Angiotensin-converting enzyme and p22(phox) polymorphisms and the risk of coronary heart disease in a low-risk Spanish population.

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Source

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Abstract

OBJECTIVE:

To evaluate the genetic contribution to myocardial infarction in a homogeneous Caucasian population (a Mediterranean Spanish population) with very low frequency of coronary heart disease (CHD).

DESIGN:

We analyzed a total of 210 subjects, younger than 55 years, considered to be a low-risk population (104 cases of myocardial infarction and 106 control), and genotyped them (using polymerase chain reaction and sequencing) for the angiotensin-converting enzyme (ACE) insertion/deletion (ACE I/D) and for the C242T polymorphism of NADPH oxidase p22(phox). Also, we sequenced 23 alleles of the ACE gene (9 D and 14 I) for the region that includes the end of the intron 16 and the exon 17.

RESULTS:

The ACE genotype-prevalence values for II, ID and DD were 4.81%, 28.85% and 66.34%, respectively, among the myocardial infarction patients, and 2.83%, 71.70% and 25.47% among controls. The statistical analysis comparing patients and controls revealed significant differences ($\chi^2=25.09$, $P=0.00000055$) between the two subpopulations. Also, we found a strong association between the genotype DD and the risk of suffering CHD (odds ratio (OR): 3.64; 95% CI: 2.37-8.07). The prevalence of the CC, TC and TT genotypes of p22(phox) gene among healthy controls proved to be 53.77%, 44.34% and 1.89%, while those of myocardial infarction were 58.65%, 39.42% and 1.93%, respectively. The association of C242T polymorphism of the p22(phox) gene with CHD was not statistically significant, ($\chi^2=0.49$, $P=0.48$). Logistic-regression analysis demonstrated that the independent risk factor for developing myocardial infarction was the DD genotype of ACE gene. Finally, our results indicate

that alleles I and D of ACE gene are differentiated at three positions (nucleotide sites 14,480, 14,488 and 14,521) of which, the positions 14,480 and 14,488 were in absolute linkage disequilibrium.

CONCLUSIONS:

Among subjects of a Mediterranean population with low risk for CHD, the presence of DD ACE genotype could be a risk factor for myocardial infarction, and we confirm the linkage disequilibrium between two nucleotide positions of the ACE gene and the polymorphism for an Alu insertion.

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