

Obstetric management of IUGR

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The intrauterine growth retardation (IUGR) takes second position after the premature births as a cause for neonate with smaller weight for its gestational age. Perinatal morbidity of retard children is important, but perinatal mortality is about eight times higher than normal weighted neonates. It is very important to make the right diagnosis of IUGR, the cause of their illness, the therapy they need and when it's necessary to find the right time, place and way of birth. The prognosis of physical and neuropsychical health of retard children is unfavorable. Normal fetal growth is determined by the genetically predetermined growth potential and further modulated by maternal, fetal, placental, and external factors. Fetal growth restriction (FGR) is a failure to reach this potential and is clinically suspected if sonographic estimates of fetal weight, size, or symmetry are abnormal. Integration of fetal anatomy assessment, amniotic fluid dynamics, uterine, umbilical, and fetal middle cerebral artery Doppler is the most effective approach to differentiate potentially manageable placenta-based FGR from aneuploidy, nonaneuploid syndromes, and viral infection. Although placental dysfunction results in a multisystem fetal syndrome with impacts on short- and long-term outcome, only cardiovascular and behavioral responses are helpful to guide surveillance and intervention. Early-onset FGR before 34 weeks ge-

station is readily recognized but challenging to manage as questions about optimal delivery timing remain unanswered. In contrast, near-term FGR provides less of a management challenge but is often missed as clinical findings are more subtle. Once placenta-based FGR is diagnosed, integrating multivessel Doppler and biophysical profile score provides information on longitudinal progression of placental dysfunction and degree of fetal acidemia, respectively. Choosing appropriate monitoring intervals based on anticipated disease acceleration and intervention when fetal risks exceed neonatal risks are the prevailing current management approaches.

Definition and classification

Intrauterine growth restriction (IUGR) describes a decrease in fetal growth rate that prevents an infant from obtaining his or her complete growth potential. Two main patterns of fetal growth restriction are observed (see Table I). If fetal growth is impaired during the first or second trimester, the infant will have symmetric growth restriction. This proportional lack of growth is caused by reduced fetal cellular proliferation of all organs and occurs in approximately 20% to 30% of IUGR infants (1). In contrast, asymmetric growth, in which an infant has a smaller abdominal size compared to head size, will occur if the decrease in growth velocity happens in the last trimester. This head-sparing phenomenon is the most common form of IUGR (~70%-80%) (1) and is attributed to the ability of the fetus to adapt, redistributing its cardiac output to the spleen, adrenal, coronary, and cerebral circulations.

Epidemiology and Etiology

The incidence of IUGR is estimated to be approximately 5% to 7%. While a large number of etiologies are not identified, the known associations involve fetal, placental, and/or maternal factors. There is a strong link between IUGR, chromosomal abnormalities, and congenital malformations.

Less frequently, IUGR may be due to first or second trimester fetal infection, including cytomegalovirus, malaria, parvovirus, and rubella. The majority of fetal etiologies lead to early gestation symmetric IUGR. Chronic maternal vascular disease due to hypertension, diabetes mellitus, renal disease, or collagen vascular disease is the most common cause of IUGR (2) in developed countries. Hypercoagulable maternal conditions such as thrombophilia and antiphospholipid antibody syndrome also inhibit growth either by placental thrombosis forma-

Table 1 - Specific Distinctions Between Symmetric and Asymmetric Intrauterine Growth Restriction (IUGR).

	Symmetric IUGR	Asymmetric IUGR
Incidence	20%-30%	70%-80%
Period of growth restriction	Begins first or second trimester	Begins third trimester
Physical characteristics	Small head and abdominal size	Large head size relative to small abdomen
Pathophysiology	Impaired cellular embryonic division Impaired cellular hyperplasia ± hypertrophy Decreased cell number ± size	Impaired cellular hypertrophy Decreased cell size
Etiology	Mostly intrinsic: chromosomal abnormalities and congenital malformations Drugs Infections Early-onset severe preeclampsia Preeclampsia <30 wk superimposed with chronic hypertension	Mostly extrinsic: placental and maternal vascular factors (eg, placental insufficiency)
Outcome	Greater morbidity and mortality	Lower morbidity and mortality

tion or by secondary effects of maternal hypertension (3, 4). Persistent maternal hypoxia due to high altitude, severe pulmonary or cardiac disease, and/or severe chronic anemia limits oxygen delivery to the fetus and attenuates fetal growth.

Maternal toxins can contribute to the development of a growth-restricted fetus. Cigarette smoking reduces uterine blood flow, limiting fetal oxygenation and attenuating growth (5). The quantity of cigarettes smoked per day correlates with the degree of IUGR (6, 7). Prolonged maternal alcohol ingestion and other drugs (eg, steroids, Coumadin, hydantoin, cocaine, and heroin) are also implicated in the development of IUGR (8).

Prenatal Management of Growth-Restricted Fetus

It is crucial that the obstetrician recognizes and accurately diagnoses a fetus with IUGR. Currently, the recommended method is by measuring anthropometric parameters, which include fetal abdominal circumference, head circumference, biparietal diameter, and femur length. These results are converted to fetal weight estimates using standard formulas and compared with population-based fetal growth curves at specific gestational ages (GA) (9). Precise initial dating by an early ultrasound will ensure that the accurate GA is used (10).

Although the diagnosis of SGA relies on biometric tests, abnormal Doppler tests are diagnostic for FGR. It is also important to realize that the assessment of growth requires at least two measurements at least 2 weeks apart (11), which will in turn differentiate normally growing fetuses from those with restricted growth. However, the biometric parameters are less useful for the management of FGR than for the detection of such cases, and have to be used in association with other techniques of antenatal surveillance to make decisions about the timing of delivery (12).

Antenatal surveillance

Doppler ultrasound, CTG analysis (non-stress test), both traditional and computerised, measurement of amniotic fluid volume, and assessment of fetal breathing, movement and tone are primary fetal assessment tools. While some physicians advocate biweekly nonstress tests, randomized controlled studies have not shown that outcomes are improved with this monitoring (13, 14). Similarly, trials assessing efficacy of using biophysical profiles as a modality to determine the optimal delivery time have not shown an association with better outcomes (15, 16, 13). Since studies demonstrate that oligohydramnios dramatically increases perinatal mortality in the growth-restricted fetus, this is often used as an independent indicator for delivery (17). Umbilical Doppler flow measurements are the most valuable current technique to distinguish the sick IUGR fetus from the well IUGR fetus (18) and, in contrast to other modalities, improve perinatal outcomes (19-22). Indeed, using this approach, fetuses with the worst placental outcome (23, 24) and the most detrimental perinatal outcome (25-27) can be identified.

Although multiple vessels have been investigated in FGR, a combination of arterial and venous vessels is the most practicable to demonstrate the degree of placental disease, level of redistribution and degree of cardiac compromise. The umbilical artery, middle cerebral artery, ductus venosus and inferior vena cava provide a comprehensive evaluation of these aspects. As the longitudinal progression of Doppler abnormalities advances from the arterial to the venous side in most cases, multivessel Doppler may be useful in planning the frequency of fetal testing (28, 29).

Umbilical artery

Umbilical artery Doppler measurement offers a completely different contribution to the management of FGR be-

cause it does not identify a high-risk group for the future but indicates whether an identified SGA fetus is affected by placental dysfunction or not. In the presence of placental insufficiency with progressive severity, there is a higher placental resistance, indicated by a high pulsatility index, absent or reversed end-diastolic component of the umbilical artery waveform (30). Absent or reversed end-diastolic flow velocities in the umbilical arteries are associated with worse perinatal outcome and high perinatal mortality, depending on gestational age (31).

Middle cerebral artery

Under conditions of limited oxygen and nutrient supply, fetal vascular redistribution in favour of vital organs can be detected by Doppler studies of the selected fetal organs. Doppler indices of resistance decrease in the middle cerebral artery, as a reflection of the brain-sparing effect of the fetus.

Venous Doppler examination

The deterioration of fetal condition due to severe FGR is usually accompanied by signs of cardiovascular changes that can be shown by venous Doppler studies. The normal forward venous blood flow is dependent on cardiac contractility, compliance and after load. Evidence of impaired cardiac function has been documented using Doppler flow studies of the precordial veins (ductus venosus, inferior vena cava and superior vena cava), hepatic veins (right, middle and left hepatic), and head and neck veins (jugular veins and cerebral transverse sinus) (32). Abnormal venous Doppler flow indices of these veins suggest impaired preload handling. A decline in the "a" wave in ductus venosus Doppler velocimetry reflects a decrease in forward flow during atrial systole. Moreover, increased umbilical venous pulsations may reflect increased central venous pressure and also tricuspid insufficiency resulting from severe cardiac dilatation.

If associated abnormalities are observed in the ductus venosus and umbilical veins, the IUGR fetus is even more compromised with a high chance of imminent death (33). This corresponds with the timing of fetal circulatory changes during a compromised state since venous alterations typically occur after arterial changes (34).

Intervention

Despite numerous approaches to managing FGR, there are no effective treatments to improve the growth pattern of a fetus. Modalities tested include maternal nutritional supplementation, plasma volume expansion, administration of amino acids and medications for the mother, such as low-dose aspirin (35). However, the universally available therapeutic option that shows improvement in outcome includes the antenatal administration of steroids in preterm pregnancies and delivery at an institution with a neonatal care unit that is able to deal with the management complexities of the growth-restricted neonate.

Antenatal steroids should be given to any growth-restricted fetus whose delivery is expected before 34 weeks' gestation (36). Although there is a trend towards the benefit of steroids given after 34 weeks (especially for elective caesarean section), this respiratory distress syndrome reduction in babies born after 34 weeks did not reach statistical significance (37).

Conclusion

Although IUGR is probably a physiologic adaptive response to various stimuli, it is associated with distinct short- and long-term morbidities. Immediate morbidities include those associated with prematurity and inadequate nutrient reserve, while childhood morbidities relate to impaired maturation and disrupted organ development, such as impaired neurodevelopment, adult type 2 diabetes and hypertension. Obstetricians should identify fetuses at risk of developing growth restriction, design a comprehensive surveillance plan, and carefully choose the time and mode of delivery. FGR due to placental insufficiency is diagnosed when decreased amniotic fluid volume, abnormal umbilical artery Doppler and failure of growth are evident using serial growth scans, provided that chromosomal abnormalities, malformations and infections are excluded. Antenatal surveillance should be instituted on the basis of the severity of the maternal or fetal condition, with an emphasis on Doppler analysis as the most important tool to grade the severity of the fetal disease.

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