Platelet collagen receptor gene polymorphisms and risk of myocardial infarction- is there a relation?

Trombosit kollajen reseptörü gen polimorfizmleri ve miyokard infarktüsü risk faktörleri arasında ilişki var mı?

Ischemic heart disease is one of the major causes of morbidity and mortality in both developed and developing countries. Approximately half of all thrombotic events occur in patients without traditional cardiovascular risk factors. For this reason, investigators have focused on the molecular genetics of thrombosis and atherosclerosis to understand the pathophysiology of arterial thrombosis. A range of specific genes contributing to cardiovascular disease risk have been identified, however the relation between most polymorphisms and cardiovascular disease is still controversial (1).

The critical role of platelets in the formation of occlusive thrombus that leads to acute myocardial infarction is now well accepted. Several platelet receptors are involved in this process, including the glycoprotein (GP) Ia-IIa (2). Polymorphisms of platelet adhesive molecules have been investigated as risk factors for arterial thrombosis in many studies (reviewed in ref. 1). The bases to these studies are; first, if the amino acid change affects function, it could affect the prothrombotic tendency of the platelet, and second, there is great heterogeneity among platelets from different donors.

Platelets have two major primary receptors for collagens, the GP Ia-IIa (integrin $\alpha 2\beta 1$) and the platelet-specific receptor GP VI. The GP Ia-IIa was the first to be considered as a potential risk factor for thrombosis. C807T dimorphism of GP Ia gene has been shown to distinguish subjects with high platelet GP Ia-IIa density (T807) from those with low density (C807) (3,4). The impact of the GP Ia gene polymorphism as a genetic risk factor for myocardial infarction has been confirmed in some but not all of the studies (5). Moshfegh et al. were the first to observe T807/A873 homozygosity as an independent risk factor for acute myocardial infarction (6). Yamada et al. studied 2819 patients with myocardial infarction and 2242 controls and compared groups in terms of 112 polymorphisms (7). They found an association between risk of myocardial infarction and connexin 37, plasminogen-activator inhibitor type 1 and stromelysin-1 genes, but not GP Ia gene. Also a study by Atherosclerosis, Thrombosis and Vascular Biology Italian Study Group, provided no evidence supporting an association between 9 polymorphism of genes encoding proteins involved in hemostasis including GP Ia gene and the development of myocardial infarction at a young age (8).

In this issue of The Anatolian Journal of Cardiology, Kömürcü et al, describe the prevalence of GP Ia gene polymorphism in patients with myocardial infarction and healthy controls (9). The findings are potentially important. The authors studied 158 patients with myocardial infarction and 145 healthy controls. They compared two groups in terms of distributions of the C807T and G873A dimorphism. The study is noteworthy because no relationship was demonstrated between GP Ia TT/AA genotype and myocardial infarction in Turkish population.

However, there are important limitations. First, the selection of the control group is very important. Controls should represent the cohort from which the patients were derived. In other words, patients and controls should be matched for age, sex and as well as known risk factors for myocardial infarction. If this restriction is adhered to, genetic differences may then be related to myocardial infarction. If not, additional statistical analysis is necessary after adjusting for risk factors for myocardial infarction. In the present study, control group is not clearly defined; they apparently were selected from a much younger population than the patients. One other limitation is that only patients who had survived a myocardial infarction were enrolled. It cannot be excluded that GP Ia gene polymorphism may have an association with more severe myocardial infarctions. However, it is hard to overcome this limitation unless a prospective study is designed and patients are followed up until they reach the end points of myocardial infarction or cardiac death. Finally, as the authors mentioned, the study was designed to establish the possible association between GP Ia genotypes and myocardial infarction. But as a secondary finding they observed an association between GP Ia TT/AA genotype and higher HDL cholesterol levels in healthy controls. This finding should be considered incidental rather than a protective role of that genotype, as no molecular mechanism has been suggested by the authors.

In conclusion, based on the findings of this study, further research should be initiated with a well-selected control group. From a clinical point of view, there is apparently no evidence to support the usefulness of screening individuals for GP Ia gene polymorphism.

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