Relationship of Endothelial Nitric Oxide Synthase Gene Polymorphism with Atherosclerotic Coronary and Carotid Arterial Disease in Egyptian Population

Background and Objectives:

Atherosclerosis is partly a heritable disorder. Various genetic polymorphisms have been linked to the atherosclerotic process and its complications. Glu298Asp polymorphism of endothelial nitric oxide synthase gene is one such genetic marker for atherosclerosis. This study aimed to assess the relationship between endothelial nitric oxide synthase Glu298Asp gene polymorphism and atherosclerotic coronary and carotid arterial disease in an Egyptian population.

Methods:

Our study included 95 Egyptian, classified into two groups: Group (1) 63 patients with ischemic heart disease and Group (2) 32 healthy control subjects (HC). They were subjected to careful history taking, thorough clinical examination, standard twelvelead surface electrocardiogram, routine laboratory investigations, echo Doppler study, carotid arterial duplex, invasive coronary angiography and analysis of the endothelial Glu298Asp gene polymorphism using polymerase chain reaction restriction fragment length polymorphism (PCR–RFLP) for detection of different genotype variants Glu/Glu (GG), Glu/Asp (GT) and Asp/Asp (TT) genotype. Determination of: total cholesterol, triglycerides, high density lipoproteins, low density lipoproteins and fasting blood glucose, was also performed.

Results:

There was a statistically significant difference in the prevalence of smoking, diabetes mellitus and hypertension in the cases compared to the HC. There was no statistically significant difference in the prevalence of family history for coronary artery disease (CAD) and obesity between the patients compared to the HC. There was a highly statistically significant difference in: total cholesterol, LDL, triglyceride and fasting blood glucose levels among patients compared to the HC. In Group (1): 59.6% (n =28) of males were GG genotype and 38.3% (n = 18) were GT genotype and 2.1% (n= 1) were TT genotype. On the other hand 75% (n= 12) of females were GG genotype and 18.8% (n = 3) were GT genotype

and 6.2% (n= 1) were TT genotype. There was no statistically significant difference in genotype frequency in males compared to females. There was no statistically significant difference in the genotype distribution between smokers compared to non smokers, diabetic compared to non diabetic, hypertensive compared to normotensive, patients with family history of CAD compared to those without family history of CAD. GT and TT genotypes were statistically significantly higher in obese patients when compared to non obese. Thus it was suggested that the heterozygous and homozygous Asp mutants were significantly associated with increased body mass index. The present study showed that the heterozygous and homozygous Asp mutants were not significantly associated with the occurrence of CAD. 63.5% of CAD patients were Glu/Glu (GG) genotype, 33.3% were Glu/Asp (GT) genotype and 3.2% were Asp/Asp (TT) genotype while in the HC, 53.1% of were Glu/Glu genotype, 43.8% were Glu/Asp genotype and 3.1% of the HC were Asp/Asp genotype. There was no statistically significant difference in the genotype distribution of GG genotype, GT genotype and TT genotype between group 1 compared to group 2 ($P > 0.05$). The present study revealed no statistically significant difference in the distribution of the T allele and G allele in patients with CAD compared to the HC (27.4 vs. 32.6 and 72.6% vs. 67.4%). The results of this study showed that the heterozygous and homozygous Asp mutants were not significantly associated with the occurrence of left ventricular systolic dysfunction. Similarly endothelial nitric oxide synthase gene polymorphism was not associated with increased carotid intimal thickening (cIMT) and Asp variant was not significantly associated with increased cIMT.

Conclusions:

Glu298Asp polymorphism in the endothelial nitric oxide synthase gene did not increase the susceptibility to coronary and carotid arteries disease in the studied patients.

Key words:

Atherosclerosis -nitric oxide synthase gene polymorphism