HOW TO MANAGE INTRAUTERINE GROWTH RESTRICTION ASSOCIATED WITH SEVERE PREECLAMPSIA AT 28-34 WEEKS OF GESTATION?

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Aim: To propose optimal management of intrauterine growth restriction (IUGR) cases associated with severe preeclampsia at 28-34 weeks of gestation.

Methods: Two hundred pregnant women with severe preeclampsia associated with growth restricted fetuses were followed with doppler velocimetry of umbilical artery between 28-34 weeks of pregnancy. Patients were grouped according to indications for termination of pregnancy, first group consisted of severely affected doppler velocity waveforms (n:100) and the second group consisted of those whose cardiotocography and biophysic profile were unfavorable (n:100). Groups were compared according to perinatal outcomes (cesarean rates, gestational age at delivery, birth weight, Apgar scores and demand for intubation and perinatal deaths).

Results: The diagnosis to delivery interval is significantly higher in the second group ($p<0.05$), whereas there was no significant difference between groups regarding gestational age at delivery and parity ($p>0.05$). Apgar scores were lower in the first group ($p<0.05$), and there was increased demand for intubation. Perinatal deaths were also lower in the second group ($p<0.05$). Cesarean rate was significantly lower compared with first group ($p<0.05$).

Conclusion: Assessment of doppler velocimetry alone may not be enough at decision for termination of pregnancy, biophysic profile and cardiotocography should be added to confirm exact time for delivery of a premature fetus and to improve perinatal outcomes.

Key words: Severe Preeclampsia, Intrauterine Growth Restriction, Doppler Velocimetry, Biophysic Profile, Perinatal Outcomes.

Eur J Gen Med 2008;5(4):212-215

INTRODUCTION

Hypertension complicates approximately 9% of all pregnancies with preeclampsia-eclampsia (up to 4%) being a major cause of maternal and perinatal morbidity and mortality. In severe preeclampsia, uteroplacental perfusion is usually diminished and this results in increased IUGR incidence, fetal hypoxia and perinatal death. Conservative treatment is usually kept limited to those with biophysic profile of 4 and above, largest vertical amniotic sac of >2 or estimated ultrasonographic fetal weight above 5th percentile (1).

MATERIALS AND METHODS

The study group consisted of 200 pregnant women with severe preeclampsia and IUGR fetuses with estimated weight of <10% for gestational age that admitted to Selcuk University Faculty of Medicine Obstetrics and Gynecology Department, tertiary referral hospital, between January 2002 and 2007. First group consisted of 100 patients with absent endiastolic flow or reverse flow and that were delivered within 24 hours after admission and the second group consisted 100 patients that had S/D ratio normal or above 2.5 and were followed up at least 24 hours, in this group delivery was planned when cardiotocography and biophysic profile were unfavorable. Steroids were administered to all patients, no repeat dose was applied.

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Table 1. Caharacteristics of patients

	First Group (n:100)	Second Group (n:100)	p
Maternal age	23.4±1.2	22.6±0.8	ns
Primiparity	71 (71%)	67 (67%)	ns
Oligohydramnios	58 (58%)	61 (61%)	ns
Normal UA velocity	_	33(33%)	<0.05
Diminished UA endiastolic velocity	-	67 (67%)	<0.05
Cesarean rate	74 (74%)	45 (45%)	<0.05

ns: Non-significant

Preeclamptic patients that had uncontrolled severe hypertension, eclampsia, trombocytopenia, high liver enzymes, persistant headache and visual symptoms were excluded from the study and delivered within 24 hours. All patients were evaluated for complete blood count, liver and renal function tests, 24 hour proteinuria and obstetrical ultrasonography and doppler velocimetry. Exact gestational week was determined according to last menstrual period and/or earliest ultrasonography. Fetal weight was obtained by Hadlock formula that uses FL, AC, and BPD.

Intrauterine growth restriction was identified when was below 10th percentile according to Yudkin et al. table. Oligohydramnios was established when the largest cord-free pocket was below 2 cms in vertical diameter. S/D ratio was measured for each patient using a color doppler ultrasound system, absence of enddiastolic flow and presence of reverse flow were noted. All doppler examinations were performed by an expert. Doppler examinations were repeated twice weekly. Detoriation in maternal condition, absence of enddiastolic flow or presence of reverse flow and abnormal heart rate tracing were accepted as indications for delivery.

Data about C/S rates, gestational age at delivery, birth weight, Apgar scores, need for intubation and perinatal deaths were selected as outcome measures.

The statistical analysis of the study were done by SPSS 11.0 for Windows programme. The data were indicated by mean and standard deviation. Comparison of data was carried out by chi-square test and t- test. The statistical significance was accepted as $p<0.05$.

RESULTS

There was no statistically significant difference between two groups regarding maternal age and parity ($p>0.05$). In the first group all patients (n:100) had absent or reverse flow at doppler velocimetry. Oligohydramnios was present in 58 patients (58%) in the first group. Most of the patients had cesarean delivery in the first group since late decelerations accompanied to doppler ultrasonographic findings or during induction of labour. In the second group, 67% of patients had S/D ratio of 2.5 and above, cesarean rate was significantly lower compared with first group ($p<0.05$).

Diagnosis to delivery interval was 21.2±1.1 (2-24) hours in the first group, whereas it was 5.2±2.1 days in the second group ($p<0.05$). Mean gestational age at delivery was 31.1±1.2 (28-34) weeks in first group and 33.6±2.2 (31-34) in the second group. Mean birth weight was 1180±250 (850-1400) gr in first group, and was 1490±310 (1250-1990) gr in second group.

There were also significant differences

Table 2. Perinatal outcomes

	First Group	Second Group	p
Gestational age at delivery, week	31.1±1.2(28-34)	33.6±2.2 (31-34)	<0.05
Mean birth weight, gr	1180±250	1490±310	<0.05
Need for intubation	95(95%)	68(68%)	<0.05
Apgar scores (5 min, <7)	81(81%)	64 (64%)	<0.05
Perinatal deaths	21 (21%)	7 (7%)	<0.05

between groups regarding gestational age at delivery and birth weights ($p<0.05$).

Considering perinatal outcomes, there were significant differences between two groups regarding mean birth weight, Apgar scores, need for intubation, perinatal deaths ($p<0.05$).

DISCUSSION

Preeclampsia, as it is well known, increases the risk for severe perinatal outcomes, mostly by its effect on reducing birth weight. Some forms of IUGR have been etiologically linked to preeclampsia, based on similar placental disease described as abnormal implantation and characterized by failure of trophoblasts to differentiate, to invade, and to remodel the spiral arteries (2).

In follow-up of pregnancies that are complicated with hypertension, doppler velocimetry is the commonly used diagnostic tool in fetal well-being nowadays.

Surveillance of high risk pregnancies, particularly IUGR, by the systematic use of Doppler ultrasound has proven to be beneficial (3,4). Doppler provides a non-invasive method to monitor blood supply in fetuses presenting intrauterine growth restriction (IUGR) (5). Inadequate placental circulation is associated with a rise in fetoplacental vascular resistance leading to a progressive decrease in the diastolic flow, thus identifying high risk pregnancies (5). The most severe cases are characterised by the absence of the diastolic velocity waveform (Doppler score, class II), and by the appearance of reverse end-diastolic flow (Doppler score, class III) (6). The presence of Doppler umbilical scores of classes II or III correlates with poor perinatal outcome (7,8).

Torres et al. (9) in their retrospective study, reported that absence of enddiastolic flow was corralated with IUGR in 100% of pregnancies and fetal death by 66.6%. Higher mortality rates are reported in those fetuses with absent or reversed end-diastolic flow on antenatal Doppler velocimetry (10,11). Similarly, in our clinic we believe that reverse or absent enddiastolic blood flow are related to increased fetal mortality according to our experiences, so terminate such gestations within a short period time, usually within 24 hours of diagnosis. And mainly the route of delivery is cesarean section in these pregnancies.

However, despite encouraging results, controversy still exists as to the optimal timing of delivery. Arguments tending towards an immediate delivery in the presence of a Doppler class II or III are counterbalanced by the risks associated with prematurity (12, 13). In most studies, intrauterine growth restriction (IUGR) has been shown to have deterious effects on mortality and morbidity in newborn infants, both in term and preterm infants (14-16). However, some studies suggest that growth restriction, presumably caused by some process that accelerates fetal maturity, may actually improve some morbidities such as respiratory distress syndrome (RDS) (17,18) and several recent neonatal articles have stated that being born small for gestational age (SGA) is associated with an increased likelihood of survival (19,20).

A fetus with growth restriction is reported to be at risk for sudden unexplained intrauterine death (21). The severity of growth restriction is directly related to an increased risk of fetal death, a relationship that holds true regardless of gestational age (22, 23).

The perinatal mortality rate is also higher among term and preterm IUGR infants, including both symmetrically and asymmetrically growth restricted (22). Lackman et al. (24) reported a 5-fold to 6-fold increased rate of death among both term and preterm infants with IUGR when using both fetal and neonatal growth curves.

In conclusion, our results support that prematurity related problems are prominant in IUGR fetuses that delivered immediately according to doppler velocimetry results that indicated increased fetal risk of intrauterine death. Our opinion is that even in the presence of class-2 or 3 doppler velocimetry findings, patients should be followed-up closely and carefully by biophysic profile and cardiotocographies in order to gain time for steroids and premature fetuses. If it is done, perinatal deaths may be decreased.

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