Discontinuity of Sacubitril/Valsartan in a Cohort of Hospitalised Individuals for Heart Failure

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INTRODUCTION

Heart failure (HF) is a complex, multifactorial clinical syndrome that originates from an alteration in the pump function of the heart, either systolic and/or diastolic. This condition typically manifests itself with symptoms such as dyspnoea, easy fatigability and water retention, which are often responsible for a reduced quality of life. The prevalence of HF increases exponentially with increasing age [1] and is on of the most main cause of hospitalisation of geriatric population. This is associated with a high mortality risk and a significant burden of comorbidities [2-3]. The management of these patients is particularly complex and relevant in public health terms. Over the years, guidelines for the management of heart failure have undergone some modifications following the introduction of new drugs. Specifically, from 2021 the guidelines ESC [4] suggest, as first-line for HF patients, the use of sacubitril/valsartan. The efficacy of sacubitril/valsartan has been investigated HF in two randomizd clinical trial (RCT): PARADIGM-HF (Prospective Comparison of Angiotensin Receptor–Neprilysin Inhibitor with Angiotensin-Converting–Enzyme Inhibitor to Determine Impact on Global Mortality and Morbidity in Heart Failure Trial) [5] and PARAGON-HF (Prospective Comparison of Angiotensin Receptor–Neprilysin Inhibitor with Angiotensin-Receptor Blockers Global Outcomes in HF with Preserved Ejection Fraction) [6].

However, few real world data is available about persistence of this pharmacological treatment.

AIM

To investigate the therapeutic discontinuity of sacubitril/valsartan in a cohort of individuals hospitalised for heart failure using data from the healthcare databases of the Lombardy region.

METHODS

The study was conducted according to a retrospective cohort design. Patients in the Lombardy Region aged between 40 and 80 years with a hospitalisation for heart failure (ICD9-CM codes: 402.01, 402.11, 402.91, 404.01, 404.03, 404.11, 404.91, 404.03, 404.13, 404.93, 427.4x and 428.x) in the period 2021-2022 were identified. For each subject, the first hospitalisation for HF was considered and the discharge date was taken as the index date. Patients with a hospitalisation for heart failure in the 5 years preceding the index date were excluded. The final cohort included all patients with a fill of sacubitril/valsartan in the first 90 days after index date.

All sacubitril/valsartan prescriptions dispensed to cohort members during follow-up were identified. The duration of each prescription was calculated by dividing the total amount of drug prescribed by the DDDs (Defined Daily Dose). From the index prescription onwards a patient was considered to be discontinuing (primary outcome) if the time lapse between the end of the prescription and the start of the next one was greater than or equal to 90 days. The first day of non-coverage of the drug was considered as the event date. A sensitivity analysis was performed considering a reduce length of 60 days for the window used to define discontinuation.

Each cohort member was followed from the index date until 31 December 2023. The proportion of discontinuation was estimated with its 95% confidence interval (95% CI). A log-binomial model was implemented to investigate the determinants of discontinuation including the following variables: gender, age at index date, the use of antihypertensive, antidiabetic, statins and antidepressants as well as Multisource Comorbidity Score (MC score at 3 classes) evaluated in the 5 years before index date. The relative risk (RR) and its confidence interval (95% CI) was reported.

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RESULTS

Final cohort was composed by 1985 patients with a first admission for HF in the period 2021-2022. The mean age was 65 (SD 10) years and 77% were male. Of these, 27% were in treatment with antidiabetics while 45% with statins and 74% with antihypertensive drugs. In addition, 11% were treated with antidepressants. Patients in the lowest MC score class were 1177 (59%) while those in the highest class were 323 (16%). The S/V discontinuation proportion was 20% (95% CI 18% to 22%). We observed that for discontinuers the proportion of alternative pharmacological drug (ACE, ARB, CCB, BB and Diuretics) during the 90 days with no S/V treatment were lower respect to their proportion during the 3 months after index date suggesting either a clinician indication or the onset of collateral effect.

The model showed that increasing age was statistically associated with a lower risk of discontinuation (RR 0.987; 95% CI 0.976 to 0.998, p-value = 0.019) while the use of antidepressants increased the risk (RR 1.430; 95% CI 1.072 to 1.91, p-value = 0.015). When the outcome was defined by considering 60 days, age was no longer significant.

CONCLUSIONS

Preliminary data based on few years after ESC guidelines showed a quite high S/V discontinuation proportion similar to that reported in other studies [7]. Young age and use of antidepressant seems to increase the risk to interrupt an efficacy treatment like S/V. Continuous monitoring of healthcare data, in the next years, will allow efficiently to evaluate the effectiveness and persistence to S/V treatment.

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