Captopril response association with angiotensin-converting enzyme (ACE) insertion/deletion polymorphisms in Mexican indigenous

COH11

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Purpose:

This study was aimed to associate the response to captopril, an antihypertensive drug, with the genotype of the insertion/deletion polymorphisms of the angiotensin-converting enzyme (ACE) in indigenous individuals from Chiapas with systemic arterial hypertension.

Introduction:

Systemic hypertension is a global health concern, contributing significantly to morbidity and mortality rates. Various factors, including genetic components, influence the development of this condition. Genetic polymorphisms in genes related to the angiotensin-converting enzyme (ACE) system, such as the insertion/deletion (I/D) polymorphism, have been implicated in hypertension pathogenesis. However, the association between these genetic variations and therapeutic responses to antihypertensive drugs remains poorly understood, particularly among the Maya indigenous population in Mexico.

The Renin-Angiotensin-Aldosterone System (RAAS) and the Angiotensin-Converting Enzyme (ACE) gene have been implicated in the development of arterial hypertension and various cardiovascular diseases. The ACE gene has a polymorphism known as insertion/deletion (I/D), where the presence or absence of 287 base pairs determines the genotype. The I/D variant of the ACE gene has been associated with diseases such as ischemic heart disease, diabetes mellitus, obesity, insulin resistance, arterial hypertension, nephropathy, and endothelial dysfunction. The DD genotype is linked to higher ACE activity, the I/D genotype to moderate activity, and the I/I genotype to the lowest activity. Studies have shown an association between the D allele and increased risk of myocardial infarction, arterial hypertension, cerebrovascular disease/stroke, and endothelial dysfunction. These findings highlight the importance of genetic variations in the ACE gene in understanding the etiology and treatment response of arterial hypertension and cardiovascular diseases.

This study is of particular significance as it focuses on an understudied population, the Maya indigenous people of Mexico, who face unique social and economic burdens. Understanding how genetic factors influence the response to antihypertensive medication in this population could potentially lead to more personalized and effective treatment strategies, ultimately reducing the social and economic burden of arterial hypertension in the Maya indigenous community.

Methods:

This was an observational, analytical, prospective, and longitudinal study aimed to associate the response to captopril, an antihypertensive drug, with the genotype of the insertion/deletion polymorphisms of the angiotensin-converting enzyme (ACE) in indigenous individuals from Chiapas with systemic arterial hypertension.

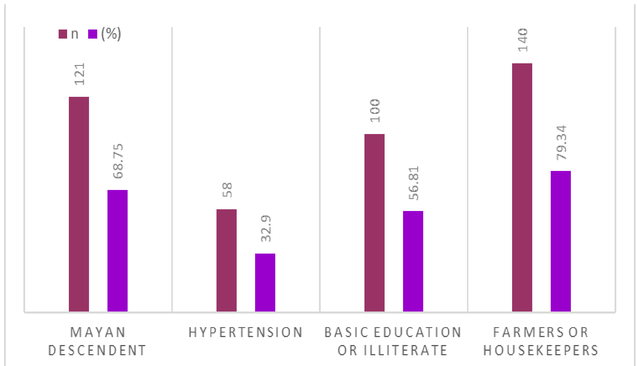
Clinical Variables from clinical history were taken, and the polymorphism were assessed from total blood as follows:

Blood samples preserved in ultra-refrigeration until the genetic material were extracted for identification of the I/D polymorphism of the ACE using the oligonucleotide sequences 5´-CTG GAG ACC ACT CCC ATC CTT TCT-3´ and 5´-AT GTG GCC ATC ACA TTC GTC AGA-3 the identification was confirmed through visualization on agarose gel and melting curves by real-time PCR.

Figure 1. Indigenous population distribution in México (Sotomayor, 2023) In Mexico, more than 20 million people are considered indigenous, which represents 19% of the country's population. The state with the highest percentage is Chiapas, with 31%, in the orange square are signaled the states with Mayan presence.

Results:

A total of 176 patients were included, of whom 68.75% (n=121) were indigenous of Mayan descent, with 32.9% (n=58) suffering from systemic hypertension, in graph 1 are showed the main demographic and clinical features of the population studied.



Graph 1: Main clinical and demographic findings in the population studied only 49 patients do not had Mayan ancestries.

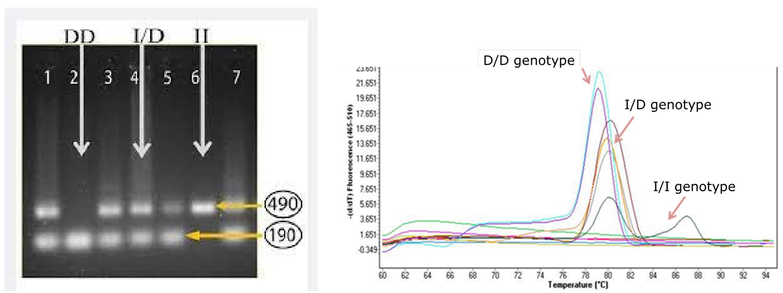
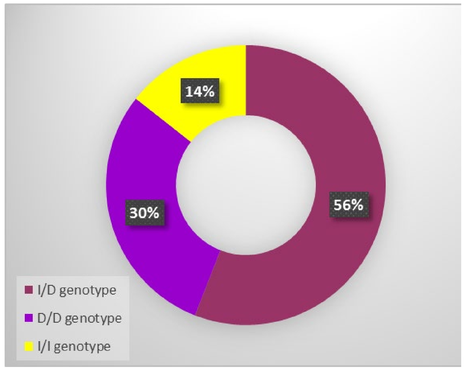


Figure 2. Representative Image of agarose gel and melting curves in the population studied

The distribution of ACE I/D genotypes are summarized in graph 2.



Graph 2. Distribution of ACE I/D polymorphism in Mayan indigenous studied

When the genotypes were analyzed estrafied by hypertensive estatus, it was observed that the D/D and I/D polymorphisms were more prevalent in the group of hypertensive indigenous individuals (89.74%), while being less frequent in the group of non-hypertensive mestizos (75%). The response to captopril was similar in both groups of hypertensive individuals (indigenous and mestizo), as both required the use of more than two antihypertensive agents to achieve effective pharmacological treatment

Conclusions:

- The D/D and I/D polymorphisms were more frequent in the hypertensive indigenous group but less prevalent in non-hypertensive mestizos.
- Response to captopril was similar in both groups of hypertensive individuals, with the need for multiple antihypertensive agents to achieve effective treatment.
- The Deletion allele was found to have a higher prevalence in the indigenous population with systemic arterial hypertension.
- Further multicenter studies are needed to explore the pharmacogenomics of antihypertensive drugs in diverse populations.
- Understanding the genetic factors influencing therapeutic response can contribute to the development of personalized treatment strategies to alleviate the social and economic burden of arterial hypertension in the Maya indigenous community.

References :

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