Vaspin in type 2 diabetes in relation to atherosclerosis

Nehal H El-Said[a], Noha A Sedik[a], Nagwa A Mohamed[b]

[a]Department of Internal Medicine, Al Kasr Al Ainy Hospital, Faculty of Medicine, Cairo University [b]Department of Clinical and Chemical Pathology, National Research Center, Cairo, Egypt

Correspondence to Noha Adly Sadik, MD, 7 Al Mahrossa Street, Ahmed Orabi, Al Mohandeseen, app 3, Giza 694, Egypt
Tel: +20 114 232 7325;
e-mail: noha_adly@yahoo.com

Received 06 May 2014
Accepted 17 August 2014

The Egyptian Society of Internal Medicine
2014, 26:130–136

Background
Vaspin is a novel adipocytokine with insulin-sensitizing effects. However, it is not known whether a correlation exists between human vaspin serum levels and markers of insulin sensitivity and glucose or lipid metabolism.

Aim of the work
To determine whether there is an association between serum vaspin levels (a novel adipocytokine with insulin-sensitizing effects), type 2 diabetes mellitus (T2D) and atherosclerosis.

Patients and methods
The study included 40 patients with T2D divided into 20 without hypertension (group 1), 20 with hypertension (group 2) and 15 age-matched and sex-matched healthy control participants (group 3). The serum vaspin level was determined by enzyme-linked immunosorbent assay. Its level was compared between both diabetic patients and controls, and between diabetic patients without hypertension and those with hypertension. All participants were subjected to an imaging procedure in the form of carotid Doppler to measure the intima — media thickness as an early marker of atherosclerosis.

Results
The serum vaspin level was significantly higher in diabetic patients compared with control participants. There was significant increase in the left carotid intima–media thickness in diabetic patients with hypertension and without hypertension compared with control participants. There was a significant positive correlation between the serum vaspin level and the BMI in diabetic patients with hypertension, a significant negative correlation between the serum vaspin level and the duration of diabetes and a significant negative correlation between the serum vaspin level and HDL in diabetic patients without hypertension.

Conclusion
There was a significantly high level of serum vaspin in T2D patients. Serum vaspin was shown to be significantly lower in T2D patients with a longer duration of illness. An increased carotid intima–media thickness in diabetic patients was not related to the vaspin level, denoting an underlying combining factor for atherosclerosis in diabetic patients other than vaspin.

Keywords:
atherosclerosis, type 2 diabetes, vaspin

Egypt J Intern Med 26:130–136

1110-7782

Introduction

Diabetes mellitus is a major risk factor for atherosclerosis [1]. Hypertension is a determinant of microangiopathy and atherothrombosis in diabetes [2]. Understanding the concept of inflammation in diabetes-accelerated atherosclerosis can be used practically to predict future cardiovascular risk by evaluating inflammatory biomarkers and to design clinical trials using inflammation as a therapeutic target [3]. Among the top contributors of inflammatory stimuli are adipokines, which are secreted from the adipose tissue [4].

Vaspin, a member of the serine protease inhibitor family, is an adipocytokine that has been isolated from the visceral adipose tissue of Otsuka Long-Evans Tokushima Fatty rats [5]. The Otsuka Long-Evans Tokushima Fatty rat is an animal model of type 2 diabetes (T2D), which is characterized by abdominal obesity, insulin resistance, hypertension and dyslipidemia [6].

To our knowledge, the comparison of the serum vaspin level between T2D patients with hypertension and without hypertension has not been investigated previously. The present study, therefore, investigated the serum vaspin level between T2D patients with hypertension and without hypertension and assessed the relation between the serum vaspin level and the carotid intima atherosclerotic media thickness, BMI and other risk factors.

Patients and methods

The study group included 40 Egyptian patients with T2D (mean age 47.95 ± 5.95 years) who were selected from the Internal medicine outpatient clinic of Al Kasr Al Ainy Cairo University Hospital between January

and May 2013. The cases were further subdivided into 20 cases without hypertension (group 1) and 20 cases with hypertension (group 2). The diagnosis and the clinical classification of diabetes mellitus were based on the guidelines of the American Diabetes Association [7]. Fifteen healthy age-matched and sex-matched participants were included as the control group (group 3) (mean age 46.87 ± 5.18 years); all were from a similar ethnic background. All patients were informed about the procedure, and a written consent was obtained. Approval of the ethical committee was also obtained. All patients were subjected to full clinical history and thorough examination, including BMI, laboratory investigations in the form of a complete blood picture, 2-h post-prandial blood glucose, serum creatinine, serum cholesterol, serum triglyceride, LDL-cholesterol, HDL-cholesterol and serum vaspin levels.

Five milliliters of fasting (12–14 h) venous blood samples were taken from each participant and divided into parts: the first part containing 2 ml was added to a tube containing EDTA for the determination of the complete blood picture on a Coulter Counter T890 (Coulter Counter, Harpenden, UK). The rest of the blood (3 ml) was left to clot, the serum was separated by centrifugation for 15 min at 1000×*g* and the fasting blood glucose was determined immediately on a Hitachi autoanalyzer (Hitachi 736; Roche, Japan) by the glucose oxidase method. The rest of the serum was stored at -20°C for the determination of the following: serum cholesterol, serum triglyceride, LDL-cholesterol, HDL-cholesterol and serum vaspin levels.

Determination of serum cholesterol and serum triglyceride was carried out on Hitachi 736 (Roche Diagnostics GmbH, Mannheim, Germany) by colorimetric techniques. For the determination of HDL-cholesterol, phosphotungestic acid and magnesium ions were used for precipitating all lipoproteins except the HDL fraction that was present in the supernatant and measured by an autoanalyzer. LDL-cholesterol was measured by the Friedwald formula [8].

Two milliliters of venous blood samples were taken from all patients 2 h after meals for the determination of postprandial blood glucose on a Hitachi 736 autoanalyzer (Roche, Japan).

The determination of serum vaspin was carried out using the sandwich enzyme immunoassay kit supplied from Adipogen Inc. (Incheon, Korea) [9].

All participants were subjected to an imaging procedure in the form of carotid Doppler to measure the intima–media thickness (IMT) of the distal common carotid, and the peak systolic velocity, the end-diastolic velocity and the resistivity index of the internal carotid artery by carotid ultrasound. B (brightness)-mode grey-scale, color, spectral Doppler techniques were used to investigate the carotid arteries according to the standardized protocol. The same operator interpreted all studies in a blinded manner, and the same ultrasound unit HD 5000 (USA using linar prove 7.5 MHZz) was used for scanning all participants.

Statistical analysis

Data were statistically described in terms of mean ± SD, median and range, or frequencies (number of cases) and percentages when appropriate. Comparison of numerical variables between the study groups was performed using the Student *t*-test for independent samples to compare two groups that were normally distributed. Comparison of numerical variables between more than two groups was performed using the one-way analysis of variance test with post-hoc multiple two-group comparisons. For comparing categorical data, the χ^2-test was performed. The exact test was used instead when the expected frequency was less than 5; *P* value less than 0.05 was considered statistically significant. All statistical calculations were performed using the computer program SPSS version 15 (Microsoft corporation, Chicago, IL, USA) for Microsoft Windows.

Results

Thirty out of the 40 diabetic patients were female (75%) and 10 patients were male (25%); the age group of our patients ranged from 40 to 55 years (47.95 ± 5.9) (Table 1). BMI in our patients ranged from 23 to 29, with a mean of 25.47 ± 1.95. The disease duration in our patients ranged from 1 to15 years; 13 patients were on insulin (32.5%), 16 patients were on sulphonylurea (40%) and 18 patients were on metformin (45%). Hypertension was present in 20 patients (50%). Dyslipidemia was present in 57.5% of our patients. Plaque was present in five patients (9.1%).

In Tables 2 and 3, Fig 1 and 2, there was a statistically significant increase in serum vaspin levels in T2D patients without hypertension and T2D patients with hypertension (1.03 ± 0.22 and 1.01 ± 0.26 ng/ml, respectively) compared with control participants (0.53 ± 0.09 ng/ml; *P* = 0.000).

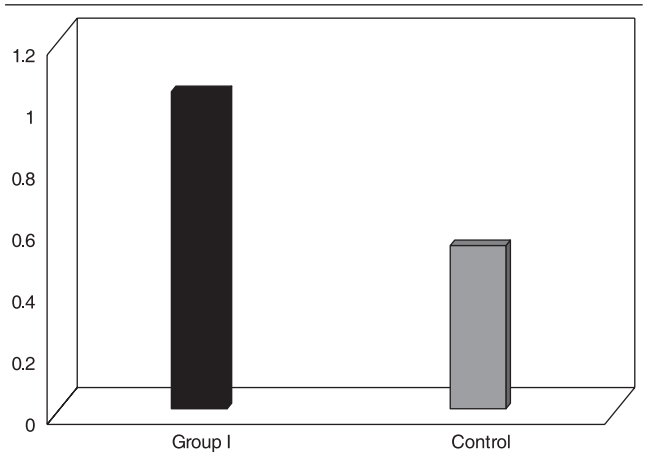
In Table 4 and Fig 3, there was no statistically significant difference in serum vaspin levels between

Table 1 Demographic data and laboratory parameters of the studied groups

ANOVA test	All cases	Group 1	Group 2	Control	*P* value
Age (years)	47.95 ± 5.95	49.55 ± 6.56	46.35 ± 4.92	46.87 ± 5.18	0.174
SBP (mmHg)	132.25 ± 13.63	142.50 ± 9.25	122.00 ± 8.65	121.67 ± 7.48	0.000*
DBP (mmHg)	78.50 ± 7.36	82.25 ± 5.95	74.75 ± 6.78	77.33 ± 9.04	0.006*
Fasting glucose (mg/dl)	175.35 ± 20.07	172.10 ± 20.76	178.6 ± 19.32	85.60 ± 10.76	0.000*
2-h PPBG (mg/dl)	221.18 ± 47.58	224.35 ± 48.80	218.00 ± 47.37	125.73 ± 8.26	0.000*
BMI (kg/m^2)	29.88 ± 3.24	30.30 ± 3.54	29.45 ± 2.93	25.47 ± 1.96	0.000*
RCM (cm)	0.08 ± 0.02	0.08 ± 0.01	0.08 ± 0.03	0.07 ± 0.01	0.81
RPSV (cm/s)	74.19 ± 5.94	70.79 ± 14.86	77.59 ± 16.64	53.25 ± 2.76	0.000
REDV (cm/s)	28.32 ± 6.27	26.65 ± 5.72	29.99 ± 6.49	23.53 ± 1.37	0.003*
RRI	0.62 ± 0.07	0.63 ± 0.07	0.61 ± 0.07	0.55 ± 0.03	0.000*
LCM (cm)	0.09 ± 0.02	0.09 ± 0.01	0.08 ± 0.02	0.06 ± 0.01	0.000*
LPSV (cm/s)	79.17 ± 3.25	77.32 ± 15.17	81.03 ± 11.09	63.39 ± 1.30	0.000*
LEDV (cm/s)	31.12 ± 8.55	28.71 ± 7.80	33.53 ± 8.78	26.98 ± 1.08	0.021*
LRI	0.64 ± 0.12	0.65 ± 0.15	0.62 ± 0.07	0.54 ± 0.03	0.007*
Cholesterol (mg/dl)	195.53 ± 57.42	198.15 ± 56.06	192.90 ± 60.09	98.07 ± 12.78	0.000*
Triglycerides (mg/dl)	124.35 ± 48.65	130.15 ± 61.12	118.55 ± 32.42	65.60 ± 9.63	0.000*
LDLC (mg/dl)	135.52 ± 30.42	140.25 ± 35.60	130.80 ± 24.18	47.13 ± 10.47	0.000*
HDLC (mg/dl)	49.00 ± 21.83	51.05 ± 27.67	46.95 ± 14.26	52.87 ± 9.52	0.648
Vaspin (ng/ml)	1.02 ± 0.20	1.03 ± 0.22	1.01 ± 0.20	0.53 ± 0.09	0.000*

Values are expressed as mean ± SD; ANOVA, analysis of variance; DBP, diastolic blood pressure; HDLC, high-density lipoprotein cholesterol; LCM, left carotid intima–media thickness; LDLC, low-density lipoprotein cholesterol; LEDV, left end-diastolic velocity; LPSV, left peak systolic velocity; LRI, left resistivity index; PPBG, postprandial blood glucose; RCM, right carotid intima–media thickness; REDV, right end-diastolic velocity; RPSV, right peak systolic velocity; RRI, right resistivity index; SBP, systolic blood pressure; *P < 0.05 is significant.

Figure 1



The serum vaspin level in diabetic patients without hypertension compared with the control group (mean ± SD).

Table 2 Comparison of serum vaspin levels between diabetic patients without hypertension and controls

Student *t*-test	Group 1	Control	*P* value
Vaspin (ng/ml)	1.03 ± 0.22	0.53 ± 0.09	0.000*

Values are expressed as means ± SD; *P < 0.05 is significant.

Table 3 Comparison of serum vaspin levels between diabetic patients with hypertension and controls

Student *t*-test	Group 2	Control	*P* value
Vaspin (ng/ml)	1.01 ± 0.20	0.53 ± 0.09	0.000*

Values are expressed as means ± SD; *P < 0.05 is significant.

Table 4 Comparison of serum vaspin levels between diabetic patients with hypertension and diabetic patients without hypertension

Student *t*-test	Group 1	Group 2	*P* value
Vaspin (ng/ml)	1.03 ± 0.22	1.01 ± 0.20	1.000

Values are expressed as means ± SD.

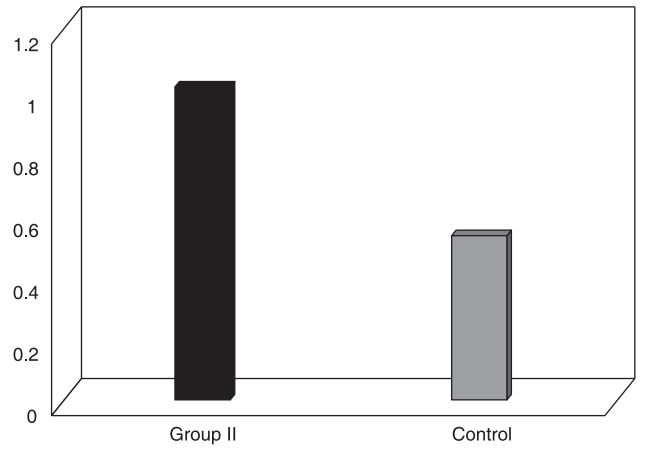
diabetic patients with hypertension and diabetic patients without hypertension.

In Table 5, there was a statistically significant negative correlation between serum vaspin levels and diabetes duration in all cases (r = -0.330, P = 0.037). There was a statistically significant positive correlation between serum vaspin levels and HDL in control participants (r = 0.575, P = 0.025) and a negative correlation between serum vaspin levels and HDL in T2D patients without hypertension (r = –0.459, P = 0.042), but there was no statistically significant correlation between serum vaspin levels and cholesterol, LDL or triglycerides in all the studied groups. There was no statistically significant correlation between serum vaspin levels and parameters of carotid intimal thickness.

Discussion

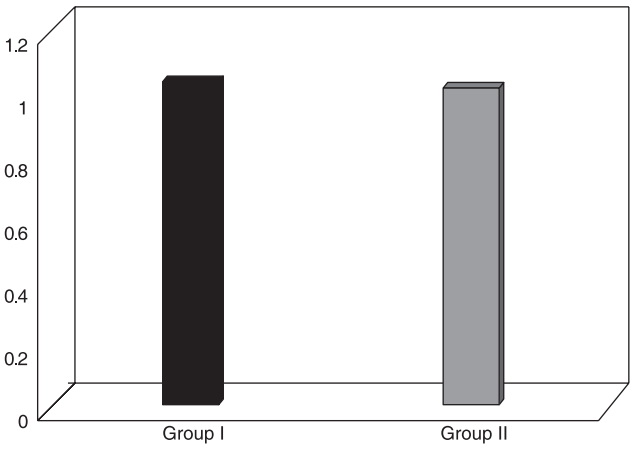
Vaspin is a new adipocytokine-linking adipose tissue related to systemic insulin resistance and thereby contributing to the pathogenesis of diabetes [10]. However, the relationship between vaspin and diabetes is still controversial; the present study aimed to investigate the role of vaspin in the pathogenesis of T2D and its metabolic parameters.

Figure 2



The serum vaspin level in diabetic patients with hypertension compared with the control group.

Figure 3



The serum vaspin level between diabetic patients without and with hypertension (mean ± SD).

Table 5 Correlation of serum vaspin with different demographic, laboratory and doppler findings in the studied groups

Group parameters	Serum vaspin in all cases		Serum vaspin in group 1		Serum vaspin in group 2		Serum vaspin in control	
	r	*P*	*r*	*P*	*r*	*P*	*r*	*P*
Age (years)	−0.179	0.269	−0.226	0.338	−0.154	0.517	−0.236	0.396
SBP (mmHg)	−0.055	0.736	−0.119	0.618	−0.134	0.572	0.066	0.815
DBP (mmHg)	−0.176	0.277	−0.306	0.190	−0.153	0.521	0.025	0.930
Fasting glucose (mg/dl)	0.092	0.574	−0.047	0.844	0.272	0.245	0.183	0.513
2-h PPBG (mg/dl)	0.190	0.241	0.268	0.252	0.096	0.687	0.196	0.484
BMI (kg/m^2)	0.259	0.106	0.091	0.703	0.480	0.032*	0.078	0.784
RCM (cm)	−0.15	0.926	−0.186	0.433	0.098	0.682	−0.421	0.118
RPSV (cm/s)	−0.39	0.809	0.223	0.345	−0.286	0.221	−0.169	0.546
REDV (cm/s)	−0.120	0.461	−0.057	0.813	−0.174	0.464	−0.227	0.416
RRI	−0.073	0.653	0.145	0.543	−0.311	0.182	0.021	0.940
LCM (cm)	−0.286	0.073	−0.255	0.277	−0.336	0.147	0.342	0.212
LEDV (cm/s)	0.124	0.446	0.266	0.258	0.018	0.941	0.143	0.611
LRI	0.115	0.480	0.230	0.329	−0.173	0.465	0.256	0.357
Cholesterol (mg/dl)	0.170	0.296	0.427	0.061	−0.431	0.109	−0.431	0.109
Triglycerides (mg/dl)	0.077	0.637	0.114	0.633	0.061	0.109	0.061	0.830
LDLC (mg/dl)	0.181	0.263	0.431	0.058	0.194	0.490	0.194	0.490
HDLC (mg/dl)	−0.297	0.063	−0.459	0.042*	0.575	0.025*	0.575	0.025*
Disease duration	−0.330	0.037*	−0.609	0.004*	0.142	0.550	—	—

DBP, diastolic blood pressure; HDLC, high-density lipoprotein cholesterol; LCM, left carotid intima–media thickness; LDLC, low-density lipoprotein cholesterol; LEDV, left end-diastolic velocity; LRI, left resistivity index; PPBG, postprandial blood glucose; RCM, right carotid intima–media thickness; REDV, right end-diastolic velocity; RPSV, right peak systolic velocity; RRI, right resistivity index; SBP, systolic blood pressure; *$P < 0.05$ is significant.

In our study, there was a statistically significant increase in serum vaspin levels in T2D patients without hypertension and T2D patients with hypertension (1.03 ± 0.22 and 1.01 ± 0.26 ng/ml, respectively) compared with control participants (mean 0.53 ± 0.09 ng/ml; $P = 0.000$), but there was no statistically significant difference in serum vaspin levels between diabetic patients with hypertension and diabetic patients without hypertension. This result was in agreement with other studies [10–12] that revealed significantly elevated levels of vaspin in T2D patients compared with control participants.

Youn *et al.* [13] did not detect a difference in circulating vaspin levels between individuals with normal glucose tolerance (NGT) and patients with T2D of different durations. Also, other studies [14,15] found no difference in serum vaspin levels between diabetic patients and NGT individuals.

As an adipocytokine, vaspin was supposed to be associated with obesity. However, the relationships between the vaspin level and body fat indexes remain controversial [14,16].

In our study, there was a statistically significant positive correlation between serum vaspin levels and BMI only

in diabetic patients with hypertension (r = 0.480, P = 0.032). Youn *et al.* [13] reported that vaspin was positively correlated with BMI in NGT individuals, whereas in diabetic patients, this correlation was not confirmed. However, after a 4-week intensive exercise training, reduced BMI was an independent predictor of increased vaspin concentration [13].

Feng *et al.* [17] showed that vaspin was positively related to BMI in healthy controls, but not in the patient groups. He explained this difference to exist because diabetes is a complicated metabolic disorder and it might simultaneously disturb the secretion of vaspin in some independent ways, which may eliminate the effects of body weight on vaspin levels, but Youn *et al.* [13] explained this to be a result of the dysregulation of vaspin concentrations in T2D patients and according to the diet and metformin therapy of T2D, which might contribute to the lack of association between an increased circulating vaspin and obesity.

In our study, there was no statistically significant difference between women and men with regard to serum vaspin levels both in the control participants (0.56 ± 0.08 vs. 0.50 ± 0.09 ng/ml, P = 0.190) and in all diabetic patients (1.01 ± 0.21 vs. 1.03 ± 0.19 ng/ml, P = 0.80). Our results were in agreement with the study by Ye *et al.* [10] and Domaa *et al.* [12], who did not find any statistically significant difference in the serum vaspin levels between women and men in NGT individuals and T2D patients.

Previous studies reported sexual dimorphism in the serum vaspin concentration, with higher levels in normal glucose-tolerant women compared with men [13,14], but these sex differences were not observed in T2D patients, and they suggested that metabolic alterations in T2D including chronic hyperglycemia and decreased insulin sensitivity modulate the vaspin serum concentration [13].

In our study, we did not find any statistically significant correlation between serum vaspin levels and age in the studied groups. This result was in disagreement with both Feng *et al.* [17] and Ye *et al.* [10], who found a positive correlation between serum vaspin levels and age in healthy controls, but not with T2D patients, and Seeger *et al.* [14], who found a positive correlation between serum vaspin levels and age in individuals with a normal glomerular filtration rate.

In our study, there was a statistically significant positive correlation between serum vaspin levels and HDL in the control participants (r = 0.575, P = 0.025) and a negative correlation between serum vaspin levels and HDL in T2D patients without hypertension (r = -0.459, P = 0.042), but there was no statistically significant correlation between serum vaspin levels and cholesterol, LDL or triglycerides in all the studied groups.

Our result was in agreement with the study by Domaa *et al.* [12], who found a statistically significant negative correlation between serum vaspin levels and HDL in T2D patients, but a statistically significant positive correlation between serum vaspin levels and cholesterol, LDL and triglycerides in T2D patients. Also, our results were in agreement with the study by Feng *et al.* [17], who did not find any statistically significant correlation between serum vaspin levels and cholesterol, LDL and triglycerides in T2D Chinese patients; he also did not find a significant correlation between serum vaspin levels and HDL.

We found a statistically significant negative correlation between serum vaspin levels and diabetes duration in all cases (r = -0.330, P = 0.037). This was in agreement with the study by Feng *et al.* [17], who found that patients with a longer diabetes duration had significantly lower serum vaspin levels than those with a shorter duration of diabetes, and he explained this by the fact that poor glucose control and insulin resistance might affect the levels of vaspin independently, with worsening of diabetes.

Carotid-wall IMT is a surrogate measure of atherosclerosis [18] associated with cardiovascular risk factors [19].

The study by Li *et al.* [20] showed that serum vaspin levels were statistically significantly lower in T2D patients with plaque than in T2D patients with no plaque. They postulated that the increased vaspin production in human adipose tissue in the early stage of T2D may be a compensatory mechanism associated with obesity, severe insulin resistance and T2D, and that vaspin could serve as a novel marker and a protective factor for macrovascular lesions. As the compensatory capacities of vaspin secretion gradually decrease with a prolonged duration of diabetes or cardiovascular disease and aggravation of vascular sclerosis, the levels of vaspin slowly decrease, as reported elsewhere [21,22]. Poor control of several risk factors for atherosclerosis might shorten the compensatory stage of vaspin upregulation, and decreased production of vaspin may contribute to accelerated progression of atherosclerosis [20].

In our study, there were no statistically significant differences in the vaspin levels in T2D patients with plaque (1.02 ± 0.23 ng/ml, P = 0.877), but there was a statistically significant difference in the left carotid IMT in T2D patients without hypertension

(0.09 ± 0.01 cm, P = 0.000) and T2D patients with hypertension (0.08 ± 0.02 cm, P = 0.002) compared with control participants. These results may be due to the small number of patients proved to have plaque (five patients), and all our patients had no clinical manifestation of atherosclerosis.

Conclusion

The results of the present study demonstrated significantly high levels of serum vaspin in T2D patients with and without hypertension compared with control participants, but there was no statistically significant difference in the serum vaspin levels between diabetic patients with hypertension and diabetic patients without hypertension. Serum vaspin was shown to be significantly lower in T2D patients with a longer duration than in those with a shorter duration of diabetes. Hence, vaspin might be a used as a predictor of poor glycemic control and insulin resistance of T2D patients. Increased carotid IMT in diabetic patients was not related to the vaspin level, denoting an underlying combining factor for atherosclerosis in diabetic patients other than vaspin. We recommend that further studies using a large patient sample may prove that vaspin may be involved in the development of the metabolic syndrome, and may confirm the associations that were observed previously in several other studies. We cannot suggest that the association of vaspin with T2D and metabolic parameters is population specific. Further studies are necessary to elucidate the mechanisms mediating these changes in vaspin regulation in patients with T2D. Vaspin could serve as a novel marker and a protective factor for macrovascular lesions. A possible therapeutic implication for vaspin in T2D patients should be investigated.

Acknowledgements

Conflicts of interest

There is no conflicts of interest.

References

1 Shaw JE, Sicree RA, Zimmet PZ. Global estimates of the prevalence of diabetes for 2010 and 2030. Diabetes Res Clin Pract 2010; 87:4–14.

2 Stas SN, El Atat FA, Sowers JR. Pathogenesis of hypertension in diabetes. Rev Endocr Metab Disord 2004; 5:221–225.

3 Maiti R, Agrawal NK. Atherosclerosis in diabetes mellitus: role of inflammation. Indian J Med Sci 2007; 61:292–306.

4 Ernst MC, Sinal CJ. Chemerin: at the crossroads of inflammation and obesity. Trends Endocrinol Metab 2010; 21:660–667.

5 Lago F, Dieguez C, Gómez-Reino J, Gualillo O. The emerging role of adipokines as mediators of inflammation and immune responses. Cytokine Growth Factor Rev 2007; 18:313–325.

6 Kawano K, Hirashima T, Mori S, Saitoh Y, Kurosumi M, Natori T. Spontaneous long-term hyperglycemic rat with diabetic complications. Otsuka Long-Evans Tokushima Fatty (OLETF) strain. Diabetes 1992; 41:1422–1428.

7 American Diabetes Association. Report of the Expert Committee on the diagnosis and classification of diabetes mellitus. Diabetes care 2003; 26:5–20.

8 Friedwald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low density lipoprotein cholesterol in plasma without use of the preparative ultracentrifuge. Clin Chem 1972; 18:499–502.

9 Inoue J, Wada J, Teshigawara S, Hida K, Nakatsuka A, Takatori Y, *et al.* The serum vaspin levels are reduced in Japanese chronic hemodialysis patients. BMC Nephrol 2012; 313:163.

10 Ye Y, Hou XH, Pan XP, Lu JX, Jia WP. Serum vaspin level in relation to postprandial plasma glucose concentration in subjects with diabetes. Chin Med J (Engl) 2009; 122:2530–2533.

11 El-Mesallamy HO, Kassem DH, El-Demerdash E, Amin AI. Vaspin and visfatin/Nampt are interesting interrelated adipokines playing a role in the pathogenesis of type 2 diabetes mellitus. Metabolism 2011; 60:63–70.

12 Domaa AM, El-Bagori NN, El- Sayd MM. The clinical significance of vaspin and chemerin in diabetic obese Libyan patients. Curr Sci Int 2012; 2:1–5.

13 Youn BS, Kloting N, Kratzsch J, Lee N, Park JW, Song ES, *et al.* Serum vaspin concentrations in human obesity and type 2 diabetes. Diabetes 2008; 57:372–377.

14 Seeger J, Ziegelmeier M, Bachmann A, Lossner U, Kratzsch J, Bluher M, *et al.* Serum levels of the adipokine vaspin in relation to metabolic and renal parameters. J Clin Endocrinol Metab 2008; 93:247–251.

15 Gulcelik NE, Karakaya J, Gedik A, Usman A, Gurlek A. Serum vaspin levels in type 2 diabetic women in relation to microvascular complications. Eur J Endocrinol 2009; 160:65–70.

16 Klöting N, Berndt J, Kralisch S, Kovacs P, Fasshauer M, Schon MR,*et al.* Vaspin gene expression in human adipose tissue: association with obesity and type 2 diabetes. Biochem Biophys Res Commun 2006; 339:430–436.

17 Feng RN, Wang C, Sun CH, Guo FG, Zhao C, Li Y. Vaspin in newly and previously diagnosed Chinese type 2 diabetic females: a case–control study. Asian Biomed 2011; 5:525–529.

18 Hodis HN, Mack WJ, LaBree L, Selzer RH, Liu CR, Liu CH, *et al.* Reduction in carotid arterial wall thickness using lovastatin and dietary therapy: a randomized controlled clinical trial. Ann Intern Med 1996; 124:548–556.

19 O'Leary DH, Polak JF, Kronmal RA, Savage PJ, Borhani NO, Kittner SJ, *et al.* Thickening of the carotid wall: a marker for atherosclerosis in the elderly? Stroke 1996; 27:224–231.

20 Li Z, Ma C, Li L, Pan X, Chen L. Vaspin serum concentration in patients with type 2 diabetes and carotid plaque. J Int Med Res 2012; 40:1670–1676.

21 Kadoglou NP, Gkontopoulos A, Kapelouzou A, Fotiadis G, Theofilogiannakos EK, Kottas G, *et al.* Serum levels of vaspin and visfatin in patients with coronary artery disease — Kozani study. Clin Chim Acta 2011; 412:48–52.

22 Kobat MA, Celik A, Balin M, Altas Y, Baydas A, Bulut M, *et al.* The investigation of serum vaspin level in atherosclerotic coronary artery disease. J Clin Med Res 2012; 4:110–113.