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Preliminary report: circulating levels of the adipokine vaspin in gestational diabetes mellitus and preeclampsia

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Abstract

The objective of the study was to investigate serum levels of the insulin-sensitizing adipokine vaspin in patients with gestational diabetes mellitus (GDM) and preeclampsia (PE) as compared with healthy controls of similar gestational age. Vaspin serum levels were quantified by enzyme-linked immunosorbent assay in control (n = 102), GDM (n = 40), and PE (n = 22) subjects. Median maternal vaspin concentrations were not significantly different in GDM, PE, and control subjects. Furthermore, vaspin did not significantly correlate to clinical and biochemical measures of renal function, glucose, and lipid metabolism, as well as inflammation. Circulating vaspin levels are not significantly different between GDM, PE, and control subjects and do not correlate with insulin sensitivity in pregnant subjects.

1. Introduction

Gestational diabetes mellitus (GDM) and preeclampsia (PE) are serious metabolic and cardiovascular complications in pregnancy that share risk factors with the metabolic syndrome including insulin resistance and obesity [1,2]. We have demonstrated that dysregulation of various adipocyte-secreted factors—so-called adipokines—occurs in GDM and PE and might play an important role in the pathogenesis of both disease states [3-6]. Recently, Hida and coworkers [7] characterized vaspin as an interesting novel adipokine with insulin-sensitizing effects. The authors demonstrated convincingly in the initial report that administration of vaspin to obese mice improved glucose tolerance and insulin sensitivity [7]. However, regulation of this adipokine has not been determined so far in GDM and PE. In the current study, we hypothesized that circulating levels of vaspin would (1) be decreased in GDM and PE patients and (2) positively correlate with insulin sensitivity in pregnancy.

2. Subjects and methods

Both the GDM [4] and PE [8] study populations have been described in detail recently. For the GDM study, 40 women with GDM and 80 pregnant controls matched for gestational age and fasting insulin (FI) were recruited. *Gestational diabetes mellitus* was defined as at least one elevated plasma glucose value during a 75-g 2-hour oral glucose tolerance test according to the criteria of the Austrian Diabetes Association with the following threshold glucose concentrations: fasting, at least 95 mg/dL; 1 hour, at least 180 mg/dL; and 2 hours, at least 155 mg/dL [9].

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For the PE study, 22 pregnant women with PE and 22 gestational age–matched controls were recruited from the Department of Obstetrics, University of Leipzig. *Preeclampsia* was defined as gestational blood pressure elevation greater than 140 mm Hg systolic or greater than 90 mm Hg diastolic accompanied by proteinuria in women who were normotensive before 20 weeks of gestation [10]. Patients with renal diseases or at least 2 criteria of generalized inflammation (body temperature higher than 38.5 °C or lower than 35 °C, heart rate higher than 100 beats a minute, respiratory rate higher than 20 breaths a minute, and probable or confirmed infection) were excluded from the study. The study was approved by the local Ethics Committee, and all patients gave written informed consent before taking part in the study. In all patients, blood was obtained after an overnight fast; and none of the women was in labor at the time of the blood sampling. Vaspin (Adipogen, Seoul, South Korea), adiponectin (Mediagnost, Reutlingen, Germany), and leptin (Mediagnost) were determined with enzyme-linked immunosorbent assays (ELISAs) according to the manufacturers' instructions. The sensitivity of the vaspin ELISA assay was 0.01 μg/L. Whereas the degree of precision of the ELISA system in terms of coefficient of variance (percentage) of intraassay was between 1.3 % and 3.8 %, that of interassays was between 3.3 % and 9.1 %. Spike recovery and linearity were in the range of 90% to 107 % and 100% to 109 %, respectively. All other parameters were measured in a certified laboratory by standard laboratory methods. Statistical analyses were performed with SPSS software version 11.5 (SPSS, Chicago, IL). Differences between controls on one hand and GDM and PE patients on the other hand were assessed by Mann-Whitney *U* test. Correlations were performed using Spearman rank correlation method. A *P* value of <.05 was considered as statistically significant in all analyses.

3. Results

Clinical characteristics of the subgroups studied are shown in Table 1. In the GDM study, median (interquartile range) circulating vaspin was not significantly different between GDM (2.9 [2.8] μg/L) and control (3.6 [3.6] μg/L) subjects (Table 1). Similarly, serum concentrations of the adipokine were not significantly different between PE patients (1.8 [3.9] μg/L) as compared with healthy pregnant controls of similar gestational age (3.3 [3.0] μg/L) (Table 1). Circulating vaspin did not significantly correlate with markers of renal function (creatinine), adiposity (body mass index [BMI], leptin), insulin resistance (fasting glucose, FI, homeostasis model assessment of insulin resistance [HOMA-IR], adiponectin), lipid metabolism (cholesterol, triglycerides), and inflammation (C-reactive protein) in univariate analyses in both study groups (data not shown). In contrast, the insulin-sensitizing adipokine adiponectin was significantly and negatively correlated with FI in both GDM ($r = -0.274$, $P = .003$) and PE ($r = -0.343$, $P = .023$) patients.

Table 1
Baseline characteristics of the study population

	GDM study		PE study	
	Control-GDM	GDM	Control-PE	PE
n	80	40	22	22
Vaspin (μg/L)	3.6 (3.6)	2.9 (2.8)	3.3 (3.0)	1.8 (3.9)
Age (y)	28 (5)	33 (10)*	29 (10)	33 (6)
BMI (kg/m^2)	22.3 (7.0)	24.9 (4.9)	20.9 (3.1)	22.4 (5.1)
SBP (mm Hg)	125 (16)	121 (23)	100 (18)	160 (35)†
DBP (mm Hg)	75 (13)	71 (17)	65 (13)	102 (24)†
Gestational age at blood sampling (d)	198 (39)	205 (30)	212 (25)	206 (48)
Creatinine (μmol/L)	49 (12)	46 (11)	54 (14)	66 (19)†
FG (mmol/L)	4.2 (0.4)	4.5 (0.9)*	3.6 (0.7)	3.6 (0.7)
Glucose 1 h (mmol/L)	7.5 (1.6)	10.3 (1.6)*	ND	ND
Glucose 2 h (mmol/L)	6.2 (1.8)	9.0 (2.3)*	ND	ND
FI (pmol/L)	56.5 (39.3)	60.3 (37.1)	56.8 (34.3)	42.7 (51.8)
HOMA-IR	1.4 (1.0)	1.6 (1.3)	1.2 (0.8)	1.2 (2.0)
Cholesterol (mmol/L)	6.3 (1.8)	6.6 (2.2)	6.8 (1.8)	6.5 (1.9)
TG (mmol/L)	2.1 (1.4)	2.2 (1.3)	2.4 (1.5)	3.4 (1.7)†
Leptin (μg/L)	23.1 (11.7)	24.9 (13.9)	24.5 (21.5)	53.5 (51.9)†
Adiponectin (mg/L)	7.0 (3.9)	7.3 (5.6)	6.7 (3.5)	11.9 (7.5)†
CRP (mg/L)	4.3 (4.5)	4.2 (4.9)	1.7 (2.4)	8.2 (33.6)†

Values for median (interquartile range) are shown. Parameters were analyzed by Mann-Whitney *U* test. CRP indicates C-reactive protein; DBP, diastolic blood pressure; FG, fasting glucose; ND, not determined; SBP, systolic blood pressure; TG, triglycerides.

* $P < .05$ as compared with control-GDM.

† $P < .05$ as compared with control-PE.

4. Discussion

In the current study, vaspin serum concentrations are determined for the first time in GDM and PE patients. We show that circulating levels of this adipokine are not significantly dysregulated in both patient populations in contrast to other adipokines including leptin [11-13] and adiponectin [5,14,15]. Furthermore, we are not able to demonstrate a significant association between vaspin serum concentrations and insulin sensitivity in both study populations. However, causality between circulating vaspin on one hand and GDM, PE, and insulin sensitivity on the other hand cannot be excluded because our study has a cross-sectional design and only a single measurement of serum vaspin is performed. Furthermore, it is possible that the lack of significant differences in circulating vaspin concentrations between GDM, PE, and control subjects may result from the selection criteria used in the study (eg, normal BMI, low circulating insulin, and low HOMA-IR values in

all groups analyzed). Clearly, more work is needed to elucidate whether vaspin has insulin-sensitizing effects also in humans.

Taken together, we show for the first time that vaspin serum levels are not significantly different in GDM, PE, and control subjects and are not associated with markers of insulin resistance. Further work is needed to better elucidate the pathophysiologic significance of vaspin in pregnancy-related complications and in human glucose metabolism.

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