INTRAUTERINE GROWTH RESTRICTION - STILL A GREAT CHALLENGE FOR THE NEONATOLOGIST - A REVIEW ARTICLE

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Abstract

This article makes a review of literature data on an extremely special category of infants – premature neonates with intrauterine growth restriction (IUGR). The antenatal recognition of a true fetal growth restriction helps prevent or decrease the mortality rate and neonatal morbidity. Prenatal and postnatal Doppler velocimetry has a great contribute to the differentiation of healthy SGA and real IUGR but also a challenge to predict which of the fetuses are at high risk for negative outcomes, and there are currently few understandable things about monitoring and treatment strategies most appropriate for preterm infants with RCIU. An international initiative to address these issues would be of great importance to improve the care of the group with IUGR.

Key words: premature neonates, intrauterine growth restriction

Introduction

IUGR remains an important health problem in developing countries around the world, being one of the "major obstetrical syndromes" associated with placental defects, but also one of the topical issues of neonatology, and in particular the association between IUGR and prematurity under 32 weeks of gestation. Neonatal morbidity and mortality remain significant and has an important economic impact. The need for more stringent diagnostic criteria remains a problem.

Intrauterine growth restriction (IUGR) was defined as the fetal growth rate that is below normal related to the growth potential of a child, specific for race and sex. (4) This was also described as a deviation or reduction from the expected growth pattern and is usually the result of a reduced hereditary growth potential or multiple adverse effects on the fetus. The "normal" newborn is the one whose birth weight is between the 10th and 90th percentiles for gestational age, sex, and race without any malnutrition and growth restriction characteristics. The terms "IUGR" and "SGA" have been used as synonyms in medical literature, although there are differences between the two. The definition of SGA is based on cross-sectional evaluation (either prenatal or postnatal) and this term has been used for those newborns whose birth weight is less than the 10th percentile for gestational age or two standard deviations below the population norms represented on the growth charts, and the definition only considers birth weight without any specification of intrauterine growth or other physical characteristics at birth (1-4).

SGA refers to a weight below the 10th percentile for gestational agerepresented on the population growth graphs. It can still be classified as (1-5):

- mild: birth weight between 3 and 10th percentile
- severe: birth weight lower than percentile 3

IUGR classification:

There are 3 types of IUGR:

- Asymmetrical IUGRs (undernourished children)
- Symmetrical IUGRs (hypoplasic small for date)
- Mixed IUGRs.

In mixed IUGR newborns have smaller numbers and smaller cell sizes as well as clinical characteristics of both types of IUGR at birth (symmetrical and asymmetrical)(Table 1). This type of IUGR results when early IUGR is affected during the pregnancy by placental cause (1-5).

Causes of IUGR

IUGR is the common end result of maternal, placental, fetal or genetic factors.

Antenatal diagnosis of IUGR

The purpose of antenatal monitoring is early detection of IUGR so that antenatal management is optimized in order to obtain better neonatal outcomes. Unfortunately, despite these initiatives, the generalized result of these IUGRs has not changed much over time. Careful monitoring will lead to changes regarding the time of birth or management of birth, but there is still controversy over the appropriate type and timing of monitoring.

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Table 1. Characteristics of symmetrical and asymmetrical types of IUGR.

Characteristics	Symmetrical IUGR	Asymmetrical IUGR
Injury period	First part of pregnancy	Late period of pregnancy
Incidence of IUGR	20 – 30%	70 – 80%
Etiology	Genetic diseases or fetal intrauterine infections	Utero-placental insufficiency
Prenatal ultrasound: head circumference, abdominal circumference, biparietal diameter, femur length	All are reduced proportionally	Abdominal circumference-low; biparietaldiam, head circumf; normal femoral length
Number of cells	Low	Normal
Cells dimension	Normal	low
IP	Normal (>2)	low (<2)
Postnatal anthropometric indices:weight, lenght, head circumf.	Low	Low weight; length and head circumf.– normal (brain sparing)
Difference between cranial and thoracic circumference in term IUGR	< 3 cm	➢ 3 cm
Characteristics of malnutrition	Less pronounced	More obvious
Prognosis	Poor	Good

(1-5)

The necessary investigation for mothers at high risk of having fetuses with IUGR includes assessment of risk factors in maternal and family history, maternal anthropometry with pre-pregnancy weight and height, maternal nutrition status, exact gestational dating, palpation of uterine height, cardiotocography, Doppler ultrasound, and precise measurement of fetal weight using biometric measures (abdominal circumference [AC], head circumference [HC], biparietal diameter and femur length [FL]). The HC / AC ratio was used for diagnosed fetuses with asymmetric growth restriction (FGR) (5-9).

The appropriate gestational age should be calculated using both the date of the last menstrual period and the length of the fetus in the first trimester of pregnancy. The specific weight gains charts (depending on race and ethnical origin) can be used to diagnose IUGR. To accurately highlight IUGR using echocardiography, serial examinations should be made (at least every three weeks to reduce false-positivity rates in diagnosing asymmetrical restriction).

Once identified maternal and IUGR risk factors, further investigations are needed: fetal karyotype for chromosomal abnormalities, TORCH profile, syphilis serology, malaria - especially in the endemic areas. A detailed anatomical fetal study, TIFFA (target imaging for fetal abnormalities) and Doppler on the uterine arteries should be performed by a fetus specialist if severe SGA is identified at the 18-20 week evaluation.

Extensive antenatal Doppler ultrasound allows assessment of well-fetal status and detection of IUGR and Doppler on uterine arteries, umbilical arteries, and on middle cerebral arteries. Although almost all veins and large arteries have been studied through Doppler in the case of IUGR neonates, however, in practical management is used Doppler velocytometry on the umbilical arteries and middle cerebral artery. Umbilical arteries were the first Dopplerevaluated. Doppler waves at their level have a characteristic appearance of "saw teeth". In the case of fetuses suspected of having IUGR, if the Doppler waves in the umbilical arteries look normal and the intrauterine growth curve ascends over a period of two weeks, the fetus may be considered to be healthy, small constitutional. The abnormal appearance of Doppler wavelengths of the umbilical arteries is an early sign of fetal suffering. The average time interval between the absence of enddiastolic flow in the umbilical arteries and the onset of delayed deceleration was estimated at about 12 days (0-49 days). Also, studies have demonstrated a progressive increase in velocimetric flow velocity in the umbilical arteries to extreme cases of inverted enddiastolic flow (Fig. 1). Increasing diastole at the MCA level is a fetal compensatory mechanism that is reactive to uteroplacentral failure ("brainstorming" mechanism). If compensatory mechanisms are overcome, fetal damage occurs rapidly. Therefore, the serial Doppler ultrasounds will estimate the duration of use of fetal compensatory mechanisms, the abnormal venous Doppler appearance indicating fetal deterioration and the need for emergency cesarean section (Fig. 2). (5-9)

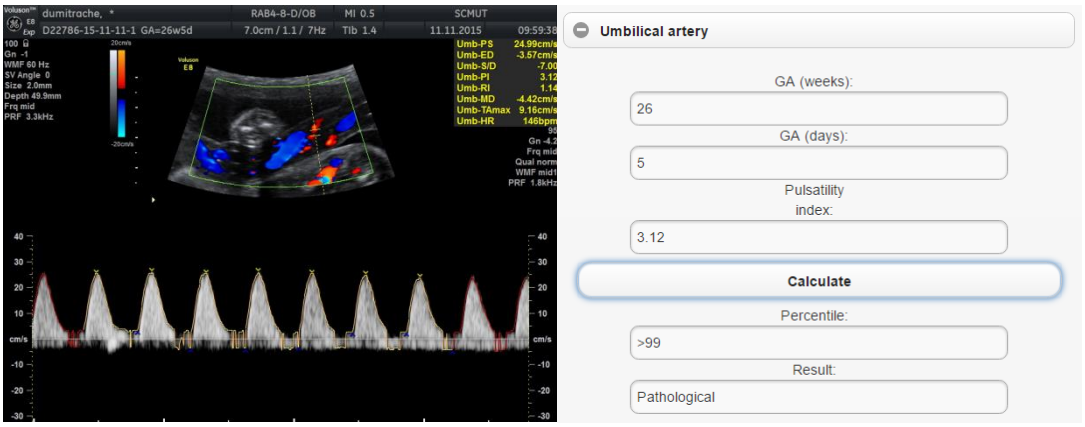

Fig. 1. Example of pulse rate index / umbilical artery resistivity index in a pregnancy 26 weeks of gestation with early RCIU http://medicinafetalbarcelona.org/calc/

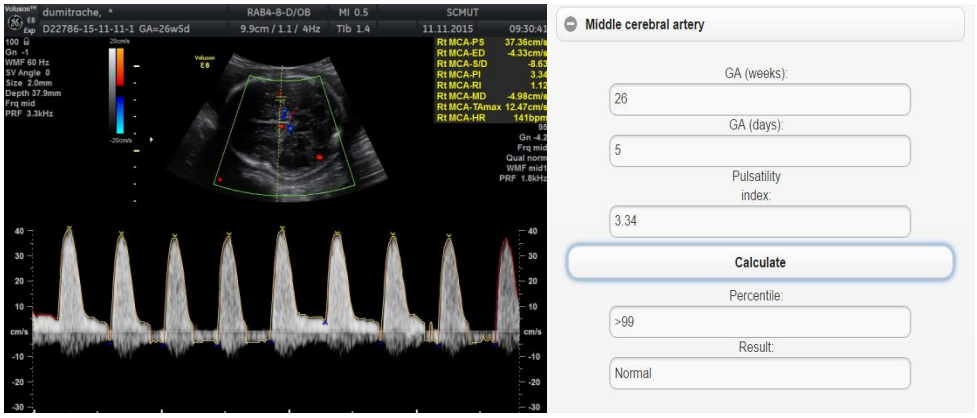

Fig. 2. Example of index pulsatility index / middle cerebral artery resistivity index and cerebro-placental index in a26 weeks of gestationpregnancy with early IUGR http://medicinafetalbarcelona.org/calc/

Postnatal diagnosis of IUGR

1. The postnatal diagnosis of IUGR includes clinical examination, anthropometry, weight index, clinical evaluation of nutrition score (CAN), cephalic index, middle arm circumference and ratio of middle arm / head circumference.(1-9)

Early and late neonatal development in a IUGR prematureis influenced by fetal hypoxia that activates a series of biophysical, cardiovascular, endocrinological and metabolic responses. Fetal cardiovascular response to hypoxia, include changes in heart rate, increase in blood pressure, and redistribution of cardiac output to vital organs are probably the most important adaptation responses to maintaining homeostasis. Redistribution of blood flow to the fetal brain is known as the "brain-sparing effect". Despite numerous attempts to manage the fetal growth restriction, there are no effective treatments to improve fetal growth. The tested methods include maternal nutritional supplements, plasma volume expanders, amino acid and medicines given to the mother- such as aspirin in low doses. moreover, maternal hyperoxygenation found in fetal pO2 reaching or nearing normal value. Even fetal glucose supplements have been tried and have proven to be of no benefit, and can exacerbate acidosis. (10-13) However, the available universal therapeutic outlook for outcome improvements includes antenatal steroid administration in preterm pregnancies and birth in an institution with a neonatal care unit that is able to cope with the complexity of neonatal growth restriction management. Antenatal corticosteroids should be administered to each affected growth-restricted fetus whose birth is expected before 34 weeks of gestation. Although there is a tendency to consider corticosteroids to be beneficial after 34 weeks of gestation (especially in certain cesarean surgeries), the reduction in respiratory distress syndrome in infants over 34 weeks has not reached statistical significance. The gestational age of the fetus is a critical component in the decision process of birth. Unfortunately, there are no randomized group studies in the total clinical spectrum of the fetal growth restriction to assess the optimal moment of birth. In principle, the moment of birth in term newborns is directly correlated with the time when fetal lung maturity was documented, if fetal distress is present or maternal causes determine birth. The management is more complicated in pregnancies between

25-32 weeks of gestation, where every day gained in the uterus can improve survival by 1-2%..(1-9) Early births in neonates with IUGR with abnormal wave on the umbilical artery (after corticosteroid treatment completed antenatally) offers the benefit of an increased rate of live birth fetuses and the disadvantage of increased neonatal mortality.(1-3)) Birth delay until fetal distress is evident may be associated with the increase in fetus mortality by about 5 times higher and neonatal death prior to discharge decreased by more than a third, although total mortality was unchanged. (1-3) It seems that there was insufficient evidence to convince those enthusiastic about this idea that it is wrong both for immediate and delayed birth. When timing is selected, assessment of fetal status should be correct to avoid predictable adverse effects. As a result, the final effect of the antenatal management protocols on the results would probably be very good if the critical results were predicted correctly prenatally. Such results include the risk of fetal death and moderate to severe peripartum acidosis, which has been associated with poor neurological development. (9-13)

Conclusions

Fetal growth restriction (FGR) is associated not only with increased perinatal mortality and morbidity but also with a long-term increased risk for complications such as poor neurological development, type II diabetes and hypertension. Obstetricians should identify fetuses at risk of developing fetal growth restriction, and develop a complet monitoring plan and carefully choose the time and the way of birth.

Main ideas

• Intrauterine growth restriction associated with prematurity under 32 weeks remains a major challenge for neonatologist and obstetrician

• Other causes of small gestational age (SGA) fetuses, such as chromosomal abnormalities and intrauterine infections, should be considered before making the diagnosis of IUGR.

• SGAnewborn is a different condition with a good prognosis and result.

• Fetal Doppler ultrasound is the most accurate and non-invasive method of evaluating placental function.

• Combined Doppler analysis performed on the umbilical artery, medium cerebral artery may show the degree of placental damage, the redistribution level and the degree of cardiac damage.

• The management of a prematur restricted fetus should include a balance between the risks of intrauterine chronic hypoxia with preterm birth and its associated risks.

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