Endocrinol Diabetes Nutr. 2018;xxx(xx):xxx–xxx

Endocrinología, Diabetes y Nutrición

www.elsevier.es/endo

ORIGINAL ARTICLE

Association of a cholesteryl ester transfer protein variant (rs1800777) with fat mass, HDL cholesterol levels, and metabolic syndrome

Daniel de Luis*, Olatz Izaola, David Primo, Emilia Gomez, Juan Jose Lopez, Ana Ortola, Rocio Aller

Center of Investigation of Endocrinology and Nutrition, Medicine School and Department of Endocrinology and Investigation, Hospital Clínico Universitario, University of Valladolid, Valladolid, Spain

Received 9 November 2017; accepted 12 March 2018

KEYWORDS
Adipokines;
Cholesteryl ester transfer protein;
Obesity;
Polymorphism;
Lipid levels;
Metabolic syndrome

Abstract
Background: There is little evidence of the association between CETP SNPs and obesity and/or related metabolic parameters.
Objective: To analyze the association of the polymorphism rs1800777 of the *CETP* gene with anthropometric parameters, lipid profile, metabolic syndrome and its components, and adipokine levels in obese subjects without type 2 diabetes mellitus or hypertension.
Design: A population of 1005 obese subjects was analyzed. Electrical bioimpedance was performed, and blood pressure, presence of metabolic syndrome, dietary intake, physical activity, and biochemical tests were recorded.
Results: Nine hundred and sixty eight patients (96.3%) had the GG genotype, 37 patients the GA genotype (3.7%) (no AA genotype was detected). Fat mass (delta: 4.4 ± 1.1 kg; $p = 0.04$), waist circumference (delta: 5.6 ± 2.1 cm; $p = 0.02$), and waist to hip ratio (delta: 0.04 ± 0.01 cm; $p = 0.01$) were higher in A allele carriers than in non-A allele carriers. HDL cholesterol levels were lower in A allele carriers than in non-A allele carriers (delta: 4.2 ± 1.0 mg/dL; $p = 0.04$). In the logistic regression analysis, the GA genotype was associated to an increased risk of central obesity (OR 7.55, 95% CI 1.10–55.70, $p = 0.02$) and low HDL cholesterol levels (OR 2.46, 95% CI 1.23–4.91, $p = 0.014$).
Conclusion: The *CETP* variant at position +82 is associated to lower HDL cholesterol levels, increased fat mass, and central obesity in obese subjects. These results may suggest a potential role of this variant gene in pathophysiology of adipose tissue.

* Corresponding author.
E-mail address: dadluis@yahoo.es (D. de Luis).

https://doi.org/10.1016/j.endinu.2018.03.006
2530-0164/

PALABRAS CLAVE
Adipocitoquinas;
Proteína trasportadora de ésteres de colesterol;
Obesidad;
Polimorfismo;
Niveles de lípidos;
Síndrome metabólico

Asociación de la variante (rs1800777) de proteína de transferencia de ésteres de colesterol con masa grasa, niveles de colesterol HDL y síndrome metabólico

Resumen
Antecedentes: Existen pocas evidencias en relación a la asociación entre los SNP de CETP y la presencia de obesidad y/o parámetros metabólicos relacionados.
Objetivo: Examinar la asociación del polimorfismo (rs1800777) del gen CETP con parámetros antropométricos, perfil lipídico, presencia de síndrome metabólico y sus diferentes componentes y los niveles de adipocitoquinas en sujetos con obesidad sin diabetes mellitus ni hipertensión.
Diseño: Se analizó una población de 1.005 sujetos con obesidad. Se registró una bioimpedancia, presión arterial, presencia de síndrome metabólico, ingesta dietética, ejercicio físico y parámetros bioquímicos.
Resultados: Novecientos sesenta y ocho pacientes (96,3%) tuvieron el genotipo GG y 37 pacientes presentaron el genotipo GA (3,7%) (no se detectó genotipo AA). La masa grasa (delta: 4,4 ± 1,1 kg; p = 0,04), circunferencia de la cintura (delta: 5,6 ± 2,1 cm; p = 0,02), relación cintura-cadera (delta: 0,04 ± 0,01 cm; p = 0,01) fueron mayores en los portadores del alelo A. El colesterol HDL fue menor en los portadores del alelo A (delta: 4,2 ± 1,0 mg/dl; p = 0,04). En el análisis de regresión logística la presencia del alelo A se asoció con un mayor riesgo de obesidad central (OR: 7,55; IC 95%: 1,10-55,70; p = 0,02) y un mayor riesgo de colesterol HDL bajo (OR: 2,46; IC 95%: 1,23-4,91; p = 0,014).
Conclusión: La variante CETP en la posición +82 se asocia a unos niveles más bajos de colesterol HDL, a un mayor porcentaje de masa grasa y obesidad central en personas con obesidad. Estos resultados podrían sugerir un posible papel de esta variante en la fisiopatología del tejido adiposo.

Introduction

An inverse and independent association between HDL cholesterol (HDL-C) concentration and risk of cardiovascular disease has been demonstrated.[1] HDL concentrations were predictive of cardiovascular events even in statin-treated individuals with LDL cholesterol concentrations < 70 mg/dl.[2] Two proteins that play important roles in HDL metabolism are ATP-binding cassette transporters A1 (ABCA1) and cholesteryl ester transfer protein (CETP). CETP participates in HDL metabolism by facilitating the transfer of cholesteryl esters from HDL to ApoB-containing lipoproteins in exchange for triglycerides being transferred to HDL.[3] The relationship of *CETP* single nucleotide polymorphisms (SNPs) with HDL-cholesterol concentrations has been extensively demonstrated.[4–9] A *CETP* polymorphism (rs1800777) located in the coding region of the gene has been previously studied. The minor allele of this SNP appears at a low frequency in general population (2–7%).[10–11] The A allele of this SNP has been associated with lower HDL-cholesterol concentrations[10] and higher CETP activity.[11] Furthermore, this SNP has been related to increase carotid intimal-medial wall thickness[12] and higher coronary calcium.

Although role of low HDL-cholesterol in cardiovascular disease is well known, other factors are strongly involved in the atherosclerotic processes.[14] These factors include high blood pressure, high triglyceride levels, hyperglycaemia, and obesity. Many of these risk factors are the ones that make up the so-called syndrome X or metabolic (MS).[15–17]

Although CETP is important for the metabolism of HDL, and *CETP* SNPs are known to be associated with differences in HDL-cholesterol concentrations,[13] association of *CETP* SNPS with anthropometric parameters, insulin resistance, metabolic syndrome and adipokine levels have not been previously reported.

In the current investigation, we examined the association of the polymorphism (rs1800777) of *CETP* gene on obesity anthropometric parameters, lipid profile, metabolic syndrome and adipokines in subjects with obesity.

Subjects and methods

Subjects and recruitment

A population of 1005 obese Caucasian subjects (body mass index ≥30) and non-diabetic patients was cross-sectional analyzed. Subjects were prospectively recruited by consecutive sampling among patients with obesity send from Primary Care Physicians to Hospital Clinico Universitario Valladolid (HCUVA). All participants provided informed consent to a protocol approved by the local ethical review boards. This study was conducted according to the guidelines laid down in the Declaration of Helsinki. All procedures involving patients were approved by the Hospital Clinico Universitario Valladolid (HCUVA) ethics committee. Subjects were excluded if had history of cardiovascular disease during the previous 24 months, history of cancer undergoing active treatment, weight loss of more than 5% of body

Please cite this article in press as: de Luis D, et al. Association of a cholesteryl ester transfer protein variant (rs1800777) with fat mass, HDL cholesterol levels, and metabolic syndrome. Endocrinol Diabetes Nutr. 2018. https://doi.org/10.1016/j.endinu.2018.03.006