An Investigation into the Effectiveness of Sacubitril and Valsartan Sodium with Percutaneous Coronary Intervention in Acute Myocardial Infarction

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To evaluate the effectiveness of emergency percutaneous coronary intervention when used in combination with sacubitril and valsartan sodium for managing patients with acute myocardial infarction. Our randomized controlled trial enrolled 78 patients with acute myocardial infarction treated at our hospital between October 2018 and October 2020. Participants were allocated randomly into two groups; observation group (n=39) received sacubitril and valsartan sodium combined with percutaneous coronary intervention, and the control group (n=39) received enalapril and percutaneous coronary intervention. In our study, in addition to comparing changes in cardiac biomarkers (troponin I and N-terminal pro-brain natriuretic peptide) before and after treatment, we also analyzed adverse reactions and changes in cardiac structure and function. After 6 mo, left ventricular end-diastolic diameter and left ventricular end-systolic diameter of observation group was obviously decreased, while the control group has no significant change. In the aspect of left ventricular ejection fraction, the observation group increased significantly, while the control group had no significant change. In the N-terminal pro-brain natriuretic peptide serum levels and the incidence of heart failure, the observation group showed advantages, compared with the control group. Sacubitril and valsartan sodium combined with emergency percutaneous coronary intervention can improve cardiac structural and functional indices, reduce the risk of heart failure, and increase long-term survival time in acute myocardial infarction patients. This approach is safe and effective and therefore warrants further consideration in clinical settings.

Key words: Sacubitril, valsartan sodium, emergency percutaneous coronary intervention, acute myocardial infarction, curative effect

Acute Myocardial Infarction (AMI) is a widespread cardiovascular disease that poses a significant threat to patients' life and well-being. AMI is a time-sensitive condition that can lead to severe complications such as malignant arrhythmias and cardiogenic shock, resulting in high disability and fatality rates. With the rise of aging populations and hypertension and hyperlipidemia, the incidence of AMI is increasing, making it a primary cause of cardiovascular-related deaths[1]. Early restoration and recanalization of criminal coronary blood supply are essential approaches to treating AMI. Emergency Percutaneous Coronary Intervention (PCI) is considered a good choice for its ability to rapidly restore myocardial blood flow and shrink the infarction area, as well as to prevent ventricular pathological remodeling, reduce acute mortality and improve long-term quality of life[2]. However, clinical studies indicate that ischemia-reperfusion injury following PCI treatment could increase the risk of cardiac diastolic and systolic disorders, causing heart failure[3]. In fact, about 17.5 % of patients with AMI following PCI eventually experience heart failure. Therefore, reducing the incidence of heart failure is crucial for improving prognoses. Sacubitril sodium is an Angiotensin Receptor Blockers (ARBs) cardiovascular drug that includes enkephalin inhibitors and valsartan sodium, which inhibit both the renin-angiotensin-aldosterone system and endorphinase. This drug is often used to treat and prevent hypertension and heart failure progression. A recent prospective study by PARADIGM-HF revealed that sacubitril can efficiently lower the possibility of hospitalization and death in heart failure patients[4]. Nonetheless, there are limited reports regarding the application of PCI with AMI. It remains unclear whether sacubitril sodium can

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inhibit pathological cardiac remodeling and improve overall prognoses. Therefore, this study reports on the efficacy of sacubitril sodium joint PCI in treating AMI, hoping to be helpful for clinical treatment. We included 78 patients with AMI in our study, all of whom were hospitalized in our undergraduate course from October 2018 to October 2020. These patients with AMI ranged from 51 y to 80 y old, with an average age of (60.32±11.46) y old, and were randomly divided into control group and observation group with the same number of patients in each group. The number of coronary artery lesions included single-vessel lesions in 29 cases, multi vessel lesions in 10 cases, Killip class III in 21 cases and IV in 8 cases. There were 22 males and 17 females aged from 48 y to 78 y with a mean age of (59.72±10.98) y. Coronary artery lesions included 31 cases of single-vessel lesions and 8 cases of multi-vessel lesions, including 21 cases of Killip III and 7 cases of IV. There was no significant difference in sex, age, number of coronary artery lesions and Killip grade between the two groups, indicating that the results were reliable and comparable. Our hospital has reviewed this study and agreed to carry out the study. Inclusion criteria for this study were all patients met AMI clinical diagnostic criteria developed by the American Heart Association (AHA), confirmed by ultrasound, electrocardiogram, and other examinations[5]; patients who met the indications for PCI treatment and had no history of drug allergies; patients with no severe diseases of critical organs and tissues such as liver, kidney, lung, or cerebrovascular and all patients joined this study voluntarily and signed informed consent. Exclusion criteria including the patients with serious heart disease; the patient had a history of AMI, heart failure or cardiac surgery; patients with malignant tumors or hyperthyroidism and patients with incomplete clinical data or incomplete treatment records. All patients underwent PCI treatment and were simultaneously administered routine antiplatelet drugs, statins and nitrates. Patients in the control group received oral enalapril (Jiangsu Hengrui Pharmaceutical Co., Ltd., H32022378) at an initial dose of 5 mg/day with an option to increase the dose to 10 mg/day, depending on the patient's blood pressure. Enalapril treatment was administered once daily and continued for 6 mo. Patients in the observation group were administered sacubitril (Swiss Novartis Pharmaceutical Co., Ltd., H20170344) at an initial dose of 50 mg, which was gradually increased to the maximum dose of 100-200 mg/day, depending on the patient's blood pressure. Sacubitril treatment was also administered once daily and continued for 6 mo. The study aimed to accomplish several objectives. The primary goal of our study was to compare the levels of Left Ventricular Ejection Fraction (LVEF), Left Ventricular End-Diastolic Diameter (LVEDD) and Left Ventricular End-Systolic Diameter (LVESD) between the two groups before and after treatment. Secondly, to compare the levels of serum N-Terminal pro-Brain Natriuretic Peptide (NT-proBNP) and cardiac Troponin I (cTnI) between groups before and after treatment. Thirdly, the incidences of adverse reactions such as renal function damage, angioedema, symptomatic hypotension and hyperkalemia were compared between the two groups. Finally, we compared the occurrence of adverse events such as heart failure, angina pectoris, stroke and death between the two groups after treatment. The cardiac structure and function indexes such as LVEF, LVEDD and LVESD were assessed using the DC-8EXP cardiac color Doppler ultrasound diagnostic system manufactured by Mindray. The measurement of serum cTnI and NT-proBNP levels involved providing 5.0 ml of venous blood to each subject in the morning and centrifuging it at 3000 rpm for 10 min. The upper layer of the serum was for testing. We bought the kit from Shanghai Kanglang Biotechnology Co., Ltd., and detected the levels of serum cTnI and NT-proBNP by immunochemiluminescence method. In the data analysis, we used the Statistical Package for the Social Sciences (SPSS) 24.0 version. The categorical data were expressed as frequencies (percentages) and the Chi-square (χ^2) test was used to compare group differences. The continuous data were expressed as mean±standard deviation, and the differences were compared by paired t-test. It was considered statistically different when $p<0.05$. Before treatment, the cardiac structural and functional indices such as LVEF, LVEDD and LVESD of the two groups stay at the same level. However, 6 mo after treatment, the levels of LVEDD and LVESD in control group were both lower than that in the observation group and LVEF was significantly higher ($p<0.01$) as shown in Table 1. The differences in cTnI and NT-proBNP levels between groups before treatment were not significant. After 6 mo of treatment, the NT-proBNP level decreased in the observation group. However, the difference in cTnI

levels between the two groups was not significant, as presented in Table 2. The differences in the incidence of adverse reactions between groups were not significant, including renal function damage, angioedema, symptomatic hypotension and hyperkalemia ($p<0.05$) as shown in Table 3. Over the 2 y follow-up period after treatment, the differences in the incidence of death, angina pectoris and stroke between groups were not significant ($p>0.05$). However, the proportion of heart failure cases in the observation group was significantly reduced ($p<0.05$) as shown in Table 4. PCI is currently considered to be the most effective way to treat AMI patients, as it can quickly reanalyze occluded coronary arteries, restore myocardial blood supply and inhibit myocardial infarction progression, thus reducing acute mortality and improving long-term prognosis[6]. However, in actual clinical practice, patients with AMI often have severe coronary atherosclerosis, and PCI cannot address the underlying etiology. These patients may also have neuroendocrine over activation, myocardial inflammatory injury and cardiovascular structural abnormalities. Post-PCI treatment, patients can experience oxidative stress and inflammatory injury, which can lead to pathological remodeling of cardiac structure and function, and eventually cause heart failure. This is a crucial factor that impacts the postoperative prognosis of patients with AMI[7]. Previous studies have reported that, 1 mo and 1 y after PCI treatment, cardiogenic mortality rates of patients with AMI can reach 6.4 % and 6.8 %, respectively, while the rate of prehospitalization is 8.3 % and 5.2 %[8]. Thus, improving the life quality of AMI patients after PCI is a pressing clinical issue. One recent study shows that many risk factors are closely associated with heart failure in patients with AMI after PCI, including age, hypertension, post infarction angina pectoris and blood glucose levels[9]. Therefore, it is important to effectively control these risk factors to improve long-term prognosis. Current guidelines and consensus at home and abroad recommend that in the absence of contraindications, patients with AMI should be prescribed angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers as soon as possible to improve myocardial vascular conditions and long-term prognosis. Sacubitril valsartan sodium is a cardiovascular drug formed by combining sacubitril and valsartan at a 1:1 molar ratio. *In vivo*, sacubitril can be converted into active, while valsartan is an angiotensin receptor antagonist. The combination of the two can inhibit both the renin-angiotensin-aldosterone system and enkephalinase. Pharmacological studies have shown that the LBQ657, an enkephalin inhibitor generated by sacubitril metabolism, can effectively inhibit enkephalinase activity, reduce natriuretic peptide degradation *in vivo*, improve nitric oxide bioavailability, dilate blood vessels, and reduce cardiac load and pathological remodeling[10]. Sacubitril sodium is widely used in patients with heart failure and hypertension because it can effectively reduce blood pressure, inhibit cardiac remodeling and control the complications of heart failure, thereby lowering the probability of prehospitalization or death of patients[11]. Studies have also demonstrated that sacubitril valsartan can significantly enhance cardiac structure and function, and reduce the time of hospitalization in patients with heart failure[12]. Furthermore, basic studies have revealed that sacubitril valsartan sodium can inhibit myocardial fibrosis, promote angiogenesis, and delay myocardial remodeling after myocardial infarction[13]. Although there have been few reports on the treatment of PCI with sacubitril valsartan sodium, research reported by Chen *et al.*[14] have indicated that sacubitril valsartan combined with emergency PCI can effectively reverse ventricular remodeling and promote the recovery of cardiac dysfunction in AMI patients, and the hemodynamics of patients are more stable. It was showed in this study that the levels of LVEDD and LVESD in the observation group were significantly lower and the level of LVEF was significantly higher after treatment. In addition, after 6 mo of treatment, the level of NT-proBNP was significantly decreased in the observation group, which was a significant indicator of heart failure with a longer *in vivo* half-life that can better reflect cardiac function damage[15]. The results of the 2 y follow-up also revealed sacubitril valsartan sodium can significantly promote cardiac structure and function. Lastly, this study showed that the drug is safe and reliable despite serious adverse drug reactions in both groups of patients. To conclude, sacubitril sodium has demonstrated its efficacy in improving the outcomes of PCI treatment for AMI patients. It can promote the improvement of cardiac structure and function, prolong the survival time of patients and it is also safe and reliable. Therefore, it can be concluded that the use of sacubitril sodium in clinical practice is beneficial and worth popularizing.

TABLE 1: COMPARISON OF CARDIAC STRUCTURAL AND FUNCTIONAL INDICES

Group	LVEF (%)		LVEDD (mm)		LVESD (mm)	
	Before	After 6 mo	Before	After 6 mo	Before	After 6 mo
Control (n=39)	38.84±4.17	46.61±4.89[1]	54.79±2.63	52.37±2.07[1]	41.08±2.44	38.56±2.05[1]
Observation (n=39)	39.10±4.22	51.38±5.16[1]	55.10±2.44	49.65±1.88[1]	41.23±2.37	35.34±1.94[1]
t	0.45	8.56	0.88	6.04	0.23	9.05
p	0.70	0.00	0.53	0.00	0.80	0.00

Note: ([1]): Comparison between before and treatment, p<0.05

TABLE 2: GROUP COMPARISON OF THE CARDIAC STRUCTURE AND FUNCTION

Group	cTnI (ng/ml)		NT-proBNP (μg/l)	
	Before	After 6 mo	Before	After 6 mo
Control (n=39)	6.13±1.72	0.06±0.01[1]	3134.47±424.88	853.50±61.03[1]
Observation (n=39)	6.20±1.85	0.04±0.01[1]	3202.59±422.91	561.87±53.76[1]
t	0.36	1.83	0.25	15.41
p	0.73	0.1	0.88	0

Note: ([1]): Comparison between before and treatment, p<0.05

TABLE 3: GROUP COMPARISON OF THE INCIDENCE OF ADVERSE REACTIONS [n (%)]

Group	Renal dysfunction	Angioedema	Symptomatic hypotension	Hyperkalemia
Control (n=39)	3 (7.69)	1 (2.56)	7 (17.95)	0 (0.00)
Observation (n=39)	4 (10.26)	0 (0.00)	5 (12.82)	0 (0.00)
χ^2	0.69	0.87	1.05	0.00
p	0.34	0.26	0.21	1.00

TABLE 4: GROUP COMPARISON OF THE PROPORTION OF DVERSE EVENTS 2 Y AFTER TREATMENT [n (%)]

Group	Heart failure	Angina	Stroke	Death
Control (n=39)	5 (12.82)	2 (5.13)	1 (2.56)	2 (5.13)
Observation (n=39)	1 (2.56)	1 (2.56)	0 (0.00)	1 (2.56)
χ^2	3.93	0.59	0.87	0.59
p	0.04	0.65	0.26	0.65

Conflict of interests:

The authors declared no conflict of interests.

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