TSSC-2018
Theme: Medical, Health & Pharmaceutical Sciences
Category: Oral Presentation

Role of genetic & epigenetic modifications on expression of PCSK9 gene in Coronary Artery Disease

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Introduction

Proprotein convertase subtilisin/kexin type 9 (PCSK9) protein modulates plasma Low Density Lipoprotein (LDL)-cholesterol levels in hepatocytes by the promoting the degradation of LDL receptors (LDLR). Elevated levels of LDL-c associated with atherosclerosis and high risk of Coronary artery disease (CAD). Studies on various genes reported that the genetic polymorphisms and epigenetic modifications are influencing the gene expression. Thus the present study is designed to investigate the influence of PCSK9 gene R46L polymorphism, promoter DNA methylation status and serum circulating levels of PCSK9 in CAD patients.

Materials & Methods

A total of 400 (200 CAD & 200 Control) subjects were recruited as study population and genotyped for PCSK9 R46L polymorphism by PCR-RFLP method using RsaI (NEB, USA) restriction enzyme. PCSK9 serum circulating levels were estimated using R&D Systems, USA. Total cholesterol, Triglycerides & High density lipoprotein were estimated using commercially available enzymatic assay kits (Coral Clinical systems, INDIA) and LDL-c levels were calculated by Friedewald's formula. Promoter DNA methylation status was determined with Methylation-specific PCR (MSP) method. Statistical analysis was performed by appropriate tools.

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Results

Genotypic distribution of *PCSK9 R46L* polymorphism analysis revealed that the variant (T/T) genotype showed protective effect against the disease in co-dominant (OR= 0.23 (0.11-0.51), p <0.0001) model. The *PCSK9* serum circulating levels were high in CAD patients (122.84±49.08 ng/ml; p <0.01) compared to controls (71.53±28.69 ng/ml). Further these subjects were analysed to investigate the association of promoter DNA methylation status with differential expression/serum protein levels of PCSK9. In conclusion DNA methylation status might be associated with modulation of PCSK9 gene expression in coronary artery disease.

Keywords: PCSK9, LDL Receptor, Coronary artery disease, DNA methylation

Acknowledgments

We acknowledge the contribution of the participants and all the study centers staff & technicians. This work was supported by OU-DST-PURSE-II Programme (C-DST-PURSE-II/23-2017), UGC-MRP (FNo.42-52/2013(SR)), UGC-BSR Fellowship (F.4-1/2006(BSR)5-78/2007(BSR)/2013-2014/03).