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Lack of Increase of Serum Adiponectin Concentrations with a Moderate Weight Loss During Six Months on a High-Caloric Diet in Military Service Among a Young Male Finnish Population

Firoozeh Mousavinasab,[1,2] Tuula Tähtinen,[3] Jari Jokelainen,[1,2] Pentti Koskela,[5] Mauno Vanhala,[4] Jorma Oikarinen,[6] and Sirkka Keinänen-Kiukaanniemi[1,2]

[1]Department of Public Health Science and General Practice, University of Oulu, Finland; [2]Central University Hospital of Oulu, Unit of General Practice and Health Centre of Oulu, Finland; [3]Health Centre of Haukipudas, Finland; [4]Health Centre of Laukaa, Finland; [5]National Public Health Institute, Oulu, Finland; and [6]Army Health Centre, Parolannummi, Finland

An increase of insulin resistance and a worsening of lipid profile during 6 mo of military service in young male Finnish population has previously been shown by us. The present study demonstrates unfavorable changes of serum adiponectin concentrations and their association with weight loss in these particular circumstances. Adiponectin in a range of 4.3–21.2 µg/mL was present in the serum samples and had a significant negative correlation with weight, body mass index, waist to hip ratio, and insulin. Fasting serum lipids and plasma insulin significantly increased and serum adiponectin levels significantly decreased during the military service. Even the subjects with a 5–10% decrease in body weight showed the same result. In cases with more than 10% weight reduction and a significant decrease of fasting insulin concentration, the total and low density lipoprotein cholesterol significantly increased and adiponectin concentration tended to decreased. Only in severely obese cases (BMI ≥ 30 kg/m²) with more than 10% decrease in body mass index adiponectin levels tended to increase, although not statistically significantly. This study shows that serum adiponectin concentrations decreased during a 6 mo high-caloric diet in military service, and even a moderate weight reduction induced by high-energy expenditure in exercise during service did not increase its levels.

Key Words: Insulin resistance; body mass index; young population; lipids, adiponectin.

Introduction

Recent studies have pointed out that a variety of proteins secreted by adipose tissue influence the systemic metabolism and organ functions *(1)*. It has been reported that adiponectin, one of the cytokines secreted by adipose tissue, would have some potential as a treatment for insulin resistance and diabetes in animal models *(2)*. Decreased circulating adiponectin levels have been found in obese subjects, type 2 diabetic patients, and the first-degree relatives of patients with type 2 diabetes mellitus *(3–7)*, coronary artery disease (CAD), and dyslipidemia *(8,9)*. An increase in serum adiponectin levels has been noted in subjects with weight reduction *(6,10,11)*.

In our previous study, unfavorable changes in several insulin resistance–associated cardiovascular risk factors, such as plasma insulin and serum lipids, during 6 mo of military service were found in a Finnish male population *(12,13)*. As the main explanation for this, the frequent consumption of snacks such as doughnuts and confectionary between high-caloric meals was suggested *(12,13)*. Because a possible role of adiponectin in insulin resistance has been shown, we aimed in this study to investigate the serum adiponectin concentrations and their changes over 6 mo of military service, during which the unfavorable changes in insulin resistance–linked metabolic markers have been demonstrated.

Results

Serum Adiponectin Concentrations and Their Correlation with Insulin Resistance–Associated Metabolic Markers

The mean adiponectin concentrations and other insulin resistance–associated markers at baseline and after 6 mo military service are presented in Table 1. Adiponectin in a range of 4.3–21.2 µg/mL was present in the serum samples and had a significant negative correlation with weight (Spearman correlation coefficient $r = -0.14$), body mass index (BMI) ($r = -0.17$), waist to hip ratio (WHR) ($r = -0.304$), and fasting plasma insulin levels ($r = -0.23$) at the baseline. Serum adiponectin concentrations significantly decreased during the 6 mo military service compared to the baseline, while total, low and high density lipoprotein cholesterol, triglycerides, and insulin significantly increased in the whole popu-

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Author to whom all correspondence and reprint requests should be addressed: Firoozeh Mousavinasab, Department of Public Health Science and General Practice, University of Oulu, Aapistie 1, P.O.Box 5000, Fin-90014, Finland. E-mail: fmousavi@student.oulu.fi

Table 1
Mean Adiponectin Concentrations and Other Insulin Resistance–Associated Markers at Baseline and After 6 mo Military Service

	At the baseline	After 6 m	Difference	
Value	Mean (SD)	Mean (SD)	Mean (SD)	*p*-value
Adiponectin (μg/mL)	11.30 (3.63)	10.31 (3.66)	0.99 (2.09)	<0.001
Total cholesterol (mmol/L)	3.72 (0.68)	4.38 (0.79)	–0.66 (0.62)	<0.001
LDL cholesterol (mmol/L)	2.19 (0.60)	2.57 (0.69)	–0.37 (0.54)	<0.001
HDL cholesterol (mmol/L)	1.15 (0.29)	1.29 (0.30)	–0.14 (0.22)	<0.001
Triglycerides (mmol/L)	0.83 (0.45)	1.16 (0.69)	–0.32 (0.66)	<0.001
Insulin (mU/L)	9.20 (4.46)	9.88 (4.96)	–0.68 (4.60)	<0.005
Body Mass Index (kg/m^2)	25.14 (4.48)	24.75 (3.92)	0.39 (1.72)	<0.001
Weight (kg)	79.57 (15.48)	78.29 (13.77)	1.28 (5.51)	<0.001
Waist (cm)	87.41 (12.36)	85.54 (11.54)	1.87 (6.16)	<0.001
Hip (cm)	98.69 (8.73)	97.16 (9.83)	1.52 (6.66)	<0.001

Table 2
Results of Backward Stepwise Regression Analysis with Adiponectin Change During Military Service as a Dependent Variable

Variable change	Regression coefficient	SD	*F*-value	*p*-value
Weight change (kg)	–0.063	0.028	5.1	0.025
QUICKI change	–0.174	0.065	7.2	0.008
LDL change (nmol/L)	–0.528	0.276	3.7	0.057
Triglycerides change (nmol/L)	–0.726	0.283	6.6	0.011

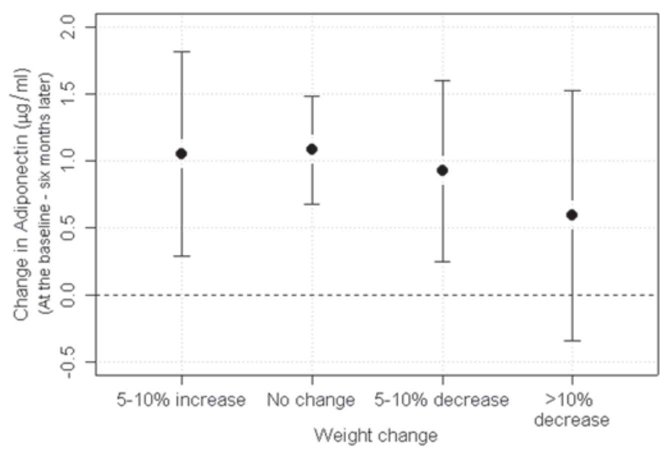

Fig. 1. Changes of adiponectin concentrations with their 95% confidence intervals according to the changes of body weight.

lation (Table 1). Insulin sensitivity measured by the Quantitative Insulin Sensitivity Index (QUICKI) decreased significantly (0.35 vs 0.34, $p < 0.001$) during the same period.

Multivariate regression analysis showed that the changes in QUICKI, triglycerides (TG), low density lipoprotein (LDL) cholesterol, and body weight were independently related to the change in serum adiponectin concentration (Table 2).

Association of Serum Adiponectin with Weight Changes

When the subjects were stratified according to their weight changes into four groups (5–10% weight gain, no change, 5–10% weight loss, and more than 10% weight loss), a significant decrease in the follow-up adiponectin levels was shown, even in the subjects who lost 5–10% of their weight during the 6 mo. In the subjects losing more than 10% of their body weight, the adiponectin concentration deceased also, but not significantly statistically. The changes of adiponectin concentrations with their 95% confidence intervals according to the changes of body weight are presented in Fig. 1.

Among the subjects with 5–10% decrease in body weight, the total cholesterol, LDL cholesterol, TG, and insulin increased significantly (Table 3). Subjects with more than 10% body weight reduction had a significant decline in insulin, but the total and LDL cholesterol continued to be significantly higher and adiponectin level tended to be lower in this group (Table 3).

In severely obese cases (BMI ≥ 30 kg/m^2) with more than a 10% decrease in body weight ($n = 5$ mean BMI = 32.3), the adiponectin levels increased (8.0 μg/mL vs 8.9, $p = 0.42$), insulin significantly decreased (15.50 mU/L vs 9.56, $p = 0.015$) but the total and LDL cholesterol significantly increased (3.38 mmol/L vs 4.38, $p = 0.004$ and 2.0 mmol/L vs 2.58, $p = 0.036$, respectively).

Discussion

The associations among obesity, insulin resistance, and type 2 diabetes are well known. However, the mechanisms underlying these relations and the role of adipocytokines such as adiponectin in relation to insulin resistance warrant additional investigations.

Table 3
Change of Plasma Lipids and Insulin According to Weight Changes During 6 mo Military Service

	Weight changes											
	>5–10% increase (*n* = 34)			No change (*n* = 110)			>5–10% decrease (*n* = 38)			>10% decrease (*n* = 23)		
	Mean	SD	*p*-value	Mean	SD	*p*-value	Mean	SD	*p*-value	Mean	SD	*p*-value
Total cholesterol (mmol/L)												
baseline	3.82	0.73		3.79	0.67		3.60	0.68		3.39	0.60	
after 6 mo	4.51	0.79		4.45	0.79		4.28	0.68		4.01	0.89	
Difference	–0.68	0.58	<0.001	–0.66	0.62	<0.001	–0.67	0.68	<0.001	–0.62	0.59	<0.001
LDL cholesterol (mmol/L)												
baseline	2.27	0.65		2.25	0.58		2.14	0.62		1.92	0.55	
after 6 mo	2.80	0.77		2.58	0.67		2.48	0.62		2.34	0.75	
Difference	–0.54	0.58	<0.001	–0.32	0.51	<0.001	–0.34	0.61	<0.001	–0.43	0.49	<0.001
TG (mmol/L)												
baseline	0.81	0.34		0.83	0.51		0.79	0.34		0.94	0.46	
after 6 mo	0.85	0.45		1.22	0.70		1.28	0.80		1.08	0.57	
Difference	–0.04	0.49	N.S	–0.39	0.67	<0.001	–0.50	0.74	<0.001	–0.14	0.54	N.S
Insulin (mU/L)												
baseline	6.10	2.22		8.95	4.54		9.89	4.58		12.51	4.33	
after 6 mo	9.15	4.34		9.64	4.96		11.53	6.06		9.36	3.16	
Difference	–2.19	3.67	<0.001	–0.69	4.51	N.S.	–1.64	4.63	<0.001	3.15	4.41	<0.001

Our present results demonstrated that, during the period of military service, the serum adiponectin level decreased and even a moderate (5–10%) weight reduction did not result in a rise of the serum adiponectin level. Associations of hyperlipidemia with low plasma adiponectin concentrations and an increase in adiponectin concentration with an improvement of plasma lipid profiles have been found *(9, 14)*. Increase in plasma adiponectin through insulin-sensitising agents such as rosiglitazone, which increase the subcutaneous adipose tissue mass while decreasing lipid profiles, has been shown *(15–18)*.

We have already reported a high caloric diet–induced insulin resistance increase during 6 mo of military service in a Finnish male population. The caloric content of ordinary meals served in the Finnish army is 3200–3600 kcal per day *(12)*, and additional energy is obtained from the snacks such as doughnuts and confectionary that are for sale in the cafeterias in the daytime between the meals and in the evenings. According to the questionnaires, servicemen reported that they consumed more snacks during the service compared to their normal life *(13)*. This high caloric diet was suggested to be the main reason for the increase of plasma lipids during the 6 mo of military service.

In the present study, we found that despite the over 10% weight reduction and increased amount of physical exercise, which is obvious on the basis of increase in HDL cholesterol level (Table 1), total and LDL cholesterol significantly increased during the 6 mo of military service. In agreement with our results, a negative lipid profile change, despite a significant weight loss during 1 yr, was shown in the subjects on a high-fat diet *(19)*.

Our data did not show an increase in serum adiponectin with moderate weight loss, although some studies *(6,10,11)* have reported that weight reduction could result in a rise of the serum adiponectin level. In one study *(6)*, plasma adiponectin rose after a 10% BMI reduction in subjects on a calorie-restricted diet in hospital. In two other studies *(10, 11)*, plasma adiponectin concentrations increased in severely obese patients who underwent in gastric surgery and had a marked loss of body weight. In the present study, most of those who lost 5–10% of their weight were moderately overweight (BMI mean = 27.9) but not severely obese, and they did not take a calorie-restricted diet. The age and ethnic difference between our cases and the subjects of the other studies must be considered.

In agreement with our results, two investigations have shown that moderate amounts of weight loss in obese and overweight women *(20,21)* were not associated with an increase in serum adiponectin. It therefore seems that a substantial (>10%) weight loss by severely obese (BMI ≥ 30 kg/m^2) persons is necessary to increase the serum adiponectin concentrations, as in the current study serum adiponectin in severely obese subjects with more than 10% weight loss started to increase, although not significantly.

To our knowledge the mechanisms for reported changes of adiponectin with weight change have not been elucidated. With the result of this study it is not completely clear why the serum adiponectin levels decreased, but it seems that the increase of the plasma lipids could be a suppressor for secretion of adiponectin. Whether lipids affect the adiponectin gene expression, or whether other mechanisms are involved, needs to be further investigated.

We conclude from our data that serum adiponectin levels could decrease due to the increase of plasma lipids achieved from a 6 mo high caloric diet, and its levels do not change even with a moderate weight reduction in this situation. It is possible also that, apart from the diet, a marked weight loss in more obese persons is necessary to increase serum adiponectin. Further studies are thus needed to better understand the role of serum adiponectin and the mechanisms involved in adiponectin change related to weight change.

Materials and Methods

Subjects and Study Design

A study population of 205 Finnish servicemen (17–28 yr) were recruited. This population consisted of 127 males from the Ostrobothnian Brigade (OB) garrison *(15)* and 78 males from the First Signal Company (FSC) *(13)*, both located in the northern part of Finland. The study was started in 1995 and the effect of the military lifestyle on insulin resistance–associated risk factors was investigated among them. As previously described *(22)*, the Ethic Committees of the Oulu Deaconess Institute and the Finnish Defence Forces approved the study protocol. All recruited servicemen were informed about the study and gave written consent.

Methods

Serum total cholesterol, high density lipoprotein (HDL) cholesterol, low density lipoprotein (LDL) cholesterol, triglycerides (TG), plasma insulin, and glucose after an overnight fast and also systolic and diastolic blood pressure (SBP and DBP), weight, body mass index (BMI), and waist-to-hip ratio (WHR) were measured once at the baseline and 6 mo later, as described previously *(15–22)*. The proportions and frequencies of subjects in the different BMI classes in the population at the baseline were 1.4% ($n = 3$) underweight (BMI < 18 kg/m^2), 50.8% ($n = 104$) normal weight (BMI 18–24.9 kg/m^2), 33.1% ($n = 68$) overweight (BMI 25.1–30 kg/m^2), and 14.7% ($n = 30$) obese (BMI > 30.0 kg/m^2).

As we have already reported, the amount of daily energy in the food served to every Finnish serviceman is 3200–3600 kcal/d *(12)*. Snacks such as doughnuts and confectionary served as the extra energy intakes between the meals.

We defined insulin resistance with the quantitative insulin sensitivity check index (QUICKI) that can be determined from fasting insulin and glucose values according to the equation: QUICKI = 1/ [log (I0) + log (G0)], in which I0 is fasting insulin and G0 is fasting glucose *(23)*.

The serum samples were stored at −80°C until subsequent adiponectin measurement. Adiponectin concentrations were determined by the Human Adiponectin ELISA Kit (B-Bridge international, Inc., CA and USA). This ELISA is a sandwich-type enzyme-linked immunoassay consisting of primary (mouse anti-adiponectin monoclonal) antibody-coated plate, secondary (rabbit anti-human adiponectin polyclonal) antibody, detection (HRP-conjugated goat anti-rabbit IgG) antibody, substrate for HRP and (recombinant human) adiponectin standard. One human serum sample with a known adiponectin concentration was used as a reference in the ELISA measurements.

Statistical Analysis

Statistical analyses and data management were performed using SPSS (v.11.5) and SAS (v. 8.2) for Windows. The normality of the studied variables was tested using the Kolmogorov–Smirnov test. Triglyceride values were log-transformed to achieve a normal distribution. The paired *t*-test was used to evaluate the significance of the difference between the mean values at the baseline and 6 mo later. The potential univariate relationships between adiponectin levels and other values (the biological or anthropometric parameter recorded) were assessed by Pearson's and Spearman's correation coefficient analyses. After that, stepwise (with backward elimination) linear regression analysis was performed to assess the variables independently related to the change in serum adiponectin levels during service. For this purpose, only the variables showing a significant univariate association with adiponection concentration were considered for multivariate analysis. A two-sided value $p < 0.05$ was considered to be significant.

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