The Diagnosis and Management of Intra-uterine Growth Retardation

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SUMMARY
The aetiology, prediction, diagnosis and perinatal complications of intra-uterine growth retardation are reviewed. A scheme of management is presented.


For many years it has been widely recognized that low-birth-weight infants (less than 2 500 g) have an increased perinatal mortality rate and a higher incidence of impaired neurological development. More recently these infants have been divided into those born too soon (preterm infants born before 37 weeks' gestation) and those with intra-uterine growth retardation (whose birth weight is inappropriately low for their gestational age). The latter are at an increased risk of starvation and asphyxia before delivery, and early recognition and active management are therefore recommended.

TERMINOLOGY
Intra-uterine growth retardation (IUGR) is diagnosed on clinical grounds when a fetus appears stunted, wasted or undernourished at birth. The pattern of fetal growth is usually assessed at delivery by plotting birth weight for gestational age on an appropriate intra-uterine growth standard. Infants which fall on or below the 10th percentile are regarded as being small for gestational age (SGA) and in need of special care.

The choice of suitable growth standards is controversial. They should preferably be sex- and parity-specific, provide data for birth weight, crown-to-heel length and head circumference, and be based on a well-nourished population. The growth charts of Lubchenco et al. for birth weight, length and head circumference have been widely used for identifying the most severely growth-retarded infants. Infants classified as AGA (appropriate for gestational age: between the 10th and 90th percentile) on these charts may not have achieved their full growth potential, however, since these standards do not represent optimal fetal growth. To assess the adequacy of intra-uterine growth the birth-weight standards of Thomson et al., which reflect a well-nourished population, are recommended.

The use of words such as premature and postmature should be replaced by preterm (less than 37 weeks' gestation), and post-term (42 weeks or more). The term 'dysmaturity' is confusing, and the classification of an infant as SGA or AGA is preferable.

CLASSIFICATION OF IUGR
While birth weight for gestational age is usually used to assess fetal growth, it is now realized that other measurements of body size such as length, head circumference or weight/length ratio are also important — for example, a wasted infant, growth-retarded due to a brief period of severe undernutrition before delivery, frequently has a low weight/length ratio in spite of being classified as AGA. These infants are at particular risk of perinatal complications.

The clinical use of ultrasound has led to an increased understanding of the patterns of fetal growth. It is now possible to monitor intra-uterine growth by serial measurements of the fetal biparietal diameter (BPD) and to diagnose growth retardation during pregnancy. More recently the ratio between head and abdominal circumference or diameter has been used to provide a more detailed assessment of intra-uterine growth. Campbell has described two types of IUGR.

Symmetrical: This is characterized by proportionately reduced head and abdominal circumferences and is associated with stunting and a reduced rate of fetal growth, probably starting in the 2nd trimester.

Asymmetrical (brain-sparing): In this group the head circumference is spared in relation to the abdominal circumference. The BPD growth falls off quite late in pregnancy and the infant is usually wasted but not stunted. The early detection of this type of IUGR is not possible if the BPD alone is measured.

These two patterns probably reflect the timing of the onset of IUGR rather than the cause, and their recognition may be useful in predicting fetal outcome. The asymmetrical group appears to be associated with a higher incidence of prenatal asphyxia, while the symmetrical group may be associated with a higher incidence of retarded physical and mental development postnatally.

CAUSES OF IMPAIRED INTRA-UTERINE GROWTH
Fetal factors: (i) chromosomal abnormalities such as trisomy 18 and 21 and Turner syndrome are associated with IUGR; (ii) genetic abnormalities such as achondroplasia may cause fetal growth retardation; (iii) isolated congenital abnormalities — there is an increased incidence of both major and minor abnormalities in infants born growth-retarded; and (iv) chronic intra-uterine infections...
such as rubella, cytomegalie inclusion disease and toxoplasmosis.

Abnormal supply line: A decrease in the uteroplacental blood flow may be secondary to: (i) maternal hypertensive, cardiovascular or renal disease; (ii) smoking, which causes a decrease in the blood supply to the placenta by the direct vasospastic effect of nicotine, while the increase in maternal catecholamines and carboxyhaemoglobin may also be important (the effect is dose-related and is generally observed when 10 or more cigarettes are smoked per day); and (iii) repeated small antepartum haemorrhages.

Abnormal mother: (i) undernutrition in the mother during pregnancy results in a higher incidence of IUGR — this is probably the commonest cause of fetal growth retardation in the world today; (ii) anaemia; (iii) chronic maternal illness; and (iv) drug abuse. Excessive alcohol intake leads to the fetal alcohol syndrome, while narcotic addiction is often associated with impaired fetal growth. In most cases of IUGR an aetiological factor can be found if carefully sought, since primary placental insufficiency is extremely rare.

ANTENATAL PREDICTION OF RISK OF IUGR

The following factors are associated with an increased risk of impaired fetal growth: (i) a maternal booking weight of less than 45 kg; (ii) a maternal weight gain of less than 0.4 kg per week in the last trimester; (iii) smoking more than 10 cigarettes per day; (iv) a history of a previous SGA infant; (v) a history of hypertensive vascular disorder or chronic renal disease; (vi) bleeding at any stage of pregnancy, especially in the third trimester; (vii) low socio-economic status; and (viii) multiple pregnancy.

ANTENATAL EXAMINATION

During the antenatal period particular attention should be paid to the following: (i) the nutritional status of the mother, whose diet should be supplemented if indicated; (ii) the increase in her weight, since a total weight gain of less than 5 kg during pregnancy has been found to correlate strongly with IUGR (Elder et al. found that a weight loss of more than 454 g between two successive clinic visits, or failure to gain weight over 3 or more successive visits after 34 weeks, increased the likelihood of giving birth to an SGA infant threefold to 15%. If the mother’s weight gain was normal the odds were 20 to 1 against IUGR. This measure has limited predictive value, however, with an incidence of 84% false-positives and 51% false-negatives; (iii) maternal blood pressure changes. Page and Christiansen found an increased risk of IUGR if the mean arterial pressure (MAP = systolic + 2 diastolic) between the 18th and 26th weeks was more than 90 mmHg. Severe essential hypertension (a blood pressure of 160/110 mmHg or more), or pregnancy-induced hypertension of a similar magnitude plus proteinuria of >5 g/24 h, were associated with 44% and 31% incidences of IUGR respectively. When IUGR is suspected the fundal height and abdominal girth should be measured carefully. The amount of liquor should be estimated and the uterus palpated for irritability. The fetal presenting part should be assessed and an estimate of gestational age and size made. The fetal movement pattern should be ascertained and cognition taken of any change. In a study by L. Leader (unpublished data) using clinical parameters, only 30% of infants suspected of IUGR were found to be SGA and only 30% of SGA infants were diagnosed antenatally. This is similar to findings in other studies.

SPECIAL INVESTIGATIONS

Ultrasound Examination

Serial BPD estimations have been found to improve the antenatal diagnosis of IUGR. This measure alone is not useful in diagnosing the asymmetrical pattern of IUGR, however, and in 30 - 40% of cases the diagnosis will be missed. With the increasing availability of grey-scale ultrasonography it will soon be possible to calculate head/abdominal ratios and improve the accuracy of diagnosis. Calculating the uterine volume may also be useful, but is not practical at the present time. The other useful role of ultrasound is in the diagnosis of congenital abnormalities which may be associated with IUGR (e.g. the diagnosis of renal agenesis may be confirmed if the fetal kidneys or bladder cannot be demonstrated).

Oestriols

The measurement of maternal unconjugated oestriol (E) and total plasma E levels and 24-hour urinary E excretion is of value in assessing the condition of the fetus. Although significantly lower values of all three have been reported in association with IUGR, there is a high incidence of both false-positive and false-negative results. Measuring urinary E levels Beischer and Brown reported a sensitivity (proportion of abnormal infants giving an abnormal test) of 64%, a specificity (proportion of normal infants giving a normal result) of 80%, and a predictive value (likelihood of a compromised fetus if the result is abnormal) of 52%. Edwards et al. reported similar results using total plasma E. Goebelsman has recently suggested that a reliable sign of IUGR may be the failure of unconjugated E and total plasma E to show the accelerated rise which is commonly seen in the final 4 - 6 weeks of uncomplicated pregnancy.

Human Placental Lactogen (HPL)

Estimation of HPL has limited value in the diagnosis of IUGR, since the major determinant of the HPL level in the mother’s blood is the functional mass of the placenta and not all cases of IUGR are associated with placental disease. Published series are difficult to compare because of differing definitions of abnormal HPL values. An HPL value of less than 5 µg/ml after 36 weeks’ gestation has been found to have a sensitivity of 40 - 50%, while Edwards et al. taking an HPL value of 4 µg/ml after 36 weeks as abnormal, reported a sensitivity of 78%, a specificity of 84% and a predictive value of 59%.
Abdominal Radiography

This can support the clinical diagnosis of IUGR by showing a smaller-than-expected, poorly calcified and hyperflexed fetus with oligohydramnios, delayed appearance of epiphysial centres and an absent fat layer. It may also be helpful in the diagnosis of major congenital abnormalities such as anencephaly.

MANAGEMENT

Once IUGR is suspected on clinical examination, the patient should be hospitalized to confirm the diagnosis or to establish baseline investigations. Patients should be confined to bed and any aetiological or contributing factor should be sought and corrected if possible. Smoking should be discouraged.

Specific Treatment

1. Hypertension should be controlled with drugs that produce peripheral vasodilatation which may be useful in increasing placental blood flow.

2. Nutritional intervention may be of value if the patient is malnourished. While a high energy intake appears more important than protein supplements, a well-balanced ward diet will probably suffice. The use of partial intravenous hyperalimentation is of doubtful value.

3. Anaemia should be corrected.

4. The place of β-sympathomimetic drugs is still uncertain, but they may be of value in reducing uterine irritability and improving choriodecidual blood flow. There is no convincing evidence that the administration of heparin or hormones to the mother is of any value to the fetus.

Our management scheme at Groote Schuur Hospital is summarized in Fig. 1. Fetal growth is assessed by: (i) 2-weekly ultrasound estimations of the BPD and abdominal measurements; and (ii) weekly assessment of changes in the mother’s weight, the fundal height and the abdominal girth. Fetal well-being is monitored by: (i) charting of fetal movement for four half-hour periods per day; (ii) twice-weekly HPL and unconjugated E₂ estimations; (iii) unstressed antenatal cardiotocography and assessment of the fetal heart rate response to sound stimulation; and (iv) assessment of the fetal biophysical profile using real-time ultrasound to assess fetal activity, breathing and habituation to a repeated stimulus.

When fetal well-being appears to be normal the face of marked and clinical IUGR, a congenital abnormality should be seriously considered. If ultrasound is not available, abdominal radiography may be helpful. Amniography may be technically difficult in these cases because of oligohydramnios.

Timing of Delivery

All infants with suspected or confirmed IUGR should preferably be delivered in a hospital which can provide both prenatal and postnatal intensive care facilities. The timing of the delivery will be influenced by the standard of neonatal care available and may vary from 34 to 36 weeks. Amniocentesis should be performed to assess fetal lung maturity before delivery. A bubble score of 2+ or more suggests pulmonary maturity. If the bubble score is < 2+, either a total phospholipid (TPL) or lecithin/sphingomyelin (L/S) ratio estimation is required. The risk of hyaline membrane disease is minimal if the TPL value is > 2 μg/ml or the L/S ratio is > 2. The presence of meconium-stained liquor invalidates the tests for pulmonary maturity and probably indicates the need for urgent delivery. If these tests indicate lung immaturity and delivery needs to be expedited owing to deteriorating fetal condition, corticosteroids can be administered to the mother to accelerate fetal lung maturity. They should never be used empirically without first testing the liquor, since risks to both mother and fetus may be associated with the use of corticosteroids. Clinical experience suggests that it is most unusual to find hyaline membrane disease in SGA infants; however, a finding of pulmonary immaturity at amniocentesis does not exclude the possibility of IUGR.

Method of Delivery

If there is any malpresentation, elective caesarean section is the method of choice.

In cephalic presentations an elective caesarean section should be considered if: (i) the infant is thought to be viable and yet weighs less than 1 500 g, since the long-term neurological outcome in very-low-birthweight infants (<1 500 g) is better when they are delivered by caesarean section (D. Fairweather — personal communication); (ii) the state of the cervix is unfavourable (Bishop’s score <5); and (iii) there are no facilities for intrapartum monitoring.

Neonatal Complications of IUGR

Good neonatal care involves anticipation of possible problems with appropriate prophylaxis, or at least early recognition and intervention. The following are some of...
the problems seen in the growth-retarded infant:

**Asphyxia:** Many of these infants are born hypoxic and acidic, fail to breathe after delivery, and require skilled resuscitation. The aspiration of meconium is a particular hazard and may be prevented by pharyngeal suctioning under direct vision at delivery before the first gasp. Cerebral oedema and hypoxic brain damage (with intraventricular haemorrhage in preterm infants) are common in asphyxiated infants and associated with a high morbidity and mortality.

**Hypoglycaemia:** Intra-uterine starvation leads to a loss of both fat and hepatic glycogen stores, and the infants may also have impaired gluconeogenesis. These factors predispose to hypoglycaemia unless early feeding is instituted.

**Polycythaemia:** Chronic intra-uterine hypoxaemia results in polycythaemia (a peripheral packed cell volume of >65%) and hyperviscosity, which may interfere with blood flow to vital organs. A partial plasma exchange may be indicated if clinical signs of cardiac failure or a disturbance of central nervous system function occurs.

**Hypothermia:** Loss of deposits of white fat (for insulation) and brown fat (heat producing) plus a large surface area/weight ratio make these infants very susceptible to heat loss and hypothermia.

Associated factors such as congenital abnormalities or chronic intra-uterine infection should be kept in mind when the growth-retarded infant is examined after delivery.

**CONSEQUENCES OF IUGR**

**Growth**

A long-term study of 96 full-term SGA infants revealed that at 4 years of age the mean heights and weights were between the 10th and 25th percentile, with 35% below the 3rd and only 8% above the 50th percentile. All the infants that eventually surpassed the 3rd percentile showed an accelerated growth rate in the first 6 months.

**Neurological Development**

The long-term outcome for these infants depends on whether the IUGR was complicated by asphyxia neonatorum, meconium aspiration, hypoglycaemia, hyperviscosity or other adverse effects. If these consequences can be avoided there is a better prognosis. An earlier study of full-term SGA infants reported a 1% incidence of cerebral palsy and convulsions in 6%. Evidence of minimal brain dysfunction was present in 25%, electroencephalographic abnormalities of a minor nature were found in 59% of males and 69% of females, and speech defects were present in about 30%. Although the average IQ was normal, 50% of the boys and 36% of the girls were doing poorly at school. No correlation was found between the severity of the IUGR and the neurological deficit.

Studies of low-birthweight infants have shown that those born SGA also have a significantly higher incidence of neurological handicap than infants who are AGA.

This incidence is even higher in infants who are symmetrically growth-retarded.

**CONCLUSION**

Intra-uterine growth retardation should be prevented if possible. This requires a knowledge of the causative factors, a high quality of prenatal care, and a rational approach to the management of these patients. The timing and method of delivery should be planned by the perinatal team so that optimal conditions can be provided for the fetus during labour and for the infant in the neonatal period. Intra-uterine growth retardation represents preventable perinatal morbidity and mortality.

**REFERENCES**