Original Article

Relationship between Visfatin and some clinical and biochemical parametres in peritoneal dialysis patients

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Abstract

Objective: To characterise the relationship between visfatin levels and various clinical and biochemical parameters in peritoneal dialysis patients.

Methods: The case-control study was conducted at the Medical Faculty Hospital, Yuzuncu Yil University, Van, Turkey, between May 2007 and December 2008, and involving 41 patients on peritoneal dialysis, 20 haemodialysis patients and 20 healthy controls. Fasting visfatin level was measured with enzyme-linked immunosorpent assay (ELISA) method, and patients on peritoneal dialysis were separated into two groups according to the visfatin levels - high and low. The groups were compared in terms of some clinical (height, weight, body mass index, waist circumference, hip circumference, waist/hip ratio, heart rate, systolic and diastolic blood pressure and the kt/V and CrCl (creatanine clearance) parameters which are indicative of the dialysis adequacy) and biochemical parameters (glucose, triglycerides, cholesterol, low density lipoprotein, high density lipoprotein, aspartate aminotransferase, alanine transminase, blood urea nitrogen, creatinine, total protein, albumin, globulin, sodium, potassium, magnesium, calcium, phosphorus, ferritin, venous blood gas, parathyroid hormone and insulin). SPSS 15 was used for statistcal analysis.

Results: No statistically significant difference in the visfatin levels was found between the patients and controls (7.71 ± 4.04, 7.36 ± 3.71, 7.70 ± 1.61, respectively, $p = 0.63$). The triglyceride level of the high-visfatin group was significantly higher than that of the low-visfatin group (243.8 ± 133.2, 150.8 ± 65.8, respectively, $p<0.05$). However, there was no correlation between visfatin and triglyceride levels. No difference in the other clinical and biochemical parametres was observed between the two groups of peritoneal dialysis patients.

Conclusions: No significant difference in the serum visfatin levels of peritoneal dialysis patients compared to haemodialysis patients or healthy individuals was noticed. Further studies are needed to confirm the effect of visfatin on triglyceride levels, and, if confirmed, the mechanism of this relation.

Keywords: Visfatin, Peritoneal dialysis, Haemodialysis. (JPMA 62: 1179; 2012)

Introduction

Visfatin is a recently identified adipo-cytokine, and is also known as PBEF (Pre-B cell colony-enhancing factor). PBEF is a growth factor for early-stage B cells. Visfatin is mainly produced by the visceral adipose tissue and is found in liver, muscle, bone marrow, lung, heart, placenta, kidney tissue and peripheral lymphocytes.[1] Even though it was initially suggested that visfatin activates the insulin receptor through competitive inhibition and that it has insulin-mimetic effects, the patho-phsyiological role of visfatin is not well understood.[2,3] Subsequent in-vivo and in-vitro studies have shown that visfatin is associated with insulin resistance, type 2 diabetes mellitus, endothelial dysfunction and increased inflammation.[4,5]

In dialysis patients, dependent on the reduced renal clearance, an increase in adipo-cytokines, including visfatin, adiponectin, leptin, and tumour necrosis factor (TNF)-alpha has been observed.[6,7] However, there are a limited number of studies on the visfatin levels of peritoneal dialysis patients and its related factors.

Patients with renal failure are known to have insulin resistance. After the initiation of peritoneal dialysis, weight-gain is often observed. The weight-gain,

increase in fat content, and the glucose load due to peritoneal solutions further aggravate the existent insulin resistance.[8] In recent years, several studies have shown that obesity increases inflammation in peritoneal dialysis patients and decreases lifespan. In peritoneal dialysis (PD) patients, obesity may increase the risk of developing cardiovascular disease by causing metabolic changes.[9]

In this study, we tried to analyse the relationship of the visfatin adipo-cytokine with various biochemical and clinical parametres especially in PD patients. We hoped to find a relation between visfatin and metabolism, including metabolic syndrome parametres and obesity.

Patients and Methods

The study was conducted at the Yuzuncu Yil University, Medical Faculty Hospital, Van, Turkey, between May 2007 and December 2008. Non-diabetic patients undergoing continuous ambulatory peritoneal dialysis for at least one year at the centre, with standard lactate containing dialysis solution, were included in the study. Patients with a history of peritonitis episode within the preceding three months and those with an active inflammation were excluded from the study, leaving 41 PD patients for analysis. Twenty healthy volunteers without any acute (within 3 months) or chronic disease history served as the control group. Additionally, 20 non-diabetic haemodialysis (HD) patients (thrice weekly) for at least one year and who did not have an active inflammation were included in the study. Informed consent for the study was obtained from the patients and the controls, and the Research Ethics Committee approved the study.

After at least 12-hour fasting, venous blood samples were drawn to measure the complete blood count, C-reactive protein (CRP), various biochemical components (glucose, triglycerides, cholesterol, low density lipoprotein (LDL), high density lipoprotein (HDL), aspartate aminotransferase (AST), alanine transminase (ALT), blood urea nitrogen (BUN), creatinine, total protein, albumin, globulin, sodium, potassium, magnesium, calcium, phosphorus and ferritin), blood gas and hormones (parathyroid hormones, insulin), as well as the visfatin levels from PD patients. Blood was drawn from the control subjects and HD patients only for the measurement of visfatin. The blood for visfatin was directly collected in ethylenediaminetetraacetic acid (EDTA) containing vacutainer haemogram tube, and was immediately centrifuged. The supernatant serum was stored frozen in at -80°C until assay. The visfatin levels were measured using a commercial enzyme immunoassay kit (visfatin C- terminal (human) EIA , Phoenix Pharmaceuticals, Belmont, CA, USA)[10,11] according to the manufacturer's instruction. The detection range was 0.1-1000 ng/ml. Additionally, the following parametres were measured for all PD patients: height, weight, body mass index (BMI), waist circumference, hip circumference, waist/hip ratio, heart rate, systolic and diastolic blood pressure, mean arterial pressure, and the kt/V and creatinine clearance (CrCl) parametres which are indicative of the dialysis adequacy. The insulin resistance (IR) index was calculated using homeostatic model assessment formula: HOMA-IR= (glucose x insulin 22.5). For the healthy control group and HD patients, height, weight, BMI, systolic and diastolic blood pressure and mean arterial pressure values were recorded. PD patients were divided into two groups according to their visfatin levels. These two PD groups were compared in terms of age, gender, and biochemical and clinical parametres. Furthermore, the visfatin levels of the PD patients were compared with those of the HD and control groups.

The statistical analysis of the data was performed using SSPS 15.0. The Kolmogorov-Smirnov test was initially applied to check normal distribution. Mann-Whitney U, chi square and Spearmans correlation analysis were used for the comparison of different groups. The visfatin levels of the three groups were compared by analysis of variance (ANOVA) test. The data and the results were expressed as mean ± standard deviation and a p value less than 0.05 was considered significant.

Results

The mean visfatin levels and general information for

Table-1: General information of the subjects.

	PD patients(n=41)	HD patients(n=20)	Control subjects(n=20)	p
Visfatin(ng/mL)	7.71 ±4.04	7.36±3.71	7.70± 1.61	NS
Gender (M/F)		25/16	11/9	11/9
NS				
Age (years)	43.6±13.2	42.2±19.2	36.3±10.3	0,03*
BMI (kg/m²)	23.9±6.2	24.5±6.4	24.7±3.6	NS
Dialysis duration (month)	58.9±33.7	47.9±23.8		NS

*Between PD and healthy controls.
PD: Peritoneal dialysis. HD: Haemodialysis. BMI: Body mass index.

Table-2: Comparison of the visfatin-high and visfatin-low PD patients regarding their biochemical and clinical parametres.

	Visfatin-high group (n=20)	Visfatin-low group (n=21)	p-value
Visfatin(ng/mL)	9,9±4,4	5,4±1,7	<0.05
Age (year)	45.1±10.4	42.2±15.6	0.49
Duration of dialysis (months)	60.3±34.4	57.7±34.0	0.81
BMI (kg/m2)	23.8± 4.3	24.1± 7.7	0.87
Waist circumference (cm)	88.7±11.9	87.7±14.9	0.83
Hip circumference (cm)	99.4±8.6	97.7±15.9	0.71
Waist /Hip ratio	0.89 ± 0.08	0.90± 0.08	0.84
Systolic BP (mmHg)	132±29	117±22	0.08
Diastolic BP (mmHg)	87±20	79±15	0.19
Haemoglobin (g/dl)	11.3±2.3	11.6±2.0	0.61
Leucocyte count (106/L)	6.9±2.1	6.7±1.4	0.63
CRP (mg/L)	7.0±5.2	5.6±4.8	0.36
LDL-cholesterol (mg/dL)	116.0±34.0	150.8±65.8	0.25
HDL-cholesterol (mg/dL)	43.8±26.4	40.3±14.3	0.60
Triglycerides (mg/dL)	243.8±133.2	150.8±65.9	<0.05
Total cholesterol (mg/dL)	194.7±54.6	175.3±36.7	0.19
Fasting blood glucose (mg/dL)	98.1±24.5	102.5±36.7	0.65
BUN (mg/dL)	58.7±13.5	48.2±12.7	0.20
Creatinine (mg/dL)	9.8±1.9	10.0±2.6	0.76
ALT (U/L)	16.2±8.6	22.9±17.3	0.20
Total protein (mg/dL)	6.8±0.7	7.0±0.6	0.30
Albumin (mg/dL)	3.6±0.5	3.5±0.5	0.62
Globulin (mg/dL)	3.1±0.5	3.5±0.6	0.06
Sodium (mmol/L)	138.3±4.1	138.5±2.6	0.80
Potasium (mmol/L)	4.2±0.7	4.0±0.6	0.36
Calcium (mg/dL)	9.1±0.9	8.9±1.2	0.58
Phosphate (mg/dL)	4.3±0.9	4.0±1.2	0.40
Ferritin (ng/dL)	778±332	707±341	0.51
PTH (pg/mL)	542.5±502.8	572.4±554.3	0.86
Bicarbonate (mmol/L)	23.1±3.8	23.6±3.0	0.64
HOMA-IR	3,81±3,59	3,93±3,74	0.84

the PD and HD patients and healthy individuals were record which showed no statistically significant difference between the visfatin levels of the three groups (Table-1).

The PD patients were then divided into two groups based on their visfatin levels. There was no significant difference in age, gender and dialysis duration between the visfatin-high and visfatin-low groups (Table-2). The comparison of the two groups regarding their biochemical and clinical parametres did not yield any significant difference, except for the triglyceride levels ($p<0.05$). The triglyceride level of the visfatin-high group was 243.8±133.2 mg/dl, whereas that of the visfatin-low group was 150.8±65.8 mg/dl.

Even though the difference in triglyceride levels between visfatin-high and visfatin-low groups was statistically significant, there was no correlation between triglyceride and visfatin levels across all PD patients ($p=0.09$, $r=2.63$). The correlation of visfatin levels with other biochemical and clinical parametres were also noted (Table-3).

Table-3: Correlation analysis of visfatin and biochemical and clinical parametres.

	r (correlation coefficient)	p-value
Duration of dialysis	0.14	0.38
BMI	-0.20	0.21
Waist circumference	0.28	0.10
Hip circumference	0.27	0.12
Waist /hip ratio	0.11	0.53
Systolic BP	0.01	0.95
Diastolic BP	0.09	0.57
Haemoglobin	0.24	0.13
Leucocyte count	-0.09	0.59
CRP	-0.08	0.61
LDL-cholesterol	0.07	0.65
HDL-cholesterol	0.06	0.71
Triglycerides	-0.26	0.10
Total kolesterol	-0.01	0.96
Fasting blood glucose	0.20	0.21
BUN	-0.23	0.14
Creatinine	0.02	0.89
ALT	0.28	0.08
Total protein	0.22	0.18
Albumin	-0.14	0.39
Sodium	-0.11	0.52
Potasium	-0.23	0.15
Calcium	-0.07	0.67
Phosphate	-0.28	0.08
Ferritin	-0.06	0.70
PTH	-0.04	0.80
Bicarbonate	0.07	0.67
HOMA-IR	0,13	0.43

Discussion

Our study of PD patients showed no difference in visfatin levels when compared with HD patients or the healthy controls. We did not find any difference in the biochemical and clinical parametres between PD patients with high visfatin levels versus PD patients with low visfatin levels except triglycerides.

To the best of our knowledge, there has been only one previous study on the levels and effects of visfatin in PD patients.[12] The study with 30 PD and 31 HD patients, reported visfatin levels significantly higher in PD patients compared to HD patients or healthy subjects. This increase in visfatin levels was attributed to PD solution dependent increase of glucose load in PD patients and to the fact that the BMI of the PD patients was higher than that of the HD patients.[12] That study also showed a positive relationship between BMI and visfatin. However, in the present study, no significant correlation was found between the visfatin levels of the PD patients and their BMI, waist circumference, hip circumference, and waist/hip ratio. This may be due to the absence of a difference in BMI of the PD and HD patients in our study.

Chronic renal failure (CRF) patients have an

elevated atherogenic lipid profile, with increased triglyceride and lipoprotein levels and decreased HDL level. There has been no prior report in the literature studying the relationship between the lipid profile and the visfatin level in dialysis patients. On the other hand, there has been conflicting findings for the normal population. One study found that visfatin was positively correlated with HDL-cholesterol and apo A1, and negatively correlated with LDL-cholesterol.[13] However, another study observed no relationship between visfatin and HDL-cholesterol or other lipoproteins.[14] Yet another study found a positive correlation between visfatin levels and the HDL-cholesterol and LDL-cholesterol in women.[15] A study with obese individuals did not find any relationship between visfatin and LDL-cholesterol, total cholesterol, or triglyceride levels.[16] Another study involving 40 normal subjects and 35 hyperlipidaemic subjects with insulin resistance, reported that visfatin was positively correlated with HDL-cholesterol and negatively correlated with triglycerides.[17] In the present study, we did not observe any correlation between visfatin level and HDL-cholesterol, LDL-cholesterol, or total cholesterol in PD patients. We only found the triglyceride level to be significantly higher in visfatin-high group of PD patients compared to the visfatin-low group. Since this finding was not confirmed with the correlation analysis, a more comprehensive study is needed in order to answer whether such a relationship exists.

There are a limited number of studies with HD patients investigating the visfatin levels and its effects. As available in literature,[12] our study also showed that the visfatin level does not differ between HD patients and healthy individuals. In contrast, others found higher visfatin levels in HD patients.[6,7] In one study, 57 of the 149 patients were diabetic and the control group consisted mostly of males.[6] None of our patient was diabetic, the gender was balanced, and had lower age for both patients and the controls. On the other hand number of controls and patients were higher in one study[7] than was the case with out study, but the demographic variables in terms of age, gender and BMI and other demographic factors were similar. We could not explain the difference between these studies clearly. Thus we think further studies are needed to clarify this issue with different demographic variables.

There are hitherto no studies on PD patients investigating the relationship between visfatin levels and the metabolic syndrome criteria or the anthropometric measurements. There are conflicting findings in the literature for the normal population regarding the correlation of visfatin with the metabolic syndrome criteria or the anthropometric measurements and whether there is more visfatin release from visceral fat tissue than from the subcutan fat tissue.[13,15,18,19] In a study with 500 subjects from the normal population investigating the relationship between visfatin levels and the metabolic syndrome criteria and anthropometric measurements, visfatin level was found to be negatively correlated with BMI, but no correlation was observed with anthropometric parameters, including waist circumference, hip circumference, waist/hip ratio.[15] In our study, no correlation was observed between visfatin level and anthropometric parameters, including BMI, waist circumference, hip circumference and waist/hip ratio in PD patients.

In a study with morbidly obese individuals, visfatin levels were significantly decreased parallel to the improvement in insulin sensitivity and the weightloss following gastric banding.[20] That study supported the relationship between visfatin and metabolic syndrome. On the other hand, in that study, no significant relationship was found between visfatin and the basal insulin resistance or any measure of obesity. Some of the other studies have also been insufficient in showing the independent relationship between visfatin and insulin resistance.[5,21] One study with 189 stage-3 and 4, and 149 stage-5 chronic renal failure patients, found that stage-5 CRF patients had significantly higher visfatin levels compared to stages 3-4 patients and to healthy control group.[6] However, there was no correlation between visfatin levels and the truncal fat mass or the insulin resistance markers.[6] These findings were consistent with the in-vivo studies showing significant secretion from tissue macrophages, from bone marrow, muscle, liver tissues, and from foetal membranes.[1,22] We found no correlation between visfatin levels and the measures of insulin resistance in PD patients.

We also did not find any correlation between the visfatin levels and the systolic and diastolic blood pressures in PD patients. This result is consistent with previous studies on PD patients,12 type 2 DM patients[14] and normal individuals.[15]

The relatively small sample size was a serious limitation of our study which could not rule out type II statistical error. Also, as a potential source of bias, the cross-sectional design could not reveal the causality between the parametres. The low number of cases also prevented multivariate analysis for the dependence of the parametres.

Conclusion

No significant difference in the serum visfatin levels of the PD patients compared to HD patients or healthy individuals was found. Among the PD patients, when considering the group with high visfatin levels against the group with low visfatin levels, except for the triglyceride levels, no significant difference was found in clinical and biochemical parametres. The triglyceride levels were higher

in the visfatin-high group. However, there was no correlation between visfatin and the triglyceride levels. Thus, the finding may be an incidental one among many parametres and tests.

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