24-hour urinary sodium excretion in patients with heart failure with reduced ejection fraction treated with sacubitril/valsartan

Authors:
S Bezati1, V Stasinos2, C Kardamis1, P Dourvas1, N Makris2, V Kontogeorgi3, M Loisiou3, E Klonou3, P Flevari2, D Leftheriotis2, 1General Hospital of Corfu, Department of Cardiology - Corfu - Greece, 2Attikon University Hospital, 2nd University Cardiology Department - Athens - Greece, 3General Hospital of Corfu, Department of Biochemistry - Corfu - Greece,

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INTRODUCTION

Sodium retention is a principal component in the vicious cycle of heart failure. Recent studies target urinary sodium excretion, considered as predictor for death and cardiovascular disease, in order to adjust therapy in acute heart failure. Treatment with neprilysin inhibitors in combination with angiotensin II receptor antagonist (ARNIs) has shown beneficial effects in morbidity and mortality in patients with heart failure with reduced ejection fraction (HFrEF).

PURPOSE

We investigated the possible association between treatment with ARNIs and urinary sodium excretion.

METHODS

We enrolled a total of 52 stable patients with HFrEF eligible for treatment with ARNIs. Patients were administered a target dose of 200mg bid (97mg sacubitril/103mg valsartan) and 24-hour urine samples were collected before, 3 months and 6 months after initiation of therapy. We calculated mean and median values of 24-hour sodium excretion and changes in subgroups of patients in relation to NYHA class were tested with General Linear Model Repeated Measures test. To test changes in relative and absolute changes in urinary sodium excretion we performed Kruskal Wallis test. Spearman’s Rho correlation analysis was performed to investigate possible associations among New York Heart Association (NYHA) functional class, dose administered and absolute and relative changes in 24-hour sodium excretion.

RESULTS

Mean age was 62±10 years, 69.2% of patients were on NYHA II, 23.1% on NYHA III and 7.7% on NYHA IV functional class. 57.7% had ischemic while 42.3% dilated cardiomyopathy, 25% chronic kidney disease and 36.5% diabetes mellitus. Median values of 24-hour sodium excretion were 122mmol (IQR 128), 133mmol (IQR 76) and 139mmol (IQR 85) at baseline, three and six months of treatment, respectively. 24-hour sodium excretion increased significantly in relation to NYHA class (p=0.038) and dose administered (p=0.053) during six months of treatment. Mean relative 24-hour sodium excretion augmented 83%. Absolute and relative changes during the first three months of treatment were statistically significant in the different subgroups of patients based on NYHA class (p=0.019 and p=0.011, respectively). The following three months of treatment levels of 24-hour excretion did not present statistically significant changes (p=0.273 and p=0.191). Absolute and relative changes were correlated significantly with NYHA class and dose administered during the first three months of treatment (p=0.11 and p=0.008, respectively).
CONCLUSIONS

Stable HFrEF patients treated with sacubitril/valsartan showed elevated urinary sodium excretion during the first three months of therapy. Levels of 24-hour urinary sodium concentration remained relatively stable the following three months of treatment. Changes were more evident in NYHA III group of patients who received optimal dose of ARNIs.