Rev Port Cardiol. 2018;37(6):497–498

Revista Portuguesa de Cardiologia
Portuguese Journal of Cardiology
www.revportcardiol.org

EDITORIAL COMMENT

Sacubitril-valsartan in the real world: From theory to clinical practice☆

Uso do Sacubitril/Valsartan no ''mundo real'': da teoria à prática clínica

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Available online 19 May 2018

''In theory, theory and practice are the same. In practice, they are not.'' – Albert Einstein

Heart failure (HF) is considered the new cardiovascular epidemic of the 21st century, in view of its increasing prevalence, high mortality and enormous costs.[1] In Portugal, HF is a major public health problem for which local and national measures are urgently needed in order to change how HF-related healthcare is currently organized.[2]

Pharmacological treatment for heart failure with reduced ejection fraction (HFrEF) is based on careful titration of disease-modifying drugs, such as angiotensin-converting enzyme (ACE) inhibitors/angiotensin receptor blockers (ARBs), beta-blockers and aldosterone antagonists.[3] Recently, the PARADIGM-HF study showed that the use of sacubitril-valsartan reduced the risk of cardiovascular events by a further 20%[4] compared to ACE inhibitors and that this new strategy of neurohumoral modulation, instead of merely inhibition, increased survival by one to two years in patients with HFrEF.[5]

Given the good results of the PARADIGM-HF study, the use of sacubitril-valsartan has been included in the European Society of Cardiology guidelines as a class IB recommendation in patients who remain symptomatic despite optimal treatment.[3] The latest American guidelines for HF treatment have gone even further, recommending that patients in New York Heart Association (NYHA) class II or III who tolerate an ACE inhibitor or ARB be switched to sacubitril-valsartan to further reduce the risk of HF-related morbidity and mortality.[6]

However, despite the abundance of evidence and the recommendations in the guidelines, uptake of sacubitril-valsartan in the real world has been disappointingly slow.[7] There are various reasons for this mismatch between theory (the guidelines) and clinical practice, one of which is that patients included in clinical trials may not be representative of the real-world population. In a study examining this question by Rodrigues et al.[8] published in this issue of the *Journal*, only one in four patients with HFrEF followed in the HF clinic of a Portuguese tertiary hospital met the inclusion criteria of the PARADIGM-HF trial. Similarly, a study investigating the same issue that analyzed over 6000 consecutive patients referred to an HF clinic in the UK showed that only 21% fulfilled the PARADIGM-HF criteria,[9] although this proportion increased to 60% if the need to reach the maximum ACE inhibitor/ARB doses was ignored. These findings reveal that in many HF patients doses of ACE inhibitors/ARBs are not titrated to the maximum recommended, either because of the presence of hypotension, renal failure or other comorbidities, or due to clinical inertia in titrating drug doses in HF.

It is thus important to discuss whether titrating drugs up to the maximum dose should be mandatory before considering initiating sacubitril-valsartan. In the PARADIGM-HF trial, the benefits of the latter drug were consistent,

☆ Please cite this article as: Fontes-Carvalho R. Uso do Sacubitril/Valsartan no ''mundo real'': da teoria à prática clínica. Rev Port Cardiol. 2018;37:497–498.

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regardless of dose or background therapy.[10] In addition, around 40% of patients had to have their enalapril dose reduced during the trial, and treatment benefits were similar in these individuals.[11] Thus, since the survival benefits of sacubitril-valsartan exceed those of an increase in ACE inhibitor/ARB dose, even patients taking submaximal doses of ACE inhibitors or ARBs should be switched to equivalent doses of sacubitril-valsartan.[12]

In conclusion, the introduction of sacubitril-valsartan is undeniably an advance in the treatment of HFrEF.[13] It is indicated as a replacement for ACE inhibitors/ARBs in HF patients with ejection fraction <40% and in NYHA class II-III. In HF, delay in starting disease-modifying treatment is associated with a significant increase in mortality.[14,15] Therefore, in the knowledge that (especially in medicine) theory and practice, as Einstein pointed out, are often not the same, the success of HF treatment will depend on whether the best scientific evidence is applied in real-world clinical practice.

Conflicts of interest

The author has no conflicts of interest to declare.

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