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EDITORIAL COMMENT

Genetic determinants of arterial hypertension: A case of oxytocin receptor gene polymorphism

Determinantes genéticos de hipertensão arterial: Um caso de polimorfismo do gene do recetor de oxitocina

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Arterial hypertension is the leading preventable risk factor for cardiovascular diseases, stroke and kidney failure and a major cause of morbidity and mortality worldwide.[1,2] Currently, individuals are considered hypertensive if their usual systolic blood pressure is ≥140 mmHg or diastolic blood pressure is ≥90 mmHg. Individuals at high risk of developing cardiovascular diseases and a usual systolic blood pressure of ≥130 mmHg are also included in this category.[2]

Hypertension can be classified as essential, when the cause of the increased blood pressure is unknown, or secondary, when the increased blood pressure is caused by another medical condition. Most arterial hypertension cases are classified as essential, with only 5-10% of adult patients having a known secondary cause, which may include coarctation of the aorta, renal disease, aldosteronism, Cushing's syndrome, pheochromocytoma, thyroid disease or obstructive sleep apnea.[2]

Essential hypertension is a multifactorial disease, arising from a combination of environmental and genetic factors. In terms of environmental factors, it is estimated that 50% of all hypertension cases can be attributed to excess weight, 30% to excessive salt intake, and 16% to low physical activity. From a genetic perspective, although 30-40% of all essential hypertension cases are estimated to be hereditary, genome wide association studies have only been able to attribute 2% of all cases to specific blood pressure genetic variants. Nevertheless, in most cases essential hypertension is caused by a combination of multiple environmental and genetic factors.[3] Our lack of understanding of the genetic determinants of blood pressure has led to hypertension treatments being largely focused on managing the environmental factors, although efforts to identify gene loci that control blood pressure levels continue to provide new molecular targets for therapeutic intervention.[4]

It is against this background that authors Cicekliyurt and Dermenci[5] present, in this issue of the Journal, research into the relevance of the single-nucleotide polymorphism (SNP) *rs2268498* of the oxytocin receptor (OXTR) gene as a risk factor for hypertension in a sample of the Turkish population.

The oxytocin hormone is a neuropeptide and the key factor in the milk-ejection reflex, which has also been linked to the regulation of immunological, metabolic and endocrine activity, and human and animal social behavior.[6,7] OXTR, in turn, is a G protein-coupled receptor; it is present in

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several areas of the brain as well as the arteries, veins, heart and other organs and tissues.[8] Within the context of hypertension and the cardiovascular system, oxytocin exerts a hypotensive action and has cardioprotective effects in hypertension, cardiac ischemia and cardiomyopathies.[8] For its part, *rs2268498* is a common polymorphism of the OXTR gene, presenting as either a T or C allele in what is presumed to be the promotor region of the gene, with carriers of the C-variant displaying up to a two-fold increase in mRNA expression of the gene. *rs2268498* has been associated with social processing and functioning, and carriers of the low-expression T-variant display performances suggestive of higher emphatic skills.[7]

Given the role of oxytocin in hypertension and associated cardiovascular diseases, as well as the demonstrable effect of *rs2268498* upon OXTR expression and several social behaviors, this SNP presented itself as a likely candidate for being a genetic risk factor for arterial hypertension.

In their work presented in this issue of the Journal, Cicekliyurt and Dermenci investigated the frequency of the *rs2268498* SNP in two groups of volunteers in Turkey. The patient group consisted of 140 individuals with an average age of 64.01±9.48 years, who had been diagnosed with arterial hypertension by presenting with an average blood pressure >140/90 mmHg. Exclusion criteria for the patient group included obesity, renal impairment, excess daily salt consumption, and hemodynamic and physiologic components with deviations that could cause hypertension. The control group consisted of 140 individuals with an average age of 56.41±12.85, with no history of hypertension or cardiovascular disease.

Cicekliyurt and Dermenci found that both groups had a similar allelic distribution. The hypertension group displayed a distribution of TT=42, CT=63, CC=35 and the control group displaying a distribution of TT=41, CT=64, CC=35. When combining data from both groups, their sample from the Turkish population showed a frequency for the C allele of 48%, which is similar to the frequency of the allele in a sample of 537 Caucasian Europeans (46%) found in another study.[9] This same study showed that the incidence of the *rs2268498* SNP could reveal significant differences between populations, as the C allele had a 29% frequency in a sample of 276 individuals of Chinese ancestry.

While the CC allele of *rs2268498* has been shown to lead to up to a two-fold increase in the mRNA expression of OXTR, and carriers of the TT allele display higher emphatic skills,[7] Cicekliyurt and Dermenci found no association between the *rs2268498* SNP and the risk for the development of arterial hypertension. This corroborates a study by Jacondino et al., in which another OXTR SNP, *rs2254298*, was studied in a cohort of Brazilian elderly patients. *rs2254298* has been associated with depression and overeating, however no correlation was found between the polymorphism and cardiovascular and metabolic risk factors.[10]

Nonetheless, the relevance of oxytocin and OXTR in arterial hypertension is undeniable, and the search to identify more genetic loci that control blood pressure will continue.

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Conflicts of interest

The author has no conflicts of interest to declare.

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