Journal of Biodiversity and Environmental Sciences (JBES)
ISSN: 2220-6663 (Print) 2222-3045 (Online)
Vol. 4, No. 2, p. 347-352, 2014
http://www.innspub.net

RESEARCH PAPER OPEN ACCESS

Resistin and homeostasis model assessment insulin resistance index in obese men

Aghazadeh Javad*, Ghazvineh Mohamadhosein, Maleki Behnam, Shahriary Bahman

Department of Physical Education and Sport Sciences, Shahre Rey Branch, Islamic Azad University, Shahre Rey, Iran

Article published on February 21, 2014

Key words: Resistin, Body mass index, Insulin action.

Abstract

Resistin, an adipocyte-derived factor has been shown to be associated with inflammatory conditions, obesity and insulin-resistant rodents and humans. In order to investigate whether serum resistin is different between obese and no obese subject and whether this adipokine is related with insulin resistance in obese individuals. Fasting blood samples were collected in fifteen sedentary healthy obese and thirteen normal weight men matched for age 33 – 41 years. Blood samples were analyzed in order to measuring resistin, insulin and glucose concentrations. The insulin resistance index was assessed by homoeostasis model assessment (HOMA-IR). All subjects were no smoker and no athletes. Statistic analysis was done with SPSS 15.0 for Windows. The data showed that serum resistin in obese group was significantly higher than normal weight men (10.19 +/- 1.82 in obese versus 5.05 +/- 1.42 in normal subjects, ng/ml, $p<0.001$). There were no correlations between resistin concentrations with insulin, insulin resistance and glucose concentration in obese subjects ($p \geq 0.05$). These findings suggest a positive relation between obesity and resistin levels independent of insulin resistance in these subjects.

***Corresponding Author:** Aghazadeh Javad ✉ javad_agazadeh60@yahoo.com

Introduction

In recent years it has been found that adipose tissue secretes a number of active peptides and proteins that are collectively known as adipocytokines (Guerre-Millo, 2004). Adipocytokines secreted by adipose tissue can function as autocrine substances, paracrine substances or endocrine hormones, and affect metabolic functions of other organs (You *et al.*, 2008). Among adipocytokines, resistin has a molecular weight of 5/12 kDa (Al-Harithy *et al.*, 2005). In humans, serum resistin in the obese is higher than in lean subjects and resistin levels are associated with BMI and visceral fat (Weyer, 2001).
This adipocytokine causes impaired insulin sensitivity and is associated with insulin resistance and obesity. In rodents, through inhibition of insulin signaling in skeletal muscle, liver and adipose tissue, resistin causes glucose intolerance (Calabro *et al.*, 2007). Further studies in rodents suggest that the levels of mRNA resistin are higher in abdominal fat stores than in thigh fat reserves (Weyer, 2001). Based on the conducted studies, patients with diabetes have a higher concentration of resistin than normal subjects, which is associated with obesity and insulin resistance (Al-Harithy *et al.*, 2005).

This adipocytokine is secreted addition to adipocytes, in muscle, pancreatic islets, and mononuclear cells and in human placenta (Reilly *et al.*, 2005). In contrast to resistin expression in rats, human resistin is expressed primarily in macrophages rather than adipose tissue (Tomaru *et al.*, 2009). In humans and rodents, increased levels of serum resistin are associated with insulin resistance. Impaired glucose tolerance and reduced insulin function by resistin indicate that resistin is effective in the link between obesity and diabetes (Steppan[a] *et al.*, 2001). Preliminary studies have shown that resistin increases in obesity and insulin resistance and reduces insulin sensitivity, however, its neutralization leads to reduced hyperglycemia and improved insulin sensitivity (Steppan *et al.*, 2001). Resistin consumption leads to impaired glucose tolerance and inhibits or loss of resistin improves glucose tolerance and insulin sensitivity (Muse *et al.*, 2004; Sensio *et al.*, 2004l Banerjee *et al.*, 2004).

Scientific evidence suggests that resistin affects energy homeostasis and resistance Insulin although its direct performance in some other tissues such as adipose tissue mass, liver and beta cells is not yet known (Bjorbaek *et al.*, 2004; Sandoval *et al.*, 2003; Brunetti *et al.*, 2004). The study of Lee *et al* showed that resistin levels in obese rat models are higher compared with their lean counterparts (Lee *et al.*, 2005). Injection of resistin into lean rats causes or increases insulin resistance while neutralizing it improves insulin sensitivity in insulin resistant rats (Bastard *et al.*, 2006). Further studies in rodents suggest that the levels of mRNA resistin are higher in abdominal fat stores than in thigh fat reserves (Weyer, 2001). Based on the conducted studies, patients with diabetes have a higher concentration of resistin than normal subjects, which is associated with obesity and insulin resistance (Al-Harithy *et al.*, 2005). This study also attempts to compare the serum levels of serum resistin between obese men and men normal weight, and look into its connection with insulin resistance in non-athletic obese men.

Method and subjects

Subjects

This study involved fifteen sedentary healthy adult obese men (BMI: 31.6 ± 1.5 kg/m2) and thirteen normal weight men (BMI: 22.9 ± 0.35 kg/m2) that matched for age (obese; 38.3 ± 2.19, normal; 37.6 ± 1.56 years). All participants reported being weight stable (±1kg) for 6 months prior to the study and engaged in physical activity less than once per month. After the nature of the study was explained in detail, informed consent was obtained from all participants.

Inclusion or Exclusion criteria

Inclusion criteria were male, aged 33 - 41 years, BMI between 30 – 36 in obese group and 20-25 kg/m2 in normal groups. Neither the obese and normal subjects had participated in regular exercise for the preceding 6 months, nor did all subjects have stable

body weight. Exclusion criteria included disease, use of medicine, daily smoking, and first degree relatives with type 2 diabetes.

Measurements of anthropometrical and clinical markers

Blood samples were obtained for biochemical assays, and anthropometric measurements were taken, including measurement of height and weight and other physical markers. All anthropometric measurements were made by the same trained general physician and under the supervision of the same pediatrician following standard protocols. Body composition monitor (BF508-Omron made in Finland) with a precision error of less than 100 g was used to measure weight and body fat percentage of the subjects. Body mass index was measured for each individual by division of body weight (kg) by height (m2). Abdominal circumference and hip circumference were measured in the most condensed part using a non-elastic cloth meter. Abdominal to hip circumference ratio was measured by dividing the abdominal circumference into that of the hip.

Resistin, insulin and glucose levels were measure after an overnight fast between 8:00 and 9:00 a.m. in two groups. Insulin resistance was determined according to the HOMA-IR as the product of fasting plasma glucose (mM) and insulin (μU/ml) divided by the constant 22.5 (Keskin *et al.*, 2005).Serum resistin and insulin were measured by ELIZA method respectively using (Demeditec insulin ELIZA DE2935, Germany) and (Biovendor-Laboratoria medicina A.S. Czech) laboratory kits. Glucose was determined by the oxidase method (Pars Azmoun, Tehran, Iran).

Statistical analysis

Data were analyzed by computer using SPSS software version 15.0. Kolmogorov-Smirnov test was used to determine of normal status of the data. Differences between groups were calculated using the independent samples t-test. The association between serum resistin concentration and other clinical parameters were assessed using Pearson's correlation coefficient.

Results

Table 1 and 2 show the descriptive anthropometric and biochemical features of obese and normal weight groups respectively. All values are given as mean and standard deviation. Data of table I and 23 show that serum resistin in obese subjects is significant higher than normal subject ($p \leq 0.001$). We also observed that insulin resistance and serum insulin were significant higher in obese group when compared with normal group ($p \leq 0.001$). Fasting glucose was higher than normal in obese subjects ($p = 0.021$).

There were no correlations between serum resistin concentrations with insulin resistance in obese group ($p = 0.09$, $r = 0.46$). In addition, there were no correlations between serum resistin concentrations and glucose ($p = 0.55$, $r = 0.17$) and serum insulin ($p = 0.07$, $r = 0.48$) in obese subjects.

Table 1. Mean and standard deviation of anthropometrical and clinical markers in obese group.

	Mean	Std. Deviation
Age (year)	38.27	2.187
Height (cm)	172.80	4.263
Weight (kg)	94.40	6.957
Abdominal (cm)	104.67	4.271
Hip (cm)	105.87	4.155
WHO	.9887	.01636
BMI (kg/m2)	31.58	1.533
Body fat (%)	32.68	1.909
Visceral Fat	13.27	1.981
Glucose (mg/dl)	93.00	13.120
Insulin (μIU/ml)	20.1067	7.31080
Insulin Resistance	4.7140	2.03955
Resistin (ng/ml)	10.1933	1.82149

Discussion

Despite the reduced levels of some adipocytokines in obesity, weight gain, especially adipose tissue weight, is associated with increased systemic levels of inflammatory mediators such as resistin; as increased resistin levels in adipose tissue and blood have been reported in obese rodents (Samad *et al.*, 1996). The findings of the present study support increased serum levels of resistin in obese men compared with normal weight men. Based on the findings of this study, it was found that obese men have twice resistin levels compared with men of normal weight.

Table 2. Mean and standard deviation of anthropometrical and clinical markers in normal weight group.

	Mean	Std. Deviation
Age (year)	37.62	1.557
Height (cm)	171.15	2.154
Weight (kg)	67.15	1.951
Abdominal (cm)	86.92	2.532
Hip (cm)	94.46	3.178
WHO	.9213	.04472
BMI (kg/m2)	22.92	.353
Body fat (%)	21.64	.879
Visceral Fat	7.54	1.050
Glucose (mg/dl)	85.00	12.774
Insulin (IU/ml)	14.4692	1.08581
Insulin Resistance	3.0485	.58994
Resistin (ng/ml)	5.0538	1.42163

In animals resistin is produced mainly in adipose tissue (Steppan *et al.*, 2001) and decreases insulin sensitivity in adipose tissue and skeletal muscles by reducing insulin-dependent glucose transport (Palanivel *et al.*, 2006; Palanivel *et al.*, 2005; Steppan *et al.*, 2005) and regulates blood glucose levels by increasing release of hepatic glucose (Banerjee *et al.*, 2004). Preliminary studies on the regulation of resistin suggest that resistin decreases during hunger and rapidly increases after satiety (Steppan[b] *et al.*, 2001). Circulating resistin levels increase in obese rats and obese rats fattened by high fat diet.

It is known that increased levels of serum resistin are associated with improvements in insulin resistance (Takashi *et al.*, 2006). Also in some laboratory studies, infusion of resistin in lean animals has been associated with an increase in insulin resistance, whereas neutralizing its effect by certain antibodies has been associated with improved insulin sensitivity in obese insulin resistant animals (Zhang *et al.*, 1994). Resistin reduces insulin-dependent glucose transport while the use of antibodies against resistin is associated with increased membrane transport of glucose (Kim *et al.*, 2001). These findings somehow support the role of resistin in the correlation of adipose tissue, obesity and insulin resistance. If resistin is regulated by insulin, then the main function of resistin is to cause insulin resistance and forming a sensitive positive feedback loop between insulin and resistin (Feng *et al.*, 2008). Although the inhibitory effects insulin on resistin has been reported (Haugen *et al.*, 2001; Shojima *et al.*, 2002), these data do not support the role of resistin in insulin resistance (Haugen *et al.*, 2001). The findings of this study also indicate that the serum resistin levels are not associated with insulin resistance in the research population.

In addition, in the present study, no significant correlation was observed between resistin serum levels and blood glucose and insulin concentrations. Confirming these finding, in a recent study, no correlation was observed between plasma resistin levels and body mass index and insulin resistance in humans (Landt *et al.*, 1997). Considering the lack of correlation between insulin and resistin levels in the said study, the researchers point out that insulin is not a major regulator of resistin in rodents. It has also been stated that resistin is not able to change the signals of insulin receptors but it probably affects insulin-dependent glucose uptake due to a decrease of intracellular activity of glucose transporter cells (Palanivel *et al.*, 2006; Palanivel *et al.*, 2005). In a

general conclusion, although the obese men had higher levels of resistin serum and insulin resistance and the literature also supports the role of both in glucose metabolism, no significant relationship was found between them. It is also possible that resistin and insulin resistance each affects blood glucose levels independently. On the other hand, regarding these statements, the lack of a significant relationship in them may have root in the small number of samples studied.

References

Al-Harithy RN, Al-Ghamdi S. 2005. Serum resistin, adiposity and insulin resistance in Saudi women with type 2 diabetes mellitus. Annals of Saudi Medicine **25(4),** 283-7.

Banerjee RR, Rangwala SM, Shapiro JS, Rich AS, Rhoades B, Qi Y, Wang J, Rajala MW, Pocai A. 2001. Regulation of fasted blood glucose by resistin. Science **303,** 1195-1198.

Banerjee RR, Rangwala SM, Shapiro JS, Rich AS, Rhoades B, Qi Y. 2004. Regulation of fasted blood glucose by resistin. Science **303,** 1196-98.

Bastard JP, Maachi M, Lagathu C, Kim MJ, Caron M, Vidal H, Capeau J, Feve B. 2006. Recent advances in the relationship between obesity, inflammation, and insulin resistance. European Cytokine Network **17(1),** 4-12.

Bjorbaek C, Kahn BB. 2004. Leptin signaling in the central nervous system and the periphery. Recent progress in hormone research **59,** 305–331.

Brunetti L, Orlando G, Recinella L, Michelotto B, Ferrante C, Vacca M. 2004. Resistin, but not adiponectin, inhibits dopamine and norepinephrine release in the hypothalamus. European Journal of Pharmacology **493,** 41–44.

Calabro P, Yeh ET. 2007. Obesity, inflammation, and vascular disease: the role of the adipose tissue as an endocrine organ. Sub-cellular biochemistry **42,** 63-91.

Feng Liu, Hong-Qi Fan, Jie Qiu, Bin Wang, Min Zhang, Nan Gu. 2008. A paradox: Insulin inhibits expression and secretion of resistin which induces insulin resistance. World Journal *of* Gastroenterology **14(1),** 95-100.

Guerre-Millo M. 2004. Adipose tissue and adipokines: for better or worse. Diabetes Metabolism **30(1),** 13-9.

Haugen F, Jorgensen A, Drevon CA, Trayhurn P. 2001. Inhibition by insulin of resistin gene expression in 3T3-L1 adipocytes. Federation of European Biochemical Societies letters **507,** 105-108.

Keskin M, Kurtoglu S, Kendirci M. 2005. Homeostasis model assessment ismore reliable than the fasting glucose/insulin ratio and quantitative insulin sensitivity check index for assessing insulin resistance among obese children and adolescents. Pediatrics **115,** 500–3.

Kim KH, Lee K, Moon YS, Sul HK. 2001. A cysteine-rich adipose tissue-specific secretory factor inhibits adipocyte differentiation. Journal of Biological Chemistry **276,** 11252.

Landt M, Lawson GM, Helgeson JM. 1997. Prolonged exercise decreases serum leptin concentrations. Metabolism **46(10),** 1109-12.

Lee JH, Bullen JW, Stoyneva VL, Mantzoros CS. 2005. Circulating resistin in lean, obese and insulin-resistant mouse models: lack of association with insulinemia and glycemia. American Journal of Physiology - Endocrinology and Metabolism **288,** 625–632.

Muse ED, Obici S, Bhanot S, Monia BP, McKay RA, RajalaMW, Scherer PE, Rossetti L. 2004. Role of resistin in diet-induced hepatic insulin

resistance. Journal of Clinical Investigation **114,** 232–239.

Palanivel R, Maida A, Liu Y, Sweeney G. 2006. Regulation of insulin signalling, glucose uptake and metabolism in rat skeletal muscle cells upon prolonged exposure to resistin. Diabetologia **49,** 183-190.

Palanivel R, Sweeney G. 2005. Regulation of fatty acid uptake and metabolism in L6 skeletal muscle cells by resistin. Federation of European Biochemical Societies letters **579,** 5049-5054.

Reilly MP, Lehrke M, Wolfe ML, Rohatgi A, Lazar MA, Rader DJ. 2005. Resistin is an inflammatory marker of atherosclerosis in humans. Circulation **111(7),** 932-9.

Samad F, Yamamoto K, Loskutoff DJ. 1996. Distribution and regulation of plasminogen activator inhibitor-1 in murine adipose tissue in vivo. Induction by tumor necrosis factor-alpha and lipopolysaccharide. Journal of Clinical Investigation **97,** 37.

Sandoval DA, Davis SN. 2003. Leptin metabolic control and regulation. Journal of Diabetic Complications **17,** 108–113.

Sensio C, Cettour-Rose P, Theander-Carrillo C, Rohner-Jeanrenaud F, Muzzin P. 2004. Changes of glycemia by leptin administration or high fat feeding in rodent models of obesity/type 2 diabetes suggest a link between resistin expression and control of glucose homeostasis. Endocrinology **145,** 2206-13.

Shojima N, Sakoda H, Ogihara T, Fujishiro M, Katagiri H, Anai M, Onishi Y, Ono H, Inukai K, Abe M, Fukushima Y, Kikuchi M, Oka Y, Asano T. 2002. Humoral regulation of resistin expression in 3T3-L1 and mouse adipose cells. Diabetes **51,** 1737-1744.

Steppan CM, Wang J, Whiteman EL, Birnbaum MJ, Lazar MA. 2005. Activation of SOCS-3 by resistin. Molecular Cell Biology **25,** 1569-1575.

Steppan[a] CM, Bailey ST, Bhat S. 2001. The hormone resistin links obesity to diabetes. Nature **409(6818),** 307–312.

Steppan[b] CM, Brown EJ, Wright CM, Bhat S, Banerjee RR, Dai CY. 2001. A family of tissue-specifi c resistin-like molecules. Proceedings of the National Academy of Sciences of the United States **98,** 502-506.

Takashi K, Toshimasa Y, Naoto K, Kazuo H, Kohjiro U, Kazuyuki T. 2006. Adiponectin and adiponectin receptors in insulin resistance, diabetes, and the metabolic syndrome. Journal of Clinical Investigation **116,** 1784–1792.

Tomaru T, Steger DJ, Lefterova MI, Schupp M, Lazar MA. 2009. Adipocyte-specific expression of murine resistin is mediated by synergism between peroxisome proliferator-activated receptor γ and CCAAT/enhancerbinding proteins," The Journal of Biological Chemistry **284(10),** 6116–6125.

Weyer C. 2001. Hypoadiponectinemia in obesity and type 2 diabetes: close association with insulin resistance and hyperansulinemia. Journal of Clinical Endocrinology & Metabolism **86,** 1930-1935.

You T, Nicklas J. 2008. Effects of exercise on adipokines and the metabolic syndrome. Current Diabetes Reports **8,** 7–11.

Zhang Y, Proenca R, Maffei M, Barone M, Leopold L, Friedman JM. 1994. Positional cloning of the mouse obese gene and its human homologue. Nature **372(6505),** 425-32.