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Efficacy of trimetazidine combining with metoprolol on plasma BNP in coronary heart disease patients with heart failure

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ABSTRACT

Objective: To explore the effect of combined application of trimetazidine and metoprolol on plasma BNP in coronary heart disease patients with heart failure and the clinical efficacy. **Methods:** A total of 140 cases of coronary heart disease patients with heart failure treated in Cardiology Department of our hospital from May 2012 to January 2015 were selected and divided into study group and control group by random number table method. The control group received digitalis, diuretics, ACEI (angiotensin-converting enzyme inhibitor) and other conventional drugs for treatment, the study group received combined use of trimetazidine and metoprolol on the basis of routine treatment of the control group, and treatment duration was 12 weeks. Then plasma BNP, systolic blood pressure, heart rate, left ventricular end diastolic diameter (LVEDD), left ventricular end systolic end (LVESD) and left ventricular ejection fraction (LVEF) of two groups before and after treatment were statistically analyzed, and the overall effect was evaluated. **Results:** Before treatment, there were no significant differences in plasma BNP, blood pressure, heart rate, LVEDD, LVESD and LVEF between the two groups; after treatment, plasma BNP, blood pressure, heart rate, LVEDD and LVESD of both groups decreased and LVEF increased, but the changes in study group were better than those in control group. **Conclusion:** Trimetazidine combined with metoprolol has better application effect in plasma BNP decrease and heart function improvement in coronary heart disease patients with heart failure.

1. Introduction

In recent years, with the improvement of living standard and life style change, the incidence of coronary heart disease is higher and higher, and especially in middle-aged and elderly population, the incidence remains at a high level[1,2]. Development of coronary heart disease may induce a variety of complications, and especially when developing into advanced stage, it can often induce extremely dangerous complications, more common one of which is heart failure[3]. Because of the decrease of heart function in patients with heart failure, ventricular systolic and diastolic capacity reduces, causing that the ability of blood to carry oxygen decreases and it's difficult to meet the demand for oxygen in tissues of the body, and restricted to current medical level, there are recently no potent drugs to treat heart failure[4]. Prolonged ventricular blood residue in patients with heart failure causes increased ventricular load, brain natriuretic peptide (BNP) has the effect of vasodilation, natriuresis and diuresis, and its plasma level is often used as a standard for determining heart failure[5]. Metoprolol is a β_1-receptor blocker and common drug for patients with heart failure, and trimetazidine is a new type of long-chain 3-ketoacyl-coenzyme A thiolase inhibitor and can effectively improve cardiac function[6]. The research explored the effect of trimetazidine combined with metoprolol on plasma BNP in coronary heart disease patients with heart failure and the therapeutic effect, and the following was a detailed report of the research.

2. Information and methods

2.1. General information

A total of 140 cases of coronary heart disease patients with heart failure treated in Cardiology Department of our hospital from May

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2012 to January 2015 were selected and divided into study group and control group by random number table method. Study group had 70 cases, including 43 male cases and 27 female cases with age range of 61-78 years and average age of (69±3) years; control group had 70 cases, including 40 male cases and 30 female cases with age range of 63-76 years and average age of (71±2) years. Comparison of general information between two groups was shown in Table 1.

Table 1.
Statistical table of general information of two groups.

Groups	*n*	Gender (*n*)	Age (years)		
		Male	Female	Age range	Average age
Study	70	43	27	61-78	69±3
Control	70	40	30	63-76	71±2
t		2.704	1.932		
P		0.062	0.074		

2.2. Including criteria

Patients selected in the research needed to meet the following criteria before they were enrolled: (1) all patients were diagnosed of coronary heart disease with heart failure (referring to diagnostic criteria of heart failure proposed by NYHA in US[7]); (2) all patients were without diseases in brain, liver, kidney and other systems; (3) all patients had good drug compliance; (4) treatment options got consent from all patients and their families before implementation; (5) there were no statistical differences in gender and age of two groups (P>0.05).

2.3. Treatment methods

After admitted to hospital, both groups received digitalis, diuretics, ACEI (angiotensin-converting enzyme inhibitor) and other conventional drugs for treatment. Study group, based on conventional treatment, received combined application of trimetazidine and metoprolol for treatment, which was as follows: initial dose of metoprolol was 7 mg/d and used in twice every day, and then with disease progression, the dose could be gradually increased, which was 80 mg/d at most and could be applied in three times accordingly; the dose of trimetazidine was 60 mg/d and taken in three times. Metoprolol was purchased from AstraZeneca (China) Pharmaceutical Co., Ltd., batch No.: J20100098; trimetazidine was purchased from Servier (Tianjin) Pharmaceutical Co., Ltd., batch No.: H20055465. Treatment duration was 12 weeks.

2.4. Monitoring indexes

Plasma BNP, systolic blood pressure, heart rate, left ventricular end diastolic diameter (LVEDD), left ventricular end systolic end (LVESD) and left ventricular ejection fraction (LVEF) of two groups before and after treatment were statistically analyzed.

2.5. Statistical methods

All data in the research was statistically analyzed by SPSS19.0 software, measurement data was by t value test, comparison between groups was by *chi*-square χ^2 test, test standard was α=0.05, and P<0.05 indicated that there were statistical significance.

3. Results

3.1. Plasma BNP and heart function of two groups before treatment

Comparison of plasma BNP, SBP (systolic blood pressure), HR (heart rate), LVEDD (left ventricular end diastolic diameter), LVESD (left ventricular end systolic end) and LVEF (left ventricular ejection fraction) of two groups before treatment was shown in the following Table 2.

It could be seen from the above table that before treatment, there were no significant differences in plasma BNP, systolic blood pressure, heart rate, left ventricular end diastolic diameter, left ventricular end systolic end and left ventricular ejection fraction of two groups (P>0.05).

3.2. Plasma BNP and heart function of two groups after treatment

Comparison of plasma BNP, SBP (systolic blood pressure), HR (heart rate), LVEDD (left ventricular end diastolic diameter), LVESD (left ventricular end systolic end) and LVEF (left ventricular ejection fraction) of two groups after treatment was shown in the following Table 3.

It could be seen from the above table that after 12 weeks of treatment, plasma BNP, systolic blood pressure, heart rate, left ventricular end diastolic diameter, left ventricular end systolic end and left ventricular ejection fraction of both study group and control group were significantly improved, but the improvement in study group was more significant (P<0.05), and especially in comparison of plasma BNP, the improvement in study group was more significant (P<0.01).

4. Discussion

Coronary arteriosclerotic heart disease, called coronary heart disease (CHD) for short, is caused by coronary artery stenosis-induced myocardial ischemia and also called ischemic cardiomyopathy[8]. There are many complications of CHD, mainly including angina, myocardial infarction, myocardial fibrosis and heart failure, among which heart failure is a more serious concurrent disease in advanced coronary heart disease. Pathogenesis of coronary heat disease with heart failure is mainly that long-term

Table 2.
Statistical table of plasma BNP and heart function of two groups before treatment.

Groups	*n*	BNP (pg/mL)	SBP (mmHg)	HR (times/min)	LVEDD (mm)	LVESD (mm)	LVEF (%)
Study	70	295.3±12.4	153.5±9.7	97.2±3.9	64.7±2.5	45.2±2.4	48.5±5.8
Control	70	294.7±13.5	152.8±8.3	97.4±4.5	63.9±2.8	45.8±2.7	49.3±6.3
t		3.731	3.563	1.284	2.638	0.983	1.683
P		0.063	0.060	0.087	0.072	0.091	0.082

Table 3.
Statistical table of plasma BNP and heart function of two groups after treatment.

Groups	*n*	BNP (pg/mL)	SBP (mmHg)	HR (times/min)	LVEDD (mm)	LVESD (mm)	LVEF (%)
Study	70	227.1±11.8	127.5±5.3	73.6±4.3	51.9±3.2	35.5±2.6	59.4±4.7
Control	70	265.5±12.3	136.8±4.6	84.5±5.2	59.6±2.7	40.8±2.3	52.8±5.1
t		19.408	14.284	12.326	11.607	9.636	10.927
P		0.007	0.028	0.033	0.038	0.047	0.042

atherosclerosis leads to ventricular ischemia and causes insufficient myocardial oxygen supply, and long-term insufficient oxygen supply in myocardial cells causes myocardial cell necrosis, apoptosis and a series of changes[9,10]. Apoptosis and necrosis of large areas of myocardial cells cause decreased ventricular systolic capacity and compliance, leading to heart failure. Conventional treatment of coronary heart disease with heart failure is centered on digitalis, diuretics, ACEI (angiotensin-converting enzyme inhibitor) and other drugs, and the main treatment mechanism is to reduce oxygen consumption in myocardial cells, expand collateral circulation of the heart and enhance myocardial diastolic and systolic capacity, but there are few therapeutic drugs that improve the metabolism of myocardial cells to treat disease, and it is more difficult to achieve ideal therapeutic effect[11].

Trimetazidine is a long-chain 3-ketoacyl-coenzyme A thiolase inhibitor (3-KAT inhibitor) and its main function is to antagonize the positive chronotropic, inotropic and dromotropic effect of epinephrine, norepinephrine and vasopressin on the heart[12]. It can increase the generation of ATP by promoting mitochondrial function activation and achieve the effect of promoting myocardial cell metabolism. A more important role of trimetazidine is that it can directly promote the consumption of myocardial cells to glucose to increase myocardial energy supply without affecting blood flow to the heart itself[13]. Metoprolol is a β_1-receptor blocker and has selective blocking effect on β_1-receptor of myocardial cells. Its main mechanism of treatment of heart failure is to block the combination of epinephrine, norepinephrine, vasopressin and other catecholamine hormones with β_1-receptor, reduce the effect of these hormones on the heart and decrease the cardiac oxygen consumption while keep the sympathetic and parasympathetic nerve sensitivity and maintain sympathetic and parasympathetic nerve function[14]. On the other hand, metoprolol has extremely low first pass elimination rate, around 20%, and is suitable for oral use, but the liver metabolic deactivation rate is high and long-term use is needed to get the treatment effect. Brain natriuretic peptide (BNP) has the effect of vasodilation, natriuresis and diuresis, and its plasma level is often used as a standard for determining heart failure[15].

The research explored the therapeutic effect of combined use of trimetazidine and metoprolol on coronary heart disease with heart failure on the basis of conventional treatment. It was found out that before treatment, comparison of plasma BNP level and heart function between study group and control group showed no significant differences (P>0.05). And after 12 weeks of differentiation treatment, meaning that control group received conventional treatment and study group, based on conventional treatment, received combined use of trimetazidine and metoprolol, plasma BNP level and heart function of both study group and control group were improved than those before treatment, but the improvement in study group was more significant (P<0.05) and the improvement in plasma BNP of study group, in particular, was much better than that of control group (P<0.01). To sum up, trimetazidine combined with metoprolol has better application effect in plasma BNP decrease and heart function improvement in coronary heart disease patients with heart failure.

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