RENIN-ANGIOTENSIN SYSTEM GENES AND EXERCISE TRAINING-INDUCED CHANGES IN SODIUM EXCRETION IN AFRICAN AMERICAN HYPERTENSIVES

Objective: To determine whether angiotensin-converting enzyme (ACE) and angiotensinogen (AGT) genotypes could predict changes in urinary sodium excretion in response to short-term aerobic exercise training (AEX).

Design: Longitudinal intervention.

Setting: The study was conducted at the University of Maryland at College Park and at Baltimore, and the University of Pittsburgh General Clinical Research Center.

Participants: 31 (age 53 ± 2 years) sedentary, hypertensive (146 ± 2/88 ± 2 mm Hg) African Americans.

Intervention: Aerobic exercise training (AEX) consisted of seven or eight consecutive days, 50 minutes per day, at 65% of heart rate reserve. Participants underwent a 24-hour period of ambulatory blood pressure (BP) monitoring and urine collection at baseline and 14–18 hours after the last exercise session.

Main Outcome Measures: Angiotensogen (AGT) M235T and ACE I/D genotype and sodium excretion and ambulatory BP.

Results: Average sodium excretion for the entire group independent of genotype increased after AEX (108 ± 9 vs 143 ± 12 mEq/day, P = .003). Sodium excretion significantly increased after exercise training in the ACE II (114 ± 22 vs 169 ± 39 mEq/day, P = .04), but not in the ID (100 ± 8 vs 133 ± 17 mEq/day, P = .12) or DD (113 ± 18 vs 138 ± 11 mEq/day, P = .13) genotype groups. In the II genotype group, the increase in sodium excretion was significantly and inversely correlated with decreases in 24-hour diastolic (r = −.88, P = .02) and mean (r = −.95, P = .004) BP. The AGT TT and MT+MM genotype groups similarly increased their sodium excretion by 34 ± 16 (P = .03) and 37 ± 17 (P = .05) mEq/day respectively.

Conclusions: These results suggest that African American hypertensives with the ACE II genotype may be more susceptible to sodium balance and BP changes with exercise training compared with those with the ID and DD genotypes. (Ethn Dis. 2006;16:666–674)

Key Words: Blood Pressure, Exercise, Genetics, Sodium

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INTRODUCTION

The renin-angiotensin system (RAS) is associated with long-term blood pressure (BP) regulation through its influence on the cardiovascular and renal systems. Angiotensinogen (AGT) is the substrate for the RAS and is produced in many tissues involved in BP regulation, including the kidney. Angiotensinogen (AGT) is cleaved by renin to form angiotensin I, which is converted to biologically active angiotensin II by angiotensin-converting enzyme (ACE). Angiotensin II causes vasoconstriction of the vasculature and sodium reabsorption in the kidney. Because of the roles that ACE and AGT play in sodium handling, genes that encode for ACE and AGT can contribute to sodium handling.

Much research has focused on the ACE insertion/deletion (I/D) gene polymorphism, defined by the presence or absence of a 287-bp DNA sequence in intron 16 at the ACE locus and its association with cardiovascular disease (CVD) risk factors. A number of studies have demonstrated that the ACE I/D gene polymorphism accounts for a substantial portion of plasma and tissue ACE-level variability. Evidence suggests that hypertension among African Americans may be related to RAS function and renal sodium handling. When the ACE I/D allele frequency was assessed in those of African descent, the D allele frequency was significantly higher than in Caucasians, but evidence conflicts on whether the ACE I/D polymorphism is associated with ACE activity in those of African descent.

The methionine-to-threonine amino acid substitution at codon 235 (M235T) is caused by a thymine-to-cytosine transition at nucleotide 704 in exon 2 at the AGT locus. Studies have reported a higher frequency of T alleles in both Caucasian and Japanese hypertensives. The M235T polymorphism has also been associated with AGT levels, in which those with the T allele demonstrated greater plasma AGT levels. Studies have also investigated the M235T polymorphism’s association with hypertension in those of African descent. The T allele is more frequent among those of African descent compared to Caucasians, but reports have shown no association between the M235T polymorphism and hypertension among those of African descent.

A relationship between dietary sodium and BP has been described in ecologic, epidemiologic, and experimental human studies. Research has also shown a relationship between di-