Short reports

The angiotensin-I converting enzyme (ACE) gene I/D polymorphism and ACE levels in Pima Indians

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Abstract

An insertion/deletion (I/D) polymorphism of the angiotensin converting enzyme (ACE) gene is associated with plasma ACE levels in white populations. The occurrence of the I/D polymorphism and relationship to ACE levels was examined in a Pima Indian group (n=305). The frequency of the D allele was lower in Pimas than whites (0.29 v 0.52 respectively). ACE levels were significantly associated with genotype in both groups (p=0.0001), which accounted for 6.5% of the variation in ACE levels in Pimas and 18% in whites. The association of the I/D polymorphism with ACE levels confirms the relationship across ethnic groups. The low frequency of the D allele in Pima Indians shows that ethnic differences should be accounted for when studying the ACE gene.

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Key words: angiotensin-I converting enzyme; insertion deletion polymorphism; ethnicity.

studies (146 male, 159 female), median age 45 years (range 35-69), and a white comparison group (n=80; 42 male, 38 female), median age 48 years (range 20-70), were recruited. DNA was extracted and PCR performed to detect the I/D polymorphism as previously described.^{2,9} Homozygous DD samples were typed with primers specific for the insertion to confirm genotype.¹⁰ Plasma samples were obtained from 300 of the Pima Indians and 73 of the white group, and ACE levels were determined by hydrolysis of furanacryloyl-1-phenylalanyl-glycylglycine (FAPGG) with subsequent decrease in absorbance at 340 nm being a measure of ACE activity. The coefficient of variation at 80 IU/l was 6% and at 250 IU/l was 3.5-4%. The figure shows amplification of samples with the I/D primers. Using the insertion specific primers one Pima subject was recategorised as an I/D. Table 1 shows the I/D genotyping results obtained, which were in Hardy-Weinberg equilibrium.

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A polymorphic region of the angiotensin-I converting enzyme (ACE) gene has been related to plasma ACE levels.¹ Detection of the polymorphism by PCR is based on the presence or absence of a 287 bp sequence in intron 16.² Homozygotes for the deletion (DD) have levels of circulating ACE approaching twice that of those homozygous for the insertion (II). The DD genotype has been associated with an increased risk of coronary artery disease (CAD) and myocardial infarction (MI) in family and population based studies.^{3,4} However, other studies have failed to show this association,^{5,6} which may be because of differences in ascertainment of disease status or that the ACE genotype/phenotype interaction varies across ethnic groups. Pima Indians from Arizona, USA, have a low prevalence of heart disease compared to the total US population.^{7,8} The aim of this study was to determine the prevalence of the I/D polymorphism and its relationship to ACE levels in this population.

Pima Indians from Arizona, USA (n=305) participating in continuing epidemiological

Amplification of the I/D polymorphism. Lanes 1, 6, and 9 II homozygotes, lanes 2 and 7 DD homozygotes, lanes 3-5 and 8 ID homozygotes, lane 10 blank control.

Table 1 Prevalence of the ACE I/D genotype in Pima Indians and whites

ACE genotype	Pima Indians	Whites
II	155 (50.8%)	19 (23.8%)
ID	125 (41.0%)	39 (48.8%)
DD	25 (8.2%)	22 (27.5%)
Total	305	80

Table 2 Mean plasma ACE levels (standard deviations) according to ACE I/D genotype

ACE genotype	Pima Indians	Whites
II	74.5 (31.7) n=153	58.7 (21.1) n=16
ID	90.2 (39.5) n=124	81.9 (29.3) n=35
DD	103.7 (46.6) n=23	94.6 (29.6) n=22

The frequency of the D allele was lower in Pimas than whites, frequencies (95% confidence intervals) 0.29 (0.25, 0.32) and 0.52 (0.44, 0.60) respectively. The frequency of the D allele in the white group was similar to reported frequencies for other white populations.⁴ Table 2 shows mean plasma ACE levels according to I/D genotype. Univariate analysis showed no evidence of a relationship between ACE levels and age or sex in either population ($p>0.1$). ACE levels were strongly associated with genotype ($p=0.0001$), and after allowing for genotype there was evidence of higher ACE levels in the Pima Indians than the white group ($p=0.03$). The variation in ACE levels explained by the ACE polymorphism was 6.5% in the Pima Indians and 18% in the whites.

The results of the present study show that the D allele has a significantly lower frequency in Pima Indians than in whites. Previous studies have shown a lower frequency of the D allele in several non-European populations including Japanese, Chinese, Samoans, and Yanomami Indians.¹¹⁻¹³ In all groups, a strong relationship existed between the I/D genotype and circulating ACE levels, as previously observed in white populations. Future studies of the ACE gene and vascular disease would take into ac-

count the ethnic origin of the patients under study.

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