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Lifestyle modification increases circulating adiponectin concentrations but does not change vaspin concentrations

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ABSTRACT

The objective of the study was to evaluate the effects of a 10-month lifestyle intervention on the components of the metabolic syndrome (MetSyn) in Koreans with MetSyn as well as on blood concentrations of adiponectin and vaspin. One hundred thirty-eight patients with MetSyn, recruited from a community health care center, were consecutively enrolled in the study; 12 patients dropped of the intervention, leaving 126 subjects (76 men and 50 women; age, 65.3 ± 9.0 years). All participants followed a 10-month lifestyle modification interventional program, including dietary counseling, advice on increasing physical activity, and recommendations to stop or limit smoking and alcohol drinking. Anthropometric and biochemical parameters related to the components of the MetSyn, including blood concentrations of adiponectin and vaspin, were assessed pre- and postintervention. At baseline, adiponectin concentrations were moderately negatively correlated to insulin concentrations and insulin resistance evaluated by the homeostasis model assessment. In response to lifestyle modification, statistically significant changes were found in systolic and diastolic blood pressure, total cholesterol, triglyceride, and insulin concentrations, as well as in homeostasis model assessment of insulin resistance. Adiponectin concentrations postintervention, compared with the preintervention levels, increased (7.2 ± 4.0 vs 6.8 ± 3.9 μg/mL, respectively; $P < .05$), whereas vaspin concentrations remained unchanged (0.25 ± 0.19 vs 0.26 ± 0.20 ng/mL, respectively; $P = .64$). A 10-month lifestyle modification program in Korean patients with MetSyn led to favorable changes in metabolic parameters and adiponectin but not vaspin concentrations.

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1. Introduction

The metabolic syndrome (MetSyn) is a clinical entity characterized by a constellation of metabolic abnormalities and cardiovascular risk factors, including obesity, insulin resistance and glucose intolerance, dyslipidemia, and hypertension [1]. Lifestyle modification, namely, changes in diet and physical activity aiming mainly, but not exclusively, at weight management, constitutes the first-line intervention for the treatment of this syndrome [2]. Weight loss has been found to result in significant improvements in the components of the MetSyn and/or in MetSyn resolution, even at high posttreatment body mass index (BMI) levels [3-8]. However, changes in metabolic parameters may occur in the absence of significant weight loss: previous studies have shown improvements in glycemic control, lipid profile, and blood pressure in response to dietary intervention despite the fact that body weight remained constant [9,10].

Blood levels of several adipokines, adipocyte-secreted molecules playing important roles in insulin resistance and the pathogenesis of the MetSyn, have also been investigated in response to lifestyle modification. Adiponectin, an adipocyte-secreted endogenous insulin sensitizer, is among the most extensively studied adipokines. Low adiponectin concentrations are associated with insulin resistance and inflammation and predict risk for developing diabetes [11-15]. Several studies so far have shown an increase in blood adiponectin levels in response to a diverse array of diet and/or physical activity interventions [16-19]. Vaspin, a member of the serine protease inhibitor (serpin) family, is a newly discovered adipokine [20], originally proposed to represent an intrinsic compensatory mechanism of the adipose tissue in response to decreased insulin sensitivity or glucose impairment [21]. However, its role in insulin resistance and the MetSyn still remains to be elucidated. In obese mice, the administration of recombinant human vaspin significantly improved insulin sensitivity and glucose tolerance [20]. In humans, some studies, but not all of them, support the positive association between serum vaspin levels, BMI, and insulin sensitivity [22-28]. Furthermore, recent evidence indicates that weight loss, induced by lifestyle intervention, pharmacotherapy, or bariatric surgery, reduces serum vaspin concentrations [29-31]. The aim of this study was to evaluate the effect of a 10-month lifestyle intervention on the components of the MetSyn as well as on the circulating levels of 2 adipokines, namely, adiponectin and vaspin, which may potentially mediate the metabolic effects of dietary and exercise interventions, in a group of Korean middle-aged and elderly MetSyn patients.

2. Methods and procedures

2.1. Subjects

Participants in this study were recruited from a community health care center (Guro-Gu Public Health Centre) between March and May 2008. One hundred thirty-eight patients with MetSyn were consecutively enrolled (83 men and 55 women; >40 years old). The diagnosis of the MetSyn was based on the presence of at least 3 of the following 5 metabolic parameters, according to the National Cholesterol Education Adult Treatment Panel III criteria, modified for the Korean population [32,33]: (1) waist circumference greater than 90 cm in men and greater than 80 cm in women, (2) blood triglyceride levels greater than 150 mg/L, (3) high-density lipoprotein cholesterol levels less than 40 mg/dL in men and less than 50 mg/dL in women, (4) blood pressure at least 130/85 mm Hg or use of antihypertensive medication, and (5) fasting plasma glucose levels at least 110 mg/dL or treatment of diabetes mellitus. Ninety-six subjects (71.4%) had diabetes, and 112 (81.7%) had hypertension. Exclusion criteria included presence of severe diabetic complications (eg, diabetic foot or severe diabetic retinopathy), liver dysfunction (aspartate aminotransferase or alanine aminotransferase >2.5 times the reference level), or renal dysfunction (serum creatinine >132 μmol/L); medical history of congestive heart failure, angina pectoris, myocardial infarction, or stroke based on physician's diagnosis; and presence of pregnancy, lactation, or other medical problems that could affect study results or trial participation. Seven men and 5 women dropped out of the intervention (because of time constraints and/or reported inability to attend the program), leaving 126 subjects (76 men and 50 women) for analysis. All participants provided written informed consent. The Korea University Institutional Review Board, in accordance with the Declaration of Helsinki of the World Medical Association, approved the study protocol. At pre- and post-intervention (10 months later), study participants underwent anthropometric and clinical assessment; a blood sample was also obtained in the morning (around 9:00 AM to 10:00 AM) after an overnight food deprivation.

2.2. Intervention

All patients followed a 10-month lifestyle modification interventional program. The intervention was undertaken by 2 nurses who were appropriately trained by a physician and a qualified dietitian. At baseline, participants visited the Guro-Gu Public Health Centre for an initial evaluation. During this visit, usual dietary intake was assessed through a 3-day food record. The lifestyle modification was then individually tailored and planned. Because the traditional Korean diet is high in sodium (because of the sodium content of kimchi foods, stirred vegetables, and meat), one of the primary aims of the intervention was to educate participants on the food sources of sodium, as well as to encourage them to improve food choices by including in their dietary plan fresh vegetables and high-quality protein foods to achieve a balanced, healthy dietary pattern low in sodium. Patients' self-efficacy was enhanced through the provision of simple and goal-oriented nutritional information and individualized dietary plans, as well as by the use of self-monitoring. With regard to physical activity, in addition to information on its metabolic benefits, patients were provided with an exercise plan, customized to their lifestyle, mainly in relation to everyday activities (preferential use of stairs, walking instead of taking the subway, etc). In addition, all participants were encouraged to stop or limit smoking and drinking alcohol.

During the 10-month intervention period, patients visited the Guro-Gu Public Health Centre every other week for lifestyle modification counseling. The sessions were held on an individual basis (10-20 minutes). If patients were unable to attend the sessions, the nurses visited them at their homes or met them online through an ubiquitous medical environment [34]. Furthermore, patients received booster information in the form of health messages via a short message system service 3 times a week. The aim of this strategy was to increase participants' motivation and improve adherence to the lifestyle goals. The messages contained information on nutrition facts, healthy food choices, and ways to increase their physical activity levels.

2.3. *Anthropometric, clinical, and biochemical analyses*

Height and weight were measured without shoes and in light clothing to the nearest 0.5 cm and 100 g, respectively. Body mass index was calculated as weight (kilograms) divided by height (meters) squared. Waist circumference (centimeters) was measured halfway between the 12th rib and the iliac crest. Arterial blood pressure was measured with the patient in a sitting position after having at least 30 minutes of rest.

Blood biochemical analyses were undertaken at the Korea University Guro Hospital laboratory (Seoul, Korea). The glucose oxidase method was used to measure plasma glucose. A human insulin-specific radioimmunoassay kit (Roche, Indianapolis, IN) was used to measure insulin levels, with a coefficient of variation (CV) of 2.2%. Insulin resistance was estimated using the homeostasis model assessment (HOMA-IR) [35]. Serum total cholesterol, triglycerides, and high-density lipoprotein cholesterol were determined by enzymatic methods using a chemical analyzer (Hitachi 747, Tokyo, Japan). Plasma adiponectin levels were measured using an adiponectin enzyme immunoassay kit (Mesdia, Seoul, Korea), with a CV for intra- and interassays of 4.1% to 5.9% and 3.7% to 6.3%, respectively. Plasma vaspin levels were measured using a Quantikine kit (AdipoGen, Seoul, Korea) with a CV for intra- and interassays of 1.6% to 3.9% and 3.4% to 8.7%, respectively.

2.4. *Statistical analysis*

Continuous variables are presented as mean values ± standard deviation, whereas categorical variables are presented as frequencies. Normality tests were applied using the Kolmogorov-Smirnov criterion. Adiponectin, HOMA-IR, insulin, and vaspin levels were log-transformed because of their skewed distributions. Changes in the investigated variables between periods were evaluated by applying the paired-samples *t* test procedure (*t* statistic). Pearson correlation coefficients were also calculated. All reported *P* values were based on 2-tailed tests with significance levels of 5%. The Statistical Package for Social Sciences software, version 13.0 (SPSS 2003, Chicago, IL), was used for the statistical calculations.

3. Results

Age and anthropometric and metabolic characteristics of the study participants at preintervention are presented in Table 1. Their mean BMI was 26.5 ± 3.6 kg/m^2, serum adiponectin concentrations were 6.8 ± 3.9 μg/mL, and serum vaspin concentrations were 0.32 ± 0.40 ng/mL. Correlation analyses were performed to evaluate associations between baseline characteristics and the blood concentrations of the adipokines investigated (Table 2). Insulin and HOMA-IR levels were moderately negatively correlated to adiponectin concentrations at preintervention (r = −0.24, P = .008 and r = −0.27, P = .002) in the entire study sample, as well as in men and women separately, but not to vaspin concentrations.

Statistically significant changes were found in systolic and diastolic blood pressure, total cholesterol, triglyceride, and adiponectin and insulin concentrations, as well as in HOMA-IR levels at postintervention compared with the preintervention levels (Table 1). Vaspin concentrations were not modified (preintervention, 0.26 ± 0.20 ng/mL; postintervention, 0.25 ± 0.19 ng/mL; P = .54). Similarly, no changes were found with

Table 1 – Anthropometric and metabolic parameters of the study participants pre- and postintervention (mean ± standard deviation).

	Preintervention			Postintervention		
	Total sample (N = 126)	Women (n = 50)	Men (n = 76)	Total sample (N = 126)	Women (n = 50)	Men (n = 76)
Age (y)	65.3 ± 9.0	66.1 ± 7.8	64.8 ± 9.7			
Weight (kg)	67.1 ± 10.7	62.9 ± 9.0	70.9 ± 10.5	67.2 ± 10.7	62.0 ± 8.9	70.5 ± 10.6
BMI (kg/m^2)	26.5 ± 3.6	27.3 ± 4.5	26.0 ± 3.2	26.3 ± 3.5	26.9 ± 4.0*	25.8 ± 3.3
Waist circumference (cm)	90.8 ± 7.1	90.6 ± 6.8	91.0 ± 7.4	90.4 ± 7.6	89.8 ± 7.9	90.8 ± 7.5
SBP (mm Hg)	139.1 ± 12.1	136.8 ± 12.5	140.6 ± 11.8	129.1 ± 13.0†	128.1 ± 13.6†	129.8 ± 12.6†
DBP (mm Hg)	83.2 ± 10.4	79.7 ± 11.7	85.6 ± 8.7	76.0 ± 8.7†	74.8 ± 8.6*	76.7 ± 8.8†
FPG (mg/dL)	124.6 ± 34.8	123.4 ± 31.8	125.3 ± 36.8	120.4 ± 34.6	128.3 ± 40.0	115.2 ± 29.6*
Total cholesterol (mg/dL)	194.7 ± 39.0	201.1 ± 45.0	190.5 ± 34.1	164.3 ± 35.6†	172.8 ± 39.4†	158.6 ± 31.9†
Triglycerides (mg/dL)	207.6 ± 94.1	221.8 ± 98.2	198.0 ± 90.6	156.4 ± 64.3†	162.1 ± 63.4†	152.6 ± 65.1†
Insulin (μIU/mL)	5.7 ± 4.1	6.1 ± 3.5	5.5 ± 4.4	4.8 ± 3.5*	5.2 ± 3.8	4.6 ± 3.3
HOMA-IR	1.77 ± 1.54	1.84 ± 1.10	1.71 ± 1.78	1.47 ± 1.20*	1.68 ± 1.28	1.33 ± 1.13*
Adiponectin (μg/mL)	6.8 ± 3.9	8.3 ± 4.5	5.6 ± 3.2	7.2 ± 4.0*	8.6 ± 4.3	6.2 ± 3.4*
Vaspin (ng/mL)	0.26 ± 0.20	0.24 ± 0.17	0.27 ± 0.22	0.25 ± 0.19	0.25 ± 0.20	0.25 ± 0.19

SBP indicates systolic blood pressure; DBP, diastolic blood pressure; FPG, fasting plasma glucose.

* P < .05, compared with the preintervention values.

† $P \leq$ 01, compared with the preintervention values.

Table 2 – Correlations with baseline variables in study participants

	Men			Women		
	Adiponectin (μg/mL)	Vaspin (ng/mL)	HOMA	Adiponectin (μg/mL)	Vaspin (ng/mL)	HOMA
Age	0.222 *	−0.176	−0.176	0.006	0.082	−0.221
Height (cm)	0.086	0.076	0.086	−0.221	0.220	0.150
Weight (kg)	−0.043	−0.128	0.220 *	−0.136	−0.075	0.111
BMI (kg/m^2)	−0.094	−0.102	0.233 *	−0.035	−0.153	0.041
Waist (cm)	0.127	−0.064	0.216 *	−0.021	0.209	0.027
SBP (mm Hg)	−0.083	−0.169	−0.056	0.153	0.116	−0.145
DBP (mm Hg)	−0.033	−0.001	0.048	−0.038	0.261	−0.159
FPG (mg/dL)	−0.164	0.140	0.269 *	−0.053	−0.104	0.066
Total cholesterol (mg/dL)	0.080	−0.253 *	0.167	0.285 *	0.038	0.095
Triglycerides (mg/dL)	−0.244 *	−0.179	0.148	−0.157	−0.067	−0.102
Insulin (μIU/mL)	−0.281 *	0.063	0.955 *	−0.263 *	0.079	0.964 *
Adiponectin (μg/mL)	1.000	−0.006	−0.317 *	1.000	−0.139	−0.281 *
Vaspin (ng/mL)	−0.006	1.000	0.165	−0.139	1.000	0.051
HOMA-IR	−0.317 *	0.165	1.000	−0.281 *	0.051	1.000

Values for adiponectin, vaspin, insulin, and HOMA-IR were log transformed.
* $P < .05$.

regard to body weight, BMI, and waist circumference in the study participants.

4. Discussion

The main finding of the study was that a 10-month lifestyle intervention in patients with MetSyn led to favorable changes in metabolic parameters in the absence of any significant change in BMI or waist circumference. In addition, the intervention had a statistically significant positive effect on adiponectin blood concentrations; however, no changes on vaspin concentrations were observed during this period. So far, the literature is inconclusive on whether improvements of the metabolic profile are mediated by body weight loss. Although most evidence supports that changes in adiponectin levels reflect changes in body weight and mediate improvements of the MetSyn [16,17,36,37], increases in adiponectin concentrations, along with favorable changes in insulin resistance markers, were also observed in the absence of or regardless of weight loss [18,19]. In our cohort, we found an increase in adiponectin, as well as in insulin sensitivity, as assessed by the HOMA-IR index, despite no significant effect on body weight. Possibly, a small but biologically significant change in visceral trunk fat could explain this finding, despite no detectable or measurable changes in waist circumference, as the latter and other anthropometric indices are only moderately correlated with visceral fat evaluated by criterion standard methods [38]. Alternatively or additionally, changes in adiponectin and insulin resistance levels may have been induced by specific dietary factors that were modified in response to the lifestyle intervention. Epidemiological studies provide evidence for the beneficial effect of fruits, whole-grain cereals, dietary cereal fiber intake, and moderate alcohol consumption on adiponectin levels [39-41], whereas adherence to a Mediterranean or other healthy dietary patterns induced increases in adiponectin concentrations and metabolic outcomes [42,43]. However, adherence to the dietary guidelines and lifestyle advice was not evaluated.

Importantly, available evidence so far remains inconsistent with regard to vaspin in relation to the MetSyn. The results of the present intervention study confirm earlier reports indicating that vaspin does not correlate with indices of insulin and glucose metabolism [44], especially among patients with type 2 diabetes mellitus [45]. They are also in accordance with the work of Chang et al [30], who found that serum vaspin concentrations decreased significantly only in those subjects who reduced their body weight by at least 2% from baseline levels, whereas no change was observed in those who were classified as nonresponders, that is, achieving less than 2% reduction in baseline weight.

Interestingly, no association was found between adiponectin concentrations and BMI values of the study participants at baseline. Although in most population groups adiponectin concentrations are negatively correlated with BMI, this has not always been the case. For example, Mente et al [46], in their recent publication, reported no association between adiponectin and BMI in Canadians of South Asian origin. The authors hypothesized that the absence of association may reflect the lack of specificity of measuring central adiposity using BMI in this specific population or may reflect different pathogenic pathways including the type, amount, and distribution of adipose tissue accumulation as well as dietary and genetic influences that may exist among South Asians. Further studies are needed to explore differences between whites and Koreans and/or South Asians in more detail.

An important limitation of the present analysis is the absence of a control group, that is, subjects receiving no intervention. Thus, we cannot rule out the possibility that the observed changes were not the result of the intervention, but rather a normative change over time. One would have expected, however, the components of the MetSyn to worsen and not improve over time. Moreover, it has been previously shown that within-individual variability of adiponectin over 3 years is small, with a correlation of 0.73 [47]. In addition, the fact that adiponectin changes occurred in parallel with changes to HOMA-IR supports our hypothesis that the adiponectin levels were improved in response to the intervention and are not due to random changes or natural evolution over time. Variability and/or random errors in laboratory measurements, as well as imprecision or misclassification in anthropometric measurements, might have also been possible. Such random error/misclassification would have suppressed effect estimates and would have been expected to lead to less significant results. Thus, the results reported herein are valid; and to the extent that no bias was introduced in the selection of study subjects, this information can be generalized to the Korean population, but it remains to be evaluated whether these observations hold true in other populations.

In summary, a 10-month lifestyle modification program for patients with MetSyn, including biweekly individual counseling sessions as well as reminders/booster information via short message system, resulted in significant improvements in metabolic parameters and adiponectin levels, despite no change in BMI or waist circumference. Furthermore, the findings that vaspin levels were not associated with components of MetSyn at baseline and were not altered in response to lifestyle modification indicate that this recently recognized adipokine may not play a role as an insulin-sensitizer factor or marker, comparable to that of adiponectin, in this population group.

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REFERENCES

[1] Pi-Sunyer X. The metabolic syndrome: how to approach differing definitions. Med Clin North Am 2007;91:1025-40 vii.
[2] Magkos F, Yannakoulia M, Chan JL, et al. Management of the metabolic syndrome and type 2 diabetes through lifestyle modification. Annu Rev Nutr 2009;29:223-56.
[3] Christ M, Iannello C, Iannello PG, et al. Effects of a weight reduction program with and without aerobic exercise in the metabolic syndrome. Int J Cardiol 2004;97:115-22.
[4] Villareal DT, Miller III BV, Banks M, et al. Effect of lifestyle intervention on metabolic coronary heart disease risk factors in obese older adults. Am J Clin Nutr 2006;84:1317-23.
[5] Muzio F, Mondazzi L, Sommariva D, et al. Long-term effects of low-calorie diet on the metabolic syndrome in obese nondiabetic patients. Diabetes Care 2005;28:1485-6.
[6] Case CC, Jones PH, Nelson K, et al. Impact of weight loss on the metabolic syndrome. Diabetes Obes Metab 2002;4:407-14.
[7] Kukkonen-Harjula KT, Borg PT, Nenonen AM, et al. Effects of a weight maintenance program with or without exercise on the metabolic syndrome: a randomized trial in obese men. Prev Med 2005;41:784-90.
[8] Phelan S, Wadden TA, Berkowitz RI, et al. Impact of weight loss on the metabolic syndrome. Int J Obes (Lond) 2007;31:1442-8.
[9] Appel LJ, Sacks FM, Carey VJ, et al. Effects of protein, monounsaturated fat, and carbohydrate intake on blood pressure and serum lipids: results of the OmniHeart randomized trial. JAMA 2005;294:2455-64.
[10] Kris-Etherton PM, Pearson TA, Wan Y, et al. High-monounsaturated fatty acid diets lower both plasma cholesterol and triacylglycerol concentrations. Am J Clin Nutr 1999;70:1009-15.
[11] Spranger J, Kroke A, Mohlig M, et al. Adiponectin and protection against type 2 diabetes mellitus. Lancet 2003;361:226-8.
[12] Daimon M, Oizumi T, Saitoh T, et al. Decreased serum levels of adiponectin are a risk factor for the progression to type 2 diabetes in the Japanese population: the Funagata study. Diabetes Care 2003;26:2015-20.
[13] Stefan N, Vozarova B, Funahashi T, et al. Plasma adiponectin concentration is associated with skeletal muscle insulin receptor tyrosine phosphorylation, and low plasma concentration precedes a decrease in whole-body insulin sensitivity in humans. Diabetes 2002;51:1884-8.
[14] Mantzoros CS, Li T, Manson JE, et al. Circulating adiponectin levels are associated with better glycemic control, more favorable lipid profile, and reduced inflammation in women with type 2 diabetes. J Clin Endocrinol Metab 2005;90:4542-8.
[15] Shetty GK, Economides PA, Horton ES, et al. Circulating adiponectin and resistin levels in relation to metabolic factors, inflammatory markers, and vascular reactivity in diabetic patients and subjects at risk for diabetes. Diabetes Care 2004;27:2450-7.
[16] Rokling-Andersen MH, Reseland JE, Veierod MB, et al. Effects of long-term exercise and diet intervention on plasma adipokine concentrations. Am J Clin Nutr 2007;86:1293-301.
[17] Mather KJ, Funahashi T, Matsuzawa Y, et al. Adiponectin, change in adiponectin, and progression to diabetes in the Diabetes Prevention Program. Diabetes 2008;57:980-6.
[18] Balagopal P, George D, Yarandi H, et al. Reversal of obesity-related hypoadiponectinemia by lifestyle intervention: a controlled, randomized study in obese adolescents. J Clin Endocrinol Metab 2005;90:6192-7.
[19] Cambuli VM, Musiu MC, Incani M, et al. Assessment of adiponectin and leptin as biomarkers of positive metabolic outcomes after lifestyle intervention in overweight and obese children. J Clin Endocrinol Metab 2008;93:3051-7.
[20] Hida K, Wada J, Eguchi J, et al. Visceral adipose tissue-derived serine protease inhibitor: a unique insulin-sensitizing adipocytokine in obesity. Proc Natl Acad Sci U S A 2005;102:10610-5.
[21] Kloting N, Berndt J, Kralisch S, et al. Vaspin gene expression in human adipose tissue: association with obesity and type 2 diabetes. Biochem Biophys Res Commun 2006;339:430-6.
[22] Gulcelik NE, Karakaya J, Gedik A, et al. Serum vaspin levels in type 2 diabetic women in relation to microvascular complications. Eur J Endocrinol 2009;160:65-70.
[23] Youn BS, Kloting N, Kratzsch J, et al. Serum vaspin concentrations in human obesity and type 2 diabetes. Diabetes 2008;57:372-7.
[24] von Loeffelholz C, Mohlig M, Arafat AM, et al. Circulating vaspin is unrelated to insulin sensitivity in a cohort of nondiabetic humans. Eur J Endocrinol 2010;162:507-13.
[25] El-Mesallamy HO, Kassem DH, El-Demerdash E, et al. Vaspin and visfatin/Nampt are interesting interrelated adipokines

playing a role in the pathogenesis of type 2 diabetes mellitus. Metabolism 2011;60:63-70.
[26] Chang HM, Park HS, Park CY, et al. Association between serum vaspin concentrations and visceral adipose tissue in Korean subjects. Metabolism 2010;59:1276-81.
[27] Stepan H, Kralisch S, Klostermann K, et al. Preliminary report: circulating levels of the adipokine vaspin in gestational diabetes mellitus and preeclampsia. Metabolism 2010;59: 1054-6.
[28] Cakal E, Ustun Y, Engin-Ustun Y, et al. Serum vaspin and C-reactive protein levels in women with polycystic ovaries and polycystic ovary syndrome. Gynecol Endocrinol 2010 Jul 13 [Epub ahead of print].
[29] Handisurya A, Riedl M, Vila G, et al. Serum vaspin concentrations in relation to insulin sensitivity following RYGB-induced weight loss. Obes Surg 2010;20:198-203.
[30] Chang HM, Lee HJ, Park HS, et al. Effects of weight reduction on serum vaspin concentrations in obese subjects: modification by insulin resistance. Obesity (Silver Spring) 2010;18:2105-10.
[31] Lee MK, Jekal Y, Im JA, et al. Reduced serum vaspin concentrations in obese children following short-term intensive lifestyle modification. Clin Chim Acta 2010;411: 381-5.
[32] Third report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. Circulation 2002;106:3143-421.
[33] Lee SY, Park HS, Kim DJ, et al. Appropriate waist circumference cutoff points for central obesity in Korean adults. Diabetes Res Clin Pract 2007;75:72-80.
[34] Yoo HJ, Park MS, Kim TN, et al. A ubiquitous chronic disease care system using cellular phones and the internet. Diabet Med 2009;26:628-35.
[35] Matthews DR, Hosker JP, Rudenski AS, et al. Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. Diabetologia 1985;28:412-9.
[36] Chan DC, Watts GF, Ng TW, et al. Effect of weight loss on markers of triglyceride-rich lipoprotein metabolism in the metabolic syndrome. Eur J Clin Invest 2008;38:743-51.
[37] Pasarica M, Tchoukalova YD, Heilbronn LK, et al. Differential effect of weight loss on adipocyte size subfractions in patients with type 2 diabetes. Obesity (Silver Spring) 2009;17: 1976-8.
[38] Storti KL, Brach JS, FitzGerald SJ, et al. Relationships among body composition measures in community-dwelling older women. Obesity (Silver Spring) 2006;14:244-51.
[39] Sierksma A, Patel H, Ouchi N, et al. Effect of moderate alcohol consumption on adiponectin, tumor necrosis factor-alpha, and insulin sensitivity. Diabetes Care 2004;27:184-9.
[40] Qi L, Rimm E, Liu S, et al. Dietary glycemic index, glycemic load, cereal fiber, and plasma adiponectin concentration in diabetic men. Diabetes Care 2005;28:1022-8.
[41] Yannakoulia M, Yiannakouris N, Melistas L, et al. Dietary factors associated with plasma high molecular and total adiponectin levels in apparently healthy women. Eur J Endocrinol 2008;159: R5-10.
[42] Fargnoli JL, Fung TT, Olenczuk DM, et al. Adherence to healthy eating patterns is associated with higher circulating total and high–molecular-weight adiponectin and lower resistin concentrations in women from the Nurses' Health Study. Am J Clin Nutr 2008;88:1213-24.
[43] Mantzoros CS, Williams CJ, Manson JE, et al. Adherence to the Mediterranean dietary pattern is positively associated with plasma adiponectin concentrations in diabetic women. Am J Clin Nutr 2006;84:328-35.
[44] Seeger J, Ziegelmeier M, Bachmann A, et al. Serum levels of the adipokine vaspin in relation to metabolic and renal parameters. J Clin Endocrinol Metab 2008;93:247-51.
[45] Nguyen QM, Srinivasan SR, Xu JH, et al. Changes in risk variables of metabolic syndrome since childhood in pre-diabetic and type 2 diabetic subjects: the Bogalusa Heart Study. Diabetes Care 2008;31:2044-9.
[46] Mente A, Razak F, Blankenberg S, et al. Ethnic variation in adiponectin and leptin levels and their association with adiposity and insulin resistance. Diabetes Care 2010;33: 1629-34.
[47] Kaplan RC, Ho GY, Xue X, et al. Within-individual stability of obesity-related biomarkers among women. Cancer Epidemiol Biomarkers Prev 2007;16:1291-3.