Natriuretic peptides, obesity and cardiovascular diseases

Peptídeos natriuréticos, obesidade e doenças cardiovasculares

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Summary

Obesity, hypertension and heart failure are conditions commonly associated with each other. Recent investigations have demonstrated that low plasmatic levels of natriuretic peptides are linked with obesity. Thus, knowing the actions of these hormones in water and salt homeostasis, it is possible to establish that low levels of natriuretic peptides may be the common denominator among obesity, hypertension and heart failure. Knowledge on this topic is crucial to develop further investigation for definitive conclusions.

Keywords: natriuretic peptides, obesity, hypertension heart failure, cardiovascular diseases, overweight.

Obesity is a significant health concern and represents an important risk factor for the development of cardiovascular diseases.[1] Despite progress in the management of this condition and the development of new health policies, the incidence of persons who are overweight or obese continues to rise. These people are at an increased risk to suffer from cardiovascular disorders with hypertension (HTN) and heart failure (HF) being the most frequent.[2,3] The pathogenesis of obesity is multifactorial resulting from interaction of biological, social and environmental factors.[4] However, current investigations have elucidated some aspects of this pathogenesis which explain an association among a high body mass index, HTN and HF.

Recent research has examined the influence of natriuretic peptides (NPs) on adipose tissue. They have demonstrated that NPs have lipolytic effects and that NP deficiency facilitates an increase in body mass index (obesity).[5,6] NPs also influence sodium and water homeostasis and are linked with HTN and HF pathophysiology. NPs facilitate diuresis, natriuresis, vasodilatation, and inhibit sympathetic outflow. These actions decrease blood pressure and reduce cardiac overload volume in patients with HF.[7,8]

From our point of view, these mechanisms suggest a relationship among low plasma levels of NPs, obesity and cardiovascular diseases (HTN and HF).

The metabolic pathway that explains the lipolytic actions of NPs was discovery recently. It begins with the production of these hormones in cardiac chambers. Then, they act through 4 guanylyl cyclase receptors of NPs located in several tissues, including adipose tissue. After a binding of the receptor they facilitate an increased production of cyclic guanosine monophosphate, which acts as a second messenger. This process is followed by an activation of protein kinase G, which induces hormone sensitive lipase phosphorylation, favoring triglycerides degradation. However, this is not the only antilipolytic mechanism of NPs. Protein kinase G can also activate p38 MAPK (mitogen activated protein kinase) enzyme turning on the brown fat thermogenic program. Brown fat stimulation increases energy expenditure and heat generation.[9]

This knowledge suggests that obesity is related to the development of HTN and HF due to decrease in a common denominator among these conditions, namely NPs.

This hypothesis should be explored in further studies. However, work published by Moro et al.[10] adds insight to this problem. These researchers found that lipid mobilization in subcutaneous adipose tissue due to physical exercise observed in overweight patients was associated with a rise in plasma levels of atrial NP. This finding supports the association between low NP concentrations and obesity and explains the beneficial effects of physical exercise in body mass reduction and improved blood pressure control.

Recently, another study demonstrated a genetic polymorphism of corin (enzyme that transforms pro-atrial

NP into atrial NP) with enhanced concentric cardiac hypertrophy in response to high systolic blood pressure in African American patients.[11] A change in corin function promotes reduction or modification in NP concentration and increases the risk of HTN and HF.

Other investigations have also found an inverse relationship between NP plasma levels and the incidence of HTN[12,13] and HF,[14,15] which supports the biological actions of these hormones. The finding of NP deficiency and the development of obesity[5,16] suggests that a primary decrease in NP concentration results in a reduction in fatty acid degradation which increases the probability of developing obesity. Simultaneously, due to low plasma levels of these hormones, there is a rise in hydrosaline retention, promotion of vasoconstriction and an increase in sympathetic outflow, increasing the probability to develop HTN and/or HF. In this case, both overweight/obesity and the above mentioned diseases appear in the same patient. This theory may be a new explanation for the associations observed among these conditions.

The possibility that low plasma levels of NPs represent the common denominator between obesity and the development of HTN and HF can open new strategies to treat these patients such as modifying NPs levels and/or intervening in their metabolic pathways. There is already a new field of investigation that involves the synthesis of NPs using amino acid insertion, substitution or deletion, which could be very useful in clinical practice.[17,18]

For now, the relationship among obesity, HTN, HF and low levels of NPs as a trigger of this association should be further evaluated. If this hypothesis is confirmed, new strategies to achieve better quality of life for our patients will need to be developed.

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ERRATUM

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In the article "Natriuretic peptides, obesity and cardiovascular diseases", published in the journal Rev Assoc Med Bras, vol. 61, n. 01: p.19-20, on page 19, where it reads:

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It should read:

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