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Effect of bisoprolol in combined with trimetazidine on the cardiac function rehabilitation in patients with chronic heart failure

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ABSTRACT

Objective: To explore the effect of bisoprolol in combined with trimetazidine on the cardiac function rehabilitation in patients with chronic heart failure (CHF). **Methods:** A total of 84 patients with CHF who were admitted in our hospital from November, 2015 to October, 2016 were included in the study and randomized into the observation group and the control group. The patients in the two groups were given oxygen inhalation, lipid regulation, diuresis, ARB, and other routine treatments. Digitalis preparations were given for those who had poor cardiac function, and bisoprolol were orally administrated in the same time. On the above basis, the patients in the observation group were given trimetazidine dihydrochloride tablets, continuously for 3 months. The morning fasting peripheral venous blood before and after treatment in the two groups was collected. CRP, IL-6, TNF-α, BNP, NE, Ang Ⅱ, ANP, ALD, and ET were detected. The cardiac color Doppler ultrasound diagnostic apparatus was used to detect LVPWT, PWS, PWD, IVSS, and IVMI. **Results:** CRP, IL-6, TNF-α, and BNP levels after treatment in the observation group were significantly lower than those in the control group. NE, Ang Ⅱ, ANP, ALD, and ET levels after treatment in the observation group were significantly lower than those in the control group. LVPWT, PWS, PWD, IVSS, and IVMI levels after treatment in the observation group were significantly lower than those in the control group. **Conclusions:** Bisoprolol in combined with trimetazidine can significantly reduce the inflammatory reaction in patients with CHF, and effectively regulate the neuroendocrine stability in order to reverse or reduce VR and improve the left ventricular function.

1. Introduction

Chronic heart failure (CHF) is the terminal stage of various heart diseases, and is a clinical syndrome characterized by VR, progressive left ventricular relaxation and or contraction dysfunction, dyspnea, reduced activity endurance, and fluid retention[1]. The abnormity of neuroendocrine activity and VR are the key links for the morbidity of CHF, and are also the important factors for causing the sudden death[2]. Bisoprolol is a high selective β1-receptor blocker, has a higher affinity to the vascular smooth muscle and bronchial β1-receptor, and is widely applied in the treatment of coronary heart disease[3]. Trimetazidine is a kind metabolic agent, and plays a role in protecting the ischemic and hypoxic myocardial cells through inhibiting the oxidation of free fatty acid, promoting the myocardial glucose oxidation, and reducing the sodium and calcium aggregation in the myocardial cells and intracellular acidosis[4]. The study is aimed to explore the effect of bisoprolol in combined with trimetazidine on the cardiac function rehabilitation in patients with CHF.

2. Materials and methods

2.1. General materials

A total of 84 patients with CHF who were admitted in our hospital

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from November, 2015 to October, 2016 were included in the study and randomized into the observation group and the control group. Inclusion criteria: (1) those who were in accordance with the diagnostic criteria of CHF[5]; (2) those whose LVEF 50%; (3) those who had no acute myocardial infarction in recent 6 months; (4) those who had signed the informed consents. Exclusion criteria: (1) those who had severe liver and renal dysfunction; (2) those who were merged with diabetes, malignant tumor, rheumatic heart disease, and hyperthyroidism; (3) those who were allergic to related drugs; (4) those who had incomplete clinical materials. In the observation group, there were 42 cases, 24 were male, and 18 were female; aged from 60 to 75 years old, with an average of (67±5) years old; course from 1 to 10 years with an average of (5±3) years; 10 in grade II, 21 in grade III, and 11 in grade IV according to NYHA grading; 12 had dilated cardiomyopathy, 25 had ischemic cardiomyopathy, and 5 had valve reflex heart disease. In the control group, there were 42 cases, 25 were male, and 17 were female; aged from 61 to 76 years old, with an average of (67±5) years old; course from 1 to 10 years with an average of (5±3) years; 12 in grade II, 20 in grade III, and 10 in grade IV according to NYHA grading; 11 had dilated cardiomyopathy, 26 had ischemic cardiomyopathy, and 5 had valve reflex heart disease. The comparison of gender, age, and NYHA grading between the two groups was not statistically significant (P>0.05).

2.2. Methods

The patients in the two groups were given oxygen inhalation, lipid regulation, diuresis, ARB, and other routine treatments. Digitalis preparations were given for those who had poor cardiac function. The patients in the control group were orally administrated with bisoprolol (produced by Beijing Huasu Pharmaceutical Co. Ltd, Approval No. H20130921), with initial dose of 1.25 mg, and the dose was gradually increased if tolerance was favorable, with maximum dose not exceeding 10 mg, 1 time/d, continuously for 3 months. On the above basis, the patients in the observation group were given trimetazidine dihydrochloride tablets (produced by Servier (Tianjin) Pharmaceutical Co. Ltd, Approval No. H20055465), 20 mg/time, 3 times/d, continuously for 3 months.

2.3. Observation indicators

(1) Cytokines: The morning fasting peripheral venous blood before and after treatment was collected. ELISA was used to detect the serum CRP, IL-6, TNF-α, and BNP. (2) Neuroendocrine factors: The morning fasting peripheral venous blood before and after treatment was collected. Radioimmunoassay was used to detect NE, AngⅡ, ANP, ALD, and ET. (3) VR: The color Doppler ultrasound diagnostic apparatus was used to detect LVPWT, PWS, PWD, and IVSS. IVMI was calculated.

2.4. Statistical analysis

SPSS 19.0 software was used for the statistical analysis. The measurement data which were complied with the normal distribution were expressed as mean±SD, and t test was used. P<0.05 was regarded as statistically significant.

3. Results

3.1. Comparison of the serum inflammatory cytokines before and after treatment between the two groups

The comparison of CRP, IL-6, TNF-α, and BNP levels before treatment between the two groups was not statistically significant (P>0.05). CRP, IL-6, TNF-α, and BNP levels after treatment were significantly reduced when compared with before treatment (P<0.05). CRP, IL-6, TNF-α, and BNP levels after treatment in the observation group were significantly lower than those in the control group (P<0.05) (Table 1).

3.2. Comparison of the neuroendocrine factors before and after treatment between the two groups

The comparison of NE, AngⅡ, ANP, ALD, and ET before treatment between the two groups was not statistically significant (P>0.05). NE, AngⅡ, ANP, ALD, and ET after treatment were significantly reduced when compared with before treatment

Table 1.

Comparison of the serum inflammatory cytokines before and after treatment between the two groups.

Time	Groups	n	CRP (ng/L)	IL-6 (ng/L)	TNF-α (ng/L)	BNP (pg/mL)
Before treatment	Control group	42	24.86±4.81	64.18±7.53	193.75±41.28	445.72±60.18
	Observation group	42	25.75±4.36	63.47±6.38	192.43±39.64	446.36±51.46
	t		-0.8885	0.4662	-0.1495	-0.0524
	P		0.3769	0.6423	0.8815	0.9584
After treatment	Control group	42	16.81±5.36*	50.74±6.39*	153.65±45.44*	328.71±49.54*
	Observation group	42	10.51±2.23*	39.75±5.35*	107.18±31.54*	252.39±47.63*
	t		-7.0329	8.5462	5.4388	7.1972
	P		0.0000	0.0000	0.0000	0.0000

*P<0.05, when compared with before treatment.

(P<0.05). NE, Ang Ⅱ, ANP, ALD, and ET after treatment in the observation group were significantly lower than those in the control group (P<0.05) (Table 2).

3.3. Comparison of VR indicators before and after treatment between the two groups

The comparison of LVPWT, PWS, PWD, IVSS, and IVMI levels before treatment between the two groups was not statistically significant (P>0.05). LVPWT, PWS, PWD, IVSS, and IVMI levels after treatment were significantly reduced when compared with before treatment (P<0.05). LVPWT, PWS, PWD, IVSS, and IVMI levels after treatment in the observation group were significantly lower than those in the control group (P<0.05) (Table 3).

4. Discussion

CHF is a kind of myocardial damage caused by various factors, which can then change the ventricular structure and function[1]. The main mechanism of CHF is VR which runs through the whole occurrence and development of the disease, while the key factor of VR is the excessive activation of neuroendocrine factors; therefore, drugs which can inhibit the excessive activation of neuroendocrine factors should be applied in the treatment of CHF[6]. It is found that[7] bisoprolol can reduce the blood pressure, extend the cardiac relaxation period, decrease the myocardial oxygen consumption, increase the coronary perfusion time, delay the progression of VR and HF, and effectively reduce the occurrence rate of cardiac sudden death. Various researches demonstrate that[8] under the condition of no contraindications, long-term application of bisoprolol in the treatment of CHF can significantly improve the cardiac function, reduce or reverse VR, and effectively alleviate the symptoms of HF. Trimetazidine can inhibit β oxidation of fatty acid, increase the glucose oxidation, prevent the reduction of intracellular ATP, maintain the energy metabolism of myocardial cells in an ischemic and hypoxic state, alleviate the intracellular electrolyte disturbance and acidosis, maintain the intracellular homeostasis, reduce the production of oxygen radicals, strengthen the anti-oxidation ability of myocardial cells, and lighten the myocardial cell damage in order to reduce the myocardial infarction area[9].

Some researches demonstrate that[10] the inflammatory reaction is closely associated with the morbidity and prognosis of CHF. The expressions of serum inflammatory cytokines are significantly elevated when there is an infection or damage, and the inflammatory cytokines are involved in VR through inducing myocardial cell apoptosis and negative inotropic effect. CRP can activate the inflammatory cells to cause anoxia and vasospasm. IL-6 can cause the cardiomyocyte hypertrophy through coupling gp130, and independently regulate the cardiac function. TNF-α can increase the ventricular inner diameter in the diastolic end, expand the left ventricle, and attenuate the left ventricular wall. The above cytokines can produce negative inotropic effect on the myocardial cells, induce myocardial cell apoptosis, and are involved in the occurrence and development of CHF[11,12]. BNP is a natural hormone synthetized by the myocardial cells, whose synthesis and release will be stimulated when there is a myocardial ischemia and damage, increased ventricular pressure load or volume, can directly or indirectly reflect the valve dysfunction and left ventricular dysfunction degree, and is a quantitative marker of HF[13]. The results in the study showed

Table 2.

Comparison of the neuroendocrine factors before and after treatment between the two groups.

Time	Groups	n	NE (ng/L)	Ang Ⅱ (pg/mL)	ANP (pg/mL)	ALD (pg/mL)	ET (mg/L)
Before treatment	Control group	42	311.83±37.54	110.58±14.23	406.61±46.31	120.53±14.56	62.45±7.11
	Observation group	42	312.45±39.26	112.87±13.37	407.26±43.34	121.42±13.28	62.33±6.54
	t		-0.0752	-0.7601	-0.0664	0.2927	0.0805
	P		0.9403	0.4494	0.9472	0.7705	0.936
After treatment	Control group	42	208.54±29.47*	75.86±8.39*	328.52±42.35*	81.34±10.41*	41.57±5.64*
	Observation group	42	115.36±19.57*	51.36±5.74*	267.47±35.16*	45.76±5.47*	28.51±3.48*
	t		17.0702	15.6191	7.188	19.6082	12.7713
	P		0.000	0.0000	0.0000	0.0000	0.0000

*P<0.05, when compared with before treatment.

Table 3.

Comparison of VR indicators before and after treatment between the two groups.

Time	Groups	n	LVPWT (mm)	PWS (mm)	PWD (mm)	IVSS (mm)	IVMI (mg/g)
Before treatment	Control group	42	11.45±1.78	13.10±1.75	14.23±1.69	12.72±1.86	2.63±0.34
	Observation group	42	11.46±1.76	13.11±1.73	14.23±1.68	12.71±1.87	2.63±0.35
	t		0.0259	-0.0263	0.0000	0.0246	0.0000
	P		0.9794	0.9791	1.0000	0.9805	1.0000
After treatment	Control group	42	9.58±0.89*	10.68±1.85*	11.65±1.87*	11.51±1.74*	2.08±0.26*#
	Observation group	42	10.71±1.62*	12.03±1.68*	12.62±1.65*	10.11±1.63*	2.32±0.27*
	t		-3.962	-3.501	-2.5341	3.8055	-4.1495
	P		0.0000	0.0008	0.0132	0.0003	0.0001

*P<0.05, when compared with before treatment.

that CRP, IL-6, TNF-α, and BNP after treatment in the observation group were significantly lower than those in the control group (P<0.05), indicating that bisoprolol in combined with trimetazidine can significantly reduce the inflammatory reaction in patients with CHF.

In CHF patients, the sympathetic nerve is in an excitatory state within 24 h, the neuroendocrine system related cytokines are activated, and NE, AngⅡ, ANP, and ALD are in a high level, resulting in heart rate acceleration and increased heart work, thus causing myocardial damage and VR[14]. Due to the continuous myocardial cell hypertrophy and strengthened RAS activity in patients with CHF, the secretion of AngⅡ, ALD, and ANP levels is increased, while ANP can inhibit the thickening of vascular smooth muscle and myocardial cells, whose content can be increased with the aggravation of disease condition[15]. Some researches demonstrate that[16] ET in a high level prevails in CHF patients, while ET exceeding the physiological dose can induce the continuous coronary contraction, and aggravate the myocardial ischemia and hypoxia. The results in the study showed that NE, AngⅡ, ANP, ALD, and ET after treatment in the observation group were significantly lower than those in the control group (P<0.05), suggesting that bisoprolol in combined with trimetazidine can regulate the excessive activation of neuroendocrine factors in patients with CHF.

VR is a kind of ventricular compensatory pathological and physiological change due to the change of cardiac primary substance and morphology. VR progression can reduce the myocardial contraction ability in patients with CHF, with gradual condition deterioration, resulting in abrupt reduction of cardiac output and inadequate tissue blood supply, thus developing into the advanced stage of CHF[17]. Some researches demonstrate that[18] collagen deposition outside the myocardial cells, the reduction of cardiac deformation, and thickening ventricular wall are involved in the main manifestations of VR, and the Doppler showed that LVPWT, PWS, PWD, IVSS, and IVMI levels are significantly elevated. In some studies by adoption of trimetazidine in combined with bisoprolol in the treatment of CHF, and the results showed that LVPWT, PWS, PWD, IVSS, and IVMI levels in the observation group were significantly reduced, significantly superior to that by single application of bisoprolol, and it is argued that trimetazidine in combined with bisoprolol can better inhibit VR progression[19]. The results in the study showed that LVPWT, PWS, PWD, IVSS, and IVMI after treatment in the study group were significantly lower than those in the control group (P<0.05), indicating that bisoprolol in combined with trimetazidine in the treatment of CHF can effectively reverse or reduce VR, and improve the left ventricular function.

In conclusion, bisoprolol in combined with trimetazidine can significantly reduce the inflammatory reaction in patients with CHF, and effectively regulate the neuroendocrine stability in order to reverse or reduce VR and improve the left ventricular function.

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