

A Clinical Study on the Influence of Shenmai Injection on the Cardiac Function and Arrhythmias in Patients with Chronic Heart Failure

L. ZHANG, H. MA AND J. SHEN*

Department of Cardiology, The Central Hospital Affiliated to Shaoxing University, Shaoxing 312030, Zhejiang Province, China

Zhang *et al.*: Influence of Shenmai Injection in Chronic Heart Failure Patients

To investigate the clinical effect of Shenmai injection on cardiac function and arrhythmias in patients with chronic heart failure. A total of 120 patients with chronic heart failure who were hospitalized in our hospital from December 2017 to June 2019 were selected and randomly divided into Shenmai group and control group after signing the informed consent form. The patients in the control group were given conventional treatment and the Shenmai group was treated with Shenmai injection on the basis of the control group. The course of the treatment in both groups was 14 d. Holter was performed in both groups before and after treatment, and the differences in the frequency and duration of atrial or ventricular arrhythmias were compared between the two groups. The main adverse cardiovascular events were recorded during 6-12 mo follow-up. The clinical total effective rate of Shenmai group was 87.66 % and that of control group was 85.96 % ($p < 0.05$). After treatment, the frequency and duration of atrial or ventricular arrhythmias in Shenmai group were significantly improved ($p < 0.05$); the frequency of atrial arrhythmias in the control group were increased and the difference was statistically significant ($p < 0.05$), but there was no significant difference in the duration of atrial arrhythmias and the frequency or duration of ventricular arrhythmias before and after treatment. There was no significant difference in main adverse cardiovascular events between the two groups after 6-12 mo of follow-up ($\chi^2 = 1.115$, $p > 0.05$). Shenmai injection has a definite effect in the treatment of chronic heart failure, which can effectively improve the heart function, arrhythmias and life quality of the patients with good safety.

Key words: Shenmai injection, chronic heart failure, arrhythmia, vasodilators

Chronic Heart Failure (CHF) is a progressive syndrome presenting with impairment of ventricular filling or ejection of blood due to organic and functional diseases of the heart. CHF is a common disease and its incidence increases with age. With an acute onset and the potential to cause considerable harm, CHF is the primary reason for many end-stage heart diseases and deaths. To date, there has been no radical cure for CHF. Medication treatment is the main type of treatment for CHF, which generally aims to relieve the symptoms of CHF and restore the cardiac functions as much as possible. Several studies conducted at home and abroad have shown that Shenmai injection has good efficacy in improving the cardiac function of patients with CHF. However, the existing studies are primarily observational studies and few are concerned with the influence of the Shenmai injection on arrhythmias and the patients' prognosis. The present study was a prospective, randomized controlled trial, which investigated the

influence of Shenmai injection on cardiac function and arrhythmias. Our research offers clues on the medication for patients with CHF. Patients with CHF treated at our hospital from December 2017 to June 2019 were recruited. They were screened according to the following criteria: Conforming to the diagnostic criteria in the 2014 Guidelines for the Diagnosis and Treatment of Heart Failure^[1]; The New York Heart Association (NYHA) functional class II-III; aged 35 to 80 y old. Exclusion criteria: Severe liver, kidney and lung failure, persistent atrial fibrillation, severe disruption of water and electrolyte balance, autoimmune diseases, malignant tumors and mental disorders. All patients signed written informed consent. The sealed envelope system was used to randomly divide the patients into the Shenmai injection group (Shenmai injection plus conventional treatment) and the control group (conventional treatment only). The control group received conventional treatment, which was further

*Address for correspondence

E-mail: shenjianyao2021@126.com

divided into non-medication and medication. The non-medication treatment included the following: Bed rest, oxygen inhalation therapy, low-salt diet, fluid restriction and moderate exercise. The medication treatment included the following: Diuretics, angiotensin-converting enzyme inhibitors, vasodilators, beta-blockers and the drugs to improve myocardial metabolism. In the meantime, the patient's fluid intake and output were carefully recorded. Symptomatic and supportive treatments to correct the disruption of water and electrolyte balance and acid-base imbalance were also given. The treatment group received Shenmai injection (Chiatai Ching Chun Bao, 50 ml/bottle) on top of the conventional treatment given in the control group. The intravenous drip of 50 ml of Shenmai injection was performed once daily for 14 d consecutively. The efficacy was evaluated in the two groups based on clinical symptoms and cardiac function classification before and after treatment: Marked efficacy: Symptoms such as chest tightness, polypnea and palpitation were dramatically improved, with a recession of edema; the breathing sounds were clear or the rales in the lungs reduced significantly; the cardiac function was considerably improved than before, with the cardiac function restored to grade 1 or by over ≥ 2 grades. Moderate efficacy: The above symptoms were relieved to a certain degree; the moist rales in the lungs reduced; the cardiac function was improved by ≥ 1 grade than before. No efficacy: The above symptoms were not improved or even aggravated after treatment. Both two groups of patients received ambulatory electrocardiography monitoring before and after treatment. The following information was recorded; the frequency and duration of atrial arrhythmias before and after treatment in the two groups; the frequency and duration of ventricular arrhythmias before and after treatment in the two groups. The two groups of patients were followed up for 6-12 mo. Main Adverse Cardiovascular Events (MACEs) were recorded, including all-cause mortality and malignant arrhythmias (ventricular fibrillation, pulseless ventricular tachycardia and torsades de pointes). Statistical Package for the Social Sciences (SPSS) 19.0 software was used for data analysis. Measurements were expressed as mean \pm standard deviation. The pairwise comparison of the measurement data was conducted using the t-test. Counts were compared between the groups using the chi-square test. $p < 0.05$ was taken to indicate a significant difference. The Shenmai injection group had 63 patients and the control group had 57 patients. The baseline data of the two groups are shown in Table 1. There were no

significant differences between the two groups in age, gender or the incidence of hypertension and diabetes ($p > 0.05$). The efficacy comparison between the two groups is shown in Table 2. The overall response rate was 87.66 % in the Shenmai injection group vs. 85.96 % in the control group, indicating a significant difference ($\chi^2 = 7.033$, $p < 0.05$). Comparison of arrhythmias before and after treatment in the two groups as shown in Table 3. The results showed that in the Shenmai injection group, both the frequency and duration of atrial and ventricular arrhythmias were reduced significantly after the treatment than before ($p < 0.05$). However, the frequency of atrial arrhythmias increased in the control group after treatment. There was also a significant difference in these aspects ($p < 0.05$). No significant differences were observed in the duration of atrial arrhythmias or the frequency and duration of ventricular arrhythmias before and after the treatment in the control group. One patient in the Shenmai injection group had an evanescent eruption. One patient in the control group had nausea and vomiting, which were relieved after discontinuation of the medication. The two groups did not differ significantly in the incidence of adverse reactions ($p > 0.05$). The two groups of patients were followed up for 6-12 mo. No MACE occurred in the Shenmai injection group. One patient in the control group died from malignant arrhythmias. However, the two groups did not differ significantly in the incidence of MACE ($\chi^2 = 1.115$, $p > 0.05$). CHF is a progressive syndrome characterized by systolic and/or diastolic dysfunction, resulting in venous system blood accumulation and artery hypoperfusion. In this condition, the cardiac output can no longer meet the metabolic requirements. In brief, CHF involves a group of symptoms related to cardiac circulation disorder. CHF mainly presents with pulmonary congestion and vena cava congestion and represents the end-stage of cardiac diseases. An epidemiological study has shown that the prevalence of CHF in the general population is 1 % to 2 %^[2]. Despite the significant progress made in the treatment of CHF in recent years, the 5 y mortality of CHF patients remains high^[3]. The prevention and treatment of CHF are important topics in both academic and clinical fields. Medication is the primary treatment for CHF at present. Western medicine treatments for CHF mainly include cardiotonic, diuretics, vasodilators and neurohormonal antagonist drugs, which can help delay the progression of CHF. In the terminology of traditional Chinese medicine, CHF is a disease associated with qi stagnation and blood stasis caused by the deficiency of heart qi and the inability of the heart to

pump. This condition further affects kidneys and liver and results from the unfavorable interactions between qi, blood and water. Studies have shown that the combination of Chinese and Western medicine can dramatically improve the prognosis, immunity and life quality of patients with CHF, while reducing the readmission rate. This approach has become an essential part of CHF management. Shenmai injection is prepared based on the formula compatibility principle and using processed red ginseng and ophiopogonis tuber. This Chinese patent medicine has the functions of tonifying qi, preventing exhaustion and restoring pulse beat. The two traditional Chinese herbal medicines have been used compatibly for over 1500 y to treat patients with deficiency of both vital energy and yin. It has been reported that^[4,5] Shenmai injection can improve myocardial metabolism and cardiac reserve capacity and increase myocardial contractility and cardiac output to reduce the cardiac load. Meanwhile, Shenmai injection can enhance immunity and regulate the endocrine balance. Several studies at home and abroad have shown^[6,7] that Shenmai injection has good efficacy in improving the cardiac function of patients with CHF. However, the existing studies are mostly observational

studies. There is a lack of randomized controlled trials and few are concerned with the effect of the Shenmai injection on arrhythmias and the patients' prognosis. To fill the research gaps, we performed a prospective, randomized controlled trial, which investigated the influence of Shenmai injection on the cardiac function, arrhythmias and prognosis of patients with CHF. We found that after 14 d of Shenmai injection on top of the conventional Western medicine treatment, the overall response rate was 87.66 %, which was significantly higher than that of the control group (85.96 %, $p<0.05$). The combination treatment group showed a marked improvement in either atrial or ventricular arrhythmias after treatment ($p<0.05$). There were no significant differences in the incidence of MACEs between the two groups during 6-12 mo of follow-up. It is necessary to expand the sample size or prolong the use of Shenmai injection or observation to verify our conclusions. Taken together, Shenmai injection plus the conventional Western medicine treatment could more effectively relieve the clinical symptoms of CHF than the standard Western medicine treatment alone. The combination treatment could dramatically improve arrhythmias and therefore is worthy of broader applications.

TABLE 1: COMPARISON OF BASELINE DATA BETWEEN THE TWO GROUPS OF PATIENTS

	Shenmai injection group (n=63)	Control group (n=57)	p value
Age (year)	63.73±8.99	64.82±9.77	0.524
Gender (male/female)	36/27	30/27	0.620
Cardiac function classification (II/III)	25/38	18/39	0.355
Hypertension	35	31	0.898
Hyperlipidemia	38	32	0.643
Diabetes	27	24	0.934
Smoking	28	20	0.296

Note: * $p<0.05$

TABLE 2: EFFICACY COMPARISON BETWEEN THE TWO GROUPS

Group	Case	Marked efficacy		Moderate efficacy		No efficacy		Overall response rate	
		Case	%	Case	%	Case	%	Case	%
Shenmai injection group	63	36	57.14	24	38.10	3	4.76	60	87.66*
Control group	57	20	35.09	29	50.88	8	14.04	49	85.96

Note: *Compared with the control group, $p<0.05$

TABLE 3: COMPARISON OF THE FREQUENCY AND DURATION OF ARRHYTHMIAS BEFORE AND AFTER TREATMENT BETWEEN THE TWO GROUPS

Group	Case	Frequency of atrial arrhythmias (Episodes/24 h)		Duration of atrial arrhythmias (Percentage %)		Frequency of ventricular arrhythmias (Episodes/24 h)		Duration of ventricular arrhythmias (Percentage %)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Shenmai injection group	63	1132.14±3211.51	126.57±94.88 [▲]	2.20±2.33	0.91±4.30 [▲]	2620.11±4964.71	570.94±1477.13 [▲]	2.67±4.01	0.78±1.94 [▲]
Control group	57	454.40±1251.18	1193.63±1076.19 [▲]	2.09±0.95	1.96±1.40	523.21±1325.79	302.28±999.62	4.03±3.55	3.73±5.98

Note: [▲]Compared with the situation before treatment, $p < 0.05$

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Conflict of interests:

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