Abstract: P1671

Safety, tolerability and discontinuation causes of sacubitril/valsartan treatment in patients with heart failure and reduced ejection fraction attending to an outpatient heart failure clinic.

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Topic(s):
Chronic Heart Failure: Pharmacotherapy

Citation:
Background
Data from controlled clinical trials indicate that sacubitril/valsartan is an effective treatment for heart failure with reduced ejection fraction (HFrEF) with an acceptable safety and tolerability profile. However, more information is needed in real world HFrEF patients.

Purpose
To describe the clinical characteristics, the safety and tolerability profile, and the discontinuation causes of the sacubitril/valsartan treatment in patients with HFrEF followed in an outpatient heart failure clinic.

Methods
We collected data from 119 consecutive patients attending to our heart failure outpatient clinic between May 2018 and November 2018. 64 (53.8%) were treated with sacubitril/valsartan. Patients were uptitrated with the goal of achieving sacubitril/valsartan 200 mg twice daily. Clinical and neurohormonal variables including those related with adverse effects and discontinuation were collected baseline and at the end of the titration period.

Results
At baseline, mean age was 63±10 and 76.6% men. Mean LVEF 28±6%. 39% ischemic etiology. 67.2% were in NYHA class II. Median NT-proBNP level 1176 pg/ml (IQR 364-3945). Mean glomerular filtration rate (GFR CKD-EPI) 71.7±20.6 mL/min and serum potassium 4.4±0.4 mEq/L. 84% received ACE inhibitors (median enalapril equivalent dose 7.5 mg/day, IQR 5-13.7) or angiotensin receptor blockers (median equivalent valsartan dose 80 mg/day, IQR 60-160). 95% received beta-blockers and 86% mineralocorticoid receptor antagonists. At the end of the titration period (6.5 weeks, IQR 3-13.2), target dose was achieved in 23 patients (40%). 24 (37.5%) needed any dose reduction. The main cause of dose reduction was hypotension, defined as systolic blood pressure (SBP) <90 mmHg (n=12, 18.8%), followed by dizziness (n=6, 9.4%), worsening of renal function, defined as serum creatinine >3.0 mg/dL (n=4, 6.3%) and diarrhea (n=2, 3.1%). 10 patients (15.6%) discontinued therapy due to adverse events. Causes for therapy discontinuation were hypotension (n=4, 6.2%), cost of medication (n=4, 6.3%), hyperkalaemia, defined as serum potassium >5.5 meq/L (n=2, 3.1%) and diarrhea (n=1, 1.6%). Angioedema was not detected. Patients with at least one adverse event were older, and with lower SBP and GFR (all p<0.05). In a multivariable analysis adjusted by age, levels of creatinine and NT-proBNP, a lower SBP (OR 0.94 95% CI 0.90-0.99) was the only variable independently associated with adverse events.

Conclusion
The treatment with sacubitril/valsartan has a tolerability profile in line with other recommended HFrEF treatments. In our cohort, hypotension remains as the main cause of reduction or discontinuation of sacubitril/valsartan. In this population of relatively young patients the cost of medication was a major cause of discontinuation. In countries with co-payment system, like ours, the non-pensioners have to pay between 40 to 60% towards the cost of medication. This aspect could be a barrier to equitable access to novel treatments.
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