INTRAUTERINE GROWTH RETARDATION

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SUMMARY

Intrauterine malnutrition continues to be an enormous public health problem . The significance of intrauterine growth retardation (IUGR) includes not only a three to ten fold increase in perinatal mortality, but also an increased morbidity in the form of birth asphyxia, meconium aspiration, persistent fetal circulation, hypothermia, hypoglycemia, hypocalcemia, polycythemia and long-term neurointellectual sequelae. Therefore our goal should be prevention of IUGR and its complications.

During early 20th century, physicians gradually became more aware of the difference between retarded growth and prematurity in small infants (1). It is important because these two problems lead to somewhat different ranges of complications in early days of life and long term sequeale (2, 3, 4).

Infants born with low birth-weights for their gestational age referred to by a variety of names (5) (small-for-dates) (SFD), fetal-malnourished, intrauterine growth-retarded (IUGR), small-for gestational age (SGA), etc.).

The most commonly used definition of IUGR includes infants who are below tenth percentile for their gestational age, according to intrauterine growth curves or more than 2 standard deviations below the mean, for gestational age (5-8).

Incidence: About 3-10% of all pregnancies results in IUGR and 20% of stillborn infants are growth retarded (9). The perinatal mortality rate is 4-8 times higher for growth retarded fetuses and serious short or long-term morbidity is noted in half of the affected surviving infants (10-12).

Fetal growth: Review of evolution of normal fetal growth will give a better perception of the need for classification of IUGR.

Winick (13) has described three phases of cellular growth in the fetus:

Phase of Cellular Hyperplasia: This phase includes an increase in cell number occuring during the first 16 weeks of embryonic and fetal life. Thereafter, the increase in cell number occurs at a slower rate with minimal increase after 32 weeks gestation. Fetal insult during this phase leads to symmetrical IUGR (type I), with the primary effect being, a reduced cell number.

Phase of Concomitant Hyperplasia and Hypertropy: This phase includes a period from 16 weeks to 32 weeks, when there is a progressive decrease in the rate of cell hyperplasia with a progressive increase in cell size. Fetal insult during this phase produces a mixed or intermediate type of IUGR, with features resembling type I, if insult occurs earlier, and type II, if insult occurs in the later stages of this phase.

Phase of Cellular Hypertrophy: This phase extends from 32 weeks to term, during which cell size rapidly increases. Insult during this phase usually occurs as a consequence of uteroplacental insufficiency, secondary to maternal medical disorders, and results in type II or asymmetrical IUGR.

Clinical Classification of IUGR

According to this classification there are two types of IUGR.

a) Type I- Symmetrical IUGR: These infants are usually proportionally small with a reduction of all external measurements, ie, weight, length, head circumference (5). The overwelming causes of type-I IUGR are intrinsic in nature, which include genetic causes and congenital anomalies (14).

Additionally, some extrinsic factors, ie, intrauterine infections, and environmental hazards including drugs, can produce type-I IUGR (15).

b) Asymmetrical IUGR or Type II: The onset of growth retardation in asymmetrical IUGR occurs in the late second trimester or early third trimester (16). Clinically the infant is small, with the head circumfe-

rence and length being relatively normal in size for gestational age. Weight/length ratio is reduced. In humans type II IUGR is predominantly a result of utero-placental insufficiency, secondary to extrinsic factors (17). This type of IUGR shows brain sparing phenomenon (14).

If the insult occurs in the second trimester there may not be significant brain sparing which then may be called intermediate type IUGR (5).

Clinical classification of IUGR has been summarized in Table I.

Complications

A- Hypoxia: IUGR infants frequently have birth asphyxia, because they tolerate the stress of labor poorly (18, 19). They are also subjected to chronic intrauterine hypoxia, which results in abnormal thickening of the smooth muscles of the small pulmonary arterioles. This reduces pulmonary blood flow and results in varying degrees of pulmonary artery hypertension. Because of this, IUGR infants are at risk of developing persistent fetal circulation (17).

Postterm IUGR infants are additionally at risk for meconium aspiration (17).

B- Hypothermia: Thermoregulation is compromised in IUGR infants because of diminished subcutaneus fat insulation (15).

C- Metabolic: Hypoglycemia is a common problem in IUGR babies due to reduced liver stores of glycogen, impaired gluconeogenesis secondary to the slow onset of action of hepatic enzymes. Symptomatic hypoglycemia is highly associated with brain damage, mental retardation and cerebral palsy (14). It is usually avoided by starting early feeding in asymptomatic babies and screening for asymptomatic hypoglycemia every 6-8 hours during the first 72 hours (20). Another metabolic disorder in babies with IUGR can be hypocalcemia which is almost always idiopathic (15).

D- Hematologic disorders: Hyperviscosity and polycythemia may be noted in babies with IUGR which result from increased erythropoietin levels secondary to fetal hypoxia asscociated with IUGR. Polycythemia may also contribute to hypoglycemia and finally leading to cerebral injury (21).

Diagnosis

Fetal Assessment (5, 16, 17, 22, 23):

1. Clinical Diagnosis: The patient's history will raise the index of suspicion regarding suboptimal growth. Manual estimations of weight, serial fundal height measurements, and maternal estimates of fetal activity are simple clinical measures (16).

2. Hormonal Evaluation: Hormonal assays were at one time popular for assessment of IUGR but are rarely used today. Maternal urinary estriol and human placental lactogen levels tend to be low in pregnancies with IUGR, though there is marked individual variation.

3. Ultrasonography: Currently, diagnostic ultrasound offers the greatest promise for diagnosis of IUGR (16).

a) Biparietal diameter (BPD): When serial measurements of BPD are less than optimal, 50-80% of infants will have subnormal birth weights.

b) Abdominal circumference: The liver is the first organ to suffer the effects of growth retardation. Reduced abdominal circumference is the earliest sign of asymmetric growth retardation and diminished glycogen storage.

c) Ratio of head circumference to abdominal circumference: The ratio normally changes as pregnancy progresses. In the second trimester the head circumference is greater than the abdominal circumference. At about 32-35 weeks of gestation, the ratio is 1:1, and after 36 weeks the abdominal measurements become larger. Persistence of a head: abdomen ratio greater than 1 late in gestation, is predictive of asymmetric IUGR.

d) Femur lengths: Femur length appears to correlate well with crown-heel length and provides, an early measurement of length. Serial measurements of femur length are as effective as head measurements for detecting type I symmetric IUGR. Absence of epiphyseal centers of the knee is also predictive of IUGR (24).

e) Placental morphology and amniotic fluid assessment: Placental aging with oligohydramnios suggests IUGR.

Neonatal Assessment

Before abnormal growth can be diagnosed in the postnatal period, one has to construct the normal growth curve for a given population (25, 26). Today Denver growth curves, developed by Lubchenco are widely used. Reduced birth weight for gestational age is the simplest method of diagnosis (27).

Table I : CLINICAL CLASSIFICATION OF IUGR

	TYPE I: SYMMETRICAL	TYPE II: ASYMMETRICAL
INCIDENCE	25%	75%
CAUSES	Intrinsic genetic anomalies "Extrinsic TORCH teratogens severe malnutrition (?), drugs, smoking, alcohol	"Extrinsic" utero placental insufficiency ie., maternal disorders
TIMING OF INSULT	28 weeks gestation	28 weeks gestation
CELL NUMBER	Decreased (hypoplastic)	Normal
CELL SIZE	Normal	Decreased (hypotrophic)
HEAD SIZE	Microcephalic	Usually normal
BRAIN SIZE	Decreased	Usually normal
LIVER-THYMUS SIZE	Decreased	Decreased
BRAIN/LIVER WEIGHT RATIO	Normal (3/1)	Increased (6/1)
PONDERAL INDEX (PI)	Normal	Decreased
CONGENITAL ANOMALIES	Frequent	Rare
ULTRASOUND		
BPD	Small	Early-normal Late-small
AC *	Small	Small
HC/AC ** RATIO	Normal	Early-increased Late-normal
POSTNATAL CATCH - UP GROWTH	Poor	Good

*** Abdominal circumference**
**** Head circumference / Abdominal circumference**

For the right diagnosis it is very useful to know the accurate gestational age. If the mother is not sure about her last menstrual period (LMP), gestational age can be dated retrospectively by using one of the well known scoring systems (28).

Since birth weight and gestational age ignores the body size and length of the neonate, some investigators have attempted to use the ponderal index (PI), (PI= birth weight (g) x 100 / crown to heel length in cm^3), to quantify the degree of thinness or obesity of the infant. Thus, a neonate that is symmetrically small, will have a normal PI as compared to one, that is asymmetically small when the PI would be low (5).

Prognosis and long term effects of IUGR

Fetuses with asymmetrical IUGR have a postnatal "catch up" growth spurt with adequate nutrition, whereas symmetrically growth retarded fetuses continue to remain in the lower percentiles and rarely exceed the 50^{th} percentile (5, 29).

The neurological outcome of SGA fetuses shows increased incidence of lower intelligence quotients, learning and behavioral disorders and neurological handicaps (3, 30, 31). The most crucial factor for predicting ultimate neurological outcome is head size in utero (BPD) or at birth (32). Fetuses with slow growth of their BPD or ultrasound in utero and neonates, with head circumference below tenth percentile at birth, have been associated with a high incidence of

subsequent neurological abnormalities (4, 32, 33).

The neurodevelopmental outcome depends also on the cause of IUGR. IUGR infants with major chromosomal disorders have a 100% incidence of handicap (10). Infants with congenital rubella or cytomegalovirus infection with microcephaly have also a poor outcome, with a handicap rate exceeding 50% (17, 20).

Prevention

Under the light of the knowledge about the adverse effects and long-term sequella of IUGR, it is needless to say that one's goal should be to prevent this outcome. Prevention requires recognition of adverse environmental influences and a high quality of prenatal care. Aspirin has already been mentioned as possibly preventing fetal growth retardation. There is also some evidence that it may improve fetal growth retardation once present. It has been shown that low dose-aspirin (150 mg/day) in the treatment of placental insufficiency during the last trimester, improved birth weight by 500 mg (34). Fetal monitoring and appropriate timing of delivery can prevent some of the complications of IUGR (5). Skilled resuscitation should be available at the time of the delivery, as birth asphyxia is common (20). Close monitoring of blood glucose calcium and central hematocrit levels are essential for the prevention of the complications of the complications of hypoglycemia, hypocalcemia and polycythemia in these babies.

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