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Research Article

ASSOCIATION OF INSERTION/DELETION POLYMORPHISM OF ACE GENE WITH HYPERTENSION IN CENTRAL INDIAN POPULATION

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A B S T R A C T

Hypertension is a major health problem throughout the world because of its high prevalence and its association with increased risk of cardiovascular disease. Advances in the diagnosis and treatment of hypertension have played a major role in recent dramatic declines in coronary heart disease and stroke mortality in industrialized countries. Hypertension is a term related to high blood pressure and it referred to the condition that affects almost one billion people worldwide, and it is a leading cause of morbidity and mortality. Renin angiotensin system (RAS) plays crucial role in the regulation of blood pressure. Association between candidate gene polymorphisms of RAS and EH has been reported in different populations. A PCR based I/D polymorphism study in central Indian patients were perform to detect ACE polymorphism and its pathophysiological role in hypertension. The pattern of genotype and allele distribution in disease and control group suggested no association of ACE I/D in Hypertension susceptibility.

INTRODUCTION

Hypertension is a term related to high blood pressure and it referred to the condition that affects almost one billion people worldwide, and it is a leading cause of morbidity and mortality. More than 20% of Americans are hypertensive, and one-third of Americans are not even aware that they are hypertensive. Therefore, the disease is sometimes called as “silent killer”. This disease is usually asymptomatic until its damaging effects of hypertension (such a stroke, myocardial infarction, renal dysfunction, visual problems, etc.) are observed. Major risk factor for coronary artery disease, myocardial infarction (“heart attacks”) and stroke is Hypertension. RAS plays a crucial role in the initiation and maintenance of vascular inflammation and vascular remodeling. Vascular inflammation leads to endothelium dysfunction. A dysfunctional endothelium is leaky and facilitates migration of inflammatory cell into the vascular wall and stimulates smooth muscle cells proliferation. The renin-angiotensin system (RAS) plays a central role in the regulation of sodium metabolism, vascular tone, blood pressure, renal haemodynamics, and vascular modelling. The ACE gene provides instructions for making the angiotensin-converting enzyme. This enzyme is able to cut (cleave) proteins. It is part of the renin-angiotensin system, which regulates blood pressure and the balance of fluids and salts in the body. By cutting a protein called angiotensin I at a particular location, the angiotensin-converting enzyme converts this protein to angiotensin II. Angiotensin II causes blood vessels to narrow (constrict), which results in increased blood pressure. This protein also stimulates production of the hormone aldosterone, which triggers the absorption of salt and water by the kidneys. The increased amount of fluid in the body also increases blood pressure. Genetic variants of its major components such as the insertion/deletion polymorphisms of angiotensin converting enzyme I (*ACE-I/D* have been implicated in the pathogenesis of hypertension, cardiovascular and renal diseases (Miller and Scholey, 2004).

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MATERIAL AND METHODS

Study population

The study population consisted of 900 unrelated subjects and comprised 450 hypertension patients and 450 ethnically matched healthy controls of Indo-European ethnicity. Cases included consecutive patients who attended the Department of Medicine at Shyam Shah Medical College, Rewa, India; Vindhya Hospital Rewa (VHRC).

DNA isolation

Genomic DNA was extracted from whole blood using a modified version of the salting-out procedure described by Miller *et al*.1987

PCR Amplification

Isolated DNA is amplified with specific primers (Ramu *et al*.,2011)
5'-CTGGAGAGCCACTCCCATCCTTTCT-3' (Forward)
5'-GACGTGGCCATCACATTCGTCAGAT-3' (Reverse).
The PCR products were run on 2% agarose gel electrophoresis. The different fragments obtained were 490bp II, 190bp DD, and 490bp and 190bp ID.

Results of detection of ACE ID

Overall genotype pattern of ACE ID gene was slightly different between case and control but statistically non significant (χ^2 =1.709, 2, d.f. =2, P value= 0.4256). Hypertension group showed slight decrease in 'I/I' genotype as compared to control group (51.3% vs *55.1*%). Genotype 'D/D' was significantly higher in HC group as compared to Hypertension group (4.4% vs. 5.7%). An odds ratio of 0.8591 of common 'I/I' genotype group respectively was consistent with little or no effect of this genotype in Hypertension susceptibility. The heterozygous genotype 'I/D' was significantly distributed in HC group as compared to Hypertension group (40.4% vs 43.0%). An odds ratio of 1.106 of 'I/D' showed no association in Hypertension susceptibility.

Fisher's Exact Test of ACE I/D Insertion and deletion Polymorphism

Genotype	Case - 450 N	%	Control 450 N	%	P Value	Odds Ratio & (CI)
I/I	231	51.3%	248	55.1%	0.2851	0.8591 (0.6610-1.117)
I/D	193	43%	182	40.4%	0.4990	1.106 (0.8482-1.442)
D/D	26	5.7%	20	04.4%	0.4495	1.318(0.7248-2.398)
Allele Frequency						
I	655	52.4%	678	61.1%	0.2368	0.8754 (0.7088-1.081)
D	245	47.6%	222	38.9%	"	
Carriage Rate						
I	424	94.2	430	95.5	0.4392	0.9095 (0.7200-1.149)
D	219	48.6	202	44.9	"	

*denotes the level of significant association between case and control.
N - Number of individuals in study group.
% - Genotype allele frequency and carriage rate expressed in percentage.

Overall allele distribution was also significant but less common 'D' allele was found in lower frequency in control as compare to Hypertension patients (38.9% vs 47.6%) and 'I' allele was found at higher frequency in case as compare to control (61.1%vs 52.4%) but the difference was significant. Carriage rate of allele 'I' was approximately equivalent to HC group and Hypertension group. Whereas carriage rate of allele 'D' was higher in control group (95.5% vs. 94.2%) but not significantly different between case and control. The pattern of genotype and allele distribution in disease and control group suggested no association of ACE I/D in Hypertension susceptibility.

DISCUSSION

Hypertension is a common and complex human disease that causes significant morbidity and mortality worldwide. Unfortunately, despite recent advances in understanding and treating hypertension, its prevalence continues to rise. Blood pressure (BP) is a highly quantitative trait and therefore it has been difficult and somewhat arbitrary to define specific levels at which high blood pressure becomes too high, i.e. hypertension. As there is a strong correlation between cardiovascular, renal complications and hypertension, a practical definition and classification of high blood pressure to assess patients and provide treatment has been agreed upon and revised (Carretero & Oparil 2000). Overall allele distribution was also significant but less common 'D' allele was found in lower frequency in control as compare to Hypertension patients (38.9% vs 47.6%) and 'I' allele was found at higher frequency in case as compare to control (61.1%vs 52.4%) but the difference was significant. Carriage rate of allele 'I' was approximately equivalent to HC group and Hypertension group. Whereas carriage rate of allele 'D' was higher in control group (95.5% vs. 94.2%) but not significantly different between case and control. The pattern of genotype and allele distribution in disease and control group suggested no association of ACE I/D in Hypertension susceptibility.

The pattern of genotype and allele distribution in disease and control group suggested lack of association of ACE I/D in Hypertension susceptibility. Previous studies already done in india shown ACE ID gene polymorphism in the Indian population showed a significant association with DD genotype and diastolic blood pressure in men (Bhavani *et al*. 2004), but other one study did not show such association with DD genotype in hypertensive men (Ashavaid *et al*. 2000). However, our results are similar with the Japanese (Higaki *et al*. 2000), Indians (Bhavani *et al*. 2005), Turkish study (Agachan *et al*. 2003), African-Americans (Duru *et al*. 1994) and Framingham heart study (O'Donnell *et al*. 1998). Some limitations of this study should be mentioned. First, the size of the sample was small, in part, because of the difficulty to select patients due to the exclusion criteria.

CONCLUSION

Our research finding suggect that pattern of genotype and allele distribution in disease and control group suggested no association of ACE I/D in Hypertension susceptibility.

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