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COMMENTARY

Sacubitril/valsartan in the treatment of arterial hypertension: an unaccomplished promise?

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Arterial hypertension continues to be the leading cause of death worldwide[1,2] and, unfortunately, remains uncontrolled in a significant percentage of hypertensive patients who do not attain the blood pressure (BP) goal that most guidelines recommend (<140/90 mm Hg). A lively debate began after the publication of the Systolic Blood Pressure Intervention Trial (SPRINT),[3] in which a goal of 120 mm Hg was reported to be adequate in a portion of the hypertensive population. This has intensified the lack of adequate BP control, as the results of SPRINT cannot be applied to all hypertensive populations. In populations not included in SPRINT but in which stroke is particularly prevalent, such as the Asian population, a trial similar to SPRINT must be conducted before the recommendations suggested by SPRINT[3] are accepted and included in the hypertension guidelines, as has been done in countries such as Canada.[4]

It is clear by the acceptance of values below 140/90 as the goal of BP control that a great deal of works remains, even in those countries that exhibit the highest rates of good BP control. This is particularly true if we take into account that, in the uncontrolled population, comorbidities such as diabetes, chronic kidney disease and obesity are particularly prevalent and make BP control more difficult and increasingly important in terms of global cardiovascular risk.[5] In addition to the need to consider the adequate implementation of lifestyle changes—particularly adequate sodium and potassium intake, control of body mass index, and increasing physical activity—the adequate use of drug combinations is also pertinent, and the triple combination of a renin-angiotensin blocker (RASB), calcium antagonist and diuretic is considered in most guidelines to be the best triple combination.[6] This has also been demonstrated in a Japanese hypertensive population with the use of a combination of an angiotensin receptor blocker, a calcium channel blocker and a diuretic.[7]

In this issue of the journal, Supasyndh *et al.*[8] describe the efficacy and safety of the combination of sacubitril and valsartan for the control of BP over a 1-year follow-up period. These data are among the most important yet published on this new combination, which unfortunately does not seem as though it will be available in the near future for the treatment of hypertension. The sacubitril/valsartan combination was up-titrated if it needed to be 400 mg QD and, subsequently, amlodipine followed by hydrochlorothiazide could be used. The overall control of systolic BP was 90.6%, whereas it was 87.6 for diastolic BP. Additionally, 66.9% of patients remained on sacubitril/valsartan monotherapy until the study ended. These results expand upon the initial data that were obtained with different doses of sacubitril/valsartan[9] and in the treatment of severe hypertension.[10] They also show that two-thirds of patients with mild to moderate hypertension attain good control with this new monotherapy and that a diuretic is the best drug to add to complete a triad of therapy that aligns with the previous results of studies in Japanese hypertensives.[7] Interestingly, the capacity of sacubitril/valsartan to control BP has been successfully tested in patients with chronic kidney disease, a frequent and dangerous comorbidity in arterial hypertension.[11]

Such positive results can only be explained by the capacity of sacubitril/valsartan to simultaneously counteract different mechanisms that facilitate the development of high BP, such as angiotensin II and aldosterone, while promoting natriuretic peptides and natriuresis.[12,13]

The impressive effects of this combination on heart failure with reduced ejection fraction demonstrated in the Prospective Comparison of ARNI (angiotensin receptor neprilysin inhibitor) with ACEI (angiotensin-converting enzyme inhibitor) to Determine the Impact on Global Mortality and Morbidity in Heart Failure Trial (PARADIGM-HF)[14] remind us that the excellent initial results obtained with ACE in this clinical entity continued on with great success for arterial hypertension, renal disease and cardiovascular risk.[15] Can these results be replicated? The initial results in the context of arterial hypertension are sufficiently positive to consider the need for an indication of sacubitril/valsartan for arterial hypertension.[16] Additional studies are required in the areas of arterial hypertension, chronic kidney disease and high cardiovascular risk. An indication for arterial hypertension would be of great value in facilitating the control of the world's 2017–0029 number one killer.

CONFLICT OF INTEREST

Dr LMR has served as an advisor and a speaker for Novartis. The remaining author declares no conflict of interest.

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