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Relationship between adiposity, adipokines, inflammatory markers and lipid profile in hemodialysis patients

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Abstract. – OBJECTIVES: Our aim is to study the correlations of leptin and adiponectin with inflammation markers, body composition and lipid profile in end stage renal disease (ESRD) patients.

PATIENTS AND METHODS: Phase angle values and fat mass as calculated using BIA, Malnutrition-Inflammation Score (MIS), leptin, adiponectin, IL-6, IL-8 triglycerides, cholesterol and other common serum markers' concentrations were analyzed using simple and multiple linear regression models in 47 hemodialysis patients.

RESULTS: In contrast to leptin, adiponectin is inversely correlated to BMI and fat mass in hemodialysis patients. Triglycerides were the only parameter that retained its statistical correlation significance with adiponectin in the multiple regression model.

CONCLUSIONS: Fat mass is of important consideration when calculating adipokines levels and their possible correlations with other variables. The inverse correlation of adiponectin with triglycerides levels should be further delineated due to the important role of vascular diseases in total mortality and morbidity of ESRD patients.

Key Words:
Leptin, Adiponectin, Triglycerides, Body composition.

Introduction

Obese dialysis patients have a lower mortality rate, a fact that can be explained by better preserved nutritional reserves or lower comorbidities[1]. However, this is hypothetical and recent studies on the association between several cardiovascular risk factors, like adiposity, adipokines, inflammatory markers and lipid profile in these patients have yielded conflicting results.

More specifically, a recent report[2] concludes that serum leptin concentration seems to be a marker of good nutrition status rather than an appetite suppressing uremic toxin in patients with chronic renal failure as some previous cross-sectional studies support[3,4]. Nevertheless, adiposity had not been taken into account in this report although body-fat mass was shown to be a factor correlating with adipokine levels[5,6] Moreover, leptin has been proposed as a negative acute-phase reactant due to its negative correlation with ferritin, although other inflammatory markers like CRP were not inversely related to serum leptin levels[2]. Likewise, the relationship of adiponectin with leptin in patients on renal replacement therapy is not clear. A negative correlation that has been shown in one study[7] was not confirmed later on[2].

A study that would examine possible correlations between the aforementioned factors would add on the complex issue of cardiovascular risk determinants in dialysis patients. The aims of our study were to quantify the serum concentrations of leptin and adiponectin in haemodialysis (HD) patients and to study the correlations of these adipokines with inflammation markers, adiposity and lipid profile.

Patients and Methods

Forty-seven hemodialysis (HD) patients (27 men and 20 women, mean age 62.6 years) agreed to participate. All of them were of Caucasian origin and had been on maintenance dialysis for at least four months before entering the study. All HD patients were on standard 4 hours, 3 times weekly, bicarbonate dialysis program, using a polysulfone, high flux, membrane.

Body Composition

Body composition was assessed with Bioimpedance analysis (BIA) (Akern BIA 101, Detroit, MI, USA) including variables of body composition like body fat, fat free mass, total body water and extracellular water, by interpreting the values

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of resistance (R), reactance (Xc) and phase angle (PA)[8]. BIA measurements were performed 10-20 minutes after completion of the HD session. The average of two readings was obtained in all patients in every visit.

Anthropometric and Laboratory Evaluation

Body weight and height assessment was performed within 10-30 min after termination of the dialysis treatment. For laboratory testing, a blood sample was drawn from a peripheral vein under fasting conditions. Leptin and adiponectin were measured by Elisa (R&D Systems, Inc, Minneapolis, MN, USA).

MIS

The malnutrition-inflammation score (MIS) was calculated for all patients. The MIS questionnaire is composed of Subjective Global Assessment (SGA), plus 3 additional parameters of assessment (BMI, serum albumin and total iron-binding capacity [TIBC]). The SGA questionnaire has been developed to assess nutritional status of hospitalized patients. It takes into account specific elements of patient's history and physical examination[9]. MIS score ranges from 0 to 30, with higher scores reflecting increased risk of malnutrition and inflammation[2]. The MIS has been proven to be a useful, short-term tool to risk-stratify HD patients[9].

Statistical Analysis

Spearman's correlation coefficients were calculated between leptin and adiponectin concentrations and clinical and laboratory variables. Based on the results of the correlations, a multiple linear regression model was developed to assess more precisely possible independent factors affecting adiponectin levels. $p < 0.05$ was considered statistically significant.

Results

Table I contains the correlations of serum leptin and adiponectin with relevant clinical and laboratory variables. As it is shown in Table I, Lleptin has a statistical significant correlation with BMI ($p < 0.004$) and body fat mass ($p = 0.017$), as calculated by BIA. Adiponectin, on the other hand, is inversely correlated with BMI ($p = 0.02$), fat mass ($p = 0.02$), triglycerides ($p = 0.03$) and phase angle ($p = 0.041$).

The correlation between leptin and adiponectin that is shown in simple linear regression model was not revealed in the multiple regression model when fat mass was added as a parameter. In more details, when factors showing a statistical significant correlation with adiponectin were studied together, triglycerides were the only parameter that retained its statistical significance ($p = 0.01$) in correlation with adiponectin.

Discussion

BIA is considered a reliable tool for the assessment of fat mass and has been correlated with prognosis in end stage renal disease patients[10]. According to regression analysis, both leptin and adiponectin are statistically significantly correlated with fat mass but not with phase angle values. As it has been hypothesized previously[1], it is possible that leptin and adiponectin are not in the causal pathway linking body composition to outcome and that they simply reflect adiposity. This may also explain the fact that the inverse correlation of these adipokines is lost when fat mass is added as an independent parameter in the multiple regression model.

Inflammation is related to malnutrition and prognosis in end stage renal disease patients[11]. In a recent study[12] ESRD patients had a marked elevation of plasma TNF-α, IL-6, IL-8 and leptin concentrations. In contrast to previous reports[4,13] we failed to show such kinds of associations between inflammatory (CRP, IL-6) or proinflammatory cytokines (IL-8) and adipokines. However, most of our patients were in better nutritional and inflammation status than in the aforementioned studies and inflammatory markers, like CRP or IL-6, were quite low.

Table I. Correlation coefficients (r) between leptin and adiponectin concentrations with clinical and laboratory variables in 47 hemodialysis patients.

	Leptin	Adiponectin
BMI (kg/m^2)	0.420 ($p < 0.004$)	-0.441 ($p < 0.002$)
Cholesterol (mg/dl)	0.037 ($p = 0.809$)	-0.069 ($p = 0.643$)
Triglycerides (mg/dl)	0.171 ($p = 0.257$)	-0.419 ($p = 0.003$)
Albumin (g/dl)	0.032 ($p = 0.832$)	-0.111 ($p = 0.456$)
TIBC (mg/dl)	0.221 ($p = 0.141$)	-0.196 ($p = 0.188$)
IL-6 (pg/ml)	0.114 ($p = 0.452$)	-0.199 ($p = 0.180$)
IL-8 (pg/ml)	0.116 ($p = 0.444$)	0.069 ($p = 0.644$)
CRP (mg/dl)	-0.277 ($p = 0.062$)	-0.106 ($p = 0.480$)
Fat Mass (kg)	0.350 ($p = 0.017$)	-0.442 ($p = 0.002$)
*P*hase angle	0.003 ($p = 0.985$)	-0.299 ($p = 0.041$)
MIS (0-30)	0.006 ($p = 0.969$)	0.046 ($p = 0.757$)

ESRD is associated with an abnormal lipid profile. In a recent study[14], adiponectin almost doubled its values in HD patients and seemed to be an important determinant in HDLc and TG levels, improving the lipid profile in these patients. It is still unknown whether there is a direct effect of adiponectin on triglycerides levels or there are other determinants of their expression. Several hypotheses exist such as the alternation of the expression of specific transcription factors, eg PPAR [15].

Conclusions

Fat mass is of important consideration when calculating adipokines levels and their possible correlations with other variables. Several discrepancies among studies regarding the relationship between adipokines with inflammatory and cardiovascular risk factors can be attributed to this fact and fat mass has always to be taken into account. The only statistically significant result found in this work, that is a constant finding throughout studies[7,16,17] is the inverse correlation of adiponectin with triglycerides levels. The correlation of adiponectin with dyslipidemia should be further investigated due to the importance of dyslipidemia in cardiovascular mortality and morbidity in ESRD patients.

Conflict of Interest

The Authors declare that there are no conflicts of interest.

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