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Distribution of Angiotensin Converting Enzyme Gene I/D Polymorphism in Normotensive University Students

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Abstract

Objectives: The aim of our study was to evaluate frequency ACE I/D polymorphism with control of hypertension in the no athlete population.

Method: A total of 72 University normotensive students (aged 22 ± 1.2 years) were included in the study. DNA extraction from was collected through buccal swabs and was used the polymerase chain reaction (PCR) to observer the polymorphism of ACE gene amplify by electrophoresis. ACE I/D genotype frequencies were determined for the students groups.

Result: The average age was approximately 22 years (range 18-29 years). The genotype distribution in students no athletes was 11 (18.1%) homozygous for the allele I, 41 (58.8%) heterozygous I/D, and 20 (29.2%) homozygous for the allele D.

Conclusion: These results suggest that normotensive students exposed to environmental, genetic and lifestyle factors may have influenced genetic variations that may be useful genetic markers in clinical practice.

Keywords: I/D; Ace genotype; Genetic polymorphisms; Hypertension

Introduction

Hypertension (HT) is one of the most commonly encountered risk factors in clinical practice associated with cardiovascular disease, and its increase prevalence in worldwide [1]. HT is a complex disease, have a multifactorial etiology, with interactions among different factors as family history, lifestyle, genetic susceptibility, and environmental factors [2].

Although, studies have reported a lower prevalence of hypertension in athletes due to healthy lifestyle, and genetic factors [3].

Recent evidence suggests that angiotensin-converting enzyme (ACE) gene, as well as other genes is linked to associate with enhanced endurance performance in athletes [4]. In this context, ACE polymorphism of clinical important role in the control of blood pressure converts angiotensin I to the angiotensin II and degrade the bradykinin [5].

In plasma ACE is produce genetically by an insertion/deletion (I/D) at 16 in the ACE gene at chromosome location 17q23, has been shown to impact ACE activity with the deletion allele (D) associated with higher levels of ACE activity then the insertion allele (I) associates with muscular endurance increase [6]. The polymorphism has been associated with different types of response to ACE inhibitors in control the blood pressure in individuals [3]. However, polymorphism has been associated with different types of response not only with blood pressure, with cardiac remodeling, thus increasing the possibility of myocardial fibrosis, reducing pumping capacity (frank starling mechanism), induced by increased peripheral resistance and remodeling (left ventricular hypertrophy) [7].

Also, it has been documented that this polymorphism is associated with an increased baseline ACE activity, increased levels of angiotensin II production and require higher doses of ACE inhibitors to achieve an adequate response to ACE inhibition [8]. The present study, with a transversal descriptive design, was performed to verify whether the frequency of ACE gene with control of hypertension in the no athlete population.

Methods

In this descriptive, transversal study, the participants were Caucasians, non-athlete university students ≥ 18 years (35 females and 37 men), from Positivo University in city of Curitiba. Verbal or written informed consent was obtained from each participant (n=72) before the initiation of the study. Ethics were reviewed and approved by the Ethics Committee of Positivo University.

Genomic DNA was extracted from buccal swabs using standard protocol according to Scott et.al. Briefly, buccal swabs were provided by each subject and stored in cell lysis solution (0.1 M EDTA, 0.1 M Tris-HCl, 1% SDS) in a controlled temperature setting. DNA was extracted through a modified version of the Qiagen buccal cell spin protocol. The ACE I/D gene polymorphisms were identified

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by polymerase chain reaction (PCR) assay, using a forward primer recognizing the insertion (I) sequence, a forward primer recognizing the deletion.

Data analysis

Statistical analyzes were performed using the software (Prism 6.0, GraphPad Software Inc, La Jolla, Calif). We used descriptive statistics to summarize data genotype and allele frequency of ACE. The data were expressed in numbers and percentage.

All the 72 students (37 males and 35 females) were recruited from Positivo University located at Curitiba, Paraná, Brazil. The mean age of the subjects was 22.8 ± 9.82 years, all were distributed throughout the periods of the physical education course (Table 1).

Genotyping of the ACE I/D polymorphisms performed by the PCR method detected the presence of a PCR DNA product band of 487 base pairs for genotype II and/or 191 bp for the DD genotype and bands of 487 and 191 bp for the ID genotype (Figure 1).

The genotype distribution in students no athletes was 11(18.1%) homozygous for the allele I, 41(58.8%) heterozygous I/D, and 20 (29.2%) homozygous for the allele D.

Discussion

This study was designed to determine the frequency of ACE polymorphism activity on blood pressure in non-athlete people.

The ACE polymorphisms are characterized by the Insertion/Deletion of a 287 bp Alu repetitive element that this associated several functions in renin-angiotensin system (RAS), such as regulating homeostasis, converting angiotensin I to angiotensin II, among other functions [9].

However, most studies have used samples of the athlete, and the loci identified completely explain only a small fraction of the clinical applications in hypertensive patients [10].

Many studies supported the hypothesis that in Caucasians population, the ACE I/D polymorphism involved in nearly half of the total phenotypic variance of intracellular, circulating and tissue [10,11].

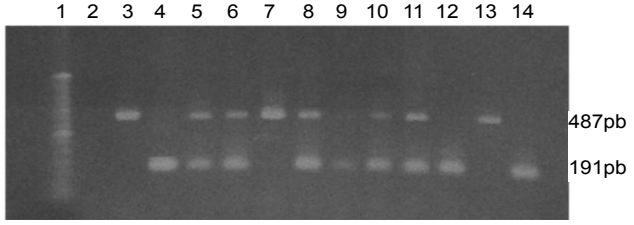

Figure 1: Visual determination of analysis of electrophoresis in agarose gel for characterization of the ACE I/d. 1 well genotypes-50 bp staircase; 2 well-negative control; Wells 3, 7 and 13-genotype II; Wells 4, 9, 12 and 14-DD genotype and wells 5, 6, 8, 10 and 11-genotype ID.

Genotype	Students (n=72)
I/I, n (%)	11 (18.1)
I/D, n (%)	41 (58.8)
D/D, n (%)	20 (29.2)
Allele	
I, n (%)	64 (44.4%)
D, n (%)	80 (55.6%)

Table 1: ACE I/D genotype and allele frequency in University students.

In the present study corroborates with findings in the literature, the ACE I/D genotypes showed relatively high with 58.8%, this genetic polymorphism is present in the studied population and is associated with higher functional performance and blood pressure control.

Durmic, et.al, reported that concentrations of ACE I/D genotypes in populations around the world, it is relatively low [12]. Considering that the homozygous DD individuals presents a higher concentration of circulating ECA than the heterozygotes ID and homozygotes II. Increased serum ACE levels may result in increased formation of Angiotensin II or increased degradation of bradykinin. Reinforcing the synergy of polymorphism with left ventricular hypertrophy (concentric hypertrophy), a deleterious mechanism for cardiac function, the studies demonstrate controversial results for changes in blood pressure values. A recent study of normotensive animals that underwent aerobic physical training did not promote cardiac hypertrophy. In this study, it can be observed that there are some changes in training response, such as a reduction in the systemic activity of ACE, physical training reduced by 20% of ACE activity in the heart compared to the sedentary group, which may partially explain the protection factor against heart remodeling. In addition, physical training reduced 50% of the gene expression of angiotensinogen in young animals. However, in the present study, participants identified with D/D (29.2), I/D (58.8) or I/I (18.1) polymorphism could be encouraged to perform aerobic physical exercises in order to minimize the effects or perhaps neutralize the mechanisms of left ventricular hypertrophy [7].

In general, the improvement of physical performance and blood pressure is probably the combined result of a multiplicity of genotypes.

The participation of this molecule in the prevention of hypertension has yet to be established; however, its participation in the systemic circulation or in the membrane supports your role of this genetic polymorphism in this pathology [13].

Conclusion

Our results suggest environmental conditions, genetic and lifestyle factors may have influenced the genetic variations that can be useful genetic markers in clinical practice and forensic medicine.

Conflict of Interest

None declared.

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