Investigation of association of PPARγ gene Pro12Ala polymorphism with metabolic syndrome variables

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PPARγ is a transcription factor that is a member of the nuclear hormone receptor family. PPARγ is believed to be a key player in metabolic syndromes, such as diabetes and obesity, and influences lipid metabolism by targeting specific genes. A coding SNP Pro12Ala (C>G rs1805192) in the PPARγ gene PPARG has been associated with insulin resistance and obesity-related traits of the metabolic syndrome, with the protective effect of the Ala (G) allele being significant. We genotyped Pro12Ala in 466 overweight/obese subjects who are at risk of the metabolic syndrome in the RISCK Study, a randomised parallel controlled trial, which aims to test the impact of specific dietary changes on cardiovascular risk factors associated with the metabolic syndrome. We tested the association of genotype with mean quantitative metabolic phenotypes, LDL-C, HDL-C, TG, TC, adiponectin, BMI and insulin sensitivity. Baseline measurements were taken after following a reference diet containing 38% energy (38%E) fat, 18%E SFA, 10%E MUFA, 6%E PUFA for 1 month. The numbers of each genotype were in Hardy–Weinberg proportions as follows: C/C 315, C/G 61, G/G 2; G-allele frequency = 0.09. A significant association was found with waist circumference in males after adjusting for age, whereby G-allele carriers had a lower waist circumference than CC homozygotes (P = 0.020). G-allele carriers also had higher HDL-cholesterol compared to CC homozygotes, although this association was insignificant after adjusting for age, gender and waist circumference (P = 0.079). No other significant associations with mean quantitative metabolic phenotypes were found after adjustment for age, gender and waist circumference. The Pro12Ala polymorphism seems to be associated with central obesity in males. The Ala (G) allele may have protective effects in maintaining a healthy lipid profile. These findings may account for small inter-individual variation in fasting HDL-cholesterol concentration in obese/overweight subjects and may therefore modulate the risk of the metabolic syndrome.