

SHORT COMMUNICATION

Serum Visfatin Levels in Patients with Anorexia Nervosa and Bulimia Nervosa

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Summary

Visfatin is an adipose tissue-derived hormone shown to correlate with visceral fat mass in patients with obesity. Its possible role in patients with different types of eating disorders is unknown. We measured fasting serum levels of visfatin and leptin and surrogate measures of insulin sensitivity in 10 untreated patients with anorexia nervosa (AN), 10 untreated patients with bulimia nervosa (BN) and 20 age-matched healthy women (C) to study the possible role of visfatin in these disorders. Patients with AN had severely decreased body mass index (BMI) and body fat content. BMI of BN group did not significantly differ from that of C group, whereas body fat content of BN group was significantly lower compared to C and higher compared to AN group, respectively. Serum glucose levels did not significantly differ among the groups studied, whereas serum insulin and leptin levels and HOMA index were significantly decreased in AN group relative to both C and BN group. In contrast, serum visfatin levels in both patients with AN and BN did not differ from those of C group. We conclude that circulating visfatin levels are not affected by the presence of chronic malnutrition in AN or binge/purge eating behavior in BN.

Key words

Anorexia nervosa • Bulimia nervosa • Visfatin • Adipose tissue

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Visfatin is a novel adipokine originally described to be produced predominantly by visceral adipose tissue and to exert insulin-mimetic and adipogenic effects (Fukuhara *et al.* 2005). Contrary to the initial report (Fukuhara *et al.* 2005), further studies concerning the association of visfatin with obesity and diabetes have brought up controversial results (Haider *et al.* 2006, Jian *et al.* 2006, Lopez-Bermejo *et al.* 2006, Chen *et al.* 2007, Dogru *et al.* 2007, Sandeep *et al.* 2007, Varma *et al.* 2007). Furthermore, the predominant contribution of visceral over subcutaneous fat depot to serum visfatin in humans has been questioned by some studies (Berndt *et al.* 2007). The effect of weight loss on circulating concentrations of visfatin in obese patients has been numerously documented, but the results are rather conflicting (Haider *et al.* 2006, Krzyzanowska *et al.* 2006, Manco *et al.* 2007).

It is currently unclear whether visfatin represents a marker of fat mass and/or function or whether it may also exert a direct regulatory role in energy metabolism. To our best knowledge, the changes and possible role of visfatin in the pathophysiology of eating disorders have not been described so far. The restrictive form of anorexia nervosa (AN) represents an extreme example of psychosomatic-based malnutrition induced by chronically decreased food intake caused by inappropriate fear of obesity and distorted body image (DSM-IV 1994). As a consequence of this abnormal self-body attitude, the severe weight and fat loss occurs in these patients.

Bulimia nervosa (BN) is an eating disorder characterized, in contrast to AN, by normal or even slightly higher body mass index (BMI). Patients with BN suffer from repeated episodes of binge eating combined with inappropriate compensatory behavior to prevent weight gain such as self-induced vomiting, misuse of laxatives, diuretics, fasting, and excessive exercise (DSM-IV 1994). The presence of either AN or BN affects body weight and fat mass and consequently energy metabolism differently, but both eating disorders are associated with alterations of various hormones, including adipokines (Baranowska *et al.* 2001, Monteleone *et al.* 2002, Housová *et al.* 2005, Dostálová *et al.* 2006, Křížová *et al.* 2007, Haluzíková *et al.* 2008). These endocrine abnormalities might contribute to the pathophysiology of AN and BN (Dostálová *et al.* 2006, 2007, Modan-Moses *et al.* 2007, Doležalová *et al.* 2007).

We measured circulating concentrations of visfatin in 10 previously untreated female patients with restrictive subtype of AN, 10 previously untreated female patients with BN and 20 age-matched healthy women to study its possible role in the pathophysiology of eating disorders. The characteristic of the study subjects is shown in Table 1.

The diagnosis of eating disorders was based on the diagnostic system (DSM-IV 1994). A clinical evaluation of the patients was performed by an experienced psychiatrist. The structured Clinical Interview MINI 5.0 was used for diagnostic assessment of patients. Patients were hospitalized on the Department of Psychiatry throughout the study. None of the studied subjects suffered from diabetes mellitus, thyroid disorder, and/or acute infectious disorder. All patients with AN had amenorrhea, whereas all patients with BN and healthy women were examined in the follicular phase of the menstrual cycle. Body weight of studied patients remained stable for at least three months prior the study. Written informed consent was provided by all participants before being enrolled in the study. The study was approved by the Human Ethical Review Committee, Institute of Endocrinology, Prague, Czech Republic, and was performed in accordance with the guidelines proposed in the Declaration of Helsinki.

All subjects were measured and weighed. Body fat content was estimated by bioimpedance analysis (Bodystat 1500, Bodystat Ltd., UK). Blood samples for visfatin evaluation were withdrawn between 7 and 8 h a.m. after 12 h of overnight fasting into tubes with aprotinin (500 U/liter). The serum was separated by

Table 1. Anthropometric, biochemical and hormonal characteristics of the studied subjects.

	Controls (n = 20)	AN (n = 10)	BN (n = 10)
Age (years)	22.6 ± 0.45	23.2 ± 1.21	21.2 ± 0.85
BMI (kg/m ²)	21.8 ± 0.36	14.5 ± 0.46* ⁺	20.1 ± 0.72
Body fat content (%)	23.7 ± 1.34	6.3 ± 1.13* ⁺	13.8 ± 1.73*
Fasting insulin (mIU/l)	6.9 ± 0.93	2.2 ± 0.29*	4.6 ± 0.18
Fasting glucose (mmol/l)	4.7 ± 0.12	4.2 ± 0.12	4.2 ± 0.08
HOMA-R	1.4 ± 0.19	0.4 ± 0.06*	0.9 ± 0.05
Fasting visfatin (ng/ml)	44.0 ± 6.27	37.9 ± 6.52	39.8 ± 2.90
Fasting leptin (ng/ml)	5.6 ± 0.64	1.7 ± 0.34* ⁺	5.0 ± 0.76

Values are expressed as mean ± S.E.M.; AN = anorexia nervosa; BN = bulimia nervosa; BMI = body mass index; HOMA-R = homeostasis model assessment of insulin resistance.*p<0.05 vs. C group; ⁺p<0.05 vs. BN group.

centrifugation and stored at -80 °C until being assayed. Serum visfatin concentrations were measured by a commercial EIA kit (Phoenix Pharmaceuticals, Inc., CA, USA). The sensitivity was 1.8 ng/ml, and the intra- and interassay variability was 5 % and 14 %, respectively. Serum insulin concentrations were measured by commercial RIA kit (Cis Bio International, Gif-sur-Yvette, France). Sensitivity was 2.0 µIU/ml, and the intra- and interassay variability was 4.2 and 8.8 %, respectively. Serum glucose concentrations were measured in the Department of Biochemistry of General University Hospital by standard laboratory methods. Homeostasis model assessment (HOMA-R) index was calculated as previously described (Matthews *et al.* 1985) using the following formula: fasting serum insulin (mIU/l) x fasting serum glucose (mmol/l)/22.5. The statistical analysis was performed on SigmaStat Software (Jandel Scientific, San Rafael, CA). The results are expressed as means ± S.E.M. The groups were compared by one-way ANOVA on ranks. Differences between groups were evaluated using unpaired t-test and Mann-Whitney rank sum test as appropriate.

The main results of the study are summarized in Table 1. Patients with AN were extremely malnourished

as evidenced by severely decreased BMI, percent of body fat and reduced serum leptin levels. BMI of BN group did not significantly differ from that of C group, whereas percent body fat of BN group was significantly lower and higher as compared to C and AN group, respectively. Fasting serum visfatin levels in either AN or BN group were not significantly different as compared to control group. Fasting serum glucose levels did not significantly differ among the groups studied, whereas fasting serum insulin and leptin levels were significantly decreased in patients with AN relative to both C and BN group. Serum insulin and leptin levels in BN group tended to be lower relative to C and higher relative to AN group, respectively, but these differences did not reach statistical significance. HOMA index values paralleled serum insulin levels, being markedly decreased in AN group, whereas no significant difference between BN and C group was found (Table 1).

The reduction of BMI significantly correlated with the changes of circulating visfatin levels after weight loss in some (Haider *et al.* 2006, Choi *et al.* 2007), but not in all previous studies (Krzyzanowska *et al.* 2006). However, all these studies were performed in obese patients undergoing bariatric surgery (Haider *et al.* 2006, Krzyzanowska *et al.* 2006, Garcia-Fuentez *et al.* 2007, Manco *et al.* 2007) or low-caloric diet combined with exercise training program (Choi *et al.* 2007). The groups of patients as well as the conditions of these studies are thus absolutely incomparable with chronic malnutrition of our patients with AN. Here we show that circulating levels of visfatin are not primarily related to the specific eating disorder. Furthermore, unchanged visfatin levels in

patients with AN and BN do not support the thesis that visceral fat mass is a major determinant of this hormone in patients with these eating disorders (Zamboni *et al.* 1997). An alternative explanation could be that circulating levels of visfatin may not accurately reflect its production and/or function in peripheral tissues, including adipose tissue. We and others have previously shown that circulating levels of adipokines do not necessarily mirror its tissue levels (Hotamisligil and Spiegelman 1994, Dostálová *et al.* 2006, Doležalová *et al.* 2007). Thus, we can not exclude the possibility that, although circulating levels of visfatin are unchanged, local visfatin effects (e.g., glucose uptake by adipocytes) within the adipose tissue might be altered in patients with eating disorders. Another possible explanation of unaltered visfatin levels in patients with AN could lie in the differences in its clearance in patients with AN (Fukuhara *et al.* 2005, Berndt *et al.* 2007).

In summary, our data show that circulating visfatin levels are not affected either by the presence of chronic malnutrition in patients with anorexia nervosa or binge/purge eating behavior in patients with bulimia nervosa. Further investigation is needed to clarify the possible role of visfatin in eating disorders or its metabolic complications.

Conflict of Interest

There is no conflict of interest.

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