Scientific Research Publishing

Case Reports in Clinical Medicine, 2021, 10, 197-202
https://www.scirp.org/journal/crcm
ISSN Online: 2325-7083
ISSN Print: 2325-7075

The Effect of Sacubitril/Valsartan in a Dialysis Patient with Severe Heart Failure*

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How to cite this paper: Kong, P.P., Dou, Y.N., Wang, X.Y., Xiao, J. and Zhao, Z.Z. (2021) The Effect of Sacubitril/Valsartan in a Dialysis Patient with Severe Heart Failure. *Case Reports in Clinical Medicine*, **10**, 197-202.
https://doi.org/10.4236/crcm.2021.107025

Received: June 15, 2021
Accepted: July 19, 2021
Published: July 22, 2021

Abstract

Heart failure (HF) is a major comorbidity in patients with end-stage renal disease (ESRD). The pathogenesis of HF in patients on renal replacement therapy represents the confluence of several traditional and nontraditional vascular risk factors, unique to the milieu of chronic kidney disease and the dialysis modality [1]. The purpose of this report is to describe the efficacy and safety of sacubitril/valsartan for an ESRD patient on hemodialysis therapy conmbined with heart failure with reduced ejection fraction (HFrEF). A 35-year-old woman was undergoing hemodialysis due to ESRD and suffering from heart failure with reduced ejection fraction. Because of worsening heart failure and hypertension, she was prescribed with sacubitril/valsartan at a dose of 50 mg twice a day, spironolactone at a dose of 20 mg three times a day and metoprolol at a dose of 23.75 mg once daily. There was a symptomatic improvement with the heart failure and reduction in NT-proBNP level, accompanied by a decrease of blood pressure after using sacubitric/valsartan. In conclusion, it is safe and effective to take sacubitril/valsartan in this hemodialysis patient with severe heart failure.

Keywords

End Stage Renal Disease, Sacubitril/Valsartan, Hemodialysis, Heart Failure, Reduced Ejection Fraction

1. Introduction

Cardiovascular disease is the main cause of death in maintenance hemodialysis patients. Many studies have shown that the proportion of dialysis patients complicated with heart failure is as high as 45% [2] [3] [4]. Heart failure is the most

*An informed consent was obtained from the patient.
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common and serious cardiovascular complication of dialysis patients, with a very high incidence and poor prognosis, which is an important reason for the progress and death of patients [5] [6]. The treatment of maintenance hemodialysis complicated with heart failure is inhibition of RAAS system (Angiotensin-converting enzyme inhibitors (ACEIs), angiotensin receptor blockers (ARBs) and aldosterone antagonist), control of hypertension, Beta-blockers, statins, etc [7]. Sacubitril/valsartan, which combines an angiotensin receptor blocker (valsartan) with a NEPi (sacubitril), was the first angiotensin receptor–neprilysin inhibitor to be developed. Natriuretic peptide system (NPS) is a kind of neuroendocrine system. It has many beneficial functions, including natriuretic, diuretic, vasodilator and anti regulation of RASS. Neprilysin (NEP or neutral endopeptidase) is the key enzyme responsible for degrading natriuretic peptides. Sacubitril/valsartan consists of the neprilysin inhibitor sacubitril and the ARB, which strengthens the protective neuroendocrine system of the heart while inhibiting the renin-angiotensin-aldosterone system, was superior to enalapril in reducing the risks of death and of hospitalization for heart failure. The PARADIGM-HF trial showed that sacubitril/valsartan reduced the risk of cardiovascular mortality among patients with heart failure with reduced ejection fraction when compared with the angiotensin-converting enzyme inhibitor enalapril, several trials in populations with heart failure. The UK HARP-III trial (United Kingdom Heart and Renal Protection-III) has demonstrated that, compared with irbesartan, sacubitril/valsartan further reduces both blood pressure and biomarkers of cardiovascular risk (troponin I and N-terminal pro-B-type natriuretic peptide), and in a wide range of people with proteinuric chronic kidney disease, adding neprilysin inhibition to angiotensin II receptor blockade has no additional effect on kidney function or albuminuria [8] [9] [10]. However, there were less reports on tolerability and outcome of patients with hemodialysis patients. The purpose of this case is to report the efficacy and safety of sacubitril/valsartan in the treatment of ESRD patients with HFrEF.

2. Case Report

A-35-year-old hemodialysis female patient was evaluated for heart failure with reduced ejection fraction (EF). Six years ago, she suffered from pre-eclampsia at 33 weeks of pregnancy. The patient was diagnosed with nephrotic syndrome and creatinine level reached 595 umol/L. After the termination of a pregnancy, she received the renal biopsy. The pathological results of renal biopsy showed focal proliferative sclerosis IgA nephropathy with pre-eclampsia pregnancy-induced renal damage. The patient was given the CCB (calcium Chanel blocker) to control the blood pressure. However, she didn't go to the hospital for regular review. Two years ago, the patient had severe chest distress and she couldn't climb the stairs. Her blood pressure was 160/100mmHg and BNP level had reached 70,000 pg/ml. At that time, severe renal impairment appeared with high creatinine value of 714.5 umol/l and low glomerular filtration rate of 5.89 $mL/min^{-1}/1.73\ m^2$. The patient began to receive hemodialysis and anti-hypertension medications

with CCB (calcium Chanel blocker) and Beta blockers. One year ago, the patient suffered severe chest tightness and inability to lie down at night, she was hospitalized in the department of cardiology. Despite medical therapy, she was 3rd times hospitalized because of decompensated heart failure. Physical examination revealed blood pressure of 140/100 and mild pitting edema in both lower extremities. The serum creatinine was 642 umol/L and an estimated glomerular filtration rate of 6.65 $mL/min^{-1}/1.73\ m^2$. She also had renal anemia and secondary hyperparathyroidism. The patient was assessed as NYHA (New York Heart Association) class 4 heart failure. The parathyroid hormone was 827.5 pg/ml, albumin was 33.7 g/L and the hemoglobin was 118 g/L at that time. The NT-proBNP level was 385,000 pg/ml. The echocardiography showed the Left ventricular function was depressed with an ejection fraction 28% and severe mitral regurgitation with a regurgitant area of 15.1 cm^2 (Table 1). She also had severe pulmonary hypertension that pulmonary artery pressure was estimated to be 56 mmHg and tricaspid incompetence with a regurgitant area of 12.7 cm^2. She was treated with 1.5 ug of calcitriol twice a week. She received the dose of 50 mg sacabitril/valsartan twice a day, 20 mg of spironolactone once a day and 23.75 mg of metoprolol once a day. The dialysis protocol of the patient was as follows: hemodialysis (HD) 5 times every two weeks and hemodiafiltration (HDF) once every month. She received high-throughput dialysis with a blood flow of 250 ml/min and a dialysate flow rate of 500 ml/min. After 1 year of active treatment, the hypertention was well controlled and there was no symptomatic hypotension. The parathyroid hormone value of the patient decreased from 827.5 pg/ml before treatment to 605.1 pg/ml at the 6^{th} month after treatment and 366.4 pg/ml at the 12^{th} month of treatment (Table 2). The albumin value also increased to the normal level. Moreover, the functional class improved from NYHA 4 to NYHA 1. Both left and right ventricular diameters estimated by echocardiography were decreased. The left ventricular diameter decreased from 23 mm to 12 mm and the right ventricular diameter decreased from 59 mm to 46 mm (Table 3). Severe tricuspid regurgitation and pulmonary hypertension also got improved and pulmonary artery pressure decreased from 56 mmHg to 14 mmHg. The ejection fraction increased from 28% to 66% and the NT-proBNP value decreased from 385,000 pg/ml to 1092 pg/ml. Now, the patient's heart failure symptoms have improved significantly, and the echocardiography indicators have improved compared to before. Because patient has been insisting on taking sacubitril/valsartan, the frequency of hospitalizations due to cardiovascular complications is also decreasing. We will continue to follow-up the condition of this patient.

3. Discussion

Cardiovascular events are the leading causes of death in patients with chronic kidney disease. Patients with chronic kidney disease receiving hemodialysis are often complicated with heart failure, and cardiac dysfunction is closely related to renal dysfunction.

Table 1. Initial echocardiography report of this patient.

Right ventricular diameter 23 mm	Ventricular septal thickness 14 mm	Left ventricular diameter 59 mm	Left ventricular posterior wall 13 mm	Aortic ring diameter 21 mm
Left atrial diameter 43 mm	Ascending aorta diameter 41 mm	Pulmonary artery ring diameter 24 mm	Pulmonary valve 0.73 m/s	Right atrium 49 × 65 mm
E peak 0.99 m/s	A peak 0.37 m/s	Aortic valve 0.97 m/s	Tricuspid regurgitation 3.1 m/s	Pulmonary artery pressure 56 mmHg
EDV 295 ml	ESV 212 m	LVEF 28%	Mitral valve orifice regurgitation area 15.1 cm^2	Tricuspid regurgitation area 12.7 cm^2

EDV: End Diastolic Volume; ESV: End Systolic Volume; LVEF: Left Ventricular Ejection Fraction.

Table 2. Comparison before and after taking sacabitril/valsartan.

	2019.1	2019.6	2019.12
BP (mmHg)	159/100	145/100	122 - 145/72 - 96
ALB (g/L)	32.2	44.7	41.7
Blood phosphorus	0.94	0.79	0.6
PTH (pg/ml)	827.5	605.1	366.4
URR (%)	65.8	74.6	75.4
KT/V	1.3	1.64	1.63

BP: Blood pressure. ALB: albumin. PTH: parathyroid hormone. URR: Urea Reduction Ratio. KT/V: Urea clearance index.

Table 3. Cardiac parameters before and after taking sacabitril/valsartan.

	Before	After
Right ventricular diameter	23 mm	12 mm
Ventricular septal thickness	14 mm	11 mm
Left ventricular diameter	59 mm	46 mm
Pulmonary artery pressure	56 mmHg	14 mmHg
LVEF	28%	66%
NT-proBNP	385,000 pg/ml	1092 pg/ml

LVEF: Left Ventricular Ejection Fraction. NYHA: New York Heart Association.

The case we describe here is an ESRD patient undergoing regular hemodialysis with severe heart failure. The patient underwent echocardiography showing a series of heart failure symptoms including decreased ejection fraction, pulmonary hypertension, severe mitral and tricuspid regurgitation, etc. She also had hypertension. She received the dose of 50 mg sacubitril/valsartan twice a day, 23.75 mg of metoprolol once a day and 20 mg of spironolactone three times a day. After a period of active treatment, the symptoms of heart failure of this ESRD patient with hemodialysis have been significantly improved. High blood pressure was effectively controlled without symptomatic hypotension and

NT-proBNP level decreased from 385,000 pg/ml to 1092 pg/ml. In terms of safety, during the use of sacubitril/valsartan, the patient did not experience heperkalemia and other side effects. Previous studies had also reported the efficacy of sacubitril/valsartan in patients with ESRD, a 67-year-old man with heart failure with reduced ejection fraction due to an ischemic cardiomyopathy and renal insufficiency undergoing hemodialysis. Because of worsening heart failure with no other therapeutic options, a treatment with sacubitril/valsartan was started. After initiation of sacubitril/valsartan, there was a symptomatic improvement with a clear reduction NT-proBNP, accompanied by a decrease in filling pressures [11] A retrospective study analysed the clinical and laboratory data of 23 HFrEF patients, found that sacubitril/valsartan could reduce the hsTnT (high-sensitive troponin) and sST2 (soluble ST2) levels and improve LVEF in HFrEF patients with ESRD, which is the first study to show the effectiveness and safety of sacubitril/valsartan in ESRD patients with HFrEF [10].

In conclusion, we found that sacubitril/valsartan could effectively and safely improve the symptoms of heart failure in this patient with ESRD on regular hemodialysis.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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