnancies. Table 1 details the clinical characteristics of the study population. There were 11 cases of perinatal death,