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Ivabradine Use in Heart Failure After Myocardial Infarction Can Help with the Titration of the Dose of ARB/ACEI or β-Blockers: A Case Report

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Abstract

Introduction: β-blockers and angiotensin receptor blocker (ARB)/angiotensin-converting enzyme inhibitors (ACEI) are well known as critical therapies for improving the prognosis in patients with acute myocardial infarction, however, their use in some case may be limited. We believe that in such cases as when β-blockers and ARB/ACEI use is limited, ivabradine plays a potential role in the improvement of individual prognoses.

Case Presentation: A 49-year-old man from Dalian, China. He was diagnosed with acute inferior myocardial infarction in Feb, 2016. And he still experienced palpitations and heart failure after drug treatment and percutaneous coronary intervention (PCI). We used metoprolol at a low dose, although the symptoms were not relieved, β-blockers could not be used or increase dose because of his hypotension. Finally, we chose ivabradine to alleviate the symptoms of the patient related to heart rate and palpitations without affecting blood pressure so as to promote the recovery of heart function. We witnessed a gradual reduction in heart rate (HR) and a gradual increase in blood pressure. Finally, we administered an ARB and increased via titration the dose of ARB and β-blocker.

Conclusions: When there are limitations to the use of ARB/ACEI and β-blockers, we can use ivabradine, which reduces HR without affecting blood pressure. Ivabradine can help with the titration of the dose of ARB/ACEI or β-blockers.

Keywords: Ivabradine, Cardiac Failure, Myocardial Infarct

1. Introduction

Myocardial infarction is the most severe type of acute coronary syndrome (ACS), and heart failure is a frequent complication of myocardial infarction. To reduce mortality, it is important to improve heart function. As the heart rate (HR) increases, so does the mortality rate (1). β-blockers and angiotensin receptor blocker (ARB)/angiotensin-converting enzyme inhibitors (ACEI) have long been considered the cornerstone therapies for heart failure after myocardial infarction; however, some patients also have low blood pressure, asthma, etc. Such conditions place a limit on β-blockers and ARB/ACEI usage. Ivabradine is a selective inhibitor of the hyperpolarization-activated cyclic-nucleotide-gated funny current (If), which is involved in pacemaker generation and the responsiveness of the sinoatrial node (SAN); ivabradine treatment leads to HR reduction with no other notable cardiovascular effects (2). Therefore, in previous studies, the role of ivabradine in arrhythmia and chronic heart failure was mainly observed. Its role in acute myocardial infarction is still unclear. This case follows a patient with heart failure after myocardial infarction who could not use ARB/ACEI or beta blockers due to low blood pressure; in this case ivabradine helped in the administration of an ARB (candesartan) and allowed for an increase in the dosage of ARB and β-blocker.

2. Case Presentation

The patient is a 49-year old man from Dalian, China, who had used β-blocker (metoprolol 25 mg $\times$ 2/die) for several years with poor control of his blood pressure. He experienced dizziness, nausea, chest tightness and difficulty breathing that lasted for hours after a bath in Feb, 2016. His symptoms were not relieved after taking the instant cardio-reliever pill, therefore he went to the Lushun people's Hospital three days after the onset of symptoms. He was diagnosed with acute myocardial infarction by electrocardiogram (ECG) and myocardial markers. The hospital is not equipped to perform a percutaneous coronary intervention (PCI) operation, and the patient did not agree to go to a better equipped hospital for the procedure due to financial reasons. He received drug treatment for one

week in the village hospital, including aspirin, clopidogrel, atorvastatin, enoxaparin and isosorbide mononitrate injection; however, he still experienced chest pain and palpitations after treatment. Re-examination of the ECG showed that the ST segment did not significantly move down. Then, after the patient's consent, he was transferred to our coronary care unit (CCU). His blood pressure was 98/72 mmHg, and his HR was 96 bpm. There was an increase in cardiac enzymes to: CK-MB 0.7 μg/L, CTNI 8.54 μg/L, and N-terminal pronatriuretic peptide (NT-proBNP) 847 pg/mL. Routine blood test, biochemical indicators, examinations were normal (Table 1).

In our CCU, we treated him with aspirin, clopidogrel and atorvastatin at the highest dosages permitted by the patient's clinical condition. As he continued to be ill and to experience chest pain for one week, we performed coronary angiography and PCI. In the evening of the first day, the patient suffered from heart failure, which preventing him from lying flat, and also occured double lung rale. His blood pressure was 87 - 98/60 - 70 mmHg, HR was 90 - 120 bpm, and NT-proBNP was 2,286 pg/mL. We used dopamine (3 - 5 μg/kg.min) to maintain blood pressure. Simultaneously, we used lyophilized recombinant human brain natriuretic peptide (Irh-BNP) to antagonize the renin-angiotensin system (RAS) and diuretics (furosemide 20 mg/qd, iv; spironolactone 20 mg/bid, oral) to reduce heart load, which may improve heart function. After several days, the symptoms of heart failure disappeared, and the patient no longer felt tightness. We measured his NT-proBNP level, which was 1,225 pg/mL; BP, which was 110/80 mmHg; and HR, which was 100 bpm. We performed ultrasound cardiography (UCG), which revealed an interior left ventricular end-diastolic diameter of 55.8 mm, Ejection fraction (EF) of 20%. It suggested left ventricular wall motion abnormality, left ventricular apical aneurysm, mild mitral valve regurgitation and poor heart function. Due to the presence of poor heart function, we used β-blockers (metoprolol) at a low dose (12.5 mg $\times$ 2/die) and monitored the patient's blood pressure, which did not notably change. After discharge, he took the medicine regularly. After one month, he returned with complaints of dyspnea and palpitations; his blood pressure was 115/88 mmHg, and his HR was 110 bpm. We increased the dose of metoprolol (25 mg/bid, oral), but he still felt palpitations. We monitored his HR, and his 24 h Holter monitor presented a total HR of 137690/23:31 h, an average HR of 97 bpm. Subsequent UCG revealed an interior left ventricular end-diastolic diameter of 55.8 mm and EF of 28%. Routine blood test, biochemical indicators, examinations were normal (Table 1). We considered increasing the dose of metoprolol but decided against it due to the patient's blood pressure fluctuating between 100 - 105/60 - 70 mmHg. The patient's HR remained high (100 - 130 bpm). As the patient's blood vessels are reperfusion and otherwise improved heart function, we concluded that the high HR was the driving force of the palpitations. Ivabradine, a drug that reduces HR in patients with sinus rhythm without affecting blood pressure, seemed to be the only rational method to control his HR and relieve the palpitations. We started with 5 mg/bid and witnessed a gradual reduction in HR and the subsequent stabilization of his clinical condition.

After approximately one week of clinical observation, we discharged the patient. We continued to monitor him via regular visits. After one week, his HR was 96 bpm, and blood pressure was 98 - 116/60 - 80 mmHg; we then increased the dose of ivabradine to 7.5 mg/bid and administered candesartan (1 mg/qd, oral). After one month, his HR was 84 bpm, and blood pressure was 100 - 118/65 - 85 mmHg; then, we increased the dose of metoprolol to 37.5 mg/morning, 25 mg/night. After seven months, based on his blood pressure (110 - 125 mmHg) and HR (75 - 90 bpm), we titrated up the dose of metoprolol to 50 mg/bid and that of candesartan to 8 mg/qd, while the dose of ivabradine was reduced to 5 mg/bid. The results have been more than satisfactory (Table 2).

3. Discussion

Heart failure during admission for acute myocardial infarction is an important predictor of short- and long-term clinical outcomes (3). Therefore, it is very important to improve the prognosis of myocardial infarction to reduce the incidence of heart failure or to allow rapid recovery from heart failure. HR reduction has been included as a treatment goal in the American College of Cardiology Foundation and the American Heart Association Heart Failure guidelines. Numerous studies have demonstrated that β-blockers exert their beneficial effects largely or solely by reducing HR (4, 5). However, β-blockers have other side-effects, such as hypotension, negative inotropy, reduced insulin sensitivity, and central nervous system-mediated fatigue (6). As a result, many patients with heart failure are unable to take β-blockers or are not able to tolerate evidence-based target doses.

This report follows a case of heart failure after myocardial infarction. Despite accepted reperfusion therapy, he also experienced palpitations and dyspnea, and his UCG indicated poor heart function. After our treatment, all of the patient's symptoms were improved, except for the palpitations. We wanted to increase the dose of β-blockers to control his HR and add ARB/ACEI to reverse ventricular remodeling, but this treatment was contraindicated due to his low blood pressure. Therefore, we needed a drug that

Table 1. Clinical Laboratory Results of the Current Case

Variables	Results	
	First Hospitalization	Second Hospitalization
Basic clinical data		
Age	48	48
Sex	Man	Man
Height, cm	164	164
Weight, kg	75	73
BMI	27.9	27.1
Systolic pressures	98	102
Diastolic pressures	72	70
History of serious diseases	Hypertension	Hypertension
Routine blood test		
White blood cell	7.02 (4 - 10) $\times 10^9$/L	6.0 (4-10) $\times 10^9$/L
Hemoglobin, g/L	155 (110 - 160)	138 (110 - 160)
Platelet	284 (100 - 300) $\times 10^9$/L	175 (100 - 300) $\times 10^9$/L
Biochemical indicators		
Alanine aminotransferase, U/L	29 (0 - 40)	26 (0 - 40)
Aspartate aminotransferase	18 (0 - 40)	19 (0 - 40)
Albumin, g/L	35 (35 - 55)	40 (35 - 55)
Creatinine, uM/L	72 (44 - 110)	80.24 (44 - 110)
Glucose, mM/L	12.92 (3.9 - 6.1)	6.0 (3.9 - 6.1)
Total cholesterol, mM/L	5.39 (1.8 - 5.17)	3.12 (1.8 - 5.17)
Triglyceride, mM/L	2.01 (0.56 - 1.7)	2.25 (0.56 - 1.7)
Cardiac troponin I, ug/L	68 (0 - 0.14)	0.6 (0 - 0.14)
Creatine kinase isoenzyme-MB, ug/L	10.2 (0 - 3.6)	0.09 (0 - 3.6)
Pro-BNP, Pg/mL	2286 (0 - 125)	1769 (0 - 125)
Echocardiography		
left ventricular end- diastolic diameter, mm	55.8	58.3
Ejection fraction, %	20	28

Table 2. The Main Variables and the Drug Use During Follow-Up.

	First Admission	Second Admission	1 Week Later	1 Month Later	7 Month Later
Heart rate, bpm	105	120	98	84	68
Blood pressure, mmHg	98/62	105/60	116/80	118/85	120/90
Ejection fraction, %	20	28	None	32	43.3
Ivabradine, mg/bid	None	5	7.5	7.5	5
Metoprolol, mg/bid	12.5	25	25	37.5 mg/morning, 25 mg/night	50
Candesartan, mg/qd	None	None	1	4	8

could reduce the HR without affecting blood pressure and thus not only could control the symptoms but also could improve heart function by reducing HR. Ivabradine was the best option.

Ivabradine was developed as a specific bradycardic agent in the 1980s and specifically inhibits the If current,

decreasing HR while avoiding the adverse effects of more traditional antianginal agents (β-blockers and calcium channel antagonists) (7, 8). Ivabradine used to treat heart failure not only reduces HR but also prolongs diastolic perfusion time, improves coronary blood flow, increases exercise capacity, and may even increase stroke volume, which may underlie its beneficial cardiac effects (9).

In this case, we chose to administer ivabradine to reduce HR, as ivabradine reduces HR without affecting blood pressure. After ivabradine treatment, his HR was gradually reduced to 70 bpm, and his palpitation was resolved. At the same time, his ventricular cardiac output increased; thus, coronary blood flow improved. Moreover, his blood pressure increased, so we were able to increase the dose of β-blockers and administered ACEI/ARB to improve his prognosis. In the guidelines, when the beta blocker reaches the target dose and/or the maximum tolerable dose, the heart rate is more than 70 times/min, and it is recommended to add ivabradine. But the role of ivabradine in acute myocardial infarction is not clear. In this case, the use of ivabradine is beyond indication. But based on the experience of this case, we believe that similar patients can use ivabradine to relieve palpitation and improve prognosis.

3.1. Conclusions

When there are limitations to the use of ARB/ACEI and β-blockers, we can use ivabradine, which reduces HR without affecting blood pressure. Ivabradine can help with the titration of the dose of ARB/ACEI or β-blockers.

Footnotes

Authors' Contribution: Zhenzhu Liu, Xiangpeng Kong and Hongyan Wang drafted the initial manuscript, were involved in the care of the patient and edited, and approved the final manuscript. Dajun Yuan and Peng Qu revised the manuscript and approved the final manuscript. All authors read and approved the final manuscript.

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