Interventional
Cardiology

Protective effect of sacubitril valsartan on acute kidney injury in patients with acute decompensated heart failure

Abstract

The interactions between the heart and kidneys are complex and a subject of great clinical and scientific interest and debate. Acute Decompensated Heart Failure (ADHF) represents the principal cause of hospitalization for Heart Failure (HF), with a prevalence that increases with age and contributes significantly to healthcare costs. Acute Kidney Injury (AKI) represents a significant adverse event among patients with ADHF, with a considerable impact on morbidity. In more than 30% of cases of ADHF, AKI develops during the course of the patient's hospitalization. The occurrence of new-onset AKI in patients with HF was associated with an elevated risk of in-patient mortality, prolonged length of stay, and increased healthcare costs compared to HF hospitalizations in which patients did not develop AKI. The management of HF in the setting of new-onset AKI represents a significant medical challenge in the acute setting due to the complex relationship between the cardiovascular and renal systems. The early detection of AKI in patients with ADHF and the implementation of appropriate interventions are of paramount importance in order to reduce the mortality rate of patients with AKI and to save money for the health insurance department. The aim of the current work is to identify effective interventions and future treatments for patients with ADHF and AKI.

Keywords: Acute kidney injury . Acute decompensated heart failure . Angiotensin receptor-neprilysin inhibitor

Introduction

Heart Failure (HF) represents a significant global health burden, affecting over 64 million individuals worldwide [1]. In particular, Acute Decompensated Heart Failure (ADHF) is a leading cause of hospitalization in older adults, with a notable impact on healthcare costs [2]. ADHF has the potential to result in significant adverse outcomes, including a decline in cardiac function, recurrent hospitalizations, and mortality. Congestion, a common feature of decompensated HF, is a significant contributing factor to Acute Kidney Injury (AKI) development [3].

AKI is a frequent coincidental syndrome among patients with HF [4]. Prior studies have demonstrated a strong association between AKI and HF [5,6]. The epidemiology of AKI serves to illustrate its considerable impact on mortality, morbidity, and healthcare costs. AKI is a complex systemic syndrome associated with a high morbidity and mortality rate. In patients with ADHF, the incidence and impact of AKI has been reported mainly in subjects hospitalized with acute HF, in which the prevalence of AKI is approximately 20% to 30% [7-9]. The growing recognition of AKI as a risk factor for HF has led to its association with prolonged hospitalization, an elevated risk of hospital readmission, and an increased risk of long-term mortality [10-13]. Prior study

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has demonstrated that a sudden decline in renal function is a more unfavorable prognostic indicator in patients with HF [14].

A number of studies have identified the mechanisms underlying AKI in patients with HF, demonstrating the involvement of common hemodynamic, neurohormonal, immunological, and biochemical feedback pathways [15-17]. The interaction between HF and AKI is complex, bidirectional, and interdependent. However, the exact mechanism remains unknown [17].

The recently released 2024 Kidney Disease Improving Global Outcomes (KDIGO) clinical practice guidelines emphasize the necessity for a comprehensive assessment of kidney risk [18]. An early diagnosis of AKI is important because it affects clinical management and improves clinical outcomes in patients with ADHF. The combination of HF and AKI has a particularly adverse outcome, underscoring the necessity for prompt detection and timely, tailored preventive and therapeutic interventions [19].

The severity or persistency of congestion is linked with adverse outcomes. This notion highlights the necessity for effective decongesting strategies using timely and adequate diuretic therapies. The onset of AKI is contingent upon a complex interplay of hemodynamic variables, including low cardiac output and congestion, and the effects of medications such as angiotensin-converting enzyme inhibitors and diuretics on kidney function.

Recently, urinary Neutrophil Gelatinase-Associated Lipocalin (uNGAL) has been described as a promising biomarker for the management of acute kidney disease. uNGAL is one of the earlier proteins released from the kidney after ischemic or toxic damage. It is a strong predictor of poor outcomes and early death in patients with AKI and ADHF. uNGAL was a good diagnostic marker for AKl development, the rise in uNGAL concentration occurred 48 hours before a jump in Serum creatinine (Scr) levels. This is significant because Scr, currently the main AKl biomarker used in clinical settings, shows a reduction in renal function has already begun and even small Scr rises are independently associated with mortality. Several clinical trials have shown that urinary and serum levels of NGAL have increased significantly in patients with AKI. Compared with other markers, uNGAL levels are closely correlated with the severity of kidney injury and early detection of AKI [20]. It was found that uNGAL is a good diagnostic marker for early prediction of AKl when the timing of the kidney injury is unknown. NGAL is also involved in the mechanism of underlying renal damage. It is a pro-inflammatory factor that promotes the progression of AKI to chronic kidney disease. Increased NGAL levels correlate with the severity of kidney injury [21].

We demonstrated that the uNGAL level in patients with ADHF complicated by AKI was increased 24 hours after hospital admission, and could be used as a biomarker to predict AKI occurrence in patients with ADHF [22]. Early detection of patients

at higher risk for AKI occurrence would help physicians to plan and initiate appropriate management to improve the renal safety of therapies, augment surveillance of cardiac and renal dysfunction, and develop renal-preserving treatments.

Sacubitril valsartan, an Angiotensin Receptor-Neprilysin Inhibitor (ARNI), has been shown to have cardiovascular benefits in chronic HF and ADHF [23]. Imbalance of the natriuretic-peptide system and over-activation of the Renin-Angiotensin-Aldosterone System (RAAS) in HF patients results in over-expression of renin and aldosterone and reduction of natriuretic peptides, which also contribute to AKI progression [22].

Our findings suggest that compared with Angiotensin-Converting-Enzyme inhibitors (ACE inhibitors) treatment, ARNI treatment in patients with ADHF combined with AKI may have a renal-protective effect by reducing the dose of loop diuretics, lowering the Scr level, improving the eGFR, and reducing the duration of hospital stay. We hypothesize that ARNI exerts a renal-protective effect by inhibiting the overactivated RASS in patients with ADHF, increasing the level of natriuretic peptides, and reducing the uNGAL level [22]. Sacubitril valsartan has demonstrated a favorable safety and efficacy profile in the treatment of patients with ADHF combined with AKI, and the results of the short communication provide a new perspective on the treatment of patients with heart failure [17,22,24].

Future treatment strategies are likely to be more individualized, i.e., tailored to the specific etiology and comorbidities of different acute heart failure phenotypes. Such as innovations in artificial intelligence technology, continued innovation in clinical trials, and research targeting individual phenotypes will also help to bring the next generation of therapies into clinical use for the benefit of more patients with acute heart failure.

Conclusion

In conclusion, the use of uNGAL allows for the early diagnosis of AKI and facilitates the early initiation of ARNI intervention for AKI. Furthermore, sacubitril valsartan has a favorable effect on cardiac function without obvious risk of adverse events in ADHF patients combined with AKI, indicating that sacubitril valsartan has the potential to become perspective treatment for these patients.

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