Management of intra uterine growth restriction

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Introduction

Intra-uterine growth restriction (IUGR) remains a complex management problem in modern obstetric practise. It is a major cause of perinatal morbidity and mortality in South Africa as well as in the developed world and is a cause of great concern for the patient, her family and doctor.

Insufficient growth that result from intrinsic fetal factors such as aneuploidy, congenital malformations and congenital infection carry a guarded prognosis that often cannot be improved by a therapeutic intervention. In comparison, IUGR related to inadequate substrates for fetal metabolism and decreased oxygen availability has a better prognosis.[1]

The challenge to the obstetrician is to identify when inadequate growth occurs abdto determine the cause and severity. This will enable fair and proper counselling of the parents concerning possible outcome and prognosis. Decisions have to be taken regarding fetal monitoring and growth evaluation and timely delivery, this after consultation with the paediatrician or neonatologist.

INITIAL DIAGNOSTIC EVALUATION

The various causes, management options and ultimate prognosis of fetuses with IUGR differ widely and it is important to examine each case individually to look for maternal, placental or fetal disorders. This is achieved by obtaining a complete history, doing a thorough physical examination, ultrasound and other special investigations.

Complete History

In addition to the normal aspects of the history, detailed attention should be given to the following:

- fetal growth restriction in previous pregnancies, because of the risk for recurrence in subsequent pregnancies
- maternal or family history of thrombosis as this can be associated with congenital and acquired trombophilia disorders.
- social habits that can play a role namely smoking, use of alcohol and of recreational drugs.

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Physical Examination

In addition to the standard clinical assessment the following aspects are important:

- Clinical suspicion of viral infections like Cytomegalovirus, Rubella, Varicella Zoster and Herpes Simplex virus must be further investigated by maternal serum testing followed, if positive, by amniotic fluid testing for DNA.
- TORCH screening should not be done routinely unless non-specific ultrasound markers of abnormality including echogenicity and calcification of the brain and liver as well as hydrops are present on sonar assessment.

Screening for inadequate growth in a low risk population is commonly performed using the symphysis-fundus height (SFH) measurement. This however has a varying sensitivity of 27-85%. Up to 50% of small for gestational age fetuses are not suspected antenataly.[2] In women with risk factors for fetal growth restriction, ultrasound assessment of fetal growth must be done in addition to serial SFH.

Imaging

Accurate dating of the pregnancy forms part of the cornerstone of the diagnosis of IUGR. Ideally duration of gestation must be confirmed by crown rump length measurement (CRL) during the first trimester or by second trimester biometry.

Estimation of fetal weight (EFW) is a critical element in diagnosis and monitoring. The EFW on ultrasound will be within 15% of the true weight in 95% of cases. Serial measurements rather than single estimates of the abdominal circumference and EFW are recommended.[3] This can be performed every 2 weeks in order to reduce false positive values due to ultrasound errors.

The Royal College of Obstetricians and Gynaecologists (RCOG) recommends plotting of values on customized growth charts.[4] In compiling these customised growth curves physiological factors known to affect fetal size are incorporated, such as gender, maternal weight, height and ethnicity. It appears to give better results than general population curves at identifying those small fetuses at risk of increased perinatal complications.[5]

Detailed anatomical survey of the fetus is essential due to the association of major fetal anomalies with IUGR. Growth

restriction is found among 20-60% of malformed infants. In comparison, 10% of IUGR is accompanied by congenital abnormalities.[6]

The anomalies associated with growth restriction include: omphalocoele, diaphragmatic hernia, skeletal dysplasia, congenital heart defects, microcephaly (rare), polyhydramnios (associated with trisomy 18). Once intrinsic fetal abnormalities have been excluded, placental insufficiency usually remains the presumed aetiological diagnosis.

Laboratory Evaluation/ Special Investigations

Fetal karyotyping is indicated in the following scenarios:

- early (<32 weeks) detection of IUGR
- severe IUGR (<3rd percentile)
- IUGR accompanied by polyhydramnios (to exclude Trisomy 18)
- structural abnormalities found during ultrasound examination. In 10-14% of structural abnormal growth restricted fetuses the karyotyping will be abnormal. However, only 2% of structurally normal growth fetuses have chromosomal abnormalities.[1]

Trisomy 18, trisomy 13 and triploidy are associated with early onset IUGR. Some of the ultrasound markers suggestive of aneuploidy include echogenic bowel, nuchal fold thickening and abnormal hand positioning.[1]

After initial assessment constitutionally small fetuses should be differentiated from truly growth restricted fetuses. These constitutionally small fetuses are anatomically normal with appropriate amniotic fluid volumes and growth rates. The outcome for this group is good. It is important to recognize ethnic and geographic differences in growth potential. This will prevent unnecessary interventions in these patients.

SUBSEQUENT OBSTETRICAL MANAGEMENT

ANTENATAL SURVEILLANCE

The purpose of antenatal surveillance is to identify fetuses at highest risk of in-utero demise, who may benefit from intervention by preterm delivery.[1]

ULTRASOUND

This is core to decision making. Growth as well as arterial and venous blood flow in the fetus can be assessed.

The frequency of serial examination must be based on severity of findings:

- monitor fetal well-being – 1-7 times per week
- fetal growth – 2-4 week

Growth is plotted on customized growth curves (where available) to detect when growth is below the 10th percentile, and in order to follow growth progress.

Doppler velocimetry is the primary surveillance tool in pregnancy with suspected IUGR.

UMBILICAL ARTERY (UA) DOPPLER

UA Doppler studies are used to stratify SGA infants into low and high risk categories. They play an important role in the initial confirmation of placental insufficiency and in ongoing surveillance and management.

It has been demonstrated that detection of abnormalities in Doppler waveforms can predict those small for gestational age babies at highest risk of prenatal mortality, with the risk of death correlating with severity of Doppler waveform deviation: odds ratio = 4.0 with absent end diastolic flow (AEDF) and reversed end diastolic flow (REDV), odds ratio = 10.6 for perinatal mortality.[7] It also influences the risk for cerebral haemorrhage, anaemia and hypoglycaemia in the neonate with increased neonatal morbidity.

Numerous randomized controlled trials showed that using Doppler velocimetry perinatal death and unnecessary induction of labour are significantly reduced.[1] Meta-analysis found that clinical action guided by Doppler ultrasound reduces the odds of prenatal death by 38% in high risk pregnancies. There were however no advantage in using this tool for screening in a low risk population.[8]

The SGA fetus with normal UA Doppler findings is unlikely to have major morbidity (normal and slightly increased umbilical Doppler flow) and it is safe to prolong and also reduce surveillance. A large prospective trial is required to determine the appropriate amount of surveillance for SGA infant with normal UA Doppler.

MIDDLE CEREBRAL ARTERY (MCA) DOPPLER

As part of the fetal response to hypoxia (mainly due to placental insufficiency) selective redistribution of blood flow is incorporated to maintain perfusion of vital organs (brain, myocardium, adrenal glands). Assessment of MCA Doppler waveform will detect reduced resistance to flow with redistribution.

Arduni et al[9] described a curvilinear relationship between the cerebral vascular response and hypoxia. Maximum vasodilation (to compensate for hypoxia) in the MCA is reached 2 weeks before the onset of fetal heart rate decelerations. Thus evidence of brain sparing is not in itself an indication for immediate delivery at very preterm gestation.

DUCTUS VENOSUS DOPPLER

Changes in Doppler velocimetry of the ductus venosus (DV) and the umbilical vein (UV) represent a late stage in cardiovascular decompensation. Urgent delivery is indicated with reversal of flow in DV or pulsation in UV.

In a high risk population an abnormal DV Doppler is a good predictor of birth acidemia with reported perinatal mortality rates of 63-100% associated with absent and reversal of flow. It is superior to measurement of UA or MCA in predicting perinatal demise.

The combined assessment in fetal surveillance is considered best practice for all preterm intra uterine growth restricted fetuses:

- UA Doppler has the highest sensitivity and negative predictive value for poor perinatal outcome.
- DV and UV parameters have the best specificity and positive predictive values.[10]

SEQUENCE IN DETERIORATION IN FETAL DOPPLER WAVEFORMS

Initially there is a decrease in AFI and increase in UA Doppler, with positive end diastolic flow. This followed by decrease in resistance in MCA (brain sparing), and the presence of AEDF in the umbilical artery. Later the resistance in the DV increases together with REDF in the umbilical artery. The end

point is reached when flow in the DV is reversed and becomes pulsatile in the UV.

OTHER SURVEILLANCE TECHNIQUES

BIOPHYSICAL SCORE OR PROFILE

Some centres find the biophysical score useful because it provides multiple acute and chronic fetal physiologic parameters, is easy to perform and appears to be reliable. Fetal death within one week of a normal biophysical profile (BPP) is extremely rare and therefore this has a good negative predictive value.[1]

Performance of this investigation is however time consuming. According to a Cochrane review there is not enough evidence to evaluate the use of BPP as a test of fetal well-being in high risk pregnancies.[11] The use of BPP in management of growth restriction is therefore not practised in our unit.

AMNIOTIC FLUID VOLUME

Amniotic fluid volume is an important component of longitudinal monitoring and gives an indication of renal perfusion of the fetus. It must be assessed serially by either measuring the single deepest vertical pocket or by calculating the amniotic fluid index (AFI).

Observational studies found that IUGR complicated by olighydramnios (defined as a single vertical pocket of fluid measuring less than 2cm x 1cm or an AFI of less than 6) is associated with a sharply increased risk of perinatal mortality. Normal fluid volume is less frequently associated with growth restriction or fetal demise, unless congenital malformations or aneuploidy are present.[1] Further analysis concluded that an AFI of/less than 5 is associated with a significant increased risk of caesarean section delivery for the indication of fetal distress and a low Apgar score at 5 minutes.

CARDIOTOCOGRAPHY(CTG)

Non-stress CTG is an indirect assessment of fetal central neurological status as reflected in its autonomic control of the fetal heart rate.

It remains the most common test used, despite paucity of evidence that it is associated with better neonatal outcome. Although a normal CTG has a good negative predictive value, in a systematic review the effectiveness could not be evaluated because of too little available evidence.[12]

Computerised CTG systems show better accuracy than the opinion of clinicians in predicting umbilical acidosis and low Apgar score.[13] One small study looked at short term variability of 4,5mm for predicting acidemia (pH<7) and showed a sensitivity of 100%, specificity of 70%, positive predictive value of 33% and negative predictive value of 100%.[14]

FETAL BLOOD SAMPLING

Intra uterine blood sampling sampling for evaluation of the fetal condition is not recommended. Adequate management is possible without invasive techniques.

THE USE OF ANTENATAL CORTICOSTEROIDS

Despite the findings from a large study that questioned the efficacy of cortciosteroids in preterm IUGR fetuses due to the inability to meet the transient increase in metabolic demand induced by steroids, the use of corticosteroids in IUGR is still recommended.[15]

According to the RCOG it is appropriate to administer a course of antenatal steroids to decrease neonatal pulmonary and central nervous system morbidity if preterm delivery occurs. It is known from multiple series that both spontaneous and indicated preterm deliveries are more common in IUGR fetuses.

The practise of administering multiple weekly courses of steroids gained support after publication of the Australasian Collaborate Trial of Repeat Steroids which showed a decrease in respiratory distress of 33 vs. 44%, and the incidence of severe lung disease of 12, compared to 20%. However, long-term infant outcome results remain to be assessed.[16]

TIMING OF DELIVERY

There is still little consensus about the optimal timing of delivery. Delivery is indicated as soon as the risk for fetal death exceeds the risk of neonatal death. The decision is determined by both gestational age and fetal condition. The availability of neonatal care facilities and expert neonatal care providers must also form part of this equation.

The difficulties surrounding this decision were explored in the Growth Restriction Intervention Trial (GRIT). The authors recommended delayed delivery in very preterm gestations if there was uncertainty about the need for intervention. They found that deaths prior to hospital discharge were similar in both groups and that the immediate delivery group had fewer stillbirths but more neonatal and infant deaths.[17] During a 2 year follow up, the proportion of children with death or severe disability was similar for both groups.[18]

REMOTE FROM TERM

Normal umbilical artery doppler is reassuring with regard to the immediate fetal outcome. Therefore, prolongation of the pregnancy to gain further fetal maturity is reasonable. Absent end diastolic flow (AEDF) or reversed end diastolic flow (REDF) are ominous findings, and prompt delivery is often indicated because of high risk for fetal demise.

Changes in the venous circulation are generally later than those in the arterial circulation. They appear to be more predictive of impending adverse outcome and warrant immediate delivery regardless of gestational age.[1]

TERM OR NEAR TERM

Delivery can be delayed until 37 weeks when pulmonary maturity is more likely as long as antepartum fetal surveillance are reassuring and there is positive end diastolic flow present on Doppler evaluation. Pregnancies should not extend beyond 40 weeks.

In the presence of maternal disease (e.g. hypertension), the finding of arrest of growth over a two to four week interval, and if the BPP score is low, and/or the UA Doppler velocimetry reveals absence or reversal of flow, delivery is indicated. However, every case must be individualized.[1]

INTRAPARTUM MANAGEMENT

IUGR fetuses may exist in a state of mild-to-moderate chronic oxygen and substrate deprivation. This may result in the occurrence of antepartum or intrapartum hypoxia and neonatal ischemic encephalopathy, fetal heart rate

abnormalities, meconium aspiration, polycytemia, hypoglycaemia, and other metabolic abnormalities.[19]

It is imperative to optimize timing of delivery and perform continuous intrapartum fetal monitorig and provide immediate skilled neonatal care.

MODE OF DELIVERY

Vaginal labour where the fetus has been found to have IUGR is still a reasonable option in the absence of any contraindications for normal vaginal delivery. As long as there is careful intrapartum monitoring that include continuous CTG and, where available, secondary tests (fetal scalp blood and ST segment analysis of the fetal electrocardiogram), and as long as rapid intervention when evidence of fetal intolerance appears, vaginal delivery can be attempted. The mode of delivery can be decided on based on the favourability of the cervix, the severity of IUGR, gestational age, fetal presentation and presence or absence of maternal complications.[20]

Some studies have shown the use of elective caesarean section for delivery of IUGR fetuses to be associated with lower rates of respiratory distress syndrome, neonatal seizures and deaths compared to vaginal delivery, but these did not reach statistical significance and the mothers were more likely to experience serious morbidity.[21]

Conclusion

IUGR remains a challenge for all obstetric health care providers. In spite of improvement in surveillance with the refinement of Doppler studies, timely diagnosis and optimal management remains complex in the high as well as low risk populations. Serious attention to antenatal surveillance may lead to improved antenatal care, better decision making re the timing and the mode of delivery, and in the individual case may lead to an improved outcome.

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