Modern management of intrauterine growth retardation

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Management of intrauterine growth retardation is an important issue in obstetric practice. Since the introduction of Doppler ultrasonography, the problems associated with screening, diagnosing, monitoring, and identifying foetuses at risk have decreased in recent years. Owing to the use of Doppler ultrasonography, there is now a trend towards early delivery.

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Introduction

Intrauterine growth retardation (IUGR) is associated with significant perinatal mortality, perinatal morbidity,[1] and long-term sequelae which include impaired neurological development and cerebral palsy in childhood, and non–insulin-dependent diabetes mellitus and hypertension in adult life.[2] There are problems associated with the diagnosis of IUGR, however. For example, the terms 'small for gestational age' (SGA) and IUGR are often erroneously regarded as being synonymous. Whereas SGA indicates that a foetus or neonate is below a reference range for size or weight for a given gestational age, IUGR means that a pathological process is operating to prevent the foetus from achieving its growth potential. The majority of SGA foetuses are normal,[3] but much unnecessary intervention can be done if they are mistaken as cases of IUGR.[4] On the other hand, growth-retarded foetuses may not be SGA.

Whether to deliver an extremely premature foetus suffering from IUGR is a dilemma. Various studies have been done to investigate the value of Doppler ultrasonography of the umbilical artery and various foetal vessels in the diagnosis and management of IUGR. The timing of the delivery as determined by conventional methods has been challenged by the use of Doppler ultrasonography.

Accurate determination of gestational age

The accurate detection of IUGR starts with the accurate determination of gestational age. Ultrasound examinations are mandatory if dates of menstruation are unreliable or if menstrual cycles are irregular. The use of ultrasound in the second trimester increases the accuracy of the predicted date of delivery compared with the use of the Naegele rule.[5,6] It is impossible in early gestation to identify all foetuses who will develop IUGR in later gestation; ultrasound determination of gestational age becomes unreliable after 24 weeks' gestation.[7] Nevertheless, the benefits of ultrasonography and its advantages in detecting foetal anomalies, multiple pregnancies, or a low-lying placenta should be weighed against the extra costs of time, human resources, and equipment required when considering its routine use.

Screening methods for intrauterine growth retardation

It is impractical to measure foetal growth rate during all pregnancies. Effective and selective screening methods are needed. The current practice is to identify women who are carrying small foetuses. Clinical methods such as identifying risk factors, and palpation detect only 49% of IUGR neonates[8]; the false-positive rate can be as high as 71%.[9] The sensitivity of serial measurements of symphysis-fundus height (SFH), however, is higher than that of clinical methods and varies from 60% to 85%.[10-12] It is a simple and inexpensive method, and is independent of the operator's experience.

A single ultrasound measurement of abdominal circumference around 34 weeks' gestation has been shown to detect 85% of growth-retarded foetuses[12] and its sensitivity was found to be better than SFH measurement.[13] The routine use of third trimester ultrasound measurement in low-risk pregnancies, however, has not been shown to be beneficial and fails to detect early-onset IUGR. Doppler studies of uterine

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artery blood flow in the second trimester may be useful in predicting pre-eclampsia and/or IUGR.[14] If a routine ultrasound scan were done around 18 to 20 weeks' gestation, Doppler studies of uterine artery blood flow could be done at the same time, and repeated around 24 weeks' gestation if a notch or high resistance is present.[15]

Identification of small for gestational age foetuses

Whether the foetus is classified as SGA depends on which foetal parameters, chart of foetal ultrasound parameters, and threshold values (10th, 5th, or 3rd percentile) are used. Estimated foetal weight has also been used as one parameter. The best single ultrasound measurement of foetal size is the abdominal circumference.[16] Commonly used growth charts do not take into account the sex of the foetus, or maternal weight, height, ethnic group, and parity. The use of customised growth charts have been proposed; these should consider maternal characteristics and the birthweight at previous pregnancies.[17] Another approach is to assess the individual growth potential of each foetus following an assessment of growth velocity in early pregnancy. This requires at least two scans during the second trimester.[18] These methods, however, cannot be used widely because of logistical problems. Although a threshold of the 10th percentile can increase the sensitivity of detecting IUGR, many normal foetuses will also be included. Not all SGA foetuses suffer from IUGR. The differentiation between the normal but small foetuses and growth-retarded foetuses is important, because while growth-retarded foetuses need intensive monitoring and timed intervention, normal foetuses do not.

Diagnosis of intrauterine growth retardation

The proper measure of IUGR is function, not size.[19] Diagnosis of IUGR should be made by serial measurements instead of single measurement of foetal parameters. It has been suggested that the distinction between symmetrical and asymmetrical IUGR can be made by ultrasound measurements of foetal head circumference, abdominal circumference, and the ratio of head to abdominal circumferences. It has been suggested that these measurements can guide further management.[20] Considerable doubt over the reliability of their usage has been expressed, however.[21] In severe IUGR, both head and abdominal circumferences will be affected. Although it has been documented that asymmetrical IUGR is associated with higher mortality and morbidity, there is evidence showing that symmetrical IUGR represents a greater risk.[22-24] It seems that the concept of symmetrical and asymmetrical IUGR is not very useful clinically.

Doppler ultrasonography

To better identify foetuses with IUGR, the efficacies of umbilical arteries and various foetal vessels have been evaluated in various studies. Doppler studies of umbilical arteries have been shown to be useful as a secondary test for foetuses who are suspected of having IUGR and in predicting adverse foetal outcome.[25-27] Foetuses who have an abnormal pulsatility index in the middle cerebral artery have a poorer perinatal outcome than those who have cerebral resistance but a normal value.[28] Using the ratio of umbilical artery to middle cerebral artery pulsatility indices has allowed a significant improvement in the diagnostic capabilities of predicting adverse foetal outcome.[29] Different parameters in the flow pattern can be used; they include the systolic to diastolic flow ratio, and pulsatility and resistance indices. All of these are highly correlated and there is no evidence suggesting that any one of them offers clear advantages over the others.[30]

Intrauterine growth retardation versus small for gestational age foetuses

The concept of growth-retarded foetuses whose size and weight are within the normal range is controversial.[3,31] Many growth-retarded foetuses may not be SGA; there may be a greater risk of abnormal foetal development than for SGA foetuses, as they are usually undetected antenatally. On the other hand, it can be argued that increased adverse outcome seems to be restricted to the very small growth-retarded foetuses.[31,32] The use of customised growth charts and routine neonatal measurement of ponderal index, mid-arm to head circumference ratio, and triceps skinfold thickness to test for malnutrition have been proposed.[33] The effects of customised growth charts on clinical practice and perinatal outcome, however, need further evaluation in prospective controlled studies; different customised growth charts would be expected for different ethnic groups. Neonatal measurements of anthropometry and skinfold thickness do not allow obstetricians to detect foetuses who are at risk during the antenatal period. For high-risk pregnancies, including those with a past obstetric history of intrauterine death, serial measurements of foetal biometry and Doppler studies in the third trimester prior to the clinical diagnosis of IUGR will enhance the detection and assessment of the growth-retarded foetus.

Investigation for causes of intrauterine growth retardation

A careful search for the causes of IUGR should be made. Factors such as smoking, alcoholism, drug addiction, or proteinuric hypertension should be fully investigated. A detailed foetal anomaly scan should be done, and markers of aneuploidy should be looked for. Screening for evidence of recent maternal infection with toxoplasmosis protozoa, or rubella, chickenpox, and herpes viruses can be considered if foetuses are symmetrically small. Karyotyping is usually not indicated in the isolated mild form of IUGR because the risk of aneuploidy remains remote. On the other hand, karyotyping should be considered when IUGR is severe but the Doppler scan is normal, or when IUGR is associated with the development of foetal anomalies.

Foetal monitoring

Foetal monitoring of pregnancies that are complicated by IUGR is essential if delivery is not contemplated. This usually includes the use of a foetal kick chart, cardiotocograph, serial measurements of foetal biometry, the amniotic fluid index, and Doppler studies. The biophysical profile is excellent for the identification of the non-hypoxaemic SGA foetus but can be a time-consuming exercise in diagnosing hypoxaemic IUGR.[34] Cordocentesis is not recommended, as it has a procedure-related foetal mortality of about 1% and it represents merely a snap-shot of the foetal acid-base and biochemical states.

The frequency of foetal monitoring depends on the findings of various tests. Small for gestational age foetuses with an otherwise normal foetal assessment can be monitored fortnightly, while those with abnormal Doppler results and/or oligohydramnios require more frequent monitoring, or delivery.[14] If an elevation of the pulsatility index of the umbilical artery or oligohydramnios is found, twice-weekly cardiotocography, weekly Doppler studies, and measurement of the amniotic fluid index are warranted. In pregnancies that are complicated by absent or reversed end-diastolic umbilical artery flow, daily foetal monitoring is needed if delivery is not considered.

Treatment

Treatment of IUGR is largely limited to early delivery. Treating anaemia,[35] quitting smoking,[3] abstaining from alcohol,[36] and slowly detoxifying the pregnant drug addict[37] are helpful. The use of aspirin or fish oil in treating IUGR has little value, if any.[38,39]

Timing of delivery

The timing of delivery depends on the results of foetal monitoring tests and the gestational age. Traditionally, delivery is indicated when there are abnormal readings from cardiotocography or a low score on the biophysical profile. Doppler studies have shown that absent or reversed end-diastolic velocity waveforms in the umbilical artery are associated with high perinatal mortality and morbidity.[40] Foetal hypoxia and acidosis have been found to be associated with pregnancies that are complicated by the loss of end-diastolic flow.[41] Absent or reversed end-diastolic umbilical artery flow merits delivery if the neonate of that gestational age or with that estimated birthweight can be handled by the local neonatal service. There is also a current trend towards earlier delivery. Recent studies report that growth-retarded foetuses who are acidotic during intrauterine life or exhibit antepartum abnormal heart rate tracings show poor neurological development at 2 years.[42,43] Growth-retarded foetuses with abnormal foetal Doppler studies of the descending thoracic aorta have a much higher neonatal mortality rate from necrotising enterocolitis and foetal haemorrhage, which may reflect inadequate perfusion of organs following foetal circulatory readjustments to foetal hypoxaemia.[44] To this end, earlier delivery has been suggested if there is any evidence of a differential shunting of blood flow to the foetal brain, even before the cardiotocography results or biophysical profile have been found to be abnormal.

While delivery of the term growth-retarded foetus is indicated when there are abnormal Doppler measurements, it is still controversial whether a preterm pregnancy should allow foetal maturity to be reached; the foetus may then become acidotic. Alternatively, the foetus could be delivered earlier to avoid damage from hypoxia and/or acidosis. It is not known whether the benefits of delivery at the stage of foetal hypoxia, but without acidosis, outweighs the risks of prematurity. This issue will be addressed in the growth restriction intervention trial.[3] The current recommendation is that results of foetal monitoring tests other than Doppler studies should also be taken into account.

Extreme prematurity

Whether to deliver a growth-retarded foetus before 32 weeks' gestation in the presence of extreme

abnormalities, as detected by foetal monitoring, is a difficult dilemma. The foetus will probably die in utero if expectant management is adopted. Both mother and obstetrician may find it difficult to face the situation of intrauterine death. In contrast, delivery by caesarean section may lead to early neonatal mortality or severe handicap, and could cloud the future obstetrical performance of the mother. Proper counselling is essential. Delivering foetuses before 26 weeks' gestation or with an estimated foetal body weight of less than 600 g may not be in the mother's interest. Before 30 weeks' gestation, continuation of the pregnancy to allow foetal maturity is preferred. Maternal oxygen therapy has been attempted to improve the foetal condition and hence to prolong the pregnancy, but the value of this has not been proven.[14]

Conclusion

Accurate dating, preferably by routine ultrasound examination, is the first step in the accurate diagnosis of IUGR. The routine use of SFH measurements, together with the selective use of single or serial ultrasound examinations in the third trimester of high-risk pregnancies would detect the majority of the cases of IUGR. No matter which limits or chart of foetal ultrasound parameters are used, diagnosis of IUGR should be made by serial measurements instead of single measurements of foetal parameters. Whenever an SGA foetus is found, Doppler studies of the umbilical artery and/or middle cerebral artery are indicated and can help the diagnosis of IUGR. Unnecessary intervention can be reduced in those pregnancies with normal foetal assessments such as Doppler studies.

While awaiting the conclusion of the growth restriction intervention trial,[3] the finding of an increase in resistance of the umbilical artery or a decrease in resistance of the foetal middle cerebral artery should be interpreted with caution when the timing of the delivery is considered. For the term growth-retarded foetus, delivery is preferred. For the preterm foetus, results of foetal monitoring tests other than Doppler studies should be taken into account. It would be reasonable not to deliver foetuses before 26 weeks' gestation or with an estimated birthweight below 600g.

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