INPLASY

The Role of Sacubitril/Valsartan in Abnormal Renal Function Patients Combined with Heart Failure: A Meta-Analysis and Systematic Review

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ADMINISTRATIVE INFORMATION

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Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 09 December 2023 and was last updated on 09 December 2023.

INTRODUCTION

Review question / Objective This study aimed to investigate the efficacy and safety of sacubitril/valsartan in abnormal renal function (eGFR<60 ml/min/1.73m2) patients combined with heart failure based on randomized controlled trials (RCTs) and observational studies.

Condition being studied Chronic kidney disease (CKD), a global health problem, has an increased risk of cardiovascular disease which often manifests as heart failure. It has been reported that heart failure is associated with elevated morbidity and mortality of patients with CKD stages 3-5 patients with heart failure. In addition, in these special patients, the management of heart failure remains a huge challenge, possibly because of drug side events and their low responsiveness to conventional therapies. So, it is essential to explore new therapeutic strategies for abnormal renal function patients combined with heart failure. Recently, sacubitril/valsartan, as a novel dual inhibitor of neprilysin and angiotensin receptor, can ameliorate the prognosis of heart failure through vasodilatation, diuresis, natriuresis and anti-remodeling properties by simultaneously restraining natriuretic peptides degradation and renin-angiotensin-aldosterone system (RAAS) activation. Clinical guidelines have recommended sacubitril/valsartan for patients with heart failure to reduce the risk of cardiovascular death. However, these guidelines are primarily applicable to patients with normal kidney function. Whether

sacubitril/valsartan is safe and effective in impaired renal function patients combined with heart failure is still unclear.

METHODS

Participant or population Abnormal renal function (eGFR<60 ml/min/1.73m2) patients combined with heart failure.

Intervention The experimental group used sacubitril/valsartan.

Comparator The control group therapy without sacubitril/valsartan.

Study designs to be included Randomized controlled trials (RCTs) and observational studies.

Eligibility criteria The following inclusion criteria were required for eligible literature: (a) Participants: the population of trial contained estimated glomerular filtration rate (eGFR) below 60ml/min/1.73m2 patients combined with heart failure;(b) Intervention: the experimental group used sacubitril/valsartan;(c) Comparisons: the control group therapy without sacubitril/valsartan;(d) Outcomes: cardiovascular events or safety outcomes were available;(e) Study design: the number of patients with CKD and heart failure was definite or can be calculated; the type of study was RCT or observational study.

Information sources We extracted the following information from the eligible trials: the trial name, number of patients, baseline eGFR, drug names and doses, duration of treatment, efficacy outcomes (the incidence of cardiovascular death or hospitalization for heart failure) and safety outcomes (changes in renal function; the incidence of hyperkalemia and hypotension).

Main outcome(s) In terms of efficacy, we analyzed the incidence of cardiovascular events and found that sacubitril/valsartan significantly reduced the risk of cardiovascular death or heart failure hospitalization in chronic kidney disease (CKD) stages 3-5 patients with heart failure. As for safety outcomes, sacubitril/valsartan prevented the serum creatinine elevation, the eGFR decline and the development of end-stage renal disease in this population. In addition, we found that the rate of hyperkalemia and hypotension also did not increase in sacubitril/valsartan group among CKD stages 3-5 patients with heart failure.

Quality assessment / Risk of bias analysis Based on the ROB tool, all included RCTs were of high quality. According to the ROBINS-I tool, nine observational studies were assessed as having a relatively low risk of bias in six areas.

Strategy of data synthesis All statistical analysis in this meta-analysis were performed on Review Manager 5.3. Dichotomous variables were described as event counts with the odds ratio (OR) and 95% confidence interval (CI) values. Continuous variables were expressed as mean ± standard deviation (SD) with 95% CIs. The heterogeneity of studies was assessed with the Q test, I2 statistic and forest maps. Heterogeneity was low when I2 was less than 25%, moderate when I2 was between 25% and 50% and high when I2 was greater than 50%. We chose a fixed-effects model when I2<50%, otherwise the random-effects model was picked. Funnel plots and Egger's test were used to assess publication bias if at least ten studies were included.

Subgroup analysis Subgroup analysis based on eGFR level.

Sensitivity analysis None.

Country(ies) involved China.

Keywords sacubitril/valsartan; chronic kidney disease; heart failure; meta-analysis; randomized controlled trials; observational studies.

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