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BRIEF GENETIC REPORT

Effect of the Pro12Ala Polymorphism of the *PPARγ2* Gene on Serum Adiponectin Changes

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The Pro12Ala polymorphism of the peroxisome *proliferator-activated receptor gamma 2* (*PPARγ2*) gene and adiponectin, a protein secreted from adipose tissue, have been associated with insulin sensitivity. The present study demonstrates that in Finnish servicemen who were on a high-caloric diet for 6 mo only subjects with the Ala 12 allele of *PPARγ2* had a significant increase in adiponectin levels with weight loss induced by heavy exercise. This study demonstrates an interaction of genetic and environmental factors in the regulation of serum adiponectin concentrations.

Key Words: Adiponectin; *PPARγ2*.

Introduction

Peroxisome proliferator activated receptor gamma 2 (*PPARγ2*), which belongs to the family of nuclear receptors, is expressed in adipose tissue and is a major regulator of adipogenesis *(1,2)*. A proline to alanine substitution in codon 12 in exon B of *PPARγ2* has been related to insulin sensitivity *(3)*.

Adiponectin, a protein secreted from adipose tissue, is assumed to be involved in the development of insulin resistance *(4)*. Conflicting data exist on the effect of Pro12Ala polymorphism of *PPARγ2* on serum adiponectin level *(5,6)*.

Our previous study among young Finnish servicemen who were on a high- caloric diet *(7,8)* showed a significant increase in the level of total cholesterol, LDL cholesterol, triglycerides, fasting glucose, and fasting insulin after 6 mo. Serum adiponectin levels significantly decreased, whereas the levels of LDL and HDL cholesterol, triglycerides, and insulin significantly increased in the entire study population *(9)*. 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 observed, even in the subjects who lost 5–10% of their weight due to physical training during the service *(9)*. We concluded from our data that the lack of increase of adiponectin level with a moderate weight reduction and its decrease during these 6 mo is possibly due to an increase in plasma lipids.

In the present study, we aimed to investigate the effect of the Pro12Ala polymorphism of *PPARγ2* on serum adiponectin changes in relation to weight change in this particular population.

Results

Altogether 170 DNA samples for subjects having complete baseline and 6 mo data were genotyped. There were 117 subjects with the Pro12Pro, 48 subjects with Pro12Ala, and 5 subjects with Ala12Ala genotypes of *PPARγ2*. Adiponectin changes against weight changes during the 6 mo in relation to the subjects' genotype were analyzed. Because there was only one homozygous subject having the Ala12Ala genotype in each weight category, he was combined with subjects having the Pro12Ala genotype, collectively named X12Ala. As shown in Fig. 1, adiponectin levels decreased in all groups, and only X12Ala subjects with more than 10% weight reduction showed a significant (10.66 vs 12.40 μg/mL, $p = 0.002$) increase in serum adiponectin levels.

Discussion

Our study of 170 young Finnish men in military service aged 17–28 yr who were on a high-caloric diet for 6 mo showed that the Pro12Ala polymorphism of *PPARγ2* modulated the change in circulating adiponectin level depending

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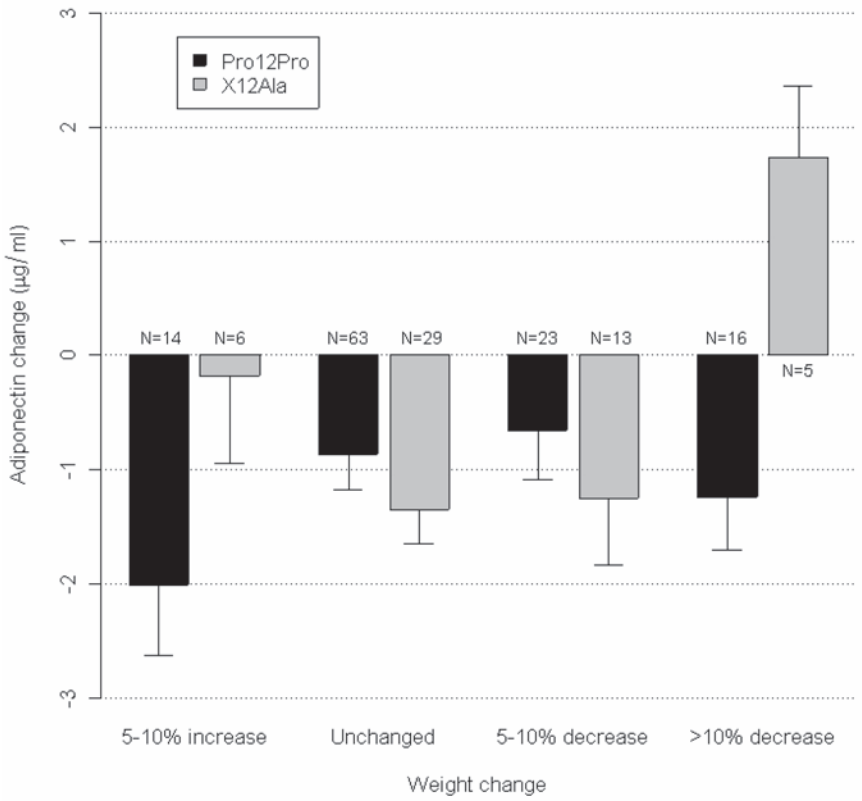

Fig. 1. Change in adiponectin serum levels among different categories of weight change according to the Pro12Ala polymorphism of *PPARγ2*.

on the genotype. The caloric content of ordinary meals served in the Finnish army is 3200–3600 kcal/d *(8)*, and additional energy is obtained from the snacks which are for sale in cafeterias. We have previously shown that a lack of increase of adiponectin level with moderate weight reduction and its decrease during 6 mo on a high caloric diet in the same population is due to an increase in plasma lipid levels *(9)*.

In the present study we found that subjects with more than 10% weight reduction and the Ala12 allele of *PPARγ2* had a significant increase in serum adiponectin concentrations even though their cholesterol continued to be significantly elevated. In contrast, subjects with more than 10% weight loss without the Ala12 allele showed a decrease in serum adiponectin levels (Fig. 1). This result indicates that moderate weight reduction has more advantageous effects on serum adiponectin level in subjects having the Ala12 allele of *PPARγ2*. We have previously shown *(10)* that serum adiponectin concentration is higher in subjects with the Ala12 Ala genotype compared to other genotypes of *PPARγ2* in this particular population. Therefore, present results could be due to a direct effect of this polymorphism on serum adiponectin level or to linkage disequilibrium of this polymorphism with other loci responsible for changes in serum adiponectin level.

In conclusion, the present study demonstrates an interaction between genetic and environmental factors in the regulation of serum adiponectin concentration.

Methods

Altogether 170 men, aged 17–28 yr (mean = 19.8 and SD = 1.4), were genotyped for the Pro12Ala polymorphism of *PPARγ2* as previously described *(10)*.

Adiponectin concentrations were determined by the Human Adiponectin ELISA Kit (B-Bridge International, Inc., CA, 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 known adiponectin concentration was used as a reference in the ELISA measurements.

Statistical analysis was performed using SPSS (v.11.5) for Windows. Paired *t*-test was used to compare the baseline adiponectin level and the level recorded 6 mo later among the different groups. p values less than 0.05 were considered significant.

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