Placental growth factor: a putative screening test for gestational diabetes mellitus in first trimester

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Summary

Purpose of Investigation: To evaluate placental growth factor as a screening test for gestational diabetes mellitus in the first trimester. *Methods:* Sixty-seven pregnant women who were admitted to the outpatient clinic of Ege University Obstetrics and Gynecology Department consecutively for first trimester bioanalysis between May 2005 and February 2006 were included in the study. The cohort of patients underwent 50 g or 100 g oral glucose tolerance tests at the 24th week of pregnancy. Placental growth factor levels were analyzed by ELISA (human PGIF, ELIZA kit, Quantikine, R&D systems, USA) from the maternal blood collected at the time of first trimester screening. *Results:* The study group of 15 patients with gestational diabetes were compared with a control group of 52 pregnant women with normal oral glucose tolerance tests. The level of placental growth factor was mean 35.79 ± 16.79 pg/ml in the study group whereas it was mean 45,12 ± 28.07 pg/ml in the control group. There was no significant difference between either group for placental growth factor maternal serum levels. *Conclusion:* Maternal placental growth factor serum levels are not useful in predicting gestational diabetes mellitus.

Key words: Placental Growth Factor; Gestational Diabetes; First trimester.

Introduction

Gestational diabetes is defined as the glucose intolerance of variable severity with onset during pregnancy and characterized by defective insulin secretion or insulin resistance. The incidence ranges from 2.2% to 8.8% of all pregnancies and this is the most common medical complication of pregnancy [1, 2]. Several studies have been done to find an optimum screening test as the high concentrations of glucose, especially in the first trimester of pregnancy, may cause several complications such as miscarriages, congenital defects, macrosomia, hypoglisemia, prematurity, cardiomyopathy and respiratuar distress. Early diagnosis and optimazing maternal blood glucose levels will decrease the complication rates and fetomaternal morbidity. The 50 g oral glucose tolarance test (OGTT) is now widely accepted all over the world as a screening test between 24-28 weeks of pregnancy; however, a screening test which can be performed in the first trimester may be a better alternative.

Diabetic pregnancy causes abnormal placental growth and fetal development. Placental growth is regulated by several growth factors including placental growth factor (PLGF), vascular endothelial growth factor (VEGF) and fibroblast growth factor (FGF). PLGF is a member of the VEGF family and the main source of PLGF during pregnancy is the placental trophoblasts [3]. It is a key molecule in angiogenesis and contributes to the regulation of placental function.

The aim of this study was to investigate PLGF as a screening test for gestational diabetes mellitus in the first trimester.

Material and Methods

The study was condıcted in accordance wtih the guidelines and approval given by the Ethical Committee of the Ege University Hospital. Sixty-seven 11-14-week pregnant women admitted to the outpatient clinic of Ege University Obstetrics and Gynecology Department consecutively for first trimester bioanalysis between May 2005 and February 2006 were included in the study. All selected pregnant women demonstrated intermediate or high-risk factors for diabetes according to the American Diabetes Association [4]. Out of 67 pregnancies three were twin pregnancies, whereas 64 were singleton pregnancies. The study group (n = 15) with gestational diabetes were compared with a control group (n = 52) with normal oral glucose tolerance tests. OGTTs (50 or 100 g) were performed on all pregnant women at the 24th week of pregnancy. The first-hour glucose level above 140 mg/dl in the 50 g OGTT was accepted as abnormal; 100 g-3-hour OGTT was performed after an overnight fast. Gestational diabetes was diagnosed with two or more high glucose levels during fasting, first hour, second hour and third hour glucose levels [5]. Blood samples were collected from the antecubital veins into heparinized vacutainer tubes. After centrifugation at 1000 g for 15 min, serum samples were incubated at –80ºC and analyzed in the Biochemistry Department laboratory. PLGF was studied with the ELISA method (human PGIF, ELIZA kit, Quantikine, R&D systems, USA).

Statistical Analysis

Statistical analysis was performed using the SPSS v. 12.0 program. Spearman's rho test was used for correlation analysis and the Mann-Whitney U test was used to compare groups. The levels were expressed in mean ± standard deviation.

Results

Age of the pregnant women (n = 67) ranged from 22 to 44 years (31 ± 4 years) and mean parity was 0.5 ± 0.7. Maternal levels of PLGF did not correlate with age. The mean birth week and birth weight were 38 ± 1.93 weeks

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and 3.296 ± 561 g, respectively. There was also no correlation between birth weight and PIGF levels. The level of placental growth factor was mean 35.79 ± 16.79 pg/ml in the study group whereas it was mean 45.12 ± 28.07 pg/ml in the control group. There was no significant difference between either group for placental growth factor maternal serum levels (Table 1).

Table 1. — *Patient characteristics and PLGF levels (n = 67) (mean ± SD).*

	GDM group (n = 15)	Control group (n = 52)
Age*	33.30 ± 4.89	29.90 ± 3.81
Birth week†	37.47 ± 2.13	38.22 ± 1.85
Birth weight†	32.76 ± 500	33.02 ± 581
Parity*	0.87 ± 0.83	0.42 ± 0.60
PlGF levels†	35.79 ± 16.79	45.12 ± 28.07

*Statistically significant difference between both groups ($p > 0.05$).
†Statistically insignificant difference between both groups ($p > 0.05$).

Fifty pregnant women underwent cesarean (C) section (74.5%). The major indication for cesarean sections was previous C section (n = 8). Others included macrosomia, fetal distress, placenta previa, prolonged labor, and breech presentation. The most common complication of the newborns was prolonged jaundice (n = 5, 7.4%). Other complications were prematurity, hypoglycemia, cardiac defects and extremity abnormalities (n = 8, 12%). According to the correlation analysis, there was no relationship between the apgar scores of the newborns and maternal serum PLGF levels.

Mean weight gain of the pregnant women was 13.59 ± 5.09 kg and out of the 67, seven had excessive weight gain (≥ 20 kg). The weight gain of the pregnant women did not correlate with PLGF levels.

Discussion

The placenta has a very critical role for both fetal development and maintenance of pregnancy. Development of the placenta is regulated by several growth factors such as PLGF, VEGF, FGF and abnormal placentation may result in a wide range of pregnancy complications.

PLGF is a homodimeric glycoprotein that is involved in the VEGF family. During pregnancy, it is expressed in trophoblasts and contributes to proliferation, migration and endothelial cell activation [6, 7]. Studies with trisomy 21 fetuses showed higher maternal serum levels of PLGF [8, 9], whereas pregnancies complicated with preeclampsia and fetal growth restriction showed lower maternal serum levels as these fetuses have defective placental development and vascularization [10].

Although there are several studies about PLGF, there is limited data about the relationship between PLGF and diabetes. It is now known that pregnancies which are complicated with gestational or pregestational diabetes have higher placental weight and this is accomponied with a delay of placental maturation [11].

Loukovaara *et al*. [12] compared the umbilical cord PLGF levels of 62 normal pregnant women, 67 pregnant women with type 1 diabetes and 28 pregnant women with gestational diabetes treated with insulin. There was no statistically significant difference between three groups. Cord serum PLGF levels did not correlate with birthweight as it was the same in our study.

Ong *et al*. [13] evaluated maternal serum PLGF levels of 82 diabetic pregnancies and 400 normal controls. There were four groups in the study including pregnant women with type 1 diabetes, type 2 diabetes, gestational diabetes and healthy pregnant controls. PLGF levels were significantly higher in the type 2 and gestational diabetes group than the control group. On the other hand, there was no statistically significant difference between the type 1 diabetes group and the controls. This was attributed to insulin resistance which is the common pathogenetic mechanism of both type 2 diabetes and gestational diabetes.

Early diagnosis of gestational diabetes is very important as maternal and fetal complications may be decreased due to the early optimization of serum glucose concentration. In this study, we did not find any relationship between maternal serum PLGF levels and gestational diabetes; however more studies with large patient populations are needed for definitive results.

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