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Original Article

Inverse association of long-acting natriuretic peptide with metabolic syndrome in peritoneal dialysis patients

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Abstract: Long-acting natriuretic peptide (LANP) is one of the peptide hormones in atrial natriuretic peptide (ANP) prohormone. Low levels of natriuretic peptide may lead to reduced lipolysis and excessive weight gain in obese patients. The aim of this study was to investigate the relationship between fasting serum LANP level and the metabolic syndrome (MetS) among peritoneal dialysis (PD) patients. Fasting blood samples were obtained from 52 PD patients among clinic outpatients. MetS and its components were defined using diagnostic criteria from the International Diabetes Federation. Serum LANP levels were measured using a commercially available enzyme immunoassay kit. Twenty-nine PD patients (55.8%) had MetS. Peritoneal dialysis patients with MetS had higher body weight, waist circumference, body mass index (BMI), body fat mass, fasting glucose, triglyceride, insulin levels, and HOMA-IR as well as lower HDL-C concentrations and LANP than those without MetS. Fasting serum LANP levels correlated negatively with body weight (r = -0.336; P = 0.015), waist circumference (r = -0.341; P = 0.013), BMI (r = -0.348; P = 0.012), and albumin (r = -0.384; P = 0.005) among the PD patients by univariate linear regression analysis. After multivariate forward stepwise linear regression analysis, fasting serum LANP levels correlated significantly inversely with waist circumference (β = -0.306, R^2 change = 0.093, P = 0.018) and albumin (β = -0.354, R^2 change = 0.147, P = 0.007) among PD patients. LANP level is significantly reduced in PD patients who were diagnosed to have MetS. Waist circumference and albumin showed an independent inverse association with serum LANP levels in PD patients.

Keywords: Albumin, long-acting natriuretic peptide, metabolic syndrome, peritoneal dialysis, waist circumference

Introduction

Cardiac natriuretic peptides consist of a family of peptide hormones that are synthesized by 3 genes and then stored as 3 different prohormones, which are 126 amino acid atrial natriuretic peptide (ANP), 108 amino acid B-type natriuretic peptide (BNP), and 103 amino acid C-type natriuretic peptide (CNP). Within the ANP prohormone are 4 peptide hormones, the long-acting natriuretic peptide (LANP; N-terminal pro-ANP 1-30), vessel dilator (N-terminal pro-ANP 31-67), kaliuretic peptide (N-terminal pro-ANP 79-98), and ANP (α-ANP), which can regulate blood pressure and plasma volume [1]. The biologic effects of the four peptide hormones of ANP are not only restricted to immune systems, blood pressure homeostasis via modulating natriuresis, vasodilatation, vasopressin antagonist, endothelin, and the renin-angiotensin-aldosterone system [2], but also exert potent lipolytic effects similar to those induced by β-adrenergic receptor agonist but through cyclic guanosine monophosphate (cGMP) dependent protein kinase, leading to perilipin and hormone-sensitive lipase phosphorylation [3, 4].

It is known that except for classic hemodynamic triggers of natriuretic peptide, some stimuli like weight loss and exercise could enhance the expression [5, 6]. On the other hand, obesity and insulin resistance are associated with lower levels of circulating natriuretic peptides, which lead to a vicious cycle resulting in the inability to resist the accumulation of fat [7]. It

then can be speculated that low levels of natriuretic peptide may lead to reduced lipolysis and excessive weight gain in obese patients, which may be one of the biological alterations that contribute to the development of obesity [8]. Moreover, lower plasma N-terminal pro-ANP levels were also associated with the development of insulin resistance and metabolic syndrome (MetS) [7, 9-11]. Although some studies showed that the serum level of natriuretic peptide was negatively associated with the occurrence of MetS in ambulatory individuals [7], hypertensive patients [9], congestive heart failure patients [10], and renal transplantation patients [11], there is no study about the association between serum LANP levels and MetS in peritoneal dialysis (PD) patients. The aim of this study was to investigate the characteristics and relationship between fasting serum LANP level and the MetS among PD patients.

Materials and methods

Patients

In October 2010, 52 patients receiving PD in a medical centre in eastern Taiwan were enrolled in this study. Forty-three patients who had been on continuous ambulatory peritoneal dialysis (CAPD, Dianeal, Baxter Health Care, Taiwan) treated with three to five dialysate exchanges per day. The other 9 patients treated with 4 to 5 dialysate exchanges each night with an automated device (automated peritoneal dialysis, APD; Dianeal, Baxter Health Care, Taiwan). Patients were excluded if they had any acute infection, such as peritonitis or catheter exit-site infection, at the time of blood sampling or co-morbidities like acute myocardial infarction, pulmonary edema, liver cirrhosis, and thyroid disease, or if they refused to provide informed consent for the study. The Protection of the Human Subjects Institutional Review Board of Tzu-Chi University and Hospital approved this study.

Anthropometric analysis

All variables of anthropometric factors were measured at fasting morning without the presence of dialysate in the abdominal cavity in the PD patients. Height was measured to the nearest half centimetre. Body weight was measured in light clothing and without shoes to the nearest half kilogram, and waist circumference was measured to the nearest half centimetre at the shortest point below the lower rib margin and the iliac crest without the presence of dialysate in the abdominal cavity in these PD patients. Body mass index (BMI) was calculated as weight (kilograms) divided by height squared (metres). Bioimpedance measurements of fat mass were performed at the bedside according to the standard, tetrapolar, whole body (hand-foot) technique, using a single-frequency (50-kHz) analyzer (Biodynamic-450, Biodynamics Corporation, Seattle, MA, USA). Measurements were carried out by the same operator without the presence of dialysate in the abdominal cavity in the PD patients; fat mass was collected and analyzed by specific formulas provided by the manufacturer [9-12].

Biochemical investigations

Patients had not made a dialysis exchange before blood sampling in the morning. Fasting blood samples of approximately 5 ml for measuring complete blood count (Sysmex K-1000, Bohemia, NY, USA) and other factors were immediately centrifuged at 3000 g for 10 min. The serum was stored at 4°C for biochemical examination within 1 hour after collection. Serum levels of blood urea nitrogen (BUN), creatinine (Cre), fasting glucose, total cholesterol (TCH), triglyceride (TG), high-density lipoprotein-cholesterol (HDL-cholesterol), albumin, globulin, and total calcium and phosp-horus were measured using an autoanalyzer (COBAS Integra 800, Roche Diagnostics, Basel, Switzerland). Serum LANP (N-terminal pro-ANP 1-30 or pre-pro-ANP 26-55, Phoenix Pharmaceuticals Inc., Burlingame, CA, USA) levels were measured using a commercially available enzyme immunoassay kit (EIA). The limit of detection calculated as the concentration of human LANP corresponding to the blank average minus 3 standard deviations was 0.1 ng/ml. The inter- and intra-assay coefficients of variation for LANP were 6.2% and 5.4%, respectively [9-12]. Serum insulin levels were measured using the MEIA (microparticle enzyme immunosorbent assay) method by an autoanalyzer (Abbott Laboratories, Abbott Park, IL, USA) [9, 10]. Insulin resistance was evaluated using a homeostasis model assessment of insulin resistance (HOMA-IR) as follows: HOMA-IR = fasting plasma glucose (mg/dl) × fasting serum insulin (μU/ml)/405 [9, 10]. Serum intact parathyroid hormone (iPTH) (Diagnostic Systems

Laboratories, Texas, USA) level was measured using a commercially available enzyme-linked immunosorbent assay (ELISA). Patients were classified as secondary hyperparathyroidism if serum iPTH was greater than 300 pg/ml.

Cumulative glucose load

The total exposure to glucose was calculated from the dialysis regime reported the day before blood sampling. The product of the volume and the glucose concentration for each exchange was calculated. For example, for an individual who was using 4×2 L exchanges (2×1.36%, 1×2.27%, and 1×3.86%), there would be 54.4+45.4+77.2 = 177.0 g of glucose per day, as described by Davies et al. [13].

Metabolic syndrome and its components

The prevalence of MetS was defined using the International Diabetes Federation definition [14]. People were classified as having MetS if they had central (abdominal) obesity with a waist circumference ≥ 90 cm (men) or ≥ 80 cm (women) (Chinese criteria) and matched 2 or more of the following criteria: fasting serum glucose of 110 mg/dl or more, TG of 150 mg/dl or higher, HDL-cholesterol level less than 40 mg/dl in men or less than 50 mg/dl in women, or blood pressure of 130/85 mmHg or higher. The use of antihypertensive medication was considered as high blood pressure in this analysis. Diabetes mellitus (DM) was determined according to World Health Organization criteria [15]. A person was regarded as having DM if the fasting plasma glucose was either 126 mg/dl or more, if the 2-hour glucose after an oral glucose tolerance test was 200 mg/dl or more, or if he/she was using diabetes medication (oral or insulin).

Statistical analysis

Data are expressed as means ± standard deviation and were tested for normal distribution by Kolmogorov-Smirnov statistics. Categorical variables were analyzed by the Chi-square test. Comparisons between patients were performed using Student's independent *t*-test (two-tailed) for the normally distributed data or the Mann-Whitney U test for the parameters that presented with non-normal distribution (fasting glucose, iPTH, insulin, HOMA-IR). Univariate linear regression analyses were used to examine the relationship between the clinical variables with serum LANP levels in PD patients. Variables that were significantly associated with LANP in PD patients were tested for independency in multivariate forward stepwise regression analysis. Data were analyzed using SPSS for Windows (version 13.0; SPSS Inc., Chicago, IL, USA). A p-value < 0.05 was considered statistically significant.

Results

Demographic, biochemical, and clinical characteristics of the 52 PD patients are presented in **Table 1**, and the clinical and laboratory characteristics of the PD patients with or without MetS are presented in **Table 2**. Peritoneal dialysis patients with MetS had higher body weight (66.22±3.3 kg vs. 57.37±13.21 kg; $P = 0.021$), waist circumference (94.69±7.49 cm vs. 83.46±9.66 cm, $P < 0.001$), BMI (26.16±3.82 kg/m^2 vs. 22.12±3.44 kg/m^2, $P < 0.001$), body fat mass (26.16±3.82% vs. 24.97±5.75%, $P < 0.001$), fasting glucose (158.21±65.13 mg/dl vs. 107.7±28.92 mg/dl, $P = 0.001$), TG concentrations (252.79±129.85 mg/dl vs. 153.91±120.61 mg/dl, $P = 0.007$), insulin levels (27.16±32.45 μU/dl vs. 10.28±7.45 μU/dl, $P = 0.004$), and HOMA-IR (11.1±14.13 vs. 2.75±2.1, $P < 0.001$) and lower HDL-C concentrations (39.0±7.81 mg/dl vs. 50.22±16.91 mg/dl, $P = 0.007$) and LANP (66.99±44.19 ng/ml vs. 114.75±74.81 ng/ml, $P = 0.006$) than PD patients without MetS.

The fasting serum LANP levels of the PD patients found by subgroup analysis (gender, DM, HTN, secondary hyperparathyroidism, and PD models and medications) are presented in **Table 3**. The co-morbidities of the PD patients included diabetes ($n = 20$; 37.3%), hypertension ($n = 31$; 58.8%) and secondary hyperparathyroidism ($n = 24$; 47.1%). The medications prescribed to the PD patients included thiazolidinediones ($n = 5$; 9.0%), sulphonylureas ($n = 11$; 19.6%), insulin ($n = 9$; 17.6%), angiotensin receptor blocker (ARB) or angiotensin-converting enzyme inhibitor (ACEi) ($n = 24$; 45.1%) and statin ($n = 18$; 35.3%). The LANP levels did not differ statistically based on gender, co-existing diabetes and/or hypertension, secondary hyperparathyroidism, and PD models and medications uses.

The univariate linear regression analysis of the relationship between the fasting serum LANP

Table 1. Clinical and laboratory characteristics of PD patients

Items	Parameter		Parameter	
Anthropometric data	Height (cm)	159.32±8.51	Waist circumference (cm)	89.72±10.14
	Body weight (kg)	62.30±13.86	Age (year)	52.85±13.16
	Body mass index (kg/m^2)	24.37±4.15	PD duration (month)	41.79±37.35
	Body fat mass (%)	29.66±7.42	SBP (mmHg)	134.04±24.00
	DBP (mmHg)	77.25±15.85		
Biochemical data	White blood count (x1000/μl)	8.20±3.05	Haemoglobin (g/dl)	9.83±1.65
	Albumin (g/dl)	3.84±0.44	Globulin (g/dl)	2.94±0.54
	Triglyceride (mg/dl)	209.06±134.13	Total cholesterol (mg/dl)	194.60±51.62
	HDL-C (mg/dl)	43.96±13.73	Creatinine (mg/dl)	10.24±3.03
	Fasting glucose (mg/dl)	135.87±57.72	Total Calcium (mg/dl)	9.65±0.66
	Phosphorus (mg/dl)	5.28±1.21	Insulin (μU/dl)	19.69±25.96
	iPTH (pg/ml)	438.96±412.83	LANP (ng/ml)	88.12±63.72
	HOMA-IR	7.41±11.36	Cumulative glucose load (g/day)	142.82±40.60

Data are expressed as means ± standard deviations. PD, peritoneal dialysis; SBP, systolic blood pressure; DBP, diastolic blood pressure; HDL-C, high-density lipoprotein cholesterol; iPTH, intact parathyroid hormone; LANP, long-acting natriuretic peptide; HOMA-IR, homeostasis model assessment of insulin resistance.

Table 2. Clinical variables of the PD patients with or without metabolic syndrome

Items	No metabolic syndrome (n = 23)	Metabolic syndrome (n = 29)	*P* value
Age (year)[a]	51.83±15.28	53.66±11.41	0.623
PD duration (month)[a]	49.17±42.10	35.93±32.68	0.207
Height (cm)[a]	160.28±9.01	158.55±8.17	0.472
Body weight (kg)[a]	57.37±13.21	66.22±13.30	0.021*
Waist circumference (cm)[a]	83.46±9.66	94.69±7.49	<0.001*
Body mass index (BMI; kg/m^2)[a]	22.12±3.44	26.16±3.82	<0.001*
Body fat mass (%)[a]	24.97±5.75	33.38±6.47	<0.001*
Systolic blood pressure (mmHg)[a]	138.65±26.01	130.38±22.05	0.220
Diastolic blood pressure (mmHg)[a]	81.57±15.39	73.83±15.62	0.080
White blood count (×1000/μl)[a]	7.42±2.64	8.81±3.25	0.104
Haemoglobin (g/dl)[a]	10.05±1.59	9.65±1.70	0.381
Albumin (g/dl)[a]	3.81±0.39	3.85±0.49	0.758
Globulin (g/dl)[a]	2.85±0.52	3.02±0.56	0.257
Fasting glucose (mg/dl)[b]	107.70±28.92	158.21±65.13	0.001*
Total cholesterol (mg/dl)[a]	195.91±56.31	193.55±48.58	0.872
Triglyceride (mg/dl)[a]	153.91±120.61	252.79±129.85	0.007*
High-density lipoprotein-cholesterol (mg/dl)[a]	50.22±16.91	39.00±7.81	0.003*
Creatinine (mg/dl)[a]	10.21±3.40	10.27±2.79	0.951
Total calcium (mg/dl)[a]	9.78±0.67	9.56±0.65	0.229
Phosphorus (mg/dl)[a]	5.14±1.36	5.38±1.08	0.482
Intact parathyroid hormone (pg/ml)[b]	474.59±438.45	410.71±396.87	0.585
LANP (ng/ml)[a]	114.75±74.81	66.99±44.19	0.006*
Insulin (μU/dl)[b]	10.28±7.45	27.16±32.45	0.004*
HOMA-IR[b]	2.75±2.10	11.10±14.13	<0.001*
Cumulative glucose load (g/day)[a]	149.32±39.59	137.66±41.33	0.308

Data are expressed as means ± standard deviations. *$P < 0.05$ was considered statistically significant after Student *t*-test or the Mann-Whitney U test. [a]Data were tested by Student *t*-test. [b]Data were tested by Mann-Whitney U test. PD, peritoneal dialysis; LANP, long-acting natriuretic peptide; HOMA-IR, homeostasis model assessment of insulin resistance.

and clinical and laboratory parameters in PD patients is presented in **Table 4**. Body weight (r = -0.336; P = 0.015), waist circumference (r = -0.341; P = 0.013), BMI (r = -0.348; P =

Table 3. Subgroup analysis of fasting serum long-acting natriuretic peptide levels of the PD patients

Characteristic		Number (%)	LANP level (ng/ml)	*P* value
Gender	Male	20 (37.3)	80.55±44.00	0.504
	Female	32 (62.7)	92.85±73.70	
DM	No	32 (62.7)	98.29±69.94	0.148
	Yes	20 (37.3)	71.84±49.62	
Hypertension	No	21 (41.2)	92.42±72.61	0.693
	Yes	31 (58.8)	85.20±58.01	
Secondary hyperparathyroidism	No	28 (52.9)	78.91±54.14	0.265
	Yes	24 (47.1)	98.86±73.07	
PD model	CAPD	43 (82.4)	83.93±63.81	0.305
	APD	9 (17.6)	108.13±62.92	
Thiazolidinediones	No	47 (91.0)	89.16±64.63	0.720
	Yes	5 (9.0)	78.27±59.90	
Sulphonylureas	No	41 (80.4)	92.56±67.01	0.335
	Yes	11 (19.6)	71.49±48.57	
Insulin	No	43 (82.4)	91.44±65.67	0.417
	Yes	9 (17.6)	72.26±53.85	
ACE inhibitor or ARB	No	28 (54.9)	101.56±71.58	0.101
	Yes	24 (45.1)	72.44±50.10	
Statin	No	34 (64.7)	89.53±65.22	0.829
	Yes	18 (35.3)	85.45±62.54	

*$P < 0.05$ was considered statistically significant after Student *t*-test. LANP, long-acting natriuretic peptide; DM, diabetes mellitus; PD, peritoneal dialysis; CAPD, continuous ambulatory peritoneal dialysis; APD, automated peritoneal dialysis, ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker.

0.012), and albumin (r = -0.384; P = 0.005) inversely correlated with fasting serum LANP levels among the PD patients.

A multivariate forward stepwise linear regression analysis on the variables that were significantly associated with fasting serum LANP levels among PD patients showed that waist circumference (β = -0.306, R^2 change = 0.093, P = 0.018) and albumin (β = -0.354, R^2 change = 0.147, P = 0.007) were independently inversely associated with the fasting serum LANP levels (**Table 5**).

Discussion

The results of our study showed that the fasting LANP level was lower for those who had MetS than for those without MetS and was inversely associated with waist circumference and serum albumin level in PD patients.

Cardiac natriuretic peptides consist of a family of six peptide hormones that are synthesized by three separate genes and then stored as three separate prohormones, ANP, BNP, and CNP. The ANP prohormone contains four peptide hormones: LANP, vessel dilator, kaliuretic peptide, and ANP [1, 16]. In addition to playing a key role in the regulation of salt and water balance and blood pressure homeostasis, natriuretic peptides have the lipolytic effects and increased transcripts of brown adipocyte-associated genes as well as markers of mitochondrial biogenesis and cellular oxygen consumption [4, 17]. Decreasing serum levels of natriuretic peptides have been considered associated with fat accumulation, which was shown by the Framingham Heart Study offspring cohort study to reduce N-terminal pro-ANP (N-ANP) and BNP in obese subjects [18]. After distinguishing the influences of hypertension and DM on the plasma level of natriuretic peptides, Wang et al. found that obese and overweight individuals have considerably lower plasma N-ANP and BNP than those with a normal BMI. In addition, those who have abdominal pattern of obesity would additionally have lower levels of natriuretic peptides [18]. In our present study, we similarly found that LANP, one of the four peptide hormones, was inversely associated with waist circumference, which is a major diagnostic component of MetS, in PD patients.

In PD patients, there is high prevalence rate of MetS, ranging from 32.1% to 47.2% in different studies, and MetS is a risk factor associated with high C-reactive protein and adverse cardiovascular outcomes [19-21]. Metabolic syndrome represents a constellation of abdominal obesity, hypertension, impaired fasting glucose, and dyslipidemia, which is indicative of insulin resistance [17]. In this study, we found that the prevalence of PD patients with MetS was 55.8%, and PD patients with MetS have a higher serum insulin level and HOMA-IR than those without MetS. It had been shown that

Table 4. Univariate linear regression analyses of parameters correlated with serum long-acting natriuretic peptide levels of PD patients

Items	Beta	*P* value
Age (year)	0.186	0.188
PD duration (month)	0.126	0.373
Height (cm)	-0.127	0.369
Body weight (kg)	-0.336	0.015*
Waist circumference (cm)	-0.341	0.013*
Body mass index (BMI; kg/m^2)	-0.348	0.012*
Body fat mass (%)	-0.219	0.118
Systolic blood pressure (mmHg)	0.079	0.576
Diastolic blood pressure (mmHg)	0.147	0.218
White blood count (×1000/μl)	-0.062	0.662
Haemoglobin (g/dl)	0.011	0.937
Albumin (g/dl)	-0.384	0.005*
Globulin (g/dl)	0.059	0.676
Fasting glucose (mg/dl)	-0.125	0.377
Total cholesterol (mg/dl)	-0.039	0.782
Triglyceride (mg/dl)	-0.178	0.206
High-density lipoprotein-cholesterol (mg/dl)	0.029	0.828
Creatinine (mg/dl)	-0.185	0.188
Total calcium (mg/dl)	0.171	0.225
Phosphorus (mg/dl)	-0.048	0.738
Intact parathyroid hormone (pg/ml)	0.071	0.615
Insulin (μU/dl)	-0.089	0.531
HOMA-IR	-0.102	0.471
Cumulative glucose load (g/day)	0.037	0.792

*$P < 0.05$ was considered statistically significant after univariate linear analyses. HOMA-IR, homeostasis model assessment of insulin resistance.

Table 5. Multivariate stepwise linear regression analysis of parameters correlated with serum long-acting natriuretic peptide levels of PD patients

Items	Beta	R square	R square change	*P* value
Albumin (g/dl)	-0.354	0.147	0.147	0.007*
Waist circumference (cm)	-0.306	0.240	0.093	0.018*

*$P < 0.05$ was considered statistically significant in the multivariate stepwise linear regression analyses.

hypertension, hypervolemia, congestive heart failure, abnormal renal function, and even dialysis treatment could influence the serum level of natriuretic peptides [22]. Moreover, it had been shown that a variety of different populations of patients who have MetS were found to have lower serum natriuretic peptides [9-11], which indicates an inter-relationship between MetS and serum natriuretic peptides. In this present study, we demonstrated that PD patients with MetS would have lower serum LANP levels than those without.

The mechanism underlying MetS with lower LANP might be bi-directional. An in vivo study showed that caloric deprivation induced a significant decrease in natriuretic peptide receptor-C (NPR-C), which is a disulfide-linked homodimer that is homologous to the extracellular domains of guanylyl cyclase-A but contained only 37 amino acids and functions as clearing natriuretic peptides, and resulted in an increase of circulating ANP levels [23]. Similarly, adipose tissue of patients having obesity and hypertension also showed elevated NPR-C gene expression, which indicates more ANP clearance [24]. On the contrary, adipocyte could also express NPR-A, which could mediate the biologic effects of natriuretic peptides. Sengenes et al. demonstrated that binding ANP to NPR-A could induce lipolysis, which indicates that a low level of natriuretic peptide could worsen the state of obesity [3].

In this present study, we found that the serum albumin level of PD patients correlated inversely with the serum LANP level. Although there is no significance, PD patients with MetS in this present study similarly have a higher average serum albumin level than those without MetS. Similarly, our previous studies conducted on hypertensive patients, congestive heart failure patients, and renal transplantation patients [9-11] showed an inverse relationship with the serum LANP level. As it had been known that serum albumin, which might be indicative of the nutritional status of PD patients, is an important predictor of survival in dialysis patients [21], serum albumin was found to be positively correlated with the occurrence of visceral fat area in other studies

[20]. Studies have documented an "obesity paradox", in which overweight and mildly obese people with chronic kidney disease have a better prognosis than patients who are underweight or severely obese [25]. The obesity paradox in dialysis patients might have multi-factorial causes such as protein-energy wasting, inflammation, under-nutrition versus over-nutrition, hemodynamic stability, circulatory cytokines, uremic toxin in adipose tissue, and endotoxin-lipoprotein interactions [26]. In this study on PD patients, we speculate that the inverse relationship between LANP and albumin might indicate the nutritional status; prospective studies are needed to elucidate the mechanism for this relationship.

Many factors, such as medications, clearance of LANP, and associated co-morbidities, might affect serum LANP levels in patients with kidney disease [5-7, 22]. Plasma angiotensin is associated with adiposity, and renin-angiotensin system blockers can improve glucose homeostasis and reduce abdominal fat [27], but traditional beta-blockers are known to worsen glucose homeostasis through plasma ANP and cGMP concentrations [28]. Studies had shown that the usage of atorvastatin in acute myocardial infarction had effects on decreasing ANP level [29], pioglitazone affected the expression of ANP through activation of peroxisome proliferator-activated receptor [30], and insulin exerted its anti-lipolytic effects in human fat cells, leading to inhibition of β-adrenergic receptor agonist and catecholamine-induced lipolysis [3]. In the subgroup analysis of this present study, there was no significant influence of the LANP level on DM, HTN, secondary hyperparathyroidism, or PD models, and no significant association between medication uses and serum LANP was found among PD patients.

Our study has some limitations. Firstly, this study was of cross-sectional design. Therefore, our findings should be investigated in long-term prospective studies before a causal relationship between serum LANP and MetS in PD patients can be established. Secondly, other N-terminal ANP prohormone peptides, such as vessel dilators or kaliuretic peptides, which have the same effects as those of LANP, also need further investigations.

In conclusion, we found that PD patients with MetS had a lower serum LANP level than those without MetS, and there was an inverse relationship between circulating fasting LANP and waist circumference among PD patients.

Disclosure of conflict of interest

None.

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