Thrombotic and Inflammatory Mechanisms in Patients with Stable Angina Pectoris: Differential Effects of Fibrinogen Genetic Variability

Background: Patients with stable angina pectoris are characterized by increased levels of thrombotic and inflammatory biomarkers including fibrinogen, interleukin 6 (IL-6) and sCD40L. However, it is unclear, whether fibrinogen genetic variability could modify these processes in those patients. Thus, we investigated the effect of a beta chain genetic polymorphism of fibrinogen on the aforementioned biomarkers.

Methods: We genotyped 402 patients with documented stable coronary artery disease (CAD) and 273 controls. The G455A (rs1800790) polymorphism was determined by polymerase chain reaction (PCR) and the specific HaeIII restriction enzyme. Serum levels of fibrinogen were measured by the von Clauss method. Both IL-6 and sCD40L levels were assessed by enzyme-linked immunosorbent assay (ELISA).

Results: GG: 54.6%, GA: 36.8%, AA: 8.6% for controls and GG: 50.1%, GA: 42.0%, AA: 7.9% for CAD. Interleukin 6 levels (pg/ml) were enhanced in patients with CAD compared to controls (4.40±3.13 vs 3.41±2.76, p<0.01). However, the G455A polymorphism failed to affect IL-6 levels between GG+GA vs AA both in CAD and controls (p=NS). Similarly, sCD40L levels (ng/ml) were significantly higher in CAD compared to controls (2.07±1.47 vs 1.82±1.68, p<0.001). Although no difference was observed in sCD40L across the study genotypes both in controls and in CAD (p=NS), the G455A polymorphism defined sCD40L levels (GG+GA vs AA) in the total population (1.91±1.41 vs 2.77±2.23, p<0.05). Finally, fibrinogen levels (mg/dl) were significantly higher in CAD compared to controls (p<0.001). Importantly, the present polymorphism affected significantly fibrinogen levels (GG+GA vs AA) not only in controls (366.6±85.8 vs 439.1±122.3, p<0.05), but also in CAD (426.0±122.7 vs 521.8±113.1, p<0.001).

Conclusions: The rs1800790 genetic polymorphism has a differential/striking effect on fibrinogen levels both in controls and in patients with coronary artery disease. In addition, it affects partly sCD40L in the total population. Our findings suggest that the G455A polymorphism affects the thrombotic process and consequently promotes atherosclerosis, especially via its significant impact on fibrinogen.