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Adipose tissue resistin levels in patients with anorexia nervosa

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Abstract

Objective: Resistin is a specific fat-derived hormone that affects fuel homeostasis and insulin action in rodents. However, its role in human physiology and pathophysiologic conditions, such as malnutrition, remains uncertain.

Methods: To enhance understanding of the role of resistin in the pathophysiology of anorexia nervosa (AN), we measured plasma resistin levels in 13 women with a restrictive type of AN and in 16 healthy age-matched women (control). Further, we measured resistin levels in the subcutaneous adipose tissue of eight women from the AN group and eight women from the control group with an in vivo microdialysis technique (CMA/107 pump, CMA/60 catheters, CMA Microdialysis AB, Solna, Sweden).

Results: Body mass index, percentage of body fat, fasting plasma leptin and insulin, and homeostasis model assessment index for insulin resistance were severely decreased in patients with AN compared with the control group. Plasma resistin levels were significantly decreased in patients with AN ($P < 0.05$), whereas subcutaneous adipose tissue resistin levels were significantly increased in patients with AN compared with the control group ($P < 0.05$). In both groups, plasma resistin levels showed no significant relation to resistin in dialysate, percentage of body fat, body mass index, homeostasis model assessment index for insulin resistance, and fasting plasma leptin levels.

Conclusion: We demonstrated that AN is associated with decreased plasma resistin levels and increased resistin levels in extracellular space of the abdominal adipose tissue. Plasma resistin levels in patients with AN or in healthy normal-weight women were not directly related to body mass index, percentage of body fat, plasma leptin levels, and insulin sensitivity.

Keywords: Resistin; Anorexia nervosa; Microdialysis; Malnutrition; Leptin

Introduction

Resistin has been proposed as a fuel homeostasis and an insulin action regulator in rodents [1] and may also be involved in hematopoesis, immune function [2], and inflammatory processes [3,4].

Whether or not human resistin is implicated in insulin resistance is still uncertain. Much speculation remains and not only due to the differences observed between human and mouse tissue expressions of the gene [5]. Studies of resistin gene expression in human adipose tissue have been inconsistent [6,7] and the role of adipose tissue resistin gene expression in human insulin resistance has not been confirmed [8]. Resistin expression tended to be higher in obese than in lean subjects [7,9] and was higher in abdominal than in other adipose depots [9,10]. Plasma resistin levels were not found to be different between non-diabetic obese and lean subjects and correlated with insulin resistance, but not with body mass index (BMI) [11]. In contrast, numerous other studies have not reported any relation between circulating resistin levels and insulin resistance [12–14].

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Initially, resistin was supposed to be under tight nutritional control, being decreased by fasting and reincreased by refeeding, suggesting that this factor may be an adipose sensor for nutritional status in rodents [1,15]. Although Valsamikis et al. [16] postulated that serum resistin levels decrease with modest weight loss in obese individuals, other studies in human seem not to support the original hypothesis [17,18]. Further, some investigators found that resistin expression in human white adipose tissue was negatively regulated by cholesterol [19] and by estrogen [20] and was not related to adiposity, blood pressure, fasting plasma glucose level [13], acute fasting, or leptin administration [12].

Anorexia nervosa (AN) is a psychiatric disorder characterized by intense fear of gaining weight, leading to deliberate food intake reduction and life-threatening weight and fat loss in affected patients [21]. As expected, severe malnutrition in AN is associated with altered glucose and lipid metabolism and multiple endocrine perturbations [22]. Some of these abnormalities may be linked to altered adipocytokine production [2]. In a study by Housova et al. [18], plasma resistin levels in patients with AN were not found to be significantly different from those in controls or patients with bulimia nervosa and showed no significant relation to BMI or fat content. However, in vivo resistin levels in human white adipose tissue have not been explored. Our group previously reported that, despite significantly decreased plasma leptin levels in patients with AN, leptin levels in adipose tissue of patients with AN are unchanged [23]. These findings underlined the importance of regional in vivo measurements for a better understanding of systemic hormone function.

Microdialysis is a powerful and safe technique that allows detection of in vivo local changes in interstitial fluid concentrations of various molecules, including hormones [24]. The spectrum of molecules and tissues studied by microdialysis is widening. For example, in our previous study [25], we documented increased sympathetic nervous system activity, especially increased norepinephrine levels, in adipose tissue of patients with AN. More recently, our group adopted the microdialysis technique to study in vivo local adipocytokine production in adipose tissue [26].

Based on our previous results, we hypothesized that resistin concentrations in the extracellular space of abdominal adipose tissue of patients with AN may be altered and may contribute to regional changes in adipose tissue metabolism in AN. Therefore, we examined resistin levels in the interstitial space of adipose tissue in patients with AN by in vivo microdialysis.

Materials and Methods

Study subjects

Thirteen women with a restrictive type of AN (age 23.4 ± 1.39 y, BMI 15.2 ± 0.54 kg/m^2, percentage of body fat [%BF] 6.3 ± 1.01) and 16 healthy control women (age 24.1 ± 1.19 y, BMI 21.2 ± 0.33 kg/m^2, %BF 22.5 ± 1.58) were enrolled in this study. All subjects were non-smokers, had no allergies, and had been free of medications for ≥3 wk before the study. The control women had no history of obesity, hypertension, gastrointestinal diseases, eating disorders, or other psychiatric disorders and had normal physical examination and electrocardiogram. Blood tests confirmed normal blood cell counts and liver and renal functions. Patients with AN were diagnosed according to the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* [27] after detailed medical and psychiatric evaluations. All patients with a restrictive type of AN were examined after 2 wk of hospitalization at the Department of Psychiatry, First Faculty of Medicine, Charles University, Prague, while still in an acute state. Patients with AN were clinically stable and in relatively good health, except for their eating disorder. All control women were in the first 2 wk of their menstrual cycle, whereas all patients with AN had amenorrhea. All subjects provided written informed consent before participation in the study, which was approved by the human ethic review committee of the Institute of Endocrinology (Prague, Czech Republic), and was performed in accordance with guidelines proposed in the Declaration of Helsinki.

Experimental procedures

Upon enrollment, subjects were prohibited from drinking coffee and alcohol and were asked to fast and drink only water the night before the study. All subjects were admitted to the Institute of Endocrinology at 0700 h. After a short medical examination (blood pressure, heart and respiratory rate measurements, and electrocardiogram), %BF was estimated by anthropometric measurement and bioimpedance (Tanita, Tokyo, Japan). All subjects were then placed in a supine position on a comfortable bed in a room kept at 23–25°C, and a venous catheter was placed in the antecubital vein. A microdialysis catheter (CMA/60, CMA Microdialysis AB, Solna, Sweden) with a membrane length of 30 mm and a molecular cut-off of 20 kDa was inserted subcutaneously under sterile conditions, 8–10 cm lateral to the umbilical scar after local anesthesia with 0.1% lidocaine. Immediately after insertion, the catheter was perfused with a physiologic solution using a portable pump (CMA/107). Sterile Krebs-Henseleit buffer [26] was used as a perfusion fluid. A constant perfusion rate of 2 μL/min was maintained throughout the study. Blood and microdialysate collections started ≥45 min after catheter insertion and bedrest to reach steady-state conditions. Microdialysate samples were collected at 45-min intervals between 0800 and 0930 h. Blood samples for resistin and leptin assay were collected into chilled polypropylene tubes containing Na_2EDTA and antilysin. Plasma was immediately separated from whole blood by centrifugation at 3000 rpm for 20 min at 4°C and stored at −20°C until being thawed and assayed.

Table 1
Clinical, anthropometric, and major laboratory characteristics of the study subjects*

	C (n = 16)	AN (n = 13)
Age (y)	24.1 ± 1.19	23.4 ± 1.39
BMI (kg/m^2)	21.2 ± 0.33	15.2 ± 0.54†
Body fat (%)	22.5 ± 1.58	6.3 ± 1.01†
Total fat skinfold (mm)	120.5 ± 12.17	42.1 ± 4.78†
Abdominal fat skinfold (mm)	12.5 ± 2.13	4.8 ± 1.59†
Leptin (ng/mL)	7.7 ± 0.79	1.5 ± 0.25†
Fasting insulin (pmol/L)	14.4 ± 2.11	3.8 ± 1.25†
Fasting glucose (mmol/L)	4.6 ± 0.20	4.3 ± 0.13
HOMA-IR	2.8 ± 0.38	0.8 ± 0.31†

AN, anorexia nervosa; BMI, body mass index; C, control; HOMA-IR, homeostasis model assessment for insulin resistance

* Values are expressed as mean ± SEM.

† Values significantly different from C group, $P < 0.05$.

Subcutaneous blood flow estimation

Subcutaneous adipose tissue blood flow in the abdominal region was estimated by the ethanol washout method [28,29]. Briefly, in our study, ethanol (50 mmol/L) was added to the perfusion fluid and its escape from the perfusate into the adipose tissue interstitial fluid was assessed by measuring changes in the dialysate/perfusate ethanol ratio. Ethanol was measured with a standard enzymatic assay (Sigma Diagnostics Inc., St. Louis, MO, USA).

Calculation of relative resistin recovery and homeostasis model assessment index

Before starting microdialysis perfusion, the relative resistin recovery was calculated in vitro. The procedure is described in detail in our previous report [26].

Insulin resistance (IR) was estimated by using the homeostasis model assessment (HOMA) and the following formula: IR = fasting insulin(pmol/L)×fasting glucose (mmol/L)/22.5[30].

Analytical procedures

Plasma and microdialysate resistin was measured by a commercial human resistin radioimmunoassay (RIA) kit (Phoenix Pharmaceuticals, Inc., Belmont, CA, USA). The detection limit of the assay was 100 pg/mL and the intra- and interassay variabilities were 4.5% and 7.4%, respectively. Plasma leptin was assayed by a commercially available RIA kit (Linco Research, St. Charles, MO, USA). Sensitivity was 0.05 ng/mL and the intra- and interassay variabilities were 4.6% and 8.7%, respectively. Plasma insulin was measured by a commercial RIA kit (Immunotech AS, Prague, Czech Republic). Sensitivity was 0.5 μIU/mL and the intraassay and interassay variabilities were 3.4% and 4.3%, respectively. Plasma glucose levels were measured in a Cobas Integra 400 plus (Roche Diagnostics, GmbH, Mannheim, Germany). All assays were run twice in duplicate.

Data analysis

All results are presented as mean ± SEM. Microdialysate resistin concentrations were corrected for in vitro relative resistin recovery. To evaluate the relation between resistin concentrations and anorexia, an analysis of covariance model was used with adjustment to constant BMI and/or %BF. To achieve Gaussian data distribution and stabilize the variance, resistin plasma and adipose tissue levels were transformed by logarithmic and rank transformations, respectively. Plasma resistin and other parameter relations were analyzed with Spearman's correlation. $P \leq 0.05$ denoted statistical significance.

Results

Characteristics of study subjects

Baseline characteristics of study subjects, including anthropometric measurements, are summarized in Table 1. Patients with AN were extremely malnourished as evidenced by severely decreased BMI, %BF, and total and abdominal skinfold relative to the control (C) group (Table 1).

In vitro relative resistin recovery and abdominal adipose tissue blood flow

At a perfusion rate of 2 μL/min, the in vitro relative resistin recovery was 3.9 ± 0.18% (Table 2). Local adipose tissue blood flow was similar in the AN and C groups (ethanol ratio 42.3 ± 1.25% versus 39.8 ± 0.98%).

Table 2
RRR in vitro at four different perfusion rates*

No. of samples	Perfusion rate (μL/min)	RRR (%)
15	0.5	6.4 ± 0.05
15	1.0	5.3 ± 0.12
15	2.0	3.9 ± 0.18
15	5.0	2.4 ± 0.15

RRR, relative resistin recovery

The CMA/60 catheter with a molecular cutoff of 20 000 Da and the CMA/107 portable pump (CMA Microdialysis AB, Solna, Sweden) were used for the performance. Fifteen samples were taken at each perfusion rate. The perfusion rate of 2 μL/min was chosen for in vivo trials.

* Values are expressed as mean ± SEM.

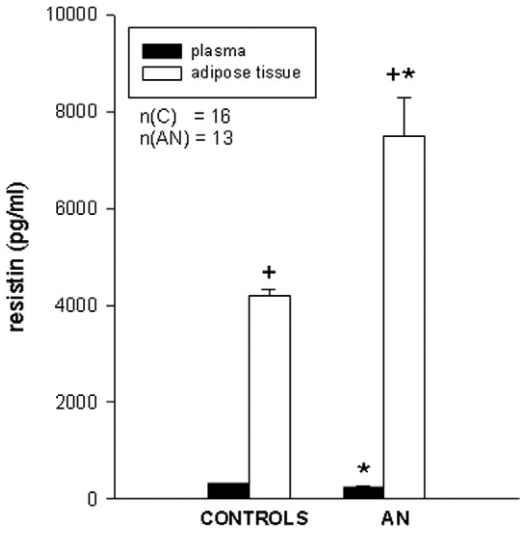

Fig. 1. Resistin concentrations (picograms per milliliter) were measured in plasma and in the extracellular space of abdominal adipose tissue in patients with AN ($n = 13$) and healthy age-matched women ($n = 16$). Resistin concentrations in the extracellular space of abdominal adipose tissue were measured in eight women from the AN group and eight women from the C group. Values are expressed as mean ± SEM. $^{*}P < 0.05$ versus C group; $^{+}P < 0.05$ versus plasma levels. AN, anorexia nervosa; C, control.

Plasma and in vivo abdominal adipose tissue concentrations of resistin, plasma glucose, insulin, leptin, and HOMA index

Fasting plasma resistin levels were significantly lower in patients with AN than in C subjects (252.9 ± 17.93 versus 324.1 ± 15.36 pg/mL, $P < 0.05$), whereas fasting dialysed resistin levels from abdominal subcutaneous adipose tissue were significantly increased in patients with AN compared with C subjects (7501.4 ± 784.85 versus 4201.8 ± 126.76 pg/mL, $P < 0.05$; Fig. 1). Detailed data on plasma and adipose tissue resistin levels of subjects undergoing microdialysis performance are presented in Table 3 for C subjects and patients with AN. Fasting plasma levels of insulin (3.8 ± 1.25 versus 14.4 ± 2.11 pmol/L, $P < 0.05$) and leptin (1.5 ± 0.25 versus 7.7 ± 0.79 ng/mL, $P < 0.05$) were significantly decreased in patients with AN compared with C subjects, whereas fasting plasma glucose was not significantly different between groups (4.3 ± 0.13 versus 4.6 ± 0.20 mmol/L). Insulin resistance estimated by HOMA was significantly decreased in patients with AN compared with C subjects (0.8 ± 0.39 versus 2.8 ± 0.38, $P < 0.05$; Table 1).

Relation of plasma resistin to other parameters

Plasma resistin levels were not significantly related to other parameters studied, including dialysed resistin levels in the abdominal adipose tissue, BMI, %BF, HOMA-IR, and fasting plasma leptin levels in patients with AN or C subjects.

Discussion

The most important finding of this study is that, although plasma resistin concentrations were significantly decreased in severely malnourished patients with a restrictive type of AN, resistin concentrations found in the extracellular space of subcutaneous abdominal adipose tissue of these patients were much higher compared with those in healthy age-matched women. Further, plasma resistin levels were not significantly related to other parameters studied, including BMI, %BF, fasting plasma insulin and leptin levels, and HOMA-IR in patients with AN or C subjects.

In the only other study published thus far, plasma resistin concentrations in patients with a restrictive type of AN tended to be lower than in C women but, in contrast to our results, the difference did not reach statistical significance [18]. Such a discrepancy might be explained by different study design (time of blood sampling between 0700 and 0800 h in that study [18] versus 0800 h in our study) and by the analytical method used for plasma resistin evaluation (enzyme-linked immunosorbent assay versus RIA). Gerber et al. [31] demonstrated the presence of different molecular isoforms of resistin in human blood, and this may raise problems when comparing data from diverse assay systems. Plasma resistin concentrations reported in previously published studies have varied very widely, from high (~50 ng/mL) [32] to low (~7 pg/mL) [33]. RIA for evaluation of plasma resistin levels in our study was run twice in duplicate, with minimal differences in duplication and between assays. Moreover, patients with AN in our study were examined after 2 wk of hospitalization at the Department of Psychiatry and all had amenorrhea. These important characteristics in addition to the age of the study subjects are not

Table 3
Detailed data on plasma and adipose tissue resistin levels in eight subjects from the control group (C1–C8) and eight subjects from the anorexia nervosa group (AN1–AN8) undergoing microdialysis study

Subjects	Plasma resistin (pg/ml)	Adipose tissue resistin (pg/ml)
C1	432.2	4703.9
C2	293.0	4408.0
C3	323.1	4324.3
C4	290.1	3909.6
C5	317.0	4252.3
C6	431.5	4215.6
C7	389.2	3500.1
C8	301.3	4300.2
Mean ± SEM	347.2 ± 21.50	4201.8 ± 126.76
AN1	202.8	5920.1
AN2	340.9	10049.9
AN3	253.9	9890.7
AN4	282.0	5659.3
AN5	250.9	5080.0
AN6	290.5	5200.2
AN7	238.8	8890.3
AN8	320.1	9320.8
Mean ± SEM	234.1 ± 31.21*	7501.4 ± 784.85*

* Values significantly diffent from the control group, $P < 0.05$.

clearly explained in the study of Housova et al. [18]. Because the factors contributing to plasma resistin levels in humans are not well established, all these points could have influenced the obtained results.

Studies that examined the relation between BMI and plasma resistin levels have produced rather contradictory results. Whereas some studies found such results correlative [34], others failed to determine such an effect [11,12,18]. In the present study, we have shown that, despite altered resistin levels in plasma and the extracellular space of abdominal adipose tissue of patients with AN, plasma resistin levels demonstrated no significant relation to BMI or %BF. We therefore suggest that neither reduction of fat mass nor severe weight loss associated with AN are important factors that affect plasma resistin levels in these patients. A possible explanation of low resistin concentrations in plasma of patients with AN may be diminished production in bone marrow [5] and eventually altered stability or clearance of resistin. It is likely that, rather than nutritional status, defective mononuclear/macrophage function [2] and altered cytokine production could contribute to decreased plasma resistin levels in patients with AN. Early cytokines, including tumor necrosis factor-α and interleukin-6, are responsible for secondary induction or enhancement of resistin expression in macrophages [35]. However, plasma levels of tumor necrosis factor-α and interleukin-6 were found to be increased [36], unchanged [37], and decreased [38] in patients with AN. Plasma resistin concentrations were associated positively with leucocytes and with the inflammatory marker high-sensitivity C-reactive protein (CRP) [39]. However, Reilly et al. [40] found that the relation of plasma resistin levels to markers of inflammation is independent of CRP. Although plasma CRP levels were found to be significantly associated with %BF, BMI, and insulin sensitivity [41], plasma levels of CRP showed no deviation from the norm [42] or were undetectable [43] in underweight patients with AN, who have increased insulin sensitivity. Studies have previously shown proinflammatory cytokines, such as interleukin-6, tumor necrosis factor-α, and leptin, to be important inducers of CRP [44], and resistin may also play a role as an inducer of CRP [45]. Thus, the decreased levels of plasma resistin in patients with AN could indicate a decreased systemic inflammatory state in these patients. Although plasma resistin levels in both groups showed no relation to resistin levels found in the extracellular space of subcutaneous abdominal adipose tissue, we can not exclude the existence of a relation between plasma and adipose tissue resistin because of the small number of microdialysated probands in our study.

The initial report by Steppan et al. [1] suggested that resistin might constitute the link between obesity and insulin resistance/diabetes. However, the role of resistin in human physiology is currently unclear and probably different from that in mice. In addition, the producing cell type, which in humans are the macrophages, and the site of the highest production, which is bone marrow [5], differ from those in mice. Nevertheless, the evidence of the production of resistin by human adipocytes was also demonstrated [7,9].

Our microdialysis experiments showed increased levels of resistin in the subcutaneous adipose tissue of patients with AN. These results are free of bias by differences in blood flow, as was verified by the ethanol washout method. Several reasons for the increase in resistin in adipose tissue of AN patients might be due to its pleiotropic character. Interestingly, minibiopsies of abdominal adipose tissue in patients with AN and in C women performed previously by our group showed that the number of adipocytes per volume is larger in AN patients than in C women [23]. Aside from macrophages, resistin is secreted by adipocytes [9], high adipose tissue resistin concentrations in patients with AN could be explained in part by the increased number of small adipocytes in the vicinity of the microdialysing membrane. However, it remains of interest as to whether resistin shows a higher expression in subcutaneous adipocytes of patients with AN.

The finding of increased resistin production in the abdominal adipose tissue of patients with AN may have interesting etiopathogenetic consequences. The changes of resistin levels in patients with AN may reflect defective mononuclear/macrophage functions [2] and/or a number of mononuclear cells. Another interesting point is the existence of multiple forms of human resistin. Because microdialysis is limited by the molecular weight of the substance, we can not exclude the possibility that the results of our study are influenced by a higher proportion of resistin monomers in the subcutaneous adipose tissue of patients with AN and this could lead to higher resistin levels in microdialysate measured in AN. Moreover, our preliminary results showed increased levels of high-sensitivity CRP mRNA in biopsies from the abdominal adipose tissue of patients with AN (our unpublished results). Because high-sensitivity CRP has been positively correlated with resistin [39], high resistin concentrations in the subcutaneous adipose tissue of patients with AN may indicate increased local inflammatory activation.

Conclusion

We have demonstrated that AN is associated with decreased plasma resistin levels and increased resistin levels in the extracellular space of subcutaneous abdominal adipose tissue. Plasma resistin levels in patients with AN or in healthy normal-weight women were not directly related to BMI, %BF, plasma leptin levels, and insulin sensitivity.

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References

[1] Steppan CM, Bailey ST, Bhat S, Brown EJ, Banerjee RR, Wright CM, et al. The hormone resistin links obesity to diabetes. Nature 2001;409:307–12.

[2] Brichard SM, Delporte ML, Lambert M. Adipocytokines in anorexia nervosa: a review focusing on leptin and adiponectin. Horm Metab Res 2003;35:337–42.

[3] Steppan CM, Lazar MA. Resistin and obesity-associated insulin resistance. Trends Endocrinol Metab 2002;13:18–23.

[4] Bokarewa M, Nagaev I, Dahlberg L, Smith U, Tarkowski A. Resistin, an adipokine with potent proinflammatory properties. J Immunol 2005;174:5789–95.

[5] Patel L, Buckels AC, Kinghorn IJ, Murdock PR, Holbrook JD, Plumpton C, et al. Resistin is expressed in human macrophages and directly regulated by PPAR gamma activators. Biochem Biophys Res Commun 2003;300:472–6.

[6] Nagaev I, Smith U. Insulin resistance and type2 diabetes are not related to resistin expression in human fat cells or skeletal muscle. Biochem Biophys Res Commun 2001;285:561–4.

[7] Savage DB, Sewter CP, Klenk ES, Segal DG, Vidal-Puig A, Considine RV, et al. Resistin/Fizz3 expression in relation to obesity and peroxisome proliferator-activated receptor-gamma action in humans. Diabetes 2001;50:2199–202.

[8] Janke J, Engeli S, Gorzelniak K, Luft FC, Sharma AM. Resistin gene expression in human adipocytes is not related to insulin resistance. Obes Res 2002;10:1–5.

[9] McTernan PG, McTernan CL, Chetty R, Jenner K, Fischer FM, Lauer MN, et al. Increased resistin gene and protein expression in human abdominal adipose tissue. J Clin Endocrinol Metab 2002;87:2407–10.

[10] Fain JN, Cheema PS, Bahouth SW, Lloyds HM. Resistin release by human adipose tissue explants in primary culture. Biochem Biophys Res Commun 2003;300:674–8.

[11] Silha JV, Krsek M, Skrha JV, Sucharda P, Nyomba BL, Murphy LJ. Plasma resistin, adiponectin and leptin levels in lean and obese subjects: correlations with insulin resistance. Eur J Endocrinol 2003; 149:331–5.

[12] Lee JH, Chan JL, Yiannakouris N, Kontogianni M, Estrada E, Seip R, et al. Circulating resistin levels are not associated with obesity or insulin resistance in humans and are not regulated by fasting or leptin administration: cross-sectional and interventional studies in normal, insulin-resistant, and diabetic subjects. J Clin Endocrinol Metab 2003;88:4848–56.

[13] Chen CC, Li TC, Li CI, Liu CS, Wang HJ, Lin CC. Serum resistin level among healthy subjects: relatioship to anthropometric and metabolic parameters. Metabolism 2005;54:471–5.

[14] Hasegawa G, Ohta M, Ichida Y, Obayashi H, Shigeta M, Yamasaki M, et al. Increased serum resistin levels in patients with type 2 diabetes are not linked with markers of insulin resistance and adiposity. Acta Diabetol 2005;42:104–9.

[15] Kim KH, Lee K, Moon YS, Sul HS. A cysteine-rich adipose tissue-specific secretory factor inhibits adipocyte differentiation. J Biol Chem 2001;276:11252–6.

[16] Valsamikis G, McTernan PG, Chetty R, Al Daghri N, Field A, Hanif W, et al. Modest weight loss and reduction in waist circumference after medical treatment are associated with favorable changes in serum adipocytokines. Metabolism 2004;53:430–4.

[17] Wolfe BE, Jimerson DC, Orlova C, Mantzoros CS. Effect of dieting on plasma leptin, soluble leptin receptor, adiponectin and resistin levels in healthy volunteers. Clin Endocrinol (Oxf) 2004;61:332–8.

[18] Housova J, Anderlova K, Krizova J, Haluzikova D, Kremen J, Kumstyrova T, et al. Serum adiponectin and resistin concentrations in patients with rescrictive and binge/purge form of anorexia nervosa and bulimia nervosa. J Clin Endocrinol Metab 2005;90:1366–70.

[19] Jove M, Planavila A, Cabrero A, Novell F, Ros E, Zambon D, et al. Reductions in plasma cholesterol levels after fenofibrate treatment are negatively correlated with resistin expression in human adipose tissue. Metabolism 2003;52:351–5.

[20] Huang SW, Seow KM, Ho LT, Chien Y, Chung DY, Chang CL, et al. Resistin mRNA levels are downregulated by estrogen in vivo and in vitro. FEBS Lett 2005;579:449–54.

[21] Ferron F, Considine RV, Peino R, Lado IG, Diaguez C, Casanueva FF. Serum leptin concentrations in patients with anorexia nervosa, bulimia nervosa and non-specific eating disorders correlate with the body mass index but are independent of the respective disease. Clin Endocrinol 1997;46:289–93.

[22] Stoving RK, Hangaard J, Hansen-Nord M, Hagen C. A review of endocrine changes in anorexia nervosa. J Psychiatr Res 1999;33:139–52.

[23] Dostalova I, Kopsky V, Duskova J, Papezova H, Pacak K, Nedvidkova J. Leptin concentrations in the abdominal subcutaneous adipose tissue of patients with anorexia nervosa assessed by in vivo microdialysis. Regul Pept 2005;128:63–8.

[24] Hansen TK, Gravholt CH, Orskov H, Rasmussen MH, Christiansen JS, Jorgensen JO. Dose dependency of the pharmacokinetics and acute lipolytic actions of growth hormone. J Clin Endocrinol Metab 2002;87:4691–8.

[25] Nedvidkova J, Dostalova I, Bartak V, Papezova H, Pacak K. Increased subcutaneous abdominal tissue norepinephrine levels in patients with anorexia nervosa: an in vivo microdialysis study. Physiol Res 2004;53:409–13.

[26] Dostalova I, Pacak K, Nedvidkova J. Application of in vivo microdialysis to measure leptin concentrations in adipose tissue. Int J Biol Macromol 2003;32:205–8.

[27] Diagnostic and statistical manual of mental disorders (DSM-IV). 4th ed. Washington, DC: American Psychiatric Association; 1994.

[28] Enoksson S, Nordenstrom J, Bolinder J, Arner P. Influence of local blood flow on glycerol levels in human adipose tissue. Int J Obes Relat Metab Disord 1995;19:350–4.

[29] Lafontan M, Arner P. Application of in situ microdialysis to measure matabolic and vascular response in adipose tissue. Trends Pharmacol Sci 1996;17:309–13.

[30] Matthews DR, Hosker JP, Rudenski AS, Nazlor BA, Treacher DF, Turner RC. Homeostasis model assessment: insulin resistance and β-cellfunction from fasting plasma glucose and insulin concentrations in man. Diabetologia 1985;28:412–9.

[31] Gerber M, Boettner A, Seidel B, Lammert A, Bar J, Schuster E, et al. Serum resistin levels of obese and lean children and adolescents: biochemical analysis and clinical relevance. J Clin Endocrinol Metab 2005;90:4503–9.

[32] Seow KM, Juan CC, Hsu YP, Ho LT, Wang YY, Hwang JL. Serum and follicular resistin levels in women with polycystic ovarian syndrome during IVF-stimulated cycles. Hum Reprod 2005;20:117–21.

[33] Lewandowski KC, Szosland K, O'Callaghan C, Tan BK, Randeva HS, Lewinski A. Adiponectin and resistin serum levels in women with polycystic ovary syndrome during oral glucose tolerance test: a significant reciprocal correlation between adiponectin and resistin independent of insulin resistance indices. Mol Genet Metab 2005;85: 61–9.

[34] Degawa-Yamauchi M, Bovenkerk JE, Juliar BE, Waston W, Kerr K, Jones R, et al. Serum resistin (FIZZ3) protein is increased in obese humans. J Clin Endocrinol Metab 2003;88:5452–5.

[35] Lehrke M, Reilly MP, Millington SC, Iqbal N, Rader DJ, Lazar MA. An inflammatory cascade leading to hyperresistinemia in humans. Plos Med 2004;1:e45.

[36] Kahl KG, Kruse N, Rieckmann P, Schmidt MH. Cytokine mRNA expression patterns in the disease course of female adolescents with anorexia nervosa. Psychoneuroendocrinology 2004;29:13–20.

[37] Brambilla F, Monti D, Franceschi C. Plasma concentrations of interleukin-1-beta, interleukin-6 and tumor necrosis factor-alpha, and of their soluble receptors and receptor antagonist in anorexia nervosa. Psychiatry Res 2001;103:107–14.

[38] Nova E, Gomez-Martinez S, Morande G, Marcos A. Cytokine production by blood mononuclear cells from in-patients with anorexia nervosa. Br J Nutr 2002;88:183–8.

[39] Kunnari A, Ukkola O, Paivansalo M, Kesaniemi YA. High plasma resistin level is associated with enhanced hsCRP and leucocytes. J Clin Endocrinol Metab 2006;91:2755–60.

[40] Reilly MP, Lehrke M, Wolfe ML, Rohatgi A, Lazar MA, Rader DJ. Resistin is an inflammatory marker of atherosclerosis in humans. Circulation 2005;111:932–9.

[41] Piche ME, Lemieux S, Weisnagel SJ, Corneau L, Nadeau A, Bergeron J. Relation of high-sensitivity C-reactive protein, interleukin-6, tumor necrosis factor-alpha, and fibrinogen to abdominal adipose tissue, blood pressure, and cholesterol and triglyceride levels in healthy postmenopausal women. Am J Cardiol 2005;96:92–7.

[42] Komorowska-Pietrzykowska R, Rajewski A, Wiktorowicz K, Sluzewska A. Immunological system activity in anorexia nervosa. Psychiatr Pol 1996;30:801–10.

[43] Cason J, Ainley CC, Wolstencroft RA, Thompson RP. Polymorphonuclear leucocytes in Crohn's disease and ulcerative proctocolitis: association between enhanced adherence to nylon fibre and disease variables. J Clin Pathol 1988;41:241–6.

[44] Maachi M, Pieroni L, Bruckert E, Jardel C, Fellahi S, Hainque B, et al. Systemic low-grade inflammation is related to both circulating and adipose tissue TNFalpha, leptin and IL-6 levels in obese women. Int J Obes Relat Metab Disord 2004;28:993–7.

[45] Al-Daghri N, Chetty R, McTernan PG, Al-Rubean K, Al-Attas O, Jones AF, et al. Serum resistin is associated with C-reactive protein and LDL cholesterol in type 2 diabetes and coronary artery disease in a Saudi population. Cardiovasc Diabetol 2005;4:10–6.