Cardiology in the Young

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Effect of Yangxin Huoxue Jiedu recipe on inflammatory factors and oxidative stress on viral myocarditis in children

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Original Article

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Abstract

Objective: This observation purposed to investigate the effect of the Yangxin Huoxue Jiedu formula on children with viral myocarditis and its effect on inflammatory factors and oxidative response. *Materials and methods:* A total of 121 children with viral myocarditis were randomly divided into two groups, namely the control group (N = 60) and the traditional Chinese medicine group (N = 61). The control group was mainly treated with routine therapy, while the traditional Chinese medicine group was treated with Yangxin Huoxue Jiedu recipes based on the control group. The creatine kinase, creatine kinase myocardial isoenzyme, aspartate aminotransferase, lactic dehydrogenase, hydroxybutyrate dehydrogenase, cardiac troponin I, brain natriuretic peptide, interleukin-6, interleukin-8, and tumour necrosis factor-alpha, superoxide dismutase and malondialdehyde in viral myocarditis patients were tested to estimate the myocardial function, inflammation, and oxidative situation. *Results:* After Yangxin Huoxue Jiedu treatment, 15 cases were recovered, 20 were excellent, and 21 were effective, which had a significant difference from the control group. The concentration of creatine kinase, creatine kinase myocardial isoenzyme, aspartate aminotransferase, lactic dehydrogenase, hydroxybutyrate dehydrogenase, cardiac troponin I and brain natriuretic peptide was decreased in the traditional Chinese medicine group. The levels of interleukin-6, interleukin-8, and tumour necrosis factor-alpha in the traditional Chinese medicine group were significantly lower than those in the control group. Superoxide dismutase was higher and malondialdehyde was lower than those in the control group. *Conclusion:* The use of Yangxin Huoxue Jiedu in the treatment of viral myocarditis has a definite clinical effect, which could improve myocardial function, reduce body inflammation, and promote oxidative recovery.

Among the cardiovascular maladies in children, viral myocarditis has a high incidence, that seriously affects the health of children.[1] Numerous pathogens can cause viral myocardial inflammation.[2] At present, the pathogenesis of viral myocarditis is not fully understood. Most scholars believe that the pathogenesis of viral myocarditis mainly includes the direct damage of the virus to myocardium, immune response mediated by virus, and molecular simulation of autoimmunity.[3–5] The conventional treatment is the first choice of free radical scavengers and other antiviral drugs in the acute phase, while in the chronic phase, the lesions are mainly autoimmune damage and cardiac insufficiency. The targeted prevention and treatment measures for the possible pathological mechanism of viral myocarditis are not ideal.[6] The research on the mechanism and prevention measures formed at the same time is also the top priority in the medical field. In addition to the treatment of Western medicine, traditional Chinese medicine plays a more and more important role in the treatment of this disease.[7] Therefore, gradual in-depth research on the treatment of viral myositis with traditional Chinese medicine has important guiding significance and application prospects.

The cardioprotective effects of herbal medicines on heart dysfunction were widely researched recently.[8,9] An observation on traditional Chinese medicine reviews that several traditional Chinese medicine prescriptions have anti-oxidation, anti-fibrosis, anti-inflammation, anti-apoptosis, and pro-angiogenesis regulatory effects in heart failure.[10] In another retrospective investigation, traditional Chinese medicine exerts a beneficial function on patients with myocardial infarction concerning decreasing cardiac death and poor prognosis during follow-up.[11] A large number of clinical data have confirmed that traditional Chinese medicine has the effect of antiviral and myocardial protection in the treatment of viral myocarditis, improving the prognosis of viral myocarditis.[12] The management of Qidong Yixin oral liquid combined with conventional treatment on viral myocarditis patients is superior to conventional treatment.[13] Nevertheless, the underlying mechanism and efficacy need further verification.

In this observation, children with viral myocarditis were recruited to demonstrate the function of a novel traditional Chinese medicine Yangxin Huoxue Jiedu recipe. This study proposes that the Yangxin Huoxue Jiedu recipe was beneficial to viral myocarditis patients via suppressing inflammatory response and oxidative disorder. Therefore, we tested the efficacy of Yangxin Huoxue Jiedu on viral myocarditis patients within 2 weeks. In addition, the impacts of Yangxin Huoxue Jiedu remedy on myocardial function inflammatory state and oxidative response were also tested.

Materials and methods

Participants recruitment

A total of 121 children with viral myocarditis received and treated in Xingtai People's Hospital from June 2019 to January 2022 were randomly divided into two groups, which were the control group (N = 60) and the traditional Chinese medicine group (N = 61). The diagnostic criteria of Western medicine were based on the diagnostic criteria of viral myocarditis (revised draft) issued in 2000.[14] The detailed criteria were as follows: (1) cardiac insufficiency, cardiogenic shock, or cardio-cerebral syndrome; (2) cardiac enlargement (one of the manifestations of X-ray and echocardiography); (3) ECG changes; (4) elevated creatine kinase myocardial isoenzyme or positive cardiac troponin (cTnI or cTnT). A clinical diagnosis of myocarditis can be made on the basis of 2 clinical criteria. Viral myocarditis can be diagnosed if the patient's endocardium, myocardium, pericardium, or pericardio-centesis fluid is positive for viral nucleic acid or specific virus antibodies. The diagnostic criteria of Chinese medicine referred to the guiding principles for Clinical Research of New Drugs of traditional Chinese medicine formulated by the Ministry of Health of the People's Republic of China.[15] The diagnostic basis of traditional Chinese medicine syndrome type included (1) palpitation, fatigue, dizziness, shortness of breath, upset and insomnia, hot heart in hands and feet; (2) chest tightness, chest pain, dry oropharynx; (3) red tongue, less fur, and thin or knot pulse. The cardiac function was documented according to the NYHA cardiac function classification.[16]

The inclusion criteria were as follows: (1) age within 2–14 years old, (2) good compliance and clear medical records; (3) diagnosis with viral myocarditis according to clinical symptoms and laboratory tests or imaging tests. The exclusion criteria were as follows: (1) complicated with other heart diseases; (2) with malignant tumours; (3) suffering from serious liver and kidney diseases; (4) could not adhere to oral traditional Chinese medicine.

Ethics statement and informed consent

The researcher introduced the experimental objectives and experimental procedures. All children and their guardians were aware of the study and signed the informed consent after being fully aware of the possible risks and benefits. These experiments were approved by the Ethics Committee of Xingtai People's Hospital and in accordance with the Declaration of Helsinki 1975. The clinical trials fully followed the requirements of good clinical practice.[17]

Randomisation and blinding

The independent statistician generated a random allocation table, and patients with viral myocarditis were given random numbers. The patients obtained traditional Chinese medicine with respective number labelling. The statistician did not participate in any other processes, including patient collection, pharmacy, packaging, distribution, index determination, et cetera.

An independent researcher was responsible for decocting Yangxin Huoxue Jiedu and labelling the drug packages. This researcher did not participate in any other trials. Other researchers and all patients were only told the code. Only the principal investigator knows the complete treatment allocations. The distribution result will not be disclosed unless the patient has serious adverse events and reactions.

Components of the Yangxin Huoxue Jiedu recipe

The prescriptions for the Yangxin Huoxue Jiedu recipe are shown in Table 1. The dosage of one day and the potential effects of each traditional Chinese medicine material are also shown in Table 1. The medicinal materials were all provided by the traditional Chinese medicine pharmacy of Xingtai People's Hospital. All the herbs in the Yangxin Huoxue Jiedu recipe were soaked in water for 30 min. The prescription herbs were decocted twice, and then, the residue was filtered. The decoctions were combined and concentrated to 400 ml, named one dose. Half dose (200 ml) was packaged in a separate container.

Placebo was manufactured on the basis of traditional Chinese medicine dilution, as described previously.[18] The placebo is a decoction made of 5% Yangxin Huoxue Jiedu decoction, ingredient (starch), bittering agent, and colouring agent to ensure the similar visual feature, taste characteristics, smell sense, transparency, and turbidity to Yangxin Huoxue Jiedu decoction. This preparation method of placebo is a routine avenue, and the placebo is similar in nature to the traditional Chinese medicine but did not have pharmacological effects.[19] The specification of the placebo was 200 ml. The placebo was also prepared by the traditional Chinese medicine pharmacy of Xingtai People's Hospital.

Management to patients

The patients in the control group were placebo and routine treatment, while those in the traditional Chinese medicine group were given Yangxin Huoxue Jiedu therapy and routine treatment. The routine treatment was symptomatic treatment according to the actual situation of the patients, including anti-virus treatment and anti-infection management. In addition, it also included nutritional guidance, oxygen support, and basic nursing. Drug options included antibiotic therapy, ribavirin, coenzyme Q10, and vitamin C. Antiviral therapy was administered with Wellbutrin at 15 mg/kg daily for 7 days of observation therapy. Improvement of myocardial metabolism was treated with coenzyme Q10 (20 mg each time, 3 times daily) and vitamin C (1 each time, twice daily) for 14 days. Penicillin was injected intramuscularly 2.5 × 104 U/ (kg-d) twice/d according to the condition. Intravenous gamma globulin 2 g/kg was administered intravenously in divided doses over 2–3 days.

The patients in the traditional Chinese medicine group were required to take the half dose (200 ml) twice in the morning and evening of one day. The patients in the control group received a 200 ml placebo in the same way as that of traditional Chinese medicine group.

Specimen obtain

The fasting venous blood of 5 ml of the two groups of patients was collected before and after a course of 14-day treatment and

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Table 1. The main components of YHJ decoction.

Chinese name	Latin name	Dosage	Potential effect
Huangqi	Astragalus membranaceus (Fisch) Bge	20 g	Invigorating qi and elevating yang, consolidating exterior and stopping sweating, inducing diuresis and relieving swelling, promoting fluid production and nourishing blood, and resolving stagnation.
Dangshen	Codonopsis pilosula (Franch.) Nannf.	18 g	Invigorating spleen and lung, nourishing blood, and promoting fluid production.
Danshen	Salvia miltiorrhiza Bge.	15 g	Promoting blood circulation and removing blood stasis, promoting meridians and relieving pain, clearing the heart and removing annoyance, cooling blood, and eliminating carbuncle.
Chuanxiong	Ligusticum chuanxiong Hort.	15 g	Promoting blood circulation and qi, dispelling wind, and relieving pain.
Chishao	Paeonia lactiflora Pall.	15 g	Clearing heat and cooling blood, removing blood stasis, and relieving pain.
Honghua	Carthamus tinctorius L.	15 g	Promoting blood circulation and dredging channels, removing blood stasis, and relieving pain.
Guizhi	Cinnamomum cassia Presl	12 g	Sweating and resolving muscles, warming and dredging meridians, helping yang to transform qi, calming chong, and lowering qi.
Lianqiao	Forsythia suspensa (Thunb.) Vahl	12 g	Clearing away heat and toxic materials, reducing swelling and dissipating stagnation, and dispersing wind and heat.
Jinyinhua	Lonicera japonica Thunb.	12 g	Clearing away heat and toxic materials and dispelling wind and heat.
Kushen	Sophora flavescens Ait.	9 g	Clearing away heat and dampness and killing insects and diuresis.
Maidong	Ophiopogon ja ponicus (L.f.) Ker-Gawl.	9 g	Nourishing yin and promoting fluid production, moistening lung, and clearing heart.
Wuweizi	*Schisandra chinensis <Turcz.> Baill.*	9 g	Convergence and astringency, benefiting qi and promoting fluid production, tonifying kidney, and calming heart.
Gancao	Glycyrrhiza uralensis Fisch	6 g	Tonifying spleen and qi, clearing heat and detoxifying, eliminating phlegm and cough, alleviating pain, and reconciling all medicines.

YHJ = Yangxin Huoxue Jiedu, a traditional Chinese medicine.

centrifuged for 5 min at 3000 r per minute. The upper serum was taken and deposited in the medical refrigerator at −80°C.

Diagnostic tests in patients with viral myocarditis

All children received routine electrocardiogram, 24-hour Holter ECG monitoring, and echocardiogram before treatment. Routine electrocardiograms were examined using an ECG-9130P 12-lead synchronised electrocardiograph (Nippon Kohden, Tokyo, Japan). A tracing speed of 25 mm per second was established to ensure that the baseline of the ECG recorded during the tracing period was stable, and the images were clear and free of interference. The ECG was monitored for 60s in the resting state of the patients, and the results were recorded. Dynamic electrocardiography was performed using a 300-4A dynamic electrocardiograph (DMS, Nevada, USA). Using high-quality electrodes special for dynamic electrocardiography, fastening the wires and electrodes, electrode sheets are correctly pasted, the conductive adhesive is evenly applied to the middle position of the electrode sheets, and all the electrode sheets need to be directly pasted on the skin of ribs and sternum. The results were automatically transmitted to the analysis system to analyse the results of 24h dynamic ECG examination. Arrhythmias mainly include sinus tachycardia, ST segment changes, and others including ventricular presystole, atrial presystole, atrioventricular block, paroxysmal supraventricular tachycardia, et cetera.

Echocardiography was performed with an HP77020AC ultrasound system from Hewlett-Packard. The left ventricular end-diastolic dimension, left ventricular end-systolic dimension, interventricular septal thickness, left ventricular ejection fraction, and cardiac enlargement (a chamber diameter or cardiothoracic ratio > 0.5[20]) were assessed by M-mode echocardiography. The measurements were repeated three times, and the average value was taken.

Curative effect standard

According to the changes in the myocardial enzyme spectrum, an electrocardiogram, and clinical symptoms, the curative outcome was estimated. The normal myocardial enzyme and electrocardiogram examination results and total disappearance of symptoms and signs mean the recovery effect of patients. When the symptoms and signs of patients obviously improved or basically disappeared, partial recovery of laboratory examination, which means excellent effect. The effectiveness was on behalf of recovery of more than one symptom or auxiliary examination. The ineffective meant no improvement in the main symptoms and examination. All these effects of Yangxin Huoxue Jiedu were distinguished by referring to the guiding principles for Clinical Research of New Drugs of traditional Chinese medicine.

Estimation of laboratory indicators

The changes of myocardial enzyme spectrum were revealed in all patients with viral myocarditis, including creatine kinase, creatine kinase myocardial isoenzyme, aspartate aminotransferase, lactic dehydrogenase, and hydroxybutyrate dehydrogenase. The serum cardiac troponin I, and brain natriuretic peptide of children with viral myocarditis were evaluated by immunoturbidimetry. ELISA method was used to detect inflammatory and oxidative factors, including serum interleukin-6, interleukin-8, tumour necrosis factor-α, and superoxide dismutase. The operation was carried

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out in strict accordance with the reagent instructions (Boster, Wuhan, China). The detection of malondialdehyde was performed based on the kit reference from Jisskang Biotechnology (Qingdao, China).

Safety assessment

During the study, the patient's liver, renal function, electrolytes, analysis of blood, and urine analysis were examined. The adverse drug reactions and medical events of patients during treatment were recorded according to the requirements of the Administrative Measures for Adverse Drug Reaction Monitoring Reports.[21]

Statistical analysis

SPSS Statistics 20.0 and GraphPad software 7.04 were used for statistical analysis. The measurement data are expressed by mean ± standard deviation, and the differences within and between groups were compared by t-test. The counting data were exhibited by n (%), and χ^2 test was used. The difference was statistically significant ($p < 0.05$).

Results

General clinicopathological information and clinical efficacy of traditional Chinese medicine

According to the random method, 61 patients were enrolled in the traditional Chinese medicine group and the other 60 patients were enrolled in the control group. The gender, age, and course of disease, NYHA cardiac function classification, clinical symptom, echocardiographic parameters, routine ECG detection results, and dynamic ECG results between the control group and traditional Chinese medicine group indicated no significant difference, and thus, these two groups were comparable (Table 2, $p > 0.05$).

Comparison of clinical efficacy between the two groups

In the control group, the number of cases with recovery, excellence, effective, and ineffective treatment was 7, 11, 27, and 15 respectively (Table 3). In the traditional Chinese medicine group, 15 patients obtained recovery results, 20 excellent, 21 effective, and 5 ineffective (Table 3). The recovery rate between the control group and traditional Chinese medicine group was significant, which indicated that Yangxin Huoxue Jiedu exerted an obvious clinical efficacy (Table 3, $p = 0.010$).

Traditional Chinese medicine improves myocardial ability

According to the results of myocardial enzyme spectrum, the content of creatine kinase, creatine kinase myocardial isoenzyme, aspartate aminotransferase, lactic dehydrogenase, and hydroxybutyrate dehydrogenase declined in patients of traditional Chinese medicine group compared with the control group, reflecting that traditional Chinese medicine could recover the myocardial ability of viral myocarditis patients (Table 4, $p < 0.05$). Additionally, cardiac troponin I and brain natriuretic peptide also showed a reduced tendency in traditional Chinese medicine group, suggesting the impacts of traditional Chinese medicine in viral myocarditis patients (Table 4, $p < 0.05$). After treatment, the left ventricular end-diastolic dimension, left ventricular end-systolic dimension, and interventricular septal thickness of the traditional Chinese medicine group were decreased compared with the control group (Table 4, $p < 0.05$). Compared to the control group, the left ventricular ejection fraction was elevated in the traditional Chinese medicine group after treatment (Table 4, $p < 0.05$). The number of left ventricular enlargement and cardiac arrhythmias showed no obvious difference between the control group and the traditional Chinese medicine group after treatment (Table 4, $p > 0.05$).

Traditional Chinese medicine ameliorated inflammatory indicators

The concentration of inflammatory activators reflected the inflammatory state before and after YHJ treatment. Before Yangxin Huoxue Jiedu treatment, the leakage of tumour necrosis factor-alpha, interleukin-6, and interleukin-8 was similar in the control group and traditional Chinese medicine group (Fig. 1a–c, $p > 0.05$). However, after 2-week treatment with Yangxin Huoxue Jiedu formula, the generation of inflammatory biomolecules in the traditional Chinese medicine group was diminished relative to control group, suggesting traditional Chinese medicine might assuage inflammatory progression (Fig. 1a–c, $p < 0.001$).

Traditional Chinese medicine impeded oxidative stress

The related indexes superoxide dismutase and malondialdehyde showcased the oxidative reaction of viral myocarditis patients. After treatment, the concentration of superoxide dismutase in the traditional Chinese medicine group was obviously higher than that in the control group (Fig. 2a, $p < 0.001$). Also, the malondialdehyde content of patients with Yangxin Huoxue Jiedu treatment declined compared with control group (Fig 2b, $p < 0.001$). Briefly, these reactions endorsed Yangxin Huoxue Jiedu recipe was beneficial to viral myocarditis via halting oxidative stress.

Clinical safety evaluation

No adverse medical events or adverse drug reactions were observed in the two groups. There were no abnormal changes in clinical laboratory indexes.

Discussion

Viral myocarditis is a disease that causes systemic damage, such as cardiac insufficiency by infiltration of inflammatory cells in the myocardial interstitium and necrosis of adjacent cardiomyocytes due to a variety of infections or other causes.[22] It is one of the common causes of cardiac impairment in childhood, but the incidence in childhood is uncertain.[23,24] The clinical manifestations of viral myocarditis are complex.[25,26] The early clinical manifestations include upper respiratory tract infection and digestive tract infection. During this period, patients will suffer from cough, shortness of breath, and irritability. Severe viral myocarditis develops rapidly, from mild symptoms to multiple organ dysfunction, accompanied by haemodynamic changes, and has a considerable mortality rate.[27] Therefore, the treatment of viral myocarditis should be paid attention to.

In Chinese medicine, the pathological causes of viral myocarditis were evil toxins invading the heart, deficiency of vital Qi, deficiency of Qi and Yin, and blood stasis.[28] In combination with trimetazidine and traditional Chinese medicine, injections had a high therapeutic value in the management of viral myocarditis.[29] In addition, a total of six single ingredients of traditional Chinese medicine were observed conducive to viral myocarditis, including Astragalus membranaceus (Fisch) Bge (Huangqi), and *Sophora flavescens* Ait. (Kushen).[30] In this observation, Huangqi and Kushen were selected to form a

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Table 2. Clinical data of all collected population.

Parameters	Control group (n = 60)	TCM group (n = 61)	p value
Gender (N)			0.526
Male	31	28	
Female	29	33	
Age (years)	9.10 ± 2.29	8.89 ± 2.65	0.634
Course of disease (days)	5.90 ± 2.11	5.75 ± 2.17	0.708
NYHA cardiac function classification (N)			0.849
II class	39	41	
III class	21	20	
Clinical symptom (N)			
Chest distress	52	56	0.395
Shortness of breath	51	48	0.481
Tachycardia	45	47	0.834
Chest pain	50	49	0.814
Echocardiographic parameters			
LVEDD (cm)	4.95 ± 1.07	4.76 ± 1.03	0.339
LVSD (cm)	3.47 ± 0.86	3.78 ± 0.97	0.070
IVSD (cm)	0.61 ± 0.17	0.64 ± 0.16	0.268
LVEF (%)	44.39 ± 2.34	43.82 ± 2.36	0.186
Routine ECG detection (N)			
Sinus tachycardia	18	16	0.645
ST segment change	12	14	0.693
Others	5	7	0.762
24-hour Holter ECG detection (N)			
Sinus tachycardia	20	19	0.847
ST segment change	13	15	0.830
Others	7	9	0.789

TCM = traditional Chinese medicine; LVEDD = left ventricular end-diastolic dimension; LVSD = left ventricular end-systolic dimension; IVSD = interventricular septal thickness; LVEF = left ventricular ejection fraction; ECG = electrocardiogram.

Table 3. Final efficacy of TCM treatment.

Efficacy	Control group (n = 60)	TCM group (n = 61)	p value
Recovery (N, %)	7, 11.67	15, 24.59	0.010
Excellent (N, %)	11, 18.33	20, 32.79	
Effectiveness (N, %)	27, 45.00	21, 34.43	
Ineffectiveness (N, %)	15, 25.00	5, 8.20	

TCM = traditional Chinese medicine.

prescription for nourishing heart, promoting blood circulation and detoxification. Several single ingredients in this traditional Chinese medicine formula were proven to be effective in treating immune abnormalities and myocardial diseases. For instance, Huangqi has the function of tonifying Qi, which has been widely used to treat cardiovascular disease.[31] The polysaccharides contained in Codonopsis pilosula (Franch.) Nannf. (Dangshen) is considered to have therapeutic effects on enhancing immunity and antioxidant (32).[32] The efficacy of Yangxin Huoxue Jiedu recipe was tested through a two-week treatment on viral myocarditis patients. The finding pinpointed that the overall prognosis of patients with Yangxin Huoxue Jiedu treatment was more satisfactory than control patients, suggesting the effectiveness of Yangxin Huoxue Jiedu recipe on viral myocarditis patients. In addition, this paper further certified the function of traditional Chinese medicine on myocardial ability via assessing the alternation of the myocardial enzyme spectrum. The levels of creatine kinase, creatine kinase myocardial isoenzyme, aspartate aminotransferase, lactic dehydrogenase, and hydroxybutyrate dehydrogenase were decreased after treatment, especially in the patients of traditional Chinese medicine group. Brain natriuretic

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Table 4. Effect of TCM treatment on myocardial function.

Indicator	Before treatment		After treatment	
	Control group	TCM group	Control group	TCM group
CK (U/L)	213.78 ± 20.64	212.70 ± 22.09	154.55 ± 16.37	87.09 ± 15.44*
CK-MB (μg/L)	29.21 ± 3.54	30.17 ± 3.82	17.76 ± 2.56	14.21 ± 1.60*
ASK (U/L)	73.10 ± 8.03	74.18 ± 8.96	35.31 ± 9.48	22.63 ± 6.99*
LDH (U/L)	220.91 ± 27.26	226.88 ± 18.94	135.15 ± 14.04	101.81 ± 10.24*
HBDH (U/L)	283.36 ± 35.51	285.37 ± 35.21	175.38 ± 27.16	93.31 ± 15.11*
cTnI (μg/L)	0.60 ± 0.17	0.62 ± 0.19	0.50 ± 0.15	0.17 ± 0.03*
BNP (pg/mL)	212.39 ± 31.40	212.07 ± 26.25	106.73 ± 21.00	80.15 ± 19.40*
LVEDD (cm)	4.95 ± 1.07	4.76 ± 1.03	3.83 ± 0.92	3.46 ± 0.76*
LVSD (cm)	3.47 ± 0.86	3.78 ± 0.97	2.84 ± 0.92	2.30 ± 0.80*
IVSD (cm)	0.61 ± 0.17	0.64 ± 0.16	0.46 ± 0.15	0.40 ± 0.10*
LVEF (%)	44.39 ± 2.34	43.82 ± 2.36	58.09 ± 2.28	59.32 ± 1.93*
Left ventricular enlargement (N)	13	15	5	2
Cardiac arrhythmias (N)	27	25	11	4

TCM = traditional Chinese medicine; CK: creatine kinase; CK-MB: creatine kinase myocardial isoenzyme; ASK: aspartate aminotransferase; LDH: lactic dehydrogenase; HBDH: hydroxybutyrate dehydrogenase; cTnI: cardiac troponin I; BNP: brain natriuretic peptide; LVEDD = left ventricular end-diastolic dimension; LVSD = left ventricular end-systolic dimension; IVSD = interventricular septal thickness; LVEF = left ventricular ejection fraction.
*$p < 0.05$.

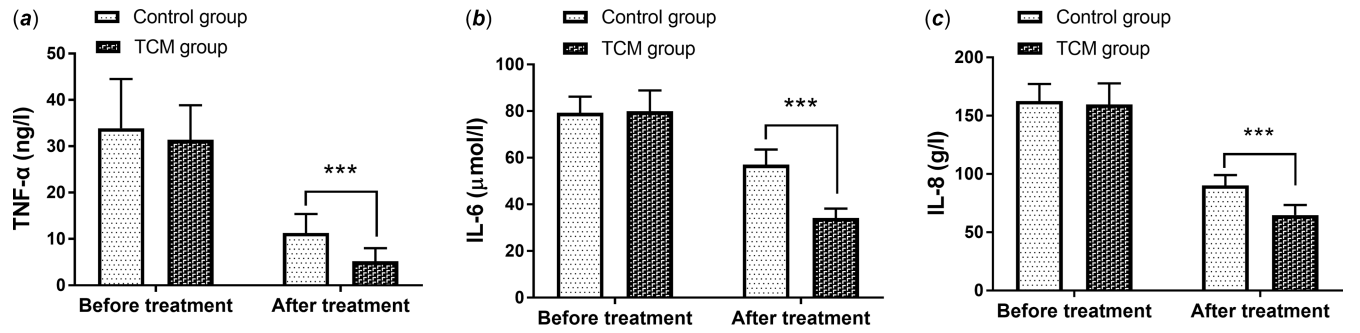

Figure 1. Inhibition of inflammation after YHJ treatment. (***a***) The TNF-α content in the TCM group was inhibited after treatment. (***b***) YHJ recipe suppressed the IL-6 generation. (***c***) The IL-8 expression in the TCM group was decreased after treatment. ***$p < 0.001$, relative to control group.

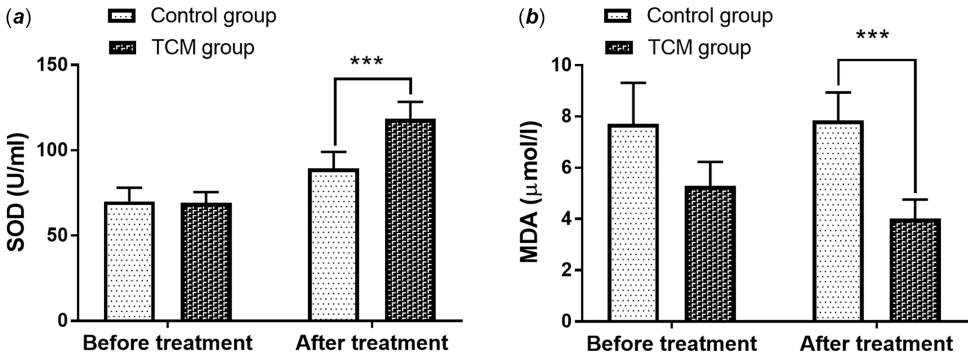

Figure 2. YHJ ameliorated the oxidative injury. (***a***) The SOD expression in TCM group was increased after treatment. (***b***) Decreased MDA content was found in TCM group after YHJ treatment. ***$p < 0.001$, relative to control group.

peptide is mainly secreted by the left ventricle and is an important index for the diagnosis of heart failure.[33] Serum cardiac troponin I is a specific protein of cardiac myocytes reflecting the myocardial function.[34] Our results indicated that traditional Chinese medicine could improve the myocardial function of patients with viral myocarditis. In addition, the left ventricular function after Yangxin Huoxue Jiedu treatment was improved significantly, indicating that Yangxin Huoxue Jiedu treatment was beneficial to Viral myocarditis treatment.

Viral myocarditis is marked as inflammation of the myocardium; thus, detection of inflammatory indicators was a method to analyse the mechanism of Yangxin Huoxue Jiedu.[35] In current

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investigation, the therapeutic effects of traditional Chinese medicine were further tested with respect to inflammation and oxidative stress. Usage of Yangxin Huoxue Jiedu recipe reduced the release of tumour necrosis factor-alpha, interleukin-6, and interleukin-8, indicating that Yangxin Huoxue Jiedu might contribute to the improvement of viral myocarditis via inhibiting inflammatory generation. Oxidative stress is another element, that is pertinent to the pathogenesis of viral myocarditis.[36] Additionally, the concentration of superoxide dismutase and malondialdehyde of viral myocarditis patients was changed obviously after Yangxin Huoxue Jiedu management, suggesting the protective roles of Yangxin Huoxue Jiedu on oxidative response. Huangqi assuages the content of tumour necrosis factor-alpha and interleukin-6 caused by COVID-9, reinforcing our finding.[37] In another experiment, Huangqi is proved as an inhibitory element on inflammation and oxidative stress.[38] Taking all results and previous outcomes into consideration, Yangxin Huoxue Jiedu recipe might have anti-oxidative and anti-inflammatory properties. In addition, no adverse medical events or adverse drug reactions happened in all patients, indicating that Yangxin Huoxue Jiedu management was safe in treating viral myocarditis. This study had some limitations, such as the small sample size, incomplete efficacy indication, and safety assessment. Besides, a limitation of this paper is that not all patients underwent MRI testing, resulting in a lack of data on clinical characteristics.

Collectively, Yangxin Huoxue Jiedu recipe could improve the therapeutic effect on viral myocarditis patients. In addition, Yangxin Huoxue Jiedu formula could ameliorate the myocardial lesions, inhibit the inflammatory situation, and moderate the oxidative stress in viral myocarditis patients, thus impeding viral myocarditis progression.

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Competing interests. None.

Ethical standards. These experiments were approved by the Ethics Committee of Xingtai People's Hospital and in accordance with the Declaration of Helsinki 1975.

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