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CLINICAL STUDY

Use of gated myocardial perfusion imaging to assess clinical value of Xinmailong injection in chronic congestive heart failure

Yan Liu, Zhiqian Wang, Wenliang Xiao, Yuan Li

Yan Liu, Zhiqian Wang, Wenliang Xiao, Department of Cardiology, the Third Hospital of Hebei Medical University, Shijiazhuang 050051, China
Yuan Li, Department of Cardiology, the Fourth Hospital of Shijiazhuang Municipality, Shijiazhuang 050051, China
Correspondence to: Prof. Zhiqian Wang, Department of Cardiology, the Third Hospital of Hebei Medical University, Shijiazhuang 050051, China. 15512172510wang@sina.com
Telephone: +86-15512172510
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Abstract

OBJECTIVE: This study used gated myocardial perfusion imaging (G-MPI) to assess the clinical value of Xinmailong injection in chronic congestive heart failure (CHF).

METHODS: A total of 102 CHF patients were randomly divided into the control group (n=51) and the Xinmailong group (n=51). Patients in the control group were routinely treated. Patients in the Xinmailong group were additionally treated with Xinmailong injection in addition to routine treatment. Before and 3 months after treatment, G-MPI was used to determine changes in the left ventricular ejection fraction (LVEF), left ventricular end-diastolic volume (LVEDV) and left ventricular end-systolic volume (LVESV). Fourteen days after treatment, changes in plasma brain natriuretic peptide (BNP) levels were determined.

RESULTS: Before treatment, there were no significant differences in LVEF, LVEDV, LVESV, and BNP levels between the two groups (all P>0.05). After treatment, LVEDV, LVESV, and BNP levels were significantly lower, and LVEF was significantly higher in the Xinmailong group than in the control group (all P<0.05).

CONCLUSION: Additional use of Xinmailong injection in addition to routine treatment improves cardiac function of CHF patients. Because of the safety and effectiveness of Xinmailong injection, this therapy should be promoted.

Key words: Myocardial perfusion imaging; Heart failure, Natriuretic peptide, brain; Xinmailong injection

INTRODUCTION

Chronic congestive heart failure (CHF) is a syndrome in which cardiac structural or functional diseases cause myocardial damage, a large ventricular load, weakened ventricular diastolic force, and reduced ventricular ejection volume. Consequently, metabolic requirements of the body cannot be met. CHF is a commonly and frequently encountered disease, and is the terminal stage of cardiac disease, with extremely high mortality. Epidemiological data have shown that for CHF, the hospitalization rate accounts for 20% and mortality for 40% of cardiovascular diseases at the same stage, and its survival rate is similar to that of tumors.[1,2] There is an increase of 200 000 CHF patients every year worldwide.[3] The incidence of CHF is increasing in China,[4] and its incidence among older people is as high as 1.3% .[5] Some CHF patients are treated with digitalis, ethyl nitrate, β receptor inhibitors, and angiotensin-converting enzyme inhibitors, but there is no ideal cure. Therefore, the clinical symptoms and prognosis of CHF need to be further improved.

Compound nucleoside bases and conjugated amino ac-

ids, which are two effective ingredients of Xinmailong injection extracted from cockroaches, can dilate the coronary artery, antagonize activation of neuroendocrine, increase blood supply to cardiac muscle, improve cardiac function, and antagonize ventricular restructuring.[6]

In this study, we examined the effect of Xinmailong injection while applying routine treatment in CHF patients by strengthening the heart and inducing urination. We used gated myocardial perfusion imaging (G-MPI) to determine changes in left ventricular ejection fraction (LVEF), left ventricular end-diastolic volume (LVEDV), left ventricular end-systolic volume (LVESV), and brain natriuretic peptide (BNP) levels before and after treatment to assess the curative effect of Xinmailong injection.

MATERIALS AND METHODS

Patients

We studied 102 CHF inpatients from the medical department of the heart, The Third Hospital of Hebei Medical University from April 2011 to October 2013.

Inclusion criteria

All patients with Ⅱ-Ⅳ cardiac function according to the guide for diagnosing and treating CHF (compiled by the cardiovascular disease branch of the China Medical Association, 2007 edition)[7] were included.

Exclusion criteria

Patients with the following conditions were excluded: hypotension, acute left heart failure, acute myocardial infarction, severe valvulopathy, hypertrophic obstructive cardiomyopathy, pulmonary heart disease, severe insufficiency of the liver and kidney, and those who were sensitive to Xinmailong.

Modeling and grouping

A total of 102 inpatients were randomly divided into the control group (n=51; serial number: 1-51) and the Xinmailong group (n=51; serial number: 52-102). Patients in the control group were routinely treated. Patients in the Xinmailong group were additionally treated with Xinmailong injection in addition toroutine treatment. In the Xinmailong group, there were 33 men and 18 women, aged 57-73 years [mean, (65±7) years]. In the control group, there were 35 men and 16 women, aged 57-75 years [mean, (66±9) years]. There were no significant differences in sex, age, hyperlipidemia, diabetes, and hypertension between the two groups (P> 0.05, Table 1). This research was approved by the ethical committee of The Third hospital of Hebei Medical University, and all of the patients signed a consent form.

Methods

Therapy: patients in both groups were treated with furosemide (Zhaohui Pharmaceutical Co., Ltd., Shanghai, China), digoxin (Xinyi Pharmaceutical Co., Ltd., Shanghai, China), and lotensin, an angiotensin invertase inhibitor (Nuohua Pharmaceutical Co., Ltd., Beijing, China). In addition to routine treatment, patients in the Xinmailong group were additionally treated with an intravenous drip of Xinmailong injection (approval number: Z20060443; Tengchong Pharmaceutical Company, Yunnan, China) at a concentration of 5 mg/kg each time, twice a day, with an interval of more than 6 h between each time, for 14 consecutive days. These patients were also administered 5% glucose injection or 200 mL of 9% NaCl injection with a drip speed of 20-40 drops per min. Patients were treated for the first time with Xinmailong injection if a skin test was negative.

Determination of curative effects

Fourteen days after treatment, curative effects were assessed in both groups. Effectiveness was defined as clinical symptoms that were obviously improved and cardiac function was ameliorated to one class. Ineffectiveness was defined as no obvious improvement in clinical symptoms, cardiac function was ameliorated to less than one class, or heart failure was aggravated or even death occurred.

Use of G-MPI

Before and 3 months after treatment in all of the patients, G-MPI was used to determine parameters of left ventricular function with an Infinia Hawkeye double probe single-photon emission computed tomography (SPECT) instrument (GE Co., Fairfield, CT, USA) and collimator with parallel holes, low energy, and high resolution.

G-MPI was used 1.5 h after intravenous injection of 111-740 MBq ^{99} Tc^{m}-MIBI. The probe was obliquely moved 45° from the right front to the left rear, and rotated in a clockwise direction 180° to collect eight images every cardiac cycle, with a 64×64 matrix. Images were analyzed with the Xeleris Functional Imaging Workstation (GE Co., Fairfield, CT, USA), and original images were restructured with filtering counter-projection. After restructuring, images of the horizontal long axis, vertical long axis, and short axis were displayed. Based on three-dimensional restructuring, quantitative gated SPECT (GE Co., Fairfield, CT, USA) was used to analyze and calculate the left ventricular functional parameters of left ventricular ejection fraction (LVEF), left ventricular end-diastolic volume (LVEDV), left ventricular end-systolic volume (LVESV).

Determination of plasma BNP levels

A BNP kit and the Triage BNP analyzer (Biosite Diagnostics Inc., San Diego, CA, USA) were used according to the manufacturer's instructions. A volume of 2 mL of venous blood was extracted from all of the patients before treatment and 14 days after treatment. Blood samples were added to a test tube with anticoagulant and it was evenly mixed. After a test plate had been placed under room temperature for 15 min, a tube was

used to extract blood samples and drip them onto the test plate. Fifteen minutes later, the test plate automatically displayed the test result.

Statistical analysis

Data are expressed by mean±standard deviation ($\bar{x} \pm s$). The *t*-test was used for comparison before and after treatment in the two groups, and for comparison between the two groups. The χ^2 test was used for enumeration data. $P<0.05$ was considered statistically significant. SPSS 16.0 software (SPSS Inc., Chicago, IL, USA) was used for statistical analysis.

RESULTS

This study was conducted as follows (Figure 1). One hundred and two CHF patients were recruited and divided into 2 groups.

Comparison of baseline data between the two groups

There were no significant differences in baseline data between the two groups (Table 1).

Comparison of curative effects between the two groups

Treatment was effective in 46 patients and ineffective in five patients, with a total efficacy rate of 90.2% in the Xinmailong group. Treatment was effective in 34 patients and ineffective in 17 patients, with a total efficacy rate of 66.7% in the control group. The Xinmailong group had a significantly better curative effect than the control group ($P<0.05$, Table 2).

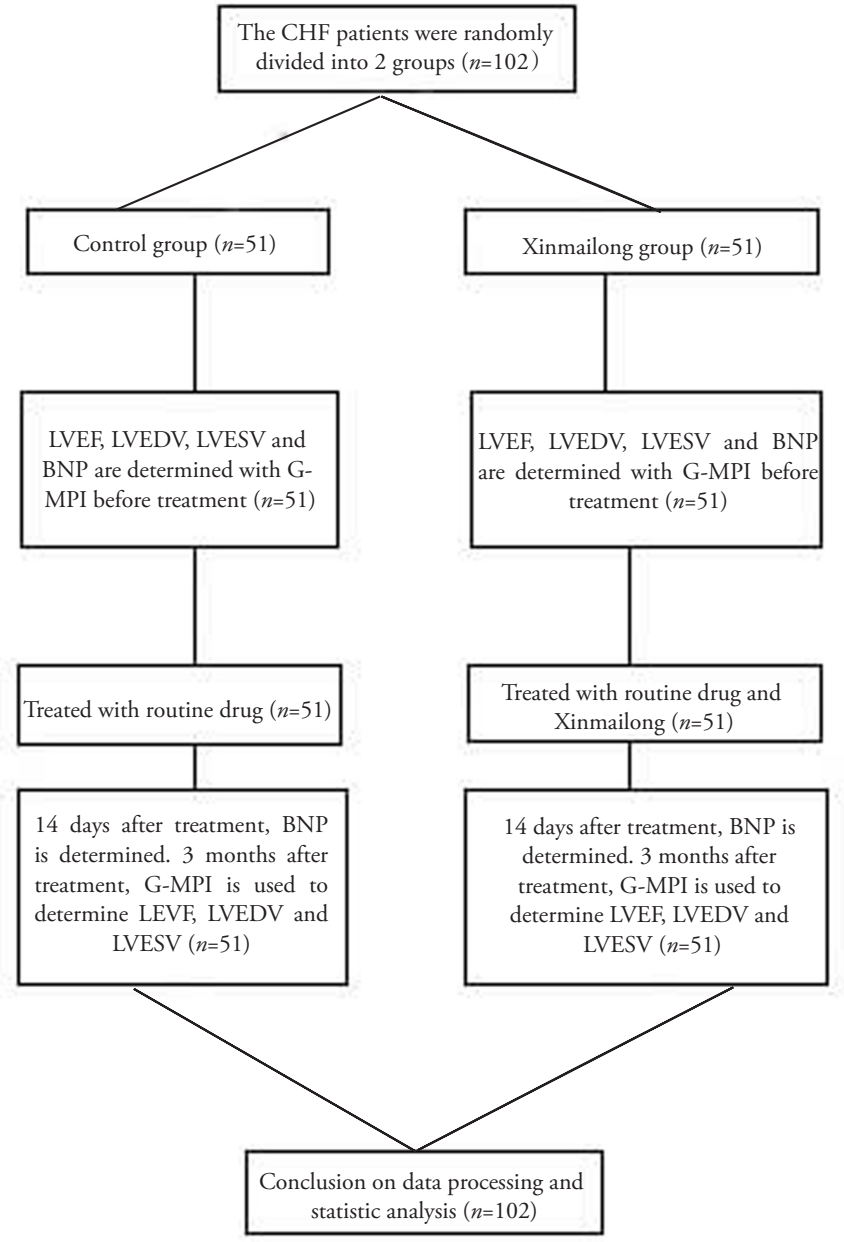

Figure 1 Diagram of the test procedure

LVEF: left ventricular ejection fraction; LVEDV: left ventricular end-diastolic volume; LVESV: left ventricular end-systolic volume; BNP: brain natriuretic peptide.

Comparison of LVEF, LVEDV, LVESV, and BNP between the two groups

There were no significant differences in LVEF, LVEDV, LVESV, and BNP levels before treatment between the two groups (P>0.05, Table 3). However, LVEDV, LVESV, and BNP levels were significantly lower, and LVEF was significantly higher after treatment in the Xinmailong group compared with the control group (all P<0.01).

DISCUSSION

Currently, treating CHF includes eliminating life-threatening factors, regulating metabolic mechanisms, antagonizing excessive activation of neurohumoral factors, and obstructing and delaying myocardial restructuring. Besides alleviating clinical symptoms, CHF patients should strive to enhance the tolerable amount of exercise, improve their quality of life, and reduce mortality.[8] Drugs currently used by patients with heart failure include angiotensin invertase inhibitors, angiotensin receptor inhibitors, β receptor inhibitors, aldehyde ketone receptor antagonists, diuretics, vasodilators, and positive inotropic drugs, such as digitalis, dobutamine, and milrinone. These drugs can improve clinical symptoms, but increase myocardial oxygen consumption, induce arrhythmia, and even increase mortality.[9]

The developer in G-MPI can be extracted by active mitochondria of myocardial cells, reflecting metabolism and activation of normal myocardial cells. When myocardial perfusion is obtained, LVEDV, LVESV, and LVEF can simultaneously be obtained, representing parameters of left ventricular function and activity of the local heart wall. G-MPI is a reliable method for assessing the structure and function of the heart.

In our study, G-MPI was applied to assess the curative effect of Xinmailong injection on CHF. We found that clinical symptoms in the Xinmailong group improved in 90.2% of patients, which was significantly better than that with only routine treatment. LVEDV and LVESV in the Xinmailong group were significantly lower than those in the control group. LVEF in the Xinmailong group was significantly higher than that in the control group. These results indicated that improvement of cardiac function in the Xinmailong group was better than that in the control group. The mechanism involved is that Xinmailong injection contains nucleosides, compound amino acids, and polypeptides, which accelerate calcium flow into myocardial cells to smoothly and persistently strengthen myocardial contractive power.[10,11] These components of Xinmailong injection can also increase calcitonin gene-related peptide content in plasma, leading to a decrease endothelin secretion and inhibition of activation of nervous endocrine.[12] In addition, these factors can dilate the renal ar-

Table 1 Comparison of baseline data between the two groups ($\bar{x}$ ±s)

Group	n	Male/female (n)	Age (years)	Hyperlipemia [n (%)]	Diabetes [n (%)]	Hypertension [n (%)]
Control	51	35/16	66±9	26 (50.98)	19 (37.25)	18 (35.29)
Xinmailong	51	33/18	65±7	25 (49.02)	20 (39.22)	19 (37.25)
P value	-	>0.05	>0.05	>0.05	>0.05	>0.05

Notes: patients in the control group were routinely treated and those in the Xinmailong group were additionally treated with Xinmailong in addition to routine treatment.

Table 2 Comparison of the curative effect between the two groups

Group	n	Effectiveness (n)	Ineffectiveness (n)	Total effective rate (%)
Control	51	34	17	66.7
Xinmailong	51	46	5	90.2

Notes: patients in the control group were routinely treated and those in the Xinmailong group were additionally treated with Xinmailong on the basis of routine treatment.

Table 3 Comparison of LVEF, LVEDV, LVESV, and BNP levels between the two groups ($\bar{x}$ ±s)

Group	n	LVEDV (mL)		LVESV (mL)		LVEF (%)		BNP (pg/mL)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control	51	119±36	104±20	73±28	58±22	37±3	48±3	1706±117	586±53
Xinmailong	51	121±39	91±18[a]	75±26	43±18[a]	37±3.5	53±3[a]	1690±115	479±44[a]
t	-	0.2828	3.4060	0.3131	3.9250	1.1608	7.5650	0.7279	11.1402
P value	-	>0.05	<0.01	>0.05	<0.01	>0.05	<0.01	>0.05	<0.01

Notes: patients in the control group were routinely treated, and those in the Xinmailong group were additionally treated with Xinmailong on the basis of routine treatment. LVEF: left ventricular ejection fraction; LVEDV: left ventricular end-diastolic volume; LVESV: left ventricular end-systolic volume; BNP: brain natriuretic peptide. [a]P<0.01, compared with data after treatment in the control group.

tery and improve microcirculation in the kidney to induce urination, alleviate the cardiac load of CHF patients, and ameliorate blood stasis in the lung.[13-15] Therefore, the curative effect of Xinmailong injection on CHF is produced by strengthening myocardial contractive power, inducing urination, dilating blood vessels, and regulating endocrine and humoral factors.

Qilin *et al* [16] found that Xinmailong further enhances cardiac function in patients with heart failure caused by acute myocardial infarction, and reduces high sensitivity-C reactive protein and N terminal pro-brain natriuretic peptide levels, improving the prognosis. Xingwen and others[17,18] have discovered that Xinmailong injection remarkably improves right ventricular systolic and diastolic function in patients with pulmonary heart disease, and its curative effect is better than that of routine treatment. Their results are similar to our current findings.

BNP is a natural hormone with biological activity and is synthesized by myocardial cells. Plasma BNP concentrations, a quantitative marker of heart failure, objectively reflect the extent of heart failure and are closely related to the prognosis of heart failure. Every increase in BNP levels by 100 ng/L in CHF patients indicates an increase in the risk of death by 35%.[19] The guide compiled by the European Heart Disease Association in 2010 stresses that an increase in BNP levels is important for diagnosing heart failure, and for the first time points out a strategy for diagnosing heart failure with symptoms. Using dynamic monitoring of BNP levels to direct diagnosis and treatment of heart failure can reduce mortality and the re-hospitalization rate owing to deterioration of heart failure.[20] In our study, plasma BNP levels in the Xinmailong group were significantly lower than those in the control group after treatment. This finding further indicates that Xinmailong injection improves clinical symptoms and the prognosis of CHF patients.

In summary, Xinmailong injection can be used to effectively treat CHF. Because of the small amount of samples and short time of observation in our study, further studies are required to determine whether Xinmailong injection improves the prognosis of CHF patients.

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