Single Nucleotide Polymorphism rs17173608 in the Chemerin Encoding Gene: Is It a Predictor of Insulin Resistance and Severity of Coronary Artery Disease in Non-Obese Type 2 Diabetes?

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Abstract: (1) Background: Chemerin, or the RARRES2 (Retinoic Acid Receptor Responder 2) gene, is found to be associated with an increased incidence of insulin resistance, endothelial dysfunction, type 2 diabetes (T2D), and coronary artery disease (CAD). This study investigates associations of RARRES2 rs17173608 with insulin resistance and the severity of CAD in non-obese T2D patients in relation to the clinical and genetic factors. (2) Methods: A total of 300 patients with T2D and CAD were recruited in this study. The associations of insulin resistance and the severity of CAD with RARRES2 rs17173608 and clinical factors were assessed. The genotyping procedures were performed using the TaqMan method. The significant associations (p < 0.05) from preliminary tests were employed to carry out the secondary analysis. (3) Results: RARRES2 rs17173608 (TT, TG, and GG polymorphisms in the preliminary analysis; TG and GG polymorphisms in a secondary analysis) was associated with insulin resistance and the severity of CAD in both the preliminary and secondary analysis (all p-values were < 0.05). Additionally, in the secondary analysis, FPG and ACEI were also associated with insulin resistance and the severity of CAD (all p-values were < 0.05). (4) Conclusion: From the preliminary findings, rs17173608 is a significant predictor of insulin resistance and the severity of CAD.

Keywords: chemerin; RARRES2; rs17173608; insulin resistance; T2D; severity of CAD

1. Introduction

Chemerin, also known as retinoic acid receptor responder protein 2 (RARRES2) and tazzarete50 induced gene 2 [1], is a chemoattractant protein involved in the pathogenesis of metabolic syndrome [2]. It is secreted in the liver, acts as a chemotactic agent, and is highly stimulated by elements of the innate immune system, such as plasmacytoid dendritic cells and macrophages [2]. Chemerin induces angiogenesis of endothelial cells and results in endothelial dysfunction [3]. Besides which, it can activate inflammatory response and oxidative stress in adipose tissue, results in insulin resistance and further enhance endothelial dysfunction [4]. Endothelial dysfunction and insulin resistance cause the progression of type 2 diabetes (T2D) and atherosclerotic coronary artery disease (CAD).

The CAD is classified as severe when the atherosclerotic plaques narrow down the vessels with stenosis by more than 50% [5]. In a study by Dahy et al., serum chemerin levels were higher in patients with T2D and metabolic syndromes than non-diabetics and patients without metabolic syndromes [4]. There is growing evidence showing a relationship between coronary atherosclerosis and chemerin. Several cross-sectional studies showed an independent correlation between chemerin concentrations and CAD. Chemerin is moderately heritable, with 16-25% of variations ascribed to genetic factors [5].