Acta Biomed 2015; Vol. 86, Supplement 1: 21-23

Original article

Obstetrical management of fetus with intra uterine growth restriction (IUGR) and late IUGR

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Summary. In this article we evaluated an important complication of pregnancy, the fetal growth restriction (IUGR). IUGR is defined as an estimated fetal weight of fetal abdominal circumference below the 10th centile measured by ultrasound according to local standards. We present the prenatal surveillance, the screening tests for late IUGR and the new diagnostic examinations, to establish the best prevention system for IUGR and late IUGR. (www.actabiomedica.it)

Key words: fetal growth restriction (IUGR); late IUGR; screening test

Introduction

An important complication of pregnancy is fetal growth restriction. A widely accepted prenatal definition of intra uterine growth restriction (IUGR) is defined as an estimated fetal weight of fetal abdominal circumference below the 10th centile measured by ultrasound according to local standards.

Perinatal mortality are increased in late preterm and term fetuses with a birth weight below the 10th population percentile. About 60% of term perinatal mortality regards children with a birth weight percentile below the 10th percentile. Yet, beyond perinatal this burden of mortality and perinatal morbidity what mostly concern clinicians are the consequences of low birth weight on for future development, especially for cardiovascular, metabolic and neurological development. ('Barker hypothesis'). It is know that adverse insults acting during intrauterine life can result in permanent changes in the physiology and metabolism of the newborn, which in turn leads to an increased risk of disease in adulthood. The "fetal origin of adult disease Hypothesis" by Barker et al identified the relationship between impaired intra-uterus growth and adult cardiovascular disease risk and death.

Fetal Programming

According to Rogers, Lillycrop and others, "the foetus appears to use the in utero environment to predict and prepare for the postnatal environment. That is, an organism alters its developmental path to produce a phenotype (observable traits, such as characteristics of behaviour, physiology, metabolism, or outward appearance) that gives it a survival or reproductive advantage in postnatal life". This process goes by the name of " predictive adaptive response". Epigenetics is the key to understanding the relationship between intrauterine environment and gene expression.

The placenta bears a central role in fetal programming. The placenta is the organ that the fetus uses during intrauterine life to transfer nutrients, and energetic

substrates from maternal blood diverted in the intervilluos space, to exchange gases and hormones. The determinant of these processes is trophoblast development both as an anatomic organ which accommodates maternal and fetal blood flow and a membrane exchange activity.

The aetiology of fetal growth restriction is multifactorial. The most common cause for fetal growth problems is a disturbance in the utero-placenta circulation. This disturbance develops in a slow process, but without intervention it can lead to fetal death. Insufficiency of the utero-placenta circulation is often associated with pregnancy induced hypertension and pre-eclampsia. Maternal diseases like hypertension, renal failure or pulmonary disease are associated with a higher risk of IUGR. Tobacco, drugs and alcohol also are associated with a higher risk of IUGR, where smoking is the most important negative factor. Other related factors are a low socio-economical status, stress, poor diet and maternal age (very young women and a high maternal age). Foetuses with congenital or genetic abnormalities are also at a higher risk for IUGR. The most important risk factors are medical diseases; especially hypertensive disorders, smoking and complications in a previous pregnancy.

Prenatal Surveillance

Antepartum fetal surveillance is essential in managing these pregnancies and timely recognition of complications. Term, growth restricted foetuses present the obstetrician with at least two difficulties. Firstly they are difficult to identify. After identification of the small fetus, the second challenge concerns, the distinction between pathologically small foetuses, most likely accompanied by a suboptimal placental function, and constitutional healthy small foetuses. Such a distinction is difficult, since most assessment tools fail during the term period. Umbilical artery Doppler fails in recognizing the fetus with true growth restriction at near term or term age. Similarly, Doppler velocimetry of the uterine arteries although more sensitive in the identification of the risk of small placentas is still just a proxy of the real maternal vascular supply line to the placenta. In spite of these limitations ultrasound measurements of the abdominal circumference and Uterine Doppler velocimetry could be considered for screening late IUGR foetuses

Screening tests for late IUGR

1. Cross sectional Abdominal circumference measurement below the 10th percentile does not represent growth, yet it represents a robust reproducible screening test between 35+0 and 37+6 wks'gestation. Intrauterine death due to growth restriction before 37+6 weeks is an exceptional event and therefore this window of gestation represent a proper timing of screen out abnormal fetal growth before delivery.

2. Uterine Doppler velocimetry in late gestation might identify foetuses at risk of IUGR due to placental vascular insufficiency, that might be lost by fetal biometry.

When recognized, another challenge is formed by limited therapeutical options. The only possible intervention consists out of adequately timing of birth. Optimal timing of elective delivery is difficult in pregnancies complicated by intra uterine growth restriction due to lack of adequate diagnostic tools. The importance of being able to identify foetuses at risk resides in the possibility to target interventions with potential adverse effects if used too liberally. This has been shown by a recent large randomized trial in which an unselected population of term foetuses with an estimated fetal weight below the 10th percentile were randomized between immediate induction of labor or expectant management. The incidence of adverse outcomes did not differ between both groups. In other words, too many constitutionally small foetuses were exposed to an unnecessary intervention with risks of complications obscuring the possible gain of early intervention in foetuses at real risk.

Many parameters have been evaluated to distinguish between constitutionally small and pathologically growth restricted foetuses with little result so far. Doppler evaluation of flow patterns in the umbilical artery are used routinely in preterm growth restricted foetuses but are normal in most cases in term small-for-gestational-age foetuses. This due to the fact that a high placental resistance occurs only when more than 1/3rd of placenta function is deficient. Oligohydramnios is not specific enough. Abnormal fetal heart rate

patterns can reliably identify fetal distress but are a late sign of impairment. Monitoring of fetal movements is subjective and reduced movements are generally also a late sign of impairment

Recently a number of new diagnostics tools have been described in small case series, which have potential in the early recognition of the term IUGR fetus at risk for adverse neonatal outcome:

New diagnostic examinations

1. Blood flow volume in the uterine artery assessed with Doppler ultrasound seem to be more sensitive than just the arterial Doppler waveform .

2. Blood flow volume in the umbilical vein can sort out minor reduction in nutritional function of the placenta notwithstanding normal Umbilical artery waveform.

3. PGF/sFlit-1 might be a useful biomarker of placental vascular dysfunction and add its predictive value in identifying small foetuses accompanied by dysfunctional placenta

4. The cerebro-placental ratio (CPR) defined as the ratio between the pulsatility index measured in these arteries has been shown to be related to MRI abnormalities and abnormal neonatal neurobehavioral development. In fact, subtle opposite changes in flow patterns of umbilical arteries and middle cerebral artery might also identify the fetus at risk.

5. Computerized CTG is of clinical relevance in identifying abnormal variability in severe growth restricted foetuses, yet short term variability and an exact identification of small and large accelerations might contribute to identify subtle changes in fetal adaptation to limited placental resources

6. Advanced analysis of fetal heart rate patterns specifically assessing changes in the autonomous regulation of fetal heart rate may also identify the IUGR fetus at increased risk. Early signs of hypoxemia are found in changes in the autonomous regulation of the fetal heart rate. This can be assessed by relatively new promising methods; spectral analysis or phase rectified signal averaging (PRSA) of the fetal heart rate, measured by electromyography. Both methods are more specific than conventional analysis in identifying hypoxemia during labour or growth restriction ante partum. Research from Munich, Utrecht, and from our group has shown abnormalities in about 30% of SGA foetuses, compared to only 5-8% with conventional computer analysis. Most of these cases were preterm and correlations with neonatal outcome have not yet been studied..

The challenge is to find combinations amongst these monitoring modalities that will identify and monitor late IUGR , in such a way that targeted intervention studies can be performed in order to optimize diagnosis and prevent long term cardiovascular and metabolic sequelae in this large subset of foetuses

Conclusions

It is clear from this brief analysis that late IUGR remains a major challenge in perinatal medicine. Unfortunately the italian ultrasound screening protocol for IUGR at 30-32 weeks of gestation represents a major problem, too late for early severe IUGR, too early for late IUGR, a total useless misleading waste of money.

Whereas the TRUFFLE protocol represents a clear cut monitoring system for early IUGR , further studies are still to be performed in order to define the optimal screening and monitoring methods for late IUGR.

Reference

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