Comparison of Somatomedin-C (SMC/IGF-I), human placental lactogen and Doppler velocimetry between appropriate and small-for-gestational-age pregnancies

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Summary

Thirty-two pregnant women with small-for-gestational-age (SGA) fetuses and 45 pregnant women with appropriate-for-gestional-age (AGA) fetuses (controls) were recruited after the 32nd week of gestation. Blood samples were collected for estimation of somatomedin-C (SMC/IGF-I) and hPL in the maternal serum and in the umbilical cord serum. The systolic/diastolic (S/D) ratio of the umbilical artery was also recorded. The results showed somatomedin-C and hPL levels in the maternal serum and in the umbilical cord to be significantly decreased and the Doppler S/D ratio to be significantly increased in the SGA group. In this group, using the multivariable regression analysis, we found significant correlations between maternal hPL, somatomedin-C, Doppler S/D ratio and birth weight.

Key words: Somatomedin-C (SMC/IGF-I) hPL; Doppler; SGA; Pregnancy.

Introduction

Fetal growth retardation usually manifests itself during the third trimester. It should be important to find a marker for the early detection of this condition so as to arrange for early surveillance and learn about the underlying mechanisms [1].

Recently, extensive evidence has accumulated showing that insulin and insulin growth factors (IGFs) are essential in regulating fetal growth and fetal weight gain [2]. Somatomedin-C (SMC/IGF-I) is produced from early on by almost all fetal organs and stimulates cell division and differentiation in an autocrine, paracrine or endocrine fashion [3].

Human placental lactogen (hPL) participates directly or indirectly in a number of metabolic processes. These putative actions include lipolysis, an increase in the levels of circulating free fatty acids and an anti-insulin action [4]. hPL has been identified to be composed of approximately 190 amino-acids in a single chain cross-linked by two sulfide bonds of cystine bridges [5]. hPL has a molecular weight of 22,308 daltons [5].

Umbilical artery Doppler velocimetry identifies abnormal blood flow in the placenta. It has been useful for the understanding of placentation and provides a foundation for our understanding of the pathophysiology of various growth disorders [6]. To our knowledge, there have been no studies correlating umbilical artery Doppler velocimetry with somatomedicin-C and hPL in pregnancy. Our aim was to evaluate umbilical artery Doppler velocimetry, somatomedin-C and hPL in the maternal and cord serum in appropriate (AGA) and small-for-gestational-age (SGA) pregnancies.

Materials and Methods

We studied two groups of pregnant women who were non-smokers, non-alcoholics and with no previous or present obstetrical or medical disorders from 33 to 41 weeks of gestation: the first group consisted of 45 women with uncomplicated AGA pregnancies and the second consisted of 32 pregnant women with SGA fetuses as documented by ultrasound and fundal height and confirmed with neonatal weight at delivery to be less than the 10th percentile for the gestational age [7]. Each woman signed an informed consent form which was approved by the Human Research Committee. Patients were recruited from Winthrop University Hospital.

We obtained 2 ml of venous blood from each woman while she was in the Department of Obstetrics or upon admission to the hospital for delivery. The duration of gestation was calculated from the last menstrual period and was correlated with ultrasound and uterine size. Two ml of cord blood were also obtained at delivery. The blood samples were centrifuged to separate the serum which was stored below –20°C until assayed.

Somatomedin-C (SMC/IGF-I) concentrations were determined by a radioimmune assay using acid ethanol extraction [8]. hPL concentration was determined quantitatively using a radioimmunoassay kit (DPC,CA).

Using continous-wave Doppler (Multigon 500A) we measured the umbilical artery systolic/diastolic (S/D) ratio in 40 AGA uncomplicated pregnancies and in 32 SGA pregnancies. The S/D ratio was considered abnormal when it was equal to or exceeded 3 after 30 weeks of gestation. Data analysis was performed using the t-test and Mann-Whitney U-test and correlation coefficient (SYSTAT 5.02 soft-wear).

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Table 1. — *Comparison of appropriate-for-gestational age (AGA) and small-for-gestational age (SGA) fetuses (Values are given as means±SE)*

	AGA		SGA		P
	N	mean±SE	N	means±SE	
Gestational age at sampling (weeks)	45	37±4	32	36±4	NS
Maternal hPL (ug/ml)	44	10±3	32	3.3±2**	<0.01
Cord hPL (ug/ml)	26	0.2±0.1	22	0.025±0.018**	0.01
Maternal Somatomedin-C (SMC/IGF-I) (U/ml)	45	1.7±0.5	31	1.044±0.317	<0.01
Cord Somatomedin-C (SMC/IGF-I) (U/ml)	25	0.623±0.19	22	0.433±0.15	<0.05
Doppler (S/D ratio)	40	2.5±0.35	32	3.7±0.66**	<0.01
Weight (g)	37	3400±500	32	2100±400**	<0.01

Results

The median gestational age at sampling was 37±4 weeks for AGA and 36±4 weeks in the SGA group. The mean maternal somatomedin-C was 1.7±0.5 U/ml in the AGA group compared to 1.044±0.317 U/ml in the SGA group ($p<0.01$). The mean cord somatomedin-C was 0.623±0.19 U/ml in the AGA group as compared to 0.433±0.15 U/ml in the SGA group ($p<0.05$). The mean maternal hPL was 10±3 ug/ml in ghe AGA group compared to 3.3±2 ug/ml in the SGA group ($p<0.01$). The mean cord hPL was 0.2±0.1 ug/ml in the AGA group as compared to 0.025±0.018 ug/ml in the SGA group ($p<0.01$). The mean S/D ratio of the umbilical artery in the AGA group was 2.5±0.35 as compared to 3.7±0.66 in the SGA group ($p<0.01$) (Table 1).

Maternal hPL shows a significant positive correlation with birth weight ($n=37$, $r=0.548$, $p<0.0001$) and with maternal somatomedin-C ($n=37$, $r=0.673$; $p<0.0001$) in the AGA group. Maternal hPL shows a negative correlation with the umbilical artery Doppler velocimetry S/D ratio ($n=40$, $r=0.472$, $p<0.002$). Cord hPL levels show no significant correlation with birth weight, while cord somatomedin-C shows significant positive correlation with birth weight in the AGA group ($n=25$, $r=0.39$, $p<0.05$).

Since all the patients in the SGA group had abnormal S/D rations (>3) by using the multivariable regression analysis of maternal hPL, maternal somatomedin-C, Doppler S/D ratio data and birth weight we found significant correlations with these variables ($n=25$, $r=0.548$, $p<0.045$). Maternal hPL shows a significant positive correlation between cord somatomedin-C and birth weight ($n=22$, $r=0.7$, $p<0.001$).

Discussion

This study shows clearly that there are statistically significant differences between maternal and cord serum hPL and somatomedin-C in AGA and SGA pregnancies.

In addition, in our material low somatomedin-C concentrations in the umbilical cord showed a significant positive correlation with birth weight. These results, which are in agreement with previous studies [9, 10, 11], also show the correlation between circulating concentrations of fetal somatomedin-C and birth weight.

Fetal circulating somatomedin-C is produced mainly by the fetal liver but also by other organs. Local production of somatomedin-C is considered to be important in the regulation of growth and in the differentiation of several tissues [12]. The main factors regulating IGF production in adults are growth hormone and nutrition. In the fetus nutrition appears to be the most important factor regulating somatomedin-C production [13].

Our data show that maternal and umbilical cord hPL levels were significantly decreased in the SGA group compared to the AGA group. This is in agreement with previous studies [14, 15]. hPL stimulates somatomedin-C production which may account for its growth-promoting activity. hPL is synthesized by the syncytiotrophoblast of the placenta; it is not secreted by the maternal or fetal pituitary, but ectopic tumor sources have been identified [5].

When we evaluated placental vascular function by umbilical artery Doppler velocimetry, maternal and umbilical cord hPL were found to be significantly decreased in women who had abnormal placental development as demonstrated by the S/D ratio. An increased S/D ratio

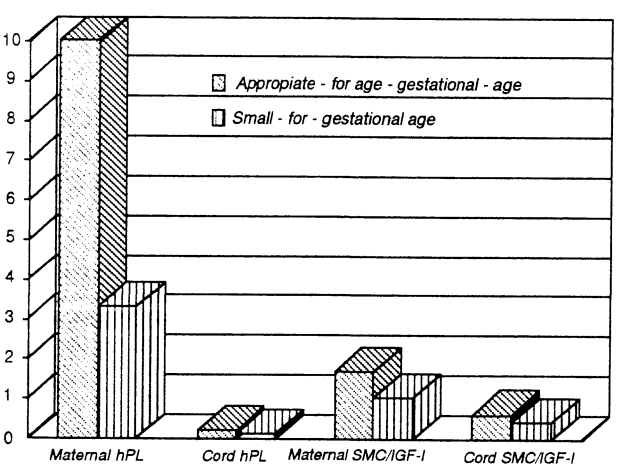

Figure 1. — Somatomedin-C (SMC/IGF-I) & hPL decreases in SGA pregnancies.

is associated with a decreased number of small muscular arteries in the villi [16]. These results suggest that hPL production during pregnancy obviously plays a part in placental growth.

In multiple gestation and in diabetic pregnancies in which placentas are larger, increased values of hPL have been observed [5]. The strong association of velocimetry with hPL and somatomedin-C indicates that growth factors play a part in the development of the vessels and the syncytiotrophoblast. The placenta has receptors for somatomedin-C and hPL. These and other growth hormones promote the angiogenesis of the placenta. The disorders of fetal growth which originate from the placenta develop early in pregnancy and more research needs to be done. Knowledge of the etiology of poor growth of the placenta could lead to treatment of the fetus early in pregnancy.

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