

SERUM LEVELS OF OMENTIN ARE NOT ALTERED IN DRUG-NAIVE PATIENTS WITH MAJOR DEPRESSION: A PILOT STUDY

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received: 9.10.2013;

revised: 14.1.2014;

accepted: 3.2.2014

SUMMARY

Background: Decreased plasma levels of omentin, a relatively novel adipokine, are shown to be associated with metabolic abnormalities and proinflammatory states. Although other adipokines such as leptin and adiponectin have been extensively investigated in patients with major depressive disorder (MDD), no studies have evaluated omentin levels in major depression. Therefore, this study sought to test the hypothesis that drug-naive patients with MDD would have lower serum omentin levels than a healthy control group similar in age, sex, and body mass index.

Subjects and methods: Thirty patients with MDD (10 men) and 30 healthy control subjects (10 men) were studied. Plasma concentration of omentin, along with other biochemical parameters, was measured after a period of fasting. The severity of depression was determined by the Beck Depression Inventory.

Results: No significant difference was found between patients with MDD (723.3±233.8 ng/ml) and healthy comparison subjects (670.7±351.8 ng/ml) in mean plasma concentrations of omentin ($p>0.05$). There was no significant correlation between plasma omentin levels and depression severity ($r=-0.147$; $p>0.05$).

Conclusions: This is the first investigation of omentin levels in patients with MDD. The hypothesis that circulating omentin levels would be different in depressed patients than in healthy controls is not supported by our data.

Key words: adipokines - major depression - omentin

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INTRODUCTION

Major depressive disorder (MDD) is one of the most common psychiatric disorders, with a lifetime prevalence of 16.2% and a 12-month prevalence of 6.6% (Kessler et al. 2003). An increasing number of observational studies indicate that depressive symptoms are associated with cardiovascular disease (CVD) or mortality, not only in patients with CVD (Barth et al. 2004), but also in individuals without CVD (Wulsin & Singal 2003). Depression is also shown to be closely related to metabolic syndrome and diabetes mellitus (Ali et al. 2006, Egede 2004, Herva et al. 2006, Kahl et al. 2012). Pathophysiological explanation of the observed connection between major depression and cardiometabolic abnormalities remains controversial, although several factors have been suggested, including unhealthy life style habits (Bonnet et al. 2005), activation of the hypothalamic-pituitary-adrenal system (Heuser 1998), oxidative damage (Maes et al. 2011), and increased platelet reactivity (Canan et al. 2012).

Recently, adipokines, secreted from adipose tissue, have emerged as novel mediators of the link between depression and metabolic abnormalities (Lu 2007). Adipokines are bioactive components that are postu-

lated to contribute to the regulation of insulin sensitivity (Dyck et al. 2006), appetite (Ata et al. 2010), energy balance (Ahima et al. 2008), blood pressure (Yiannikouris et al. 2010), and inflammation (Ouchi et al. 2011). More than 50 types of adipokines have been isolated and characterized (Lago et al. 2009). Leptin, adiponectin, ghrelin, and resistin are among the most widely investigated adipokines in patients with major depression (Lu 2007, Lutter & Elmquist 2009, Taylor & Macqueen 2010). However, to our knowledge, no studies have examined the association between depression and omentin, a relatively novel adipokine. Circulating omentin levels are reduced in patients with metabolic abnormalities (Shibata et al. 2012). Low serum levels of omentin are also associated with diabetes, cardiovascular disease, inflammation, and endothelial dysfunction (Moreno-Navarrete et al. 2011, Tan et al. 2010).

This study tested the hypothesis that drug-naive patients with major depression have lower serum omentin levels than a healthy control group matched for age, sex, diet and, various anthropometric measures. We also aimed to investigate the relationship between severity of depression and serum omentin levels in depressive patients.

SUBJECTS AND METHODS

Subjects and procedure

Thirty drug-naive, depressive outpatients, assessed in Department of Psychiatry, School of Medicine of the Izzet Baysal University, Bolu, were recruited to this study. They were selected through the Structured Clinical Interview for DSM-IV® Axis I Disorders (SCID-I) (First et al. 1995), applied by a trained psychiatrist, and met the DSM-IV criteria for a current episode of MDD. The severity of depressive episode was determined by the 21-item Beck Depression Inventory (BDI) (Beck et al. 1961), which was found to be reliable and valid in a Turkish speaking population (Hisli 1989).

The comparison group comprised volunteers selected from apparently healthy subjects who visited the Abant Izzet Baysal University Hospital for a routine checkup. They were screened for physical condition through clinical examinations, laboratory tests and electrocardiograms. Moreover, they had a mental health screening through a psychiatric interview (SCID-I) for exclusion of any present, past and family (first degree) history of axis-I diagnoses.

Patients with major depression and controls were ineligible to participate in the study if they met any of the following exclusion criteria: existence of any other mental disorders; alcohol or illicit drug abuse; treatment with any drugs or vitamin supplements within 6 months before entry; obesity (BMI >30 kg/m²); pregnancy; and heavy smoking (more than 15 cigarettes per day). Clinically significant abnormalities on the baseline physical examination, electrocardiogram or laboratory test results were also criteria for exclusion from study participation. All subjects were on a regular diet during the study period.

The study was carried out in accordance with the latest version of the Declaration of Helsinki and the study protocol was approved by the local ethical committee (Abant Izzet Baysal University Ethical Committee of Clinical Investigations). Adequate understanding and written informed consent was obtained from all participants.

Biochemical measurements

Blood samples were drawn in the morning around 10 a.m. from a forearm vein of the participants at the end of an overnight fasting period at least 10 h. Fasting blood samples were obtained for analysis of total cholesterol, triglycerides, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, uric acid, glucose, and Hemoglobin A1c with standard methods.

Omentin measurement

Venous blood samples were centrifuged within 15 min of collection, at 2,750 g for 10 min, and the super-

natant plasma was then transferred into polypropylene tubes at -80 °C until the assays were determined. Omentin concentrations were determined using enzyme-linked immunosorbent assay according to the manufacturer's protocol. Plasma omentin levels were assessed using a commercial enzyme-linked immunosorbent assay kit (Bio Vendor, Brno, Czech Republic). The linear range of the assay was 0.50–64.0 mg/l. The inter- and intra-assay coefficients of variation were 4.4 and 3.2%, respectively.

Anthropometric measurements

Anthropometric measurements obtained in this study included height, weight, body mass index (BMI), and waist circumference. BMI was calculated as body weight divided by height squared (kg/m²). Waist circumference (cm) was considered as the point midway between iliac crests and the costal margins.

Statistical Analysis

Statistical analysis was done by SPSS statistical software (SPSS for Windows 16.0, Inc., Chicago, IL, USA). Nominal parameters were compared with Student's t-test. Categorical variables were compared using chi-square test. Pearson's correlation test was used to examine relations among omentin levels and other continuous variables. Differences were considered significant at P<0.05 for all these tests.

RESULTS

Analysis of sociodemographic and biochemical data including plasma omentin levels showed no significant differences between the patient and comparison groups (Table 1), (Figure 1).

There were no significant differences between men (n=10) and women (n=20) with major depression with regard to plasma omentin concentrations (693.6±261.8 ng/ml, versus 782.7±159.8 ng/ml; p=0.334). Plasma omentin levels were not different in female patients and in female comparison subjects (p>0.05). Also, compared with the healthy male subjects, the depressive male patients had similar plasma omentin concentrations (p>0.05) (Table 2).

In the patients with MDD, plasma omentin concentrations did not significantly correlate with severity of illness as measured with the BDI (n=30; r=-0.147; p=0.357). In addition, there was not a correlation between plasma levels of omentin and BMI (r=-0.072; p=0.694), waist circumference (r=-0.220; p=0.226), fasting glucose (r=-0.014; p=0.941), total cholesterol (r=-0.113; p=0.539), HDL cholesterol (r=0.254; p=0.160), LDL cholesterol (r=-0.013; p=0.943), and triglycerides (r=-0.299; p=0.096). Omentin levels correlated inversely with age (r=-0.429; p=0.001) and hemoglobin A1c (r=-0.560; p=0.001).

Table 1. Comparison of general characteristics and biochemical parameters in drug-naive patients with major depression and healthy controls

	Controls (n=30)	Patients (n=30)	p
Age (years)*	39.7±14.2	34.9±10.9	0.154
Sex (F/M)**	20/10	20/10	0.371
Body mass index (kg/m ²)*	25.2±2.9	24.6±3.3	0.484
Waist circumference (cm)*	78.6±7.3	77.6±11.4	0.710
Fasting glucose, mg/dl*	93.8±11.0	90.6±12.5	0.310
Hemoglobin A1c, %*	5.3±0.6	5.4±0.7	0.676
Total cholesterol, mg/dl*	192±32.7	178.4±26.6	0.113
HDL cholesterol, mg/dl*	41.5±9.7	41.3±8.9	0.917
LDL cholesterol, mg/dl*	123.2±33.5	111.7±24.9	0.138
Triglycerides, mg/dl*	135.9±50.7	126.7±62.7	0.533
Plasma omentin, ng/ml*	670.7±351.8	723.3±233.8	0.498

HDL: high-density lipoprotein; LDL: low-density lipoprotein; *Mean±Standard deviation; **Frequencies

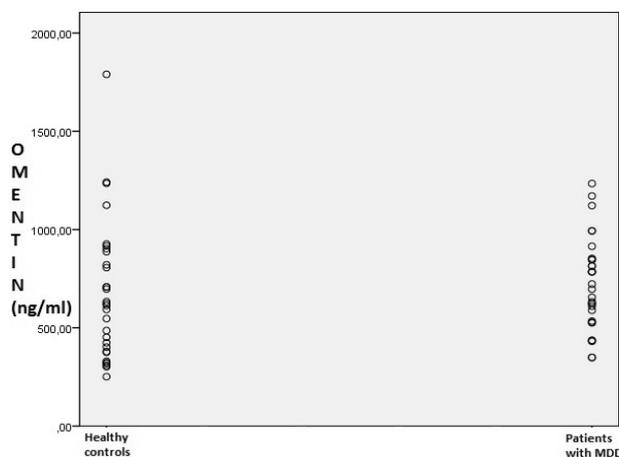


Figure 1. Scatter-plot diagram of omentin plasma levels in patients with MDD and healthy controls

Table 2. Comparison of plasma omentin levels in drug-naive female/male patients with major depression and female/male healthy controls

	Plasma omentin, ng/ml (Mean± Standard deviation)	p
Female patients (n=20)	693.6±261.8	0.351
Female controls (n=20)	595.9±381.2	
Male patients (n=10)	782.7±159.8	0.679
Male controls (n=10)	820.4±233.9	

DISCUSSION

In the present study, our goal was to provide preliminary data on omentin levels in patients with MDD. We found that patients with major depression did not have significantly different plasma omentin levels from comparison subjects with no history of mood disorders. Moreover, plasma concentrations of omentin were not associated with depressive symptom severity.

An increasing number of studies have been performed to examine the question whether adipokine levels are different in patients with MDD than in healthy controls. The results from these studies have

been mixed and conflicting, with some suggesting that adipokine levels are altered (Antonijevic et al. 1998, Diniz et al. 2012, Zeman et al. 2009) and others suggesting that they are not changed (Deuschle et al. 1996, Pan et al. 2008) in depressed individuals when compared with non-depressed comparison subjects. However, only a few studies have evaluated adipokine levels in drug-free or drug-naive depressed patients. In the study by Gecici et al (2005), 26 drug-free depressive patients with atypical features were shown to have higher serum leptin levels than healthy controls. Also, Leo et al (2006) have found that first episode, drug-naive patients with MDD exhibited lower plasma adiponectin concentrations compared to matched healthy subjects. However, Kluge et al (2009) have shown that nocturnal ghrelin secretion patterns did not differ between drug-free depressive patients and healthy volunteers. In the present study, we observed that omentin levels in drug-naive patients with MDD were comparable to those found in healthy subjects of similar age, sex, and BMI.

To date, there have been no studies on the relationship of omentin and MDD. Former studies have reported that omentin levels were decreased in proinflammatory states (Tan et al. 2010), and metabolic disorders (Shibata et al. 2012). However, as plasma omentin levels were similar in patients with MDD and in comparison subjects, the hypotheses that circulating omentin levels would be diminished in major depression, is not supported by our findings.

A sexual dimorphism for adipokine levels has been reported even after controlling for differences in body mass index (Laughlin et al. 2006). However, in our study, plasma omentin concentrations were similar between women and men with depression. In addition, neither women nor men with major depression exhibited different omentin levels when compared with female and male controls, respectively. According to these findings, we may conclude that omentin concentrations are probably not affected by gender differences in depressive patients.

Omentin levels are reported to be negatively correlated with BMI (de Souza Batista et al. 2007). Thus, in order to exclude the confounding effect of obesity, we selected only non-obese patients and comparison subjects. Moreover, in prospective studies, adipokine concentrations were shown to change after treatment with antipsychotics in patients with MDD (Ishitobi et al. 2012, Moosa et al. 2003, Weber-Hamann et al. 2007). Given these findings, drug-free status of patients in our study may contribute to rule out the possible effect of antidepressant medication on omentin concentrations. Despite these strengths, there are three important limitations to this study. First, the study sample was small; therefore our results should be replicated in a larger sample before more definitive conclusions can be drawn. Second, the determination of other adipokines such as leptin, ghrelin, and adiponectin would also have been useful to elicit information regarding information on associations among adipokines in MDD. Third, the relationship of plasma concentrations of omentin and markers of inflammation were not investigated.

CONCLUSIONS

We believe this study is the first to investigate omentin levels in patients with MDD. The findings of our study show that plasma omentin concentrations are similar in physically healthy, non-obese, never-medicated patients with major depression when compared with physically and mentally healthy individuals. Further studies are needed to investigate the effect of antidepressant treatment on omentin levels in depressive patients. It will also be of interest in future studies to determine whether omentin levels are altered in other psychiatric disorders as well.

Acknowledgements: None.

Conflict of interest: None to declare.

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