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Brief communication (Original)

Vaspin in newly and previously diagnosed Chinese type 2 diabetic females: a case-control study

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Background: Visceral adipose tissue-derived serine protease inhibitor (vaspin) is a novel adipocytokine. Several studies have indicated that vaspin may exert an important role in the development of metabolic disorders.
Objective: Evaluate serum vaspin and its relation to clinical parameters in newly and previously diagnosed Chinese type 2 diabetes mellitus (T2DM) females as a case-control study.
Materials and methods: One hundred twenty female participants (newly and previously diagnosed T2DM patients) were recruited from an affiliated hospital of Harbin Medical University. Sixty healthy female volunteers from various communities were included as controls. Anthropometric parameters, serum fasting blood glucose, fasting insulin, lipid profile, HbA1c, and vaspin were measured in each participant.
Results: Serum vaspin levels were significantly lower in previously diagnosed T2DM patients (0.51±0.29 ng/mL) than in newly diagnosed T2DM patients (0.62±0.28 ng/mL) and healthy controls (0.69±0.31 ng/mL). However, there was no difference in serum vaspin between newly diagnosed T2DM patients and healthy controls. In multiple linear regression analysis, serum vaspin was significantly and positively associated with HbA1c in both newly and previously diagnosed T2DM patients, negatively associated with homeostasis model assessment of insulin resistance in previously diagnosed patients, and positively correlated with age and body mass index in healthy controls.
Conclusion: Serum vaspin was significantly lower in previously diagnosed T2DM patients than in newly diagnosed T2DM patients and healthy controls. Serum vaspin might be a predictor of poor glucose control and insulin resistance in T2DM.

Keywords: Adipocytokine, type 2 diabetes, vaspin

Obesity is a major risk factor for the development of type 2 diabetes mellitus (T2DM) [1, 2]. Many adipocytokines may regulate insulin sensitivity, inflammation, and metabolism [3]. Recently, visceral adipose tissue-derived serpin (vaspin) was identified as a new adipocytokine [4].

According to Hida et al. [4], in visceral adipose tissue of Otsuka Long-Evans Tokushima fatty (OLETF) rats, its mRNA expression peaked at the age when obesity and insulin plasma concentrations reached maximum levels, and decreased with worsening of diabetes and body weight loss. In addition, vaspin mRNA expression could be normalized by insulin and pioglitazone treatment. More importantly, administration of vaspin could improve obese mice glucose tolerance, insulin sensitivity, and reverse expression of related genes for insulin resistance.

Vaspin has been considered as a novel link between human obesity and its related metabolic disorders, especially diabetes [5]. Klothin et al. [6] reported that the expression of vaspin was high in T2DM. However, in three different studies [7-9], the vaspin levels were not different, lower, and higher in T2DM patients.

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No report has been focused on the comparison of serum vaspin between newly and previously diagnosed T2DM patients. In this study, we evaluated vaspin levels of newly and previously diagnosed Chinese T2DM female patients and assessed the relationships between serum vaspin and clinical parameters in the respective groups.

Materials and methods

Sixty previously and 60 newly diagnosed T2DM female patients were recruited from an Outpatient Diabetes Clinics of a hospital affiliated with Harbin Medical University. Sixty healthy female volunteers from various communities were included as healthy controls. T2DM was diagnosed according to the criteria of the American Diabetes Association [10]. Exclusion criteria were cardiovascular disease, liver disease, neoplasm, currently smoking, and inflammatory disease. Each participant was provided with, and signed an informed consent. Study procedures were approved by the Ethics Committee of Harbin Medical University.

Anthropometric and laboratory determinations

Weight and height were measured to the nearest 0.1 kg and 0.1 cm, respectively. Blood pressure was measured with a standard mercury sphygmomanometer. Body mass index (BMI) was calculated as weight (kg) divided by the square of height (meters). Antecubital venous blood was collected after 12 hour overnight fasting (without any form of medication). Serum and plasma were immediately separated by centrifugation. Serum vaspin was measured using a commercial enzyme-linked immunosorbent assay kit (AdipoGen, Seoul, Korea). Serum glucose was measured using the glucose oxidase method. Serum triglycerides (TG), total cholesterol (TC), and high-density lipoprotein cholesterol (HDL-c) in the serum were assayed with standard enzymatic spectrophotometric techniques using commercial kits (Biosino Biotechnology Ltd, Beijing, China) with an auto-analyzer (AUTOLAB PM 4000, AMS, Rome, Italy). Low-density lipoprotein cholesterol (LDL-c) was calculated using the Friedwald equation [11]. Serum insulin was measured using radioimmunoassay using a commercial kit (Diagnostic Systems Laboratories, Webster, TX, USA). Insulin resistance was estimated by the homeostasis model assessment of insulin resistance (HOMA-IR): (fasting insulin fasting blood glucose)/ 22.5.

Statistical analysis

Statistical analysis was carried out with Statistical Package of Social Sciences (SPSS 13.0: Release 13.01S, China). Values were presented as means SD. Continuous variables between groups were assessed by Friedman's ANOVA (with Dunn's test for post hoc analysis). Multiple linear regression was performed in each group, including age, BMI, TG, TC, HDL-c, HbA1c, and HOMA-IR as independent variables and serum vaspin as the dependent variable. All p-values were two-tailed and a p-value of <0.05 was considered as statistically significant.

Results

Clinical parameters and vaspin levels of all participants are shown in **Table 1**. There was no significant difference between age, BMI, waist, systolic blood pressure, diastolic blood pressure, and LDL-c among the three groups. Newly and previously diagnosed Chinese T2DM patients had significantly higher mean levels of fasting blood glucose (FBG), fasting insulin, TG, TC, HbA1c, and HOMA-IR than those of the healthy controls. HDL-c level was significantly lower in T2DM patients. Previously diagnosed T2DM patients had higher TG, HOMA-IR, FBG, and fasting insulin than those of newly diagnosed T2DM patients and healthy controls.

Previously diagnosed T2DM patients had significantly lower levels of vaspin than those of newly diagnosed T2DM patients and healthy controls. However, serum vaspin levels did not differ between newly diagnosed T2DM patients and healthy controls.

Relationships between serum vaspin and other parameters

Relationships between serum vaspin and other parameters in diabetic and control groups are presented in **Table 2.** In healthy controls, multiple linear regression identified age and BMI as significant independent predictors of serum vaspin. In both newly and previously diagnosed T2DM groups, HbA1c was positively associated with serum vaspin. HOMA-IR was inversely associated with serum vaspin levels in previously diagnosed patients.

Table 1. Clinical characteristics of the study participants

Parameters	Healthy Controls	Newly diagnosed	Previously diagnosed	*P*-values
Number	60	60	60	
Vaspin (ng/mL)	0.69±0.31	0.62±0.28	0.51±0.29[a, b]	0.005
Age (year)	50.42±6.73	50.83±9.00	51.67±8.45	0.691
BMI (kg/m^2)	25.92±3.99	25.46±3.29	25.52±4.73	0.818
Waist (cm)	82.86±12.21	81.57±9.10	80.96±11.19	0.624
SBP (mmHg)	120.13±11.58	122.35±15.80	123.77±15.07	0.374
DBP (mmHg)	79.10±7.39	80.02±7.90	78.23±8.29	0.464
FBG (mmol/L)	5.21±0.60	8.38±1.64[a]	8.91±1.41[a,b]	<0.001
Fasting insulin (mU/L)	10.18±2.86	14.23±3.81[a]	16.97±5.44[a,b]	<0.001
HOMA-IR	2.37±0.75	5.18±1.35[a]	6.67±2.04[a,b]	<0.001
HbA1c (%)	5.05±0.95	7.63±1.17[a]	8.00±1.01[a]	<0.001
TC (mmol/L)	4.37±0.84	4.83±0.83[a]	4.75±1.06[a]	0.016
TG (mmol/L)	1.64±0.58	2.97±1.09[a]	3.55±1.28[a,b]	<0.001
HDL-c (mmol/L)	1.51±0.55	1.30±0.46[a]	1.27±0.34[a]	0.006
LDL-c (mmol/L)	3.41±0.58	3.54±1.07	3.71±0.79	0.135

Data are mean SD, BMI=body mass index, SBP=systolic blood pressure, DBP=diastolic blood pressure, FBG=fasting blood glucose, HOMA-IR=homeostasis model assessment, HDL-c= high-density lipoprotein cholesterol, LDL-c=low-density lipoprotein cholesterol, TC=total cholesterol, TG=triglycerides, *P* values refer to overall differences across groups as derived from ANOVA, [a]p <0.05, compared with healthy controls, [b]p <0.05, compared with newly diagnosed T2DM patients

Table 2. Multiple linear regression among controls, newly and previously diagnosed T2DM female patients with vaspin as the dependent variable

	Vaspin levels (β-coefficient)		
	Healthy controls	Newly diagnosed T2DM patients	Previously diagnosed T2DM patients
Age	0.297*	0.089	0.198
BMI	0.414*	-0.013	-0.03
HOMA-IR	-0.055	-0.077	-0.352*
HbA1c	0.183	0.442*	0.373*
TC	0.054	0.081	0.076
TG	0.204	0.154	0.069
HDL-c	0.101	-0.058	0.001

BMI=body mass index, HOMA-IR=homeostasis model assessment, TC=total cholesterol, TG=triglycerides, HDL-c=high-density lipoprotein cholesterol, *p <0.05

Discussion

This study compared the vaspin levels in newly and previously diagnosed Chinese T2DM patients for the first time. It was not consistent whether T2DM patients had lower serum vaspin levels [7-9]. Youn et al. [7] did not find any difference between vaspin levels of T2DM patients and normal glucose tolerance (NGT) participants. Another report showed higher serum vaspin in T2DM patients [9]. However, both the above studies did not mention whether T2DM patients were newly or previously diagnosed. Lower serum vaspin has also been reported in T2DM patients with microvascular complications [8]. The small sample size and different age ranged between T2DM patients, and non-diabetic participants might affect their results. To clarify this inconsistency, we conducted this study with a relatively large population and balanced age range between groups, and found

previously diagnosed T2DM patients had significantly lower serum vaspin than those of newly diagnosed patients and healthy controls.

Multiple linear regression analysis of the data agreed with some previous observations [8, 12]. Our results have shown that vaspin was positively related to BMI and age in the healthy controls. However, this was not found in the patient groups. Diabetic status might account for this difference. It is important to note that diabetes is a complicated metabolic disorder, and the diabetic status might simultaneously disturb the secretion of vaspin in some independent ways, which may eliminate the effects of body weight and age on vaspin levels. Because it has been reported that glucose could increase the expression of vaspin in primary cultured human adipose tissue [13], this supports the positive correlation between vaspin and HbA1c in newly diagnosed and previously diagnosed T2DM patients in our study. On the other hand, serum vaspin was negatively correlated with HOMA-IR in previously diagnosed T2DM patients. This suggests that insulin resistance may be related to serum vaspin. It has been reported that serum vaspin was correlated negatively with HOMA-IR in diabetic patients [8] and obese children [14]. Thus, our results, together with previous observations, indicate that patients with a longer diabetic history are prone to having lower levels of vaspin. Poor glucose control and insulin resistance might influence the levels of vaspin independently with the worsening of diabetes.

As a compensatory molecule to metabolic disorder, the administration of recombinant human vaspin can improve insulin sensitivity and glucose tolerance, and reverse the expression of genes in diet induced obese mice. It has also been shown that vaspin remarkably decreases with the worsening of diabetes in diabetic rats [4]. Pioglitazone and insulin treatment normalized vaspin gene expression in the animal study [4], and metformin decreased the vaspin levels in polycystic ovary syndrome and T2DM female patients [8, 13]. Therefore, the role and significance of vaspin in diabetes or other metabolic disorders has become of great interest.

In conclusion, serum vaspin was shown to be significantly lower in previously diagnosed Chinese T2DM patients than those of newly diagnosed T2DM groups and healthy controls for the first time. Vaspin might be a predictor of poor glucose control and insulin resistance of T2DM.

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