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Relationship Between Serum Leptin Level and Peritonitis in CAPD Patients

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ABSTRACT

Background: Leptin is produced by fat cells and is secreted into the blood stream. Leptin is freely filtered into the renal tubules but its concentration in the urine is very low. Serum leptin level is higher in continuous ambulatory peritoneal dialysis (CAPD) patients, compared to the healthy individuals. Serum leptin level may have correlation with inflammatory markers and peritonitis.
Objectives: The aim of this study was to evaluate relationship of serum leptin level with peritonitis, the major complication of CAPD, in these patients.
Patients and Methods: In a cross sectional study, 75 CAPD patients in Al-Zahra Hospital in Isfahan were enrolled from October 2007 to February 2008. Serum levels of leptin, Kt/V, demographic findings, total numbers of peritonitis and presence of peritonitis in last year, were recorded in all patients, based on history, physical exam and patients' files.
Results: Mean age of the patients was 53 ± 15 years. Mean serum leptin level in females and males were 27 ± 23μg/L and 16 ± 13μg/L respectively. At univariate general linear model (GLM), there was a significant correlation between serum leptin level with body mass index (BMI) ($P < 0.001$, $\beta = 2.7$) and duration of renal failure ($P = 0.01$). No correlation was seen between serum leptin level and total number of peritonitis in the past. However, there was negative relationship between serum leptin level and presence of peritonitis in the last year ($P = 0.004$, $\beta = 6$).
Conclusions: Presumably, we could not use serum leptin level as a marker of infection in long term; however, serum leptin level may be used as an index of peritonitis and morbidity in short time.

Implication for health policy/practice/research/medical education:
Serum leptin levels could not be used as a marker of infection in long-term but it may be applied as an index of peritonitis and morbidity in short-time.

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1. Background

Leptin is a 16000 Dalton protein that is produced by fat cells, it is secreted into the blood stream, and it attaches to the leptin binding protein, and reaches hypothalamus via CSF. It decreases neuropeptide Y (NPY), suppresses appetite, and with blockade of (melanocyte stimulating hormone) MSH, reduces hunger which in turn decreases weight (1). Kidneys play an important role in metabolism and excretion of leptin. It is freely filtered into glomeruli with very little excretion in urine (2), because it is probably reabsorbed and metabolised in tubules (3). Serum leptin level is higher in chronic renal failure, hemodialysis and CAPD patients compared to general population (4, 5). Some studies reported that the level of leptin in CAPD patients and women is higher compared to hemodialysis patients and men, respectively (6, 7). Exact cause of elevated serum leptin level in renal failure

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patients is not clear; however, some factors including decreased functional mass of kidneys, hemodialysis membrane and type of dialysis (hemodialysis versus peritoneal dialysis) (8, 9), low serum erythropoietin level (10), chronic inflammation and hyperinsulinemia (11) may also have a role. Some studies show that serum leptin level is related to inflammatory factors such as C-reactive protein (12, 13). Leptin may act as an inflammatory index or cachexia induced factor in CAPD patients (14, 15). Lam *et al*. showed that during the acute phase of peritonitis, serum leptin level increases and then returns to baseline during 42 days (16).

2.Objectives

There are few comprehensive studies on relation between serum leptin level and peritonitis or inflammatory factors which remains precisely unclear and this study was carried to investigate it further. There fore, this study was conelucted to find this relation.

3. Patients and Methods

In a cross-sectional study in Al-Zahra Hospital of Isfahan from 101 CAPD patients, 75 patients fulfilled inclusion criteria and were entered in the study. Method of sampling was convenient sampling. Patients were asked by Questionnaire and assessed by physical examination, patient file and laboratory examination. Information in the questionnaire was collected by PD nurse and from patient file from October 2007 to February of 2008. Inclusion criterion was: being at least 3 months on peritoneal dialysis, and exclusion criteria were non-compliance of patients, inadequate blood sampling and peritonitis during study. Exchange of dialysis fluid in patients was 4 to 5 times per 24 hours. Diagnosis of peritonitis was based on the presence of 2 of following criteria: 1) clinical findings such as abdominal pain, fever, turbid PD effluent, 2) presence of WBC equal or greater than 100/mL in effluent and 3) positive PD effluent culture.

Fasting blood samples were taken in the peritoneal dialysis (PD) clinic for measurement of leptin (DRG kit, radioimmunoassay (RIA), Germany), blood urea, creatinine and serum albumin (Bromo Cresol Green (BCG) method); furthermore, creatinine and urea concentrations were measured in dialysate and urine samples. Body mass index (BMI) calculated by the formula [body weight (kg) / height ^{2} (m)] and total number of peritonitis, presence of peritonitis in the last year and demographic information of patients was obtained by their files. All data collected by PD nurse and data related to calculating Kt/V analyzed by PD Adequest 2 software, Baxter, USA. All laboratory tests were carried out 10 hours of fasting and in a single laboratory. Patients were asked by Questionnaire, assessed by physical examination, patient file and laboratory examination. Separated plasma of patients were kept in -20°C environment. After collection of all samples, measurements of variables were done simultaneously. T-test and univariate general linear models (GLM) were used for the analysis of the variables statistically. A p value less than 0.05 were considered as significant. All data and information are confidential and an informed consent was taken from every patient for obtaining samples and other processes of this study.

Table 1. Distribution of Causes of End-stage Renal Disease in Peritoneal Dialysis Patients

Cause	**Patient, No.** (%)
ADPKD [a]	1 (1.3)
DM [a] + HTN	4 (5.3)
DM without HTN	32 (42.7)
DM ± HTN	36 (48)
Glomerulonephritis	1 (1.3)
Gout	1 (1.3)
Hypertension	17 (22.7)
Pregnancy	2 (2.7)
Renal stone	4 (5.3)
SLE [a]	2 (2.7)
Unknown	11 (14.6)
Total	75 (100)

[a] Abbreviations: ADPKD, Autosomal dominant polycystic kidney disease; DM, Diabetes mellitus; SLE, Systemic Lupus Erythematosus

4. Results

Average age of the patients was 53 ± 15 years. History of hemodialysis was seen in 23 patients. The most common cause of end-stage renal disease was diabetes mellitus (48%) *(Table 1)*. The mean age of DM patients was higher than patients without DM (60 *vs*. 46 years in non-DM cases) (P = 0.03). Mean serum leptin level in women and men were 27 ± 23 μg/l and 16 ± 13 μg/l (P = 0.001, r = - 0.4), respectively. At univariate GLM, has been shown in *Figure 1*, no correlation was seen between serum leptin level and total number of peritonitis in past but there was negative relationship between serum leptin level and frequency of peritonitis in the last year (P = 0.004, β = 6). There was a significant correlation between serum leptin level with BMI (P < 0.001, β = 2.7) and a negative relationship was observed between age and serum leptin level (P = 0.028, β = - 0.32). The patients with longer duration of chronic kidney disease had higher serum leptin level (P = 0.01, β = 0.09); however, no relation was seen between serum leptin concentration and duration of CAPD *(Table 2)*. There was no significant correlation between serum leptin level and Kt/V, history of hypertension, and number of peritoneal dialysis exchange per day (P > 0.05).

5. Discussion

Serum leptin level in CAPD patients is higher than that of normal population and HD patients. Higher level

Table 2. Clinical and Biochemical Parameters of Patient During the Study

Variables	Minimum	Maximum	Mean ± SD
Leptin, μg/L	0.09	101.00	22.00 ± 23.00
WEIGH, kg	36.00	95.00	66.83 ± 13.49
BMI [a], kg/m^2	14.20	33.30	24.26 ± 3.89
Kt/V	1.08	4.80	2.42 ±0.80
Frequency of peritonitis at all	0.00	8.00	0.91 ± 1.38
Frequency of peritonitis during last year	0.00	7.00	0.4533 ± 1.00
Duration of renal failure, mo	0.50	300.00	43.47 ± 56.03
Duration of peritoneal dialysis, mo	3.00	70.00	20.16 ± 13.79
Duration of hemodialysis, mo	0.00	72.00	4.27 ± 12.61
Number of PD [a] exchanges per day	2.00	5.00	3.8 ± 0.78

[a] Abbreviations: BMI ,body mass index; PD, peritoneal dialysis

of serum leptin in CAPD patients may be due to higher fat mass and serum insulin level in these patients (17). Several studies have shown that serum leptin level is higher in females with chronic kidney disease compared to males (6, 18, 19). In CAPD patients, the highest serum leptin level has been observed around 8 AM and it might be due to nocturnal glucose overload in (20). In these patients, serum leptin level does not correlate with Kt/V and protein consumption (13, 17). Similarly, we did not find relation between leptin and Kt/V and also between leptin and number of exchange during 24 hours. It means that serum leptin may be not a good index for dialysis adequacy. In the current study, serum leptin level was higher in women compared to men and serum leptin level had a linear correlation with BMI. Our result is similar to the findings of Parry (17) and Kagen (18); in contrast, it is not consistency in the data of Kim (19). The reason for these differences could be partly due to discrepancy in the number of the patients studied.

Mak *et al.* (12) reported a correlation between serum leptin level and serum CRP in rats. In addition, Lee *et al.* (20) found that serum leptin had relation with CRP and IL-6 in hemodialysis patients (21). Chen *et al.* (22) showed that leptin had no correlation with inflammatory factors (CRP-IL-6-TNFα) in CAPD patients. Yilmas *et al.* (13) and Landt *et al.* (23) also reported that there is no relation between leptin and CRP. Prez fontan *et al.* (24) showed that serum leptin level has correlation with mortaliy in CAPD patients. Based on above mentioned studies we can conclude that leptin may have a role in cachexia and malnutrition seen in CAPD patients. Lam *et al.* (16) reported that in the CAPD patients, leptin level increases in acute phase of peritonitis and then it decreases slowly to the baseline level after 42 days. Also Bracho-Riquelme *et al.* demonstrated the serum leptin level less than 10 ng/mL is a negative prognostic factor in patients with moderate to severe peritonitis of CAPD patients (25). Our study showed that serum leptin level have no relation with total number of previously reported peritonitis but leptin level is lesser in patients with peritonitis during last year. Our findings have some similarity with the findings of Lam (16); therefore, we can conclude that serum leptin level increases in acute peritonitis and gradually declines to the baseline and even lower than baseline level. Limitations of our study were small number of cases and lacking of follow up. We recommend greater prospective studies with longer duration of follow up and checking other inflammatory markers such as ESR, C-reactive protein, serum ferritin and cytokines. We conclude that serum leptin level cannot be used as a good index for total previous number of peritonitis. However, more studies are needed to be carried out to reveal the relationship between leptin and peritonitis.

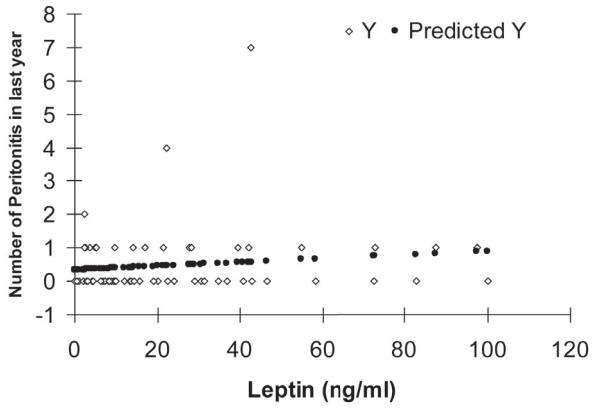

Figure 1. Relationship of Serum Leptin Level with Number of Peritonitis in Last Year

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Conflict of interest

None declared.

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