COMPARING SERUM LEPTIN AND ADIPONECTIN LEVELS IN CONTROLLED AND NON-CONTROLLED TYPE 2 DIABETES

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Abstract

INTRODUCTION: It has been demonstrated in recent studies that abnormal levels of adipocytokines may contribute to insulin resistance and type 2 diabetes. The aim of the present study was to compare serum leptin and adiponectin levels in controlled and non-controlled type 2 diabetes.

METHODS: 117 patients with controlled and non-controlled type 2 diabetes were studied. Patient, were divided into two groups based on their serum HbA1c level; there were 62 patients in the controlled group (6 %< HbA1c≤ 8%) and 55 patients in uncontrolled group (HbA1c>8%). Parameters like age, sex, duration of diabetes and biochemical indicators such as fasting blood sugar, HbA1c, insulin resistance, leptin and adiponectin were determined.

RESULTS: Higher leptin and lower adiponectin levels were observed in non-controlled type 2 diabetes. The levels of fasting blood sugar and insulin resistance were significantly higher in the non-controlled group (P<0.05).

CONCLUSION: Leptin and adiponectin may play an important role in the regulation of insulin sensitivity and control of type 2 diabetes.

Keywords: Type 2 Diabetes, Insulin resistance, Leptin, Adiponectin.

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Introduction

Type 2 diabetes mellitus is a syndrome characterized by insulin resistance and/or defective insulin secretion.[1] Recent research has demonstrated that adipose tissue is an active endocrine tissue, which secretes hormones such as leptin and adiponectin, referred to as adipocytokines.[2] In recent years, these 2 adipocytokines have been thought to possess various physiological activities.[3] Abnormal levels of adipocytokines may contribute to insulin resistance.

Leptin, the product of the obese (ob) gene,[4] is produced by adipose tissue and is secreted into the circulation. Leptin plays a critical role in the regulation of body weight by inhibiting food intake and stimulating energy expenditure.[5] Leptin resistance is related to the development of insulin resistance in individuals with type 2 diabetes.[6]

Adiponectin, a 244-amino acid protein derived from adipose tissue is released into the circulation[7] and appears to be linked to glucose homeostasis since plasma adiponectin levels are lower in diabetic subjects.[7-9] Hypoadiponectinemia was an independent risk factor for progression to type 2 diabetes.[10]

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Both adipocytokines might be exceedingly important in the regulation of inflammation related to type 2 diabetes.

The aim of the present study was to compare serum leptin and adiponectin levels in controlled and non-controlled type 2 diabetes.

Materials and Methods

One hundred seventeen Iranian type 2 diabetic patients were enrolled for this case-control study. Subjects were screened by medical history questionnaire, physical examination, and fasting blood profile. They consisted of 61 women and 56 men. The minimum duration of diabetes was 3 years (range, 3-30 years). The patients were assigned to two groups according to their HbA1c level; there were 62 patients in the controlled group (6%<HbA1c≤ 8%) and 55 patients in the uncontrolled group (HbA1c>8%). No patients had received insulin therapy. In these two groups, parameters like age, sex, duration of diabetes and biochemical indicators such as fasting blood sugar, HbA1c, insulin resistance, leptin and adiponectin were determined. All subjects gave their informed consent.

Blood was drawn in the morning after overnight fasting. The plasma fasting glucose level was measured using an automated enzymatic method. HbA1c was measured by high performance liquid chromatography. Plasma insulin was measured by a commercial radioimmunoassay kit (Bio source, USA). Serum leptin and adiponectin concentrations were measured by using commercial ELISA kits (Bio-vendor laboratory Medicine, Brno, C2ech Republic). The insulin resistance index was assessed by the homeostasis model assessment and was calculated as follows:[22,23] HOMA-R= FIRI(μu/ml)FPG(mg/dl)/405.

Data are presented as mean±SD (standard deviation). Differences between the two groups were assessed by two-tailed Student's t-test. Significance of the correlations for leptin and adiponectin was assessed by using Pearson's rank correlation analysis. Results were considered significant with two-tailed P values of <0.05.

Results

The subjects studied were all Iranian type 2 diabetic patients (56 men and 61 women) with an age range of 41-69 years. The mean±SD of the variables as well as the clinical and laboratory characteristics of patients are presented in Table 1.

Compared with controlled type 2 diabetic patients, non-controlled patients had significantly higher levels of fasting insulin, insulin resistance and HbA1c. No significant difference was observed in age, diabetes duration between the 2 groups.

Higher leptin and lower adiponectin was observed in non-controlled diabetes, but the difference was not statistically significant. In both groups (controlled and non-controlled) leptin and adiponectin levels in women were significantly higher than in men (P<0.001, table not shown). A statistically significant positive correlation was found between leptin and adiponectin (P=0.002, Figure 1).

Discussion

In this case-control study, we measured 2 serum adipocytokines, namely adiponectin and leptin. We also determined fasting insulin, insulin resistance and HbA1c. Adiponectin and leptin levels were lower in non-controlled diabetic patients and higher in controlled diabetic patients. Furthermore, we found an indirect significant relationship between adiponectin and insulin resistance, as well as a direct significant relationship between leptin and insulin resistance.

TABLE 1. Clinical and laboratory characteristics of the patients.

Variable	Diabetes (controlled)	Diabetes (non-controlled)
N	62	55
Age (years)	56.82±7.61	54.27±7.53
Diabetes duration (years)	9.94±6.75	10.89±6.41
BMI (kg/m²)	27.65±3.89	29.49±4.34
Glucose (mg/dl)	136.15±40.59	214.36±68.22
Insulin (μu/ml)	8.76±7.17	13.53±9.74*
HOMA-IR	2.64±2.95	5.67±6.96*
HbA1c (%)	7.09±0.58	8.88±0.64*
Leptin (ng/ml)	17.66±16.55	20.39±15.2
Adiponectin (μg/ml)	6.98±3.42	6.17±3.6

N: number; BMI: body mass index; HOMA-IR: homeostasis model assessment-insulin resistance; HbA1c: hemoglobin A1c. All data are shown as means±SD; *P< 0.001

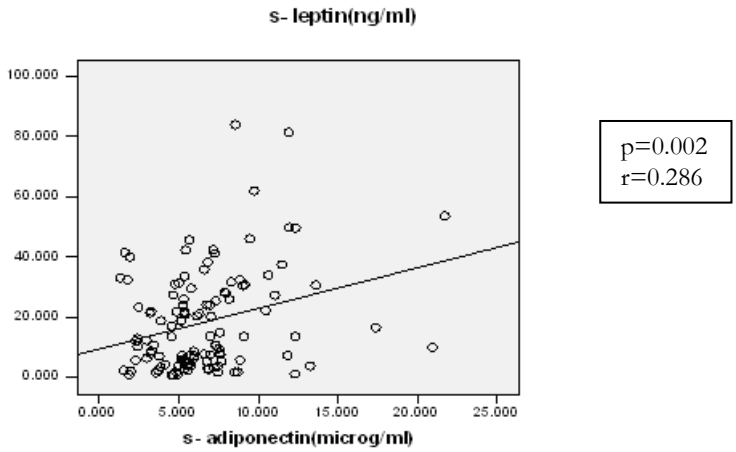

FIGURE 1. Relationship between leptin and adiponectin in all patients.

It has been demonstrated by different studies that hyperleptinemia is an independent risk factor for progression of insulin resistance in type 2 diabetes.[11,12] Adiponectin is lower in human and rodent models of obesity and type 2 diabetes. Reduced adiponectin is related to impaired insulin action in type 2 diabeticts.[13] Adiponectin concentration was significantly associated with insulin sensitivity.[14] In our study, non-controlled diabetics also had higher insulin resistance and we found an indirect significant relationship between adiponectin and insulin resistance in both groups. Koerner et al. (2005) demonstrated that lower adiponectin in non-controlled type 2 diabetics increases the risk of progression to type 2 diabetes and precedes the manifestation of diabetic complicated problems independently of all factors.[15] Adiponectin treatment reverses insulin resistance in animal models.[14] In the diabetic subjects, adiponectin and leptin levels were significantly lower and higher, respectively, than in subjects with normal glucose tolerance (NGT) and impaired glucose tolerance.[16] Several studies have shown that adiponectin levels in diabetics are lower than in those with impaired glucose tolerance (IGT) and healthy subjects,[8,9] however, Ryan et al. (2003) showed that prediabetic women have adiponectin levels twofold lower than those in normal or diabetic women.[17] Wu et al. (2004) demonstrated that leptin levels in diabetics are higher than in normal subjects.[18]

In the current study, serum leptin levels were positively correlated with serum adiponectin levels ($P<0.05$), whereas in other studies, there was a negative correlation between leptin and adiponectin levels in diabetic and normal subjects.[17,19] There was a negative correlation between leptin and adiponectin in diabetic and healthy people, but our findings raise the possibility that the negative correlation between leptin and adiponectin may be lost in diabetes.

In our study, leptin and adiponectin levels in women were significantly higher than in men (in both groups), partly as a result of inhibition by androgens and stimulation by estrogens.[20,21] Kim et al. (2005) showed (as our study) that in diabetics, the fasting adiponectin concentrations were significantly higher in women than in men;[22] however, in yet another similar study, adiponectin concentrations were higher in women overall (all groups included) but not in women classified as type 2 diabetes. These findings raise the possibility that gender differences in relation to adiponectin may be lost in diabetes.[14]

In short, leptin and adiponectin may be important in the regulation of insulin sensitivity and control of type 2 diabetes.

Serum leptin and adiponectin levels were higher and lower, respectively, in non-controlled diabetics and controlled diabetics. Furthermore, we found that these differences affected insulin sensitivity; hence, intensive control of blood sugar to bring HbA1c levels as close as possible to physiological levels (preferably less than 7 %),[23] can improve insulin sensitivity, affect adipocytokines levels and reduce complications of type 2 diabetes.

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