Hypertension and Obesity: Correlates With Renin-Angiotensin-Aldosterone System and Uric Acid

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Arterial hypertension,[1] obesity,[2] the renin-angiotensin-aldosterone system (RAAS),[3] and uric acid[4] are all independently ligated to an increased cardiovascular (CV) risk. Arterial hypertension and obesity are among the 20 leading risk factors that increase the mortality of the general population with hypertension, which is number one.[1] In turn, obesity is one of the most common factors responsible for the development of arterial hypertension.[5] On the other hand, the RAAS and uric acid have been shown to participate independently in the development and maintenance of arterial hypertension, as well as in the mechanisms leading to the development of hypertension in obesity.[4,6,7] Furthermore, RAAS as well as uric acid have been shown to be related to an increase in CV morbidity and mortality in hypertension and obesity.[8,9] In fact, uric acid could play a role in the epidemic of obesity-related metabolic syndrome and cardiorenal disease.[10] In this issue of *The Journal of Clinical Hypertension*, Zhang and colleagues[11] expand the knowledge of the participation of the RAAS and uric acid in the pathogenesis of hypertension in obesity. The authors describe that serum uric acid is strongly related to angiotensinogen in an obesity-dependent manner in untreated hypertensive patients. They also describe that serum uric acid seems to contribute to the enhancement of plasma angiotensinogen and could be involved in the pathophysiology of obesity-related hypertension where an increase in activity of RAAS is one of the mechanisms underlying the development and maintenance of arterial hypertension.[5]

The pathophysiological scene of hypertension in obesity is a vicious circle in which specific mechanisms can contribute at the same time to trigger others, leading to the progressive deterioration of the cardiorenal system. This crosstalk between hypertension and obesity is represented in the Figure where it is shown how these mechanisms are interconnected. In this context, hyperuricemia is strongly related to arterial hypertension.[4,12] At the same time, increased sympathetic activity and increased RAAS are also mechanisms underlying hypertension and obesity, where the results of Zhang and colleagues[11] also point to angiotensinogen as an important player in the pathogenesis of obesity hypertension. The high level of circulating angiotensinogen observed in untreated hypertensive obese patients is also likely

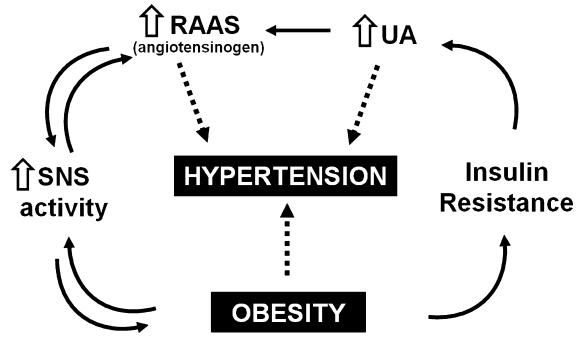

FIGURE. Common pathogenesis pathways related to hypertension and obesity. UA indicates uric acid; RAAS, renin-angiotensin-aldosterone system; SNS, sympathetic nervous system.

favored by the increase in fat mass observed in these patients. At the same time, high serum uric acid levels are a signature of the metabolic syndrome that also reflects a disturbed underlying renal hemodynamic effect. That is because the hyperinsulinemia and insulin resistance that accompanies obesity can induce the specific activation of the tubular sodium-hydrogen exchanger facilitating the active reabsorption of uric acid and decreasing its renal clearance.[13] Therefore, as the Figure shows, we know the players associated with obesity-related hypertension (as uric acid, angiotensinogen, RAAS, insulin, endothelial dysfunction, among others) and also the relationship of these factors with each other (eg, insulin resistance favors hyperuricemia and this, in turn, enhances RAAS activity). However, it is still not completely clear whether factors such as uric acid are the cause or the consequence of the cardiorenal deterioration observed in hypertension associated with obesity. Several clinical evidences have pointed out that uric acid could be an important causal factor in the onset of essential hypertension and obesity. In this sense, the observations of the Losartan Intervention for Endpoint Reduction in Hypertension (LIFE) study,[14] in which losartan-treated hypertensive patients showed reduced uric acid levels associated with reduced cardiovascular morbidity and mortality, or more recent trials in which treatment with allopurinol demonstrated decreased blood pressure in obese adolescents[15] and also delayed progression of renal disease,[16] show that drugs with uricosuric capacity may be considered as

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new therapeutic strategies in medical practice to treat obesity-related hypertension. However, larger and conclusive clinical trials are still needed to establish the specific clinical benefits of lowering uric acid in the setting of hypertension in obesity.

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