Med Clin (Barc). 2017;xxx(xx):xxx–xxx

MEDICINA CLINICA

www.elsevier.es/medicinaclinica

Original article

The *rs4285184* polymorphism of the *MGAT1* gene as a risk factor for obesity in the Mexican population☆

José C. Tapia-Rivera[a,b], Luz M. Baltazar-Rodríguez[c], Martha I. Cárdenas-Rojas[a,d], Alan Álvarez[c], Rafael Bustos-Saldaña[b], Iván Delgado-Enciso[c], Laura L. Valdez-Velázquez[e], José Guzmán-Esquivel[b,*], Mario Ramírez-Flores[a]

[a] *University Biomedical Research Center, Universidad de Colima, Colima, Mexico*
[b] *Centro Universitario del Sur, Universidad de Guadalajara, Guzmán, Jalisco, Mexico*
[c] *Faculty of Medicine, Universidad de Colima, Colima, Mexico*
[d] *Clinical Epidemiology Research Unit, Hospital General de Zona, UMF N.º 1 IMSS, Colima, Mexico*
[e] *Faculty of Chemical Sciences, Universidad de Colima, Colima, Mexico*

ARTICLE INFO

Article history:
Received 23 February 2016
Accepted 24 July 2016
Available online xxx

Keywords:
Obesity
Gene
Polymorphism
Association

ABSTRACT

Background and objective: Obesity is a factor that contributes to the morbidity of certain diseases and to worldwide mortality. MGAT1 is a glycosyltransferase involved in the synthesis of protein-bound and lipid-bound oligosaccharides and its polymorphisms are possibly involved in the etiology of obesity. We investigated the association of the *rs4285184* polymorphism of the *MGAT1* gene with obesity in adults in the State of Colima, Mexico.
Methods: A case–control study was conducted that included 244 subjects. All of them were grouped according to their percentage of body fat, determined through bioelectrical impedance, and they were genotyped for the *rs4285184* polymorphism of the *MGAT1* gene through PCR-RFLP. The results were analyzed for their association with the percentage of body fat.
Results: The G allele had a frequency of 49.19 and 38.75% for the cases and controls, respectively ($P = .020$) (OR 1.53; 95% CI 1.068–2.193). The frequency of the A/G + G/G genotype was 75% in the obese patients, which was significantly higher compared with the 57.5% of the control group ($P = .004$) (OR 2.217; 95% CI 1.287–3.821).
Conclusions: The presence of the *rs4285184* polymorphism of the *MGAT1* gene increased the risk for developing body fat associated with obesity in the Mexican population.

Polimorfismo *rs4285184* del gen *MGAT1* como factor de riesgo de obesidad en la población mexicana

Palabras clave:
Obesidad
Gen
Polimorfismo
Asociación

RESUMEN

Antecedentes y objetivo: La obesidad es un factor que contribuye a la morbilidad de ciertas enfermedades, y a la mortalidad mundial. MGAT1 es una glucosiltransferasa implicada en la síntesis de los oligosacáridos ligados a proteínas y lípidos, y es posible que sus polimorfismos estén implicados en la etiología de la obesidad. Investigamos la asociación entre el polimorfismo *rs4285184* del gen *MGAT1* y la obesidad en adultos del estado de Colima, México.

☆ Please cite this article as: Tapia-Rivera JC, Baltazar-Rodríguez LM, Cárdenas-Rojas MI, Álvarez A, Bustos-Saldaña R, Delgado-Enciso I, et al. Polimorfismo *rs4285184* del gen *MGAT1* como factor de riesgo de obesidad en la población mexicana. Med Clin (Barc). 2017. http://dx.doi.org/10.1016/j.medcli.2016.07.037

* Corresponding author.
E-mail address: pepeguzman_esquivel@outlook.com (J. Guzmán-Esquivel).

Métodos: Se realizó un estudio caso-control que incluyó a 244 sujetos. Todos ellos fueron agrupados con arreglo a su porcentaje de grasa corporal, determinado mediante impedancia bioeléctrica, y fueron genotipados para el polimorfismo *rs4285184* del gen *MGAT1* mediante PCR-RFLP. Se analizaron los resultados para buscar su asociación con el porcentaje de grasa corporal.
Resultados: El alelo G reflejó una frecuencia del 49,19% y el 38,75% para los casos y controles, respectivamente (p= 0,020) (OR 1,53; IC 95% 1,068-2,193). La frecuencia del genotipo A/G + G/G fue del 75% en los pacientes obesos, cifra significativamente superior en comparación al 57,5% del grupo control (p = 0,004) (OR 2.217; IC 95% 1,287-3,821).
Conclusiones: La presencia del polimorfismo *rs4285184* del gen *MGAT1* incrementó el riesgo de desarrollar grasa corporal asociada a la obesidad en la población mexicana.

Introduction

Obesity is a worldwide public health problem. In 2014, around 13% of the world adult population (11% of men and 15% of women) were obese.[1] The World Health Organization (WHO) defines overweight and obesity as an abnormal or excess accumulation of fat that can be detrimental to health. In Mexico in 2012, the mean prevalence of overweight and obesity was 71.3% (overweight 38.8% and obesity 32.4%), whereas in the State of Colima it was 75.3%.[2] An elevated body mass index (BMI) is an important risk factor for non-transmittable diseases with a high mortality rate, such as some cancers,[3] cardiovascular diseases,[4] and diabetes.[5] The genesis of obesity is multifactorial, resulting in a combination of causes and contributing factors that are hormonal and genetic in nature. Genetic variants of the mannosyl (α-1,3-)-glycoprotein β-1,2-N-acetylglucosaminyltransferase (MGAT1) gene have been associated with characteristic obesity phenotypes.[6,7] MGAT1 is a glycosyltransferase involved in the synthesis of protein-bound and lipid-bound oligosaccharides. MGAT1 catalyzes the first step in the conversion of oligomannose to N-glycans of glycoproteins.[8] It is located on the 5q35 chromosome.[9] Mutation or deregulation of various enzymes that are dependent on MGAT1 action are associated with human diseases such as congenital disorders of glycosylation (CDG). These are rare hereditary disorders that confer defects on the biosynthesis and transport of sugar nucleotides, glycosyltransferase events, and vesicular transport. These glycoconjugates perform critical roles in processes of metabolism, cell recognition and adhesion, cell migration, protease resistance, host defense, and antigenicity.[10,11] The mechanism(s) by which this single nucleotide polymorphisms (SNP) near the MGAT1 gene can contribute to the development of obesity is not clear, given that in the SNP map analyzed at the non-codifying regions, the probability of development is low. However, this genetic variant is on both sides of the linkage disequilibrium (LD) with the encoding exon in MGAT1, a key enzyme involved in the glycosylation of proteins and the changes in lipid expression. The changes in MGAT1 expression caused by this variant can lead to altered glycosylation, which can cause a poorly directed classification of these proteins and alter their function. This, in turn, may be important for body weight regulation.[7]

Since 1980, obesity has more than doubled throughout the world.[1] In the last few years, overweight and obesity in the State of Colima have shown an annual increase of 1.3%.[2] Therefore, the aim of the present study was to analyze the association of the genetic factor (SNP *rs4285184*) of the MGAT1 gene in subjects with different body fat percentages in the State of Colima.

Methods

Study population

A case–control study was conducted in the State of Colima, Mexico, on 244 subjects that included adult men and women above the age of 18 years that took part in an integrated health program (PrevenIMSS, 2012). Patients presenting with confirmed thyroid problems, pregnant women, and persons with any type of amputation were excluded from the study. We evaluated the case group composed of 124 patients diagnosed with obesity and the control group of 120 patients diagnosed as low-fat, normal, and over-fat, in accordance with their body fat percentage determined through bioelectrical impedance. None of the participants were blood relatives and their participation was voluntary. All of them answered a questionnaire for collecting the sociodemographic data, in which anthropometry was determined according to the anthropometric parameters by Gomez-Garcia and cols.[12] The patients were weighed on a *Tanita BC-533*® scale through bioelectrical impedance analysis (BIA). It is a simple, noninvasive technique that allows the total body water (TBW) to be estimated. Fat-free mass (FFM) is obtained through assumptions based on the tissue hydration constants, and consequently, fat mass (FM), through a simple equation of two components (FFM kg = total weight kg − FM kg), in which body impedance (Z) is in relation to 2 components or vectors: resistance "R" (of the tissues upon the passing of an electrical current) and reactance "Xc" (additional opposition due to the capacitance of those tissues and the cell membranes). Body impedance is expressed as the sum of these 2 vectors in the equation $Z^2 = R^2 + Xc^2$.[13] The patients were measured with a *Seca 208*® stadiometer. They were classified according to their body fat percentage. The cut-off points for the percentage of fat were those proposed by Bray, that are: for men, very little fat <10%, thin 10–15%, normal weight 16–19%, overweight 20–25%, obese >25%, and for women, very little fat <15%, thin 15–20%, normal weight 21–24%, overweight 25–30%, obese >30%.[14] All the participants signed statements of informed consent, following the recommendations of the Declaration of Helsinki and the study was approved by the local ethics committee.

Polymorphism analysis

DNA was extracted from buccal epithelial cells with the aid of a cytobrush from the QIAGEN Gentra Puregene Buccal Cell Kit®, following the manufacturer's instructions. The *rs4285184* polymorphism of the MGAT1 gene was studied through the polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) method. The polymerase chain reactions (PCRs) were developed in a total volume of 10 μl that contained: 1X PCR Buffer, 1.5 mM $MgCl_2$, dNTP mix (0.2 mM each one), Primers (10 μM each one) (sense 5′-catctttggagaatggcaca-3′ and anti-sense 5′-ttgtcctgcacttgttttgc-3′), 0.25 U of Taq DNA polymerase, and 100 ng of genomic DNA. The PCRs were developed in a programmable thermocycler (Stratagene, RoboCycler® Gradient 40) under the following conditions: one cycle at 94 °C for 5 min; 35 cycles at 94 °C for 30 s, 61 °C for 30 s, 72 °C for 30 s, and one final extension cycle of 72 °C for 5 min. 5 μl of PCR product (186 pb) were individually mixed with reaction buffer and 1 U of restriction enzyme, *HpyCH4IV*