Association between angiotensin converting enzyme (ACE) gene I/D polymorphism frequency and plasma ACE concentration in patients with idiopathic dilated cardiomyopathy

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Dilated cardiomyopathy (DCM) is a syndrome characterized by cardiac enlargement and impaired systolic function of one or both ventricles. The etiology of DCM is idiopathic in about half the patients. These patients present unknown cause. However, familial studies revealed that 20% to 25% of idiopathic DCM had a familial origin. This finding raised the hypothesis that gene defects might play an important role in the disease pathogenesis. Angiotensin converting enzyme (ACE) gene (Gene Bank accession number: NM 000789.2) is one of these genes affecting idiopathic DCM (1). This gene contains a polymorphism based on the presence (insertion, I) or absence (deletion, D) within intron 16, of a 287 base pair ALU repeat sequence; resulting in 3 genotypes: DD and II homozygotes and ID heterozygote. DD genotype is associated with higher concentrations of circulating ACE (2).

Plasma ACE concentration is important in regulating blood pressure and proliferation of muscle cells. As a result, ACE gene I/D polymorphism may be a genetic marker for idiopathic DCM (2-5).

We evaluated 29 (11 female and 18 male) unrelated, patients with idiopathic DCM and 20 (11 female and 9 male) healthy subjects as controls, admitted to the Research Hospital of the Osmangazi University between 2003 and 2004. DNA was extracted from venous blood by salt method and polymerase chain reaction (PCR) of amplification of DNA was performed with thermo stable taq polymerase (Sigma diagnostics, St. Louis, US) according to Gunes et al (6). The PCR products were separated by electrophoresis on 2 % agarose gel containing 4 ìl of ethidium bromide and were visualized by using CCD camera. Results were evaluated with the gel analysis Software (Lab Works, Cambridge UK).

Plasma ACE concentrations were determined by using ELISA kit (Tecemcula, CA, Chemicon International Inc.).

Echocardiograms were obtained by using Acuson-Siemens Sequoia-C256, (Acuson Corporation, Mountain View, CA, USA) with a 3.5 MHz transducer. Subjects were examined in the left lateral decubitus position according to the standardization of the American Society of Echocardiography (7). Standard views for M-mode and cross-sectional studies were obtained. Left ventricular (LV) end-diastolic dimension, LV end-systolic dimension, % fractional shortening, diastolic thickness of the ventricular septum and the posterior LV wall and LV mass were determined. The LV ejection fraction was calculated from the conventional apical 4-chamber images using the biplane Simpson’s method (8). One investigator without knowledge of the clinical characteristics analyzed all echocardiographic measurements. All examinations were recorded on videotape.

Case and control genotype frequencies were compared by χ² exact testing and plasma ACE concentrations and echocardiographic results were compared by unpaired t test. The ACE concentrations according to ACE genotypes were compared with the use of Kruskal Wallis non-parametric ANOVA test. A p-value of <0.05 was considered significant.

In this study, we have demonstrated that there was no statistically significant difference between ACE genotypes and D and I allele frequencies in idiopathic DCM patients as compared with healthy subjects (Table 1). D allele frequency was 43% in controls versus 52% in patients and I allele - 57% versus 48%, respectively. Consistently with our results Candy et al. (2), Montgomery et al. (4) and Vancura et al. (5) have demonstrated that ACE gene I/D polymorphism is not a risk factor for idiopathic DCM and there was no significant difference between genotypes and alleles compared with idiopathic DCM patients and controls. In contrast, Raynolds et al. (3) have suggested that ACE DD genotype is a risk factor for the development of end stage heart failure due to cardiomyopathy.

When we have compared the echocardiographic values between patients and controls; LV end-diastolic dimension, LV end-systolic dimension, posterior wall thickness were significantly increased and ejection fraction and fraction shortening were sig-
Nevertheless, Gunes et al. (6) have found that plasma ACE concentrations and ACE concentration and ACE gene polymorphism. (10) have found that there were no significant differences between results with the results studied in various diseases; Cambien et al. with our results (Table 1). However, when we have compared our I/D polymorphism genotypes in patients with DCM to compare association between plasma ACE concentrations and ACE gene concentrations were higher in hypertensive patients with DD genotypes.

As a conclusion, we suggest that there was no association between ACE gene I/D polymorphism and idiopathic DCM, although ACE concentration was high in this category of patients.

References