Alpha-Adducin Gly460Trp Polymorphism and Essential Hypertension in Korea

Previous studies have suggested that the Gly460Trp polymorphism of the alpha-adducin gene (ADD-1) is associated with salt sensitivity and primary hypertension. The results of linkage or association studies of ADD-1 of different populations are controversial. This study investigated the relationship between the Gly460Trp polymorphism of ADD-1 and essential hypertension in a Korean population. The subjects (n=903) were participants in a population-based study in Jangseong County, Korea. The Gly460Trp polymorphism of ADD-1 was determined using a polymerase chain reaction method. The frequency of the 460Trp allele was 59.4% in normotensives and 61.1% in hypertensives (p=0.523). The frequencies of the genotypes did not differ significantly between the hypertensive and normotensive groups (16.3% Gly/Gly, 45.8% Gly/Trp, and 38.0% Trp/Trp in normotensives; 16.2% Gly/Gly, 45.8% Gly/Trp, and 38.0% Trp/Trp in hypertensives; p=0.928). After adjusting for other risk factors, Gly/Trp and Trp/Trp were not associated with hypertension (OR 1.00, 95% CI 0.65-1.53, Gly/Trp vs. Gly/Gly; OR 1.22, 95% CI 0.79-1.90, Trp/Trp vs. Gly/Gly). These findings suggest that the Gly460Trp polymorphism of ADD-1 is not associated with hypertension.

Key Words: Hypertension; Adducin; Polymorphism, Single Nucleotide

INTRODUCTION

Essential hypertension is currently seen as a multifactorial disease caused by multiple susceptibility genes, which are modulated by various environmental factors. Alpha-adducin (ADD-1) is a ubiquitously expressed cytoskeletal protein that appears to be involved in cell-to-cell contact (1), cell membrane ion transport (2), and signal transduction (3). Abnormalities of membrane sodium transport in the kidney play an important role in hypertension. Cusi et al. (4) reported that the Gly460Trp polymorphism of ADD-1 was associated with a salt-sensitive form of hypertension. However, subsequent study results have been inconsistent (5). There is little information on its relation to hypertension in the Korean population. Therefore, we examined whether the Gly460Trp polymorphism of ADD-1 was associated with hypertension in a Korean population.

MATERIALS AND METHODS

Subjects

The study subjects were 903 individuals who participated in a population-based study in Jangseong County, Korea, in August 2000. Informed consent for participation was obtained from all subjects. The participants completed a standard questionnaire on demographic characteristics, cigarette smoking, and alcohol consumption. Body mass index (BMI, kg/m²) was calculated from height and weight measurements. Blood pressures were measured using a common protocol with a Dinamap automated blood pressure reading device (Johnson & Johnson, New Jersey, U.S.A.). Two separate readings were taken. Our analysis is based on the average systolic blood pressure (SBP) and diastolic blood pressure (DBP). Hypertension was considered present if the average of two blood pressure measurements exceeded 140 mmHg systolic or 90 mmHg diastolic, or if the subjects were currently on antihypertensive medication.

Genotyping

Genomic DNA was extracted from peripheral blood using an AccuPrep Genomic DNA Extraction Kit (Bioneer, Seoul, Korea) according to the manufacturer's protocol. The Gly460-Trp polymorphism of ADD-1 was detected using a mutagenically separated polymerase chain reaction (PCR) (6, 7). Briefly, two allele-specific primers of different lengths (FP-
RESULTS

The genotype distribution did not deviate significantly from Hardy-Weinberg equilibrium expectations (Gly/Gly, 16.3%; Gly/Trp, 47.6%; Trp/Trp, 36.1%; p=0.79). Table 1 presents the baseline characteristics of all the subjects. Age, weight, height, body mass index, SBP, and DBP differed significantly between the hypertensive and normotensive groups. Sex, smoking habit, alcohol intake, and history of diabetes mellitus did not differ between the two groups. The frequency of the 460Trp allele was 59.4% in normotensives and 61.1% in hypertensives (p=0.523). The genotype frequency did not differ significantly between the hypertensive and normotensive subjects (p=0.928). After adjusting for age, sex, body mass index, smoking, alcohol intake, and history of diabetes mellitus, the odds ratio for hypertension associated with the presence of the Gly/Trp and Trp/Trp genotypes compared with the Gly/Gly were 1.00 (0.65-1.53) and 1.22 (0.79-1.90), respectively (Table 2).

DISCUSSION

In this cross-sectional study, we investigated the association between an alpha-adducin gene polymorphism and essential hypertension in a Korean population. We found that the Gly460Trp polymorphism of ADD-1 is not associated with essential hypertension. To our knowledge, this is the first report examining the relationship between ADD-1 Gly460Trp gene polymorphism and hypertension in a sample from a general Korean population.

The frequency of the 460Trp allele varies in different populations. In this study, the frequency of the 460Trp allele was 59.4% in normotensives and 61.1% in hypertensives. These frequencies are very similar to those in Japanese (52-66%) (7, 9-11) and Chinese (42-56%) populations (12, 13). However, the frequency of the 460Trp allele is low in white populations (18% in Italy (4), 20% in France (4), and 27% in Scotland (14)) and very low (6%) in black South Africans (15). It is generally accepted that the frequency of a given variant allele in a population is determined by the biological fitness it confers in the presence of a given environment.
(15). To achieve the functional characteristics needed to cope with an adverse environment, populations pick up the appropriate allele from the available genetic pool (5).

In this study, we could not detect any association between the Gly460Trp gene polymorphism and blood pressure. Cusi et al. (4) suggested that alpha-adducin was associated with a salt-sensitive form of hypertension. Subsequent studies have reported inconsistent results (5). There are a number of possible explanations for this inconsistency. The major consideration may be ethnic differences. In Asian studies, positive associations between the Gly460Trp gene polymorphism of ADD-1 and blood pressure were found in three (10, 11, 16) of five studies (7, 9-11, 16) conducted in Japanese populations and in two (12, 13) of four (12, 13, 17, 18) in Chinese populations.

The mechanism by which ADD-1 increases blood pressure is not known. ADD-1 is thought to regulate ion transport via changes in the actin cytoskeleton (19). Adducin is thought to stimulate Na⁺–K⁺-ATPase, promoting sodium re-absorption by renal tubular cells (20). Trp/Trp individuals with this alteration in renal sodium handling will have increased sensitivity of blood pressure to sodium intake and are at increased risk for developing low-renin hypertension (21).

In summary, we failed to reveal a significant association between the Gly460Trp gene polymorphism of ADD-1 and hypertension in a Korean population.

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