



Clinical study on the effect of Tongxinluo combined with trimetazidine on cardiac function in patients with acute ST-segment elevation myocardial infarction after percutaneous coronary intervention

Qun-Xiong Fan¹, Ji-Xian Zhao¹, Huan-Xin Zhang^{1✉}, Bo Li¹, Zheng-Rong Li^{2✉}

¹ Department of Cardiology, Affiliated People's Hospital of Hubei Medical College, Wuhan 432000, China

² ICU, Affiliated People's Hospital of Hubei Medical College, Wuhan 432000, China

ARTICLE INFO

Article history:

Received 12 Jun 2017

Received in revised form 19 Jun 2017

Accepted 3 Jul 2017

Available online 14 Jul 2017

Keywords:

Tongxinluo

Trimetazidine

Acute ST-segment elevation myocardial infarction

Percutaneous coronary intervention

Cardiac function

ABSTRACT

Objective: To investigate the clinical effect of Tongxinluo combined with trimetazidine on cardiac function in patients with acute ST-segment elevation myocardial infarction after percutaneous coronary intervention. **Method:** From March 2014 to September 2016, we selected 190 patients with ST-segment elevation myocardial infarction with percutaneous coronary intervention, according to the admission time is divided into observation group and control group, the control group was treated with conventional therapy (aspirin, isosorbide dinitrate, metoprolol tartrate, clopidogrel sulfate, captopril, atorvastatin calcium and diuretics) and trimetazidine, observation group in the control group based on Tongxinluo combined treatment, each group of 95 cases, and hs-CRP, aldosterone, NT-proBNP, TNF- α , IL-6, and cardiac function (LVEDV, LVESV, LVEF, SV) were compared. **Result:** The Hs-CRP in the observation group was significantly lower than that in the control group; The aldosterone in the observation group was significantly lower than that in the control group; The levels of NT-proBNP, TNF- α and IL-6 in the observation group were significantly lower than those in the control group; LVVEV and LVESV were significantly lower in the observation group than in the control group, LVEF and SV were significantly higher than those in the control group. **Conclusion:** Tongxinluo combined with trimetazidine in patients with acute ST-segment elevation myocardial infarction after percutaneous coronary intervention in patients with clinical effect is better, stable plaque, effectively improve microcirculation and cardiac function, recommended a wide range of clinical application.

1. Introduction

Acute ST-segment elevation myocardial infarction is one of the high-risk diseases of the heart[1–4], timely and effective dredge blood vessels, restore coronary artery reperfusion is the priority to maintain cardiac function and save the lives of patients, the current clinical preferred coronary interventional therapy for the treatment, but the postoperative exist myocardial no reflow or slow blood flow, microcirculation, stent thrombosis and restenosis and other

complications, seriously affect the intervention effect and prognosis, therefore, postoperative intensive use of drugs is a key medical link to prevent vascular inflammation, improve microcirculation, myocardial reperfusion, protect myocardial cells and restore heart function[5–7]. The application of tongxinluo and trimetazidine in our hospital after percutaneous coronary intervention is satisfactory.

2. Data and methods

2.1. Clinical information

A total of 190 patients with ST-segment elevation myocardial infarction who underwent percutaneous coronary intervention (PCI) from Hubei Medical College Affiliated People's Hospital

✉Corresponding author: Zheng-Rong Li, ICU, Affiliated People's Hospital of Hubei Medical College, Wuhan 432000, China.

Tel: 13593744318

E-mail: akakhv@163.com.

Fund Project: Hubei Province Health Department of the Project (2015-53).

during in March 2014 - September 2016 were enrolled in this study. The patients were divided into two groups according to the time of admission. Set as observation group and control group, 95 cases in each group. In the observation group, there were 60 males and 35 females, aged 32-73 years old, including 53 cases of anterior wall infarction and 42 cases of inferior wall infarction. The control group was 69 males and 26 females, aged 34-74 years old, 68 cases of anterior wall infarction, 27 cases of inferior wall infarction. Inclusion criteria[8-10]: a. Diagnosis in line with the 2010 Chinese Medical Association Cardiology Branch, the Chinese Journal of Cardiovascular Disease Editorial Board and the Chinese Circulation magazine editorial jointly developed the "acute ST-segment elevation myocardial infarction diagnosis and treatment guideline" standard[3]; b. age 30-75 years; c. Consistent with indications of serum myocardial markers of ECG and myocardial necrosis;d. d. meets the indications for percutaneous coronary intervention and is approved by the family or by consent and signed informed consent; e. Onset time of less than 12 h. Exclusion criteria[11,12]: a. Neuropsychiatric abnormalities, unable to cooperate with treatment; b. Has a history of allergies; c. Blood pressure greater than 180/110 mmHg; d. Blood system disease, liver and kidney dysfunction and malignant tumor. There was no statistical difference between the two groups in terms of age, sex, and location of infarction.

2.2. Treatment

The control group received conventional therapy, aspirin (Bayer health care Co., Ltd. production, National Medicine Zhunzi J20130078) 100 mg/times, 1 times/d, oral, Isosorbide Mononitrate Sustained Release Tablets (Qilu Pharmaceutical Co., Ltd., Zhunzi H20066717) 40 mg/times, 1 times/d, oral liquor, stone sour metoprolol (Anhui Wansen Pharmaceutical Co. Ltd, Chinese Zhunzi H20066315) 100 mg/times, 2 times/d, oral, clopidogrel hydrogen sulfate(Shenzhen salubris pharmaceutical Co., Ltd., Zhunzi H20120035) 75 mg/time, 1 times/d, oral, captopril (Sichuan Pacific Pharmaceutical Co., Ltd., Chinese medicine Zhunzi H51021145) 50 mg/time, 2 times /d, oral, atorvastatin calcium (Pfizer Pharmaceutical Co., Ltd., Chinese medicine Zhunzi H20051407) 10 mg/times, 1 times/d, oral, furosemide (Huizhou Daya Pharmaceutical Co., Ltd., Chinese medicine Zhunzi H44021546) 60 mg/times, 2 times/d, oral, treatment for 12 weeks, on this basis to be treat with trimexepine hydrochloride (Ruiyang Pharmaceutical Co., Ltd., Zhunzi H20066534) 20 mg/times, 3 times/d, oral and the treatment group

was treated with Tongxinluo (Shijiazhuang Yiling Pharmaceutical Co., Ltd., Zhunzi Z19980015) on the basis of the control group. 0.78 g/time, 3 times/d, oral, treatment for 12 weeks., 3 times/d, oral, treatment for 12 weeks.

2.3. Efficacy analysis

Compare the high sensitivity C- reactive protein (hs-CRP), aldosterone, N-terminal pro-brain natriuretic peptide (NT-proBNP), tumor necrosis factor- α (TNF- α), interleukin (IL) -6, and the index of cardiac function: left ventricular end diastolic volume (LVEDV), left ventricular end systolic volume (LVESV), left ventricular ejection fraction (LVEF), stroke volume (SV) between the two groups before and after treatment. Hs-CRP[13] was detected by turbidimetric immunoassay;TNF- α and IL-6 were measured by enzyme-linked immunosorbent assay (ELISA). NT-proBNP[14] was detected by electrochemiluminescence immunoassay. LVEDV, LVESV, LVEF, SV were measured using the GEVV-7 echocardiography [15]; aldosterone was measured by radioimmunoassay [16].

2.4. Statistical methods

All data were statistically analyzed by SPSS 17.0. The results of meta-data were used by t test. $P < 0.05$ was considered statistically significant.

3. Results

3.1. Comparison of biochemical markers hs-CRP, aldosterone, NT-proBNP, TNF- α and IL-6

There was no significant difference in hs-CRP, aldosterone, NT-proBNP, TNF- α and IL-6 between the two groups before treatment ($P > 0.05$). After treatment, the biochemical indexes of the two groups were significantly lower than those before treatment ($P < 0.05$). The levels of hs-CRP, aldosterone, NT-proBNP, TNF- α and IL-6 in the observation group were (2.51 ± 0.77) mg/L, (41.75 ± 7.43) ng/dL, (27.852 ± 42.33) ng/L, (97.40 ± 14.36) ng/L, (10.31 ± 2.74) ng/L, respectively, which were significantly lower than those in the control group, the difference was statistically significant ($P < 0.05$), see Table 1 ($P < 0.05$).

Table 1.

Comparison of hs-CRP, aldosterone, NT-proBNP, TNF- α and IL-6 in both groups.

Group	n	Time	hs-CRP (mg/L)	Aldosterone (ng/dL)	NT-proBNP (ng/L)	TNF- α (ng/L)	IL-6 (ng/L)
the observation group	95	Before treatment	5.96 \pm 1.84	58.36 \pm 8.42	989.76 \pm 120.60	150.86 \pm 23.36	17.45 \pm 3.47
		After treatment	2.51 \pm 0.77 [#]	41.75 \pm 7.43 [#]	278.52 \pm 42.33 [#]	97.40 \pm 14.36 [#]	10.31 \pm 2.74 [#]
the control group	95	Before treatment	6.04 \pm 1.73	57.98 \pm 7.86	990.85 \pm 129.47	152.53 \pm 21.47	17.52 \pm 3.56
		After treatment	3.88 \pm 0.70 [*]	52.11 \pm 7.76 [*]	350.36 \pm 50.64 [*]	118.33 \pm 15.49 [*]	13.57 \pm 2.96 [*]

Note: Compared with before treatment, ^{*} $P < 0.05$; compared with the control group after treatment, [#] $P < 0.05$.

Table 2.

Comparison of two groups of cardiac function indicators.

Group	n	Time	LVEDV (mL)	LVESV (mL)	LVEF (%)	SV (mL)
the observation group	95	Before treatment	195.47±19.36	126.07±23.65	34.09±1.02	55.36±4.42
		After treatment	160.30±14.38 [#]	83.95±14.16 [#]	39.21±10.23 [#]	63.37±4.55 [#]
the control group	95	Before treatment	196.26±18.74	125.49±22.71	33.80±0.93	55.48±4.56
		Bfter treatment	175.45±15.65 [*]	90.74±15.08 [*]	36.55±7.67 [*]	58.40±4.09 [*]

Note: Compared with before treatment, ^{*} $P < 0.05$; compared with the control group after treatment, [#] $P < 0.05$.

3.2. Comparison of two groups of cardiac function

There was no significant difference in LVEDV, LVESV, LVEF and SV between the two groups before treatment ($P > 0.05$). After treatment, the cardiac function indexes of the two groups were significantly improved compared with those before treatment, LVEDV and LVESV were significantly decreased, while LVEF, SV were significantly increased ($P < 0.05$). After treatment, the levels of LVEDV and LVESV of the observation group were (160.30 ± 14.38) mL and (83.95 ± 14.16) mL respectively, which were significantly lower than those in the control group. After treatment, the LVEF and SV of the observation group were (39.21 ± 10.23)% and (63.37 ± 4.55) mL respectively, which were significantly higher than those in the control group, the difference was statistically significant ($P < 0.05$).

4. Discussion

In recent years, with the rapid socio-economic development, the incidence of myocardial infarction in all ages increased year by year, ST-segment elevation myocardial infarction is the most common. Percutaneous coronary intervention (PCI) is the first choice for the treatment of ST-segment elevation myocardial infarction[17-19], the purpose of which is to thoroughly dredge infarction artery earlier, reduce myocardial infarct size, promote the infarct area scar repair, Prevent of myocardial remodeling in non-infarcted areas, restore myocardial function[20]. But this method is not very perfect, it cannot improve myocardial infarction in patients with capillaries - microcirculation of blood flow disorder this serious problem, there is a great impact on myocardial reperfusion, can easily lead to irreversible myocardial damage in long term, and then cause congestion heart failure. Long-term clinical experience found that postoperative intensive treatment of patients with myocardial infarction is of great significance to the microcirculation blood flow. Trimethazine is a new clinical anti-myocardial ischemia, anti-angina drugs, the selectivity for effectively inhibiting mitochondrial 32 kat, hinder free fatty acid oxidation, promote glucose metabolism, and cannot rely on hemodynamics, without affecting the myocardial blood supply conditions, reduce the high energy phosphate required for the production of myocardial energy metabolism, reduce consumption oxygen, play an anti-ischemic effect, and then protect myocardial supply and demand balance and improve heart function[21,22]. Tongxinluo capsule consists of traditional Chinese

medicine preparations, including ginseng, leeches, scorpion, Eupolyphaga, centipede, cicadas, red peony and other ingredients. Which ginseng is king medicine, replenishing qi and blood, the qi and the blood flow freely, and the venation is unimpeded; Leech, wood louse insects, promoting blood circulation and removing blood stasis, combined with other drugs played a total effect of Yiqihuoxue and Tongluozhitong. The drug is currently widely used in the prevention and treatment of vascular diseases, its anti-inflammatory, antioxidant and anticoagulant lipid-lowering effect is very significant, can effectively improve vessel endothelial function and microcirculation integrity, Stabilize and eliminate vulnerable plaques, reduce the frequency of vasospasm, reduce the degree of arteriosclerosis progress, thereby promoting myocardial perfusion, increase coronary blood flow, strengthen myocardial contractility, improve ejection fraction, effectively improve myocardial ischemia and cardiac function, prevent ventricular remodeling and cardiomyocyte death[22,23]. At present, China's clinical treatment of cardiac dysfunction is still ACEI/ABR, nitrates, β -blockers and diuretics, especially in the secondary below local hospitals, the above drugs can affect hemodynamics, But long-term clinical data found that the tolerance of patients is relatively poor, and only has a strong heart, diuretic and vasodilator effect. The combination of Tongxinluo capsule and trimetazidine of Chinese and Western medicine in our hospital to achieve better efficacy, good tolerance, and significantly reduce mortality, improve heart function and prognosis, and improve the quality of life.

From the above results can be seen that in the observation group after treatment hs-CRP is lower than the control group, it can be seen that the observation group can effectively reduce the vasculitis damage reaction and improve the heart function, In the observation group after treatment, aldosterone was lower than the control group, when the body after myocardial infarction, abnormal cardiac contraction caused acute myocardial ischemia, hypoxia, adenosine triphosphate dips led to the sympathetic nervous system activated, and then aldosterone secretion increased, when the cardiac output decreased, Renal blood flow is insufficient, the renin-angiotensin-aldosterone system is activated, but also can promote aldosterone secretion increased, and aldosterone can cause water and sodium retention, increase intravascular pressure, cardiac load is more serious, at the same time, can also cause coronary contraction due to blood potassium lowering, increasing the heart burden[24]. It can be seen that the decrease of aldosterone in the observation group can effectively reduce the cardiac load after treatment; The levels of NT-proBNP, TNF- α and IL-6 in the observation group were lower than those in the control group. Since NT-proBNP[25] is

the best index to evaluate the prognosis of asymptomatic or mild symptoms of left ventricular dysfunction and advanced heart failure, and the independent predictor of heart failure, TNF-alpha and IL-6 can accelerate the formation of atherosclerosis and thrombosis, its close relationship with left ventricular remodeling after myocardial infarction and infarction, TNF-alpha and IL-6 can accelerate the formation of atherosclerosis and thrombosis, which are closely related to myocardial infarction and left ventricular remodeling after infarction.

Reference

- [1] Chinese Medical Doctor Association emergency physicians section, Chinese Medical Association cardiovascular disease branch, Chinese Medical Association laboratory medicine branch. Guideline for rapid diagnosis and treatment of acute coronary syndromes. *Chin J Emerg Med* 2016; **25**(4): 397-403.
- [2] Deng Shaoxiong, Huang Wensen, Guo Nanou. Effect of recombinant human B-type natriuretic peptide on aldosterone level and endothelial function after percutaneous coronary intervention in acute anterior myocardial infarction. *Chin J Circulation* 2014; **29**(2): 107-109.
- [3] Yang Yu, Liang Meibing, Xu Dingli. Effect of direct percutaneous coronary intervention on the effect of tirofiban on cardiac function and plasma B natriuretic peptide in patients with acute ST-segment elevation myocardial infarction. *Chin Gen Pract* 2014; **17**(16): 1866-1868.
- [4] Jia Hailian, Zhang Keqing, Liu Haitao. Effect of Tongxinluo combined with trimetazidine on high sensitivity C-reactive protein and blood lipid in patients with angina pectoris after coronary artery disease. *Pract J Cardio-Pulmonary Vascular Dis* 2012; **20**(8): 1287-1288.
- [5] Li Yanming, Zhang Han, He Ruili. Low-dose erythropoietin for acute myocardial infarction in patients with percutaneous coronary intervention after treatment efficacy and safety. *China Circulation J* 2015; **30**(1): 17-18.
- [6] He Aiyu. The effect of tongxinluo combined with trimetazidine on treatment of acute myocardial infarction after pump failure. *Chin J Rural Med* 2011; **18**(10): 40-42.
- [7] Yang Kang, Jiang Hong. Tong Xinluo capsule combined with trimetazidine treatment of unstable angina palsy Meta analysis. *Hainan Med* 2015; **26**(7): 1063-1064.
- [8] Zhou Shuting, Xiao Chunyue, Wang Aimin. Clinical study of Tongxinluo combined with trimetazidine on blood lipids and cardiac function in patients with coronary heart disease complicated with diabetes mellitus. *Chin Med J* 2013; **10** (27): 76-78.
- [9] Suh JW, Chung WY, Kim YS. The effect of intravenous administration of erythropoietin on the infarct size in primary percutaneous coronary intervention. *Int J Cardiol* 2011; **149**(19): 216-220.
- [10] Tian Zhaotao, Li Huili, Li Kun. Tongxinluo capsule intervention in acute myocardial infarction percutaneous coronary intervention in 30 cases. *Chin J Exp Tradit Chin Med* 2014; **20** (2): 196-198.
- [11] Pei Wei Na, Xie Ruiqin, Cui Wei. Comparative study on the intervention effect of Sibutramine he Cha and Nichidil on coronary artery intervention in the treatment of myocardial injury. *Chin J Circulation* 2014; **29**(4): 256.
- [12] Chen Han, Wang Jiangyou, Shang Xiaoke. Effects of atorvastatin combined with trimetazidine on perioperative myocardial injury and inflammatory factors in percutaneous coronary intervention in patients with unstable angina. *Chin J Interventional Cardiol* 2014; **22**(11): 689-690.
- [13] Dumitriu IE, Baruah P, Finlayson CJ. High levels of costimulatory receptors OX40 and 4-1BB characterize CD4+CD28 null T cells in patients with acute coronary syndrome. *Circ Res* 2012; **110**(22): 857-869.
- [14] Zheng Bo, Wang Xingang, Gong Yanjun. Effect of direct percutaneous coronary intervention on the short-term prognosis of patients with acute myocardial infarction by preoperative loading dose of atorvastatin. *Chin J Interventional Cardiol* 2013; **21**(10): 41-45.
- [15] Zhai Dongdong, Han Yaolei, Wang Lei, etc. The comparative study of protective effect of double dose and standard dose of trimetazidine on patients with unstable angina pectoris percutaneous coronary intervention during perioperative myocardial period. *China Interventional Heart Dis J* 2017; **25**(2): 77-79.
- [16] Novack V, Pencina M, Cohen DJ. Troponin criteria for myocardial infarction after percutaneous coronary intervention. *Arch Intern Med* 2012; **172**(6): 502-508.
- [17] Calvert PA, Liew TV, Gorence I. Leukocyte telomere length is associated with high-risk plaques on virtual histology intravascular ultrasound and increased proinflammatory activity. *Arterioscler Thromb Vasc Biol* 2011; **31**(9): 2157-2164.
- [18] Trabattini D, Fabbicchi F, Montorsi P. Stent thrombosis after sirolimus and paclitaxel-eluting stent implantation in daily clinical practice: Analysis of a single center registry. *Catheterizat Cardiovasc Intervent* 2007; **70**(3): 415-421.
- [19] Li Ying, Han Li, Cui Lifeng. Clinical study of Tongxinluo capsule combined with atorvastatin in the treatment of inflammatory reaction after PCI in acute myocardial infarction. *Modern Drugs Clin* 2015; **30**(1): 36-37.
- [20] Li Ying, Li Li, Song Yuexia. Effects of atorvastatin preconditioning on inflammatory factors and cardiovascular events in elderly patients with ACS. *J Integr Tradit Chin Western Med* 2008; **12**(12): 1492-1493.
- [21] Wang Siying, Li Shaodan, Liu Yi. The mechanism of Tongxinluo to improve myocardial infarction model of left ventricular structure. *Beijing Tradit Chin Med* 2017; **36**(2): 131-134 +193.
- [22] Li Dongli, Lv Tong. The application of tilofiban in acute myocardial infarction percutaneous coronary intervention. *Med Rev* 2016; **22**(6): 1135-1138.
- [23] Hu Yuecheng, Zhang Ruyan, Cong Hongliang. Effect of QuMei plexus of trimetazidine combined with hypertension coronary intervention for the treatment of patients with contrast induced acute kidney injury. *Chin J Hyperten* 2017; **25**(2): 180-182.
- [24] Shehata M. Impact of trimetazidine on incidence of myocardial injury and contrast induced nephropathy in diabetic patients with renal dysfunction undergoing elective percutaneous coronary intervention. *Am J Cardiol* 2014; **114**(3): 389-394.
- [25] Nadkarni GN, Konstantinidis I, Patel A. Trimetazidine decreases risk of contrast induced nephropathy in patients with chronic kidney disease: a meta-analysis of randomized controlled trials. *J Cardiovasc Pharmacol Ther* 2015; **20**(6): 539-546.