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Clinical efficacy of meglumine adenosine cyclophosphate combined with perindopril in treating patients with chronic heart failure.

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Abstract

Objective: To study the clinical efficacy of meglumine adenosine cyclophosphate combined with perindopril in treating patients with chronic heart failure.

Methods: Three hundred and twelve patients with chronic heart failure were enrolled and divided evenly into an observation group and a control group according to treatment methods, one hundred and fifty-six patients in each group. Patients in the observation group were treated with meglumine adenosine cyclophosphate and perindopril, while patients in the control group received conventional treatment. Clinical efficacy, heart function, mobility, brain natriuretic peptide concentration, insulin-like growth factor 1 concentration and homocysteine level were taken as investigation indexes.

Results: The overall effective rate in the observation group was higher than that of the control group; the difference was statistically significant (P<0.05). Compared with the patients in the control group, patients in the observation group had smaller Left Ventricular End Systolic Diameter (LVESD), Left Ventricular End-Diastolic Diameter (LVEDD), Interventricular Septum Thickness (IVST), Left Ventricular Posterior Wall Thickness (LVPWT), High Left Ventricular Ejection Fraction (LVEF) and longer 6-min walking distance; the differences were statistically significant (P<0.05). The differences in N-Terminal pro-Brain Natriuretic Peptide (NT-pro BNP), Insulin-Like Growth Factor 1 (IGF 1) and Homocysteine (Hcy) of the two groups had no statistical significance before treatment (P>0.05). The NT-pro BNP, IGF 1 and Hcy of both groups were better than after treatment compared to before treatment; the difference was statistically significant (P<0.05); the NT-pro BNP, IGF 1 and Hcy of the observation group were better than those of the control group after treatment (P<0.05).

Conclusions: Treating patients with chronic heart failure with meglumine adenosine cyclophosphate combined with perindopril can relieve clinical symptoms and has good clinical effects; hence it is worth clinical promotion.

Keywords: Chronic heart failure, Meglumine adenosine cyclophosphate, Perindopril.

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Introduction

Chronic heart failure is a kind of syndrome that occurs when cardiac output absolutely or relatively lower than tissue metabolism due to the disorder of myocardial systolic or diastolic function in the condition of normal venous return; its incidence has demonstrated an obvious increase in recent years, and its mortality rate ranks as high as 50% in the last five years, which makes it become a clinical syndrome seriously threatening lives of patients [1,2]. In recent years, according to the guidelines for Congestive Heart Failure (CHF) treatment, increasing myocardial contraction force, improving myocardial function and increasing cardiac output are still the major focuses of CHF treatment [3,4]. The clinical routine treatments, such as strengthening heart and dieresis, enlarging blood vessels, etc., are often performed, but it is difficult to be insisted because of its insignificant curative effect or adverse reactions [5].

Currently, Angiotensin Converting Enzyme Inhibitors (ACEI) which takes renin angiotensin aldosterone system as the therapeutic target has become the basis of clinical treatment of CHF. In addition, some new drugs have obtained good curative effects in the clinical practice of CHF treatment [6]. In recent years, a newly synthesized drug called Meglumine Adenosine Cyclophosphate (MAC), a derivative of Cyclic Adenosine Monophosphate (c AMP) with high hydrophilicity and lipotropy, has emerged. It belongs to non-digitalis positive inotropic drug and contains adenosine cyclophosphate and meglumine, which can effectively improve the level of Ca^{2+} in myocardial cells, enhance the capacity of myocardial contraction, improve the pumping force of the heart and cardiac output, inhibit the binding of vascular smooth muscle

and calcium, fully expand blood vessels, reduce cardiac load, fully expand coronary blood vessels, and improve the concentration of myocardial cells and myocardial cell metabolism level to protect myocardial cell [7,8]. Perindopril, one of the angiotensin converting enzyme inhibitors, can effectively reduce the peripheral vascular resistance, stabilize blood pressure, and reduce the bad influence of sudden change of blood pressure in myocardial cells. It also can improve myocardial ultrastructure, effectively improve left ventricular function, reduce left and right ventricular filling pressure, reduce peripheral vascular resistance, and increase cardiac output capacity and movement ability [9,10]. However, few researches concern the clinical effects of the combination of the two drugs in the treatment of CHF. This study explored the clinical efficacy of meglumine adenosine cyclophosphate in combination with perindopril in the treatment of CHF, aiming to provide a reference for clinical treatment of CHF.

Materials and Methods

Research subjects

Three hundred and twelve patients with confirmed chronic heart failure who were treated at our hospital from September 2013 to September 2013 were chosen for the study. All signed informed consent before the study. Patients who were diagnosed and confirmed with chronic heart failure were included, while patients who had serious liver, brain, and kidney dysfunction or psychiatric disorders, suffered from hypotension or anaemia, or had a serum creatinine level higher than 252.2 $\mu mol.L^{-1}$ were excluded. According to different treatment methods, patients were divided into a control group and an observation group. In the control group, there were 156 cases, 90 males and 66 females, with age ranging from 35 to 77 years old (mean 49.2 ± 14.4 years old) and the course of disease ranging from 5 to 21 years (average 7.3 ± 2.2 years); 66 cases were at grade II, 73 cases at grade III, and 17 cases at grade IV, according to clinical classification of cardiac function. In the observation group, there were 156 cases, 95 males and 71 females, with age ranging from 37 to 78 years old (mean 49.9 ± 11.8 years old) and the course of disease ranging from 3 to 23 years (average 7.1 ± 2.4 years); 64 cases were at grade II, 72 cases at grade III, and 20 cases at grade IV. The differences between two groups in gender, age, the course of disease and the stage of cardiac function had no statistical significance (P>0.05); therefore, the results were comparable.

Treatment methods

The control group: Conventional anti-heart failure treatment was given; besides, patients were given symptomatic treatment based on causes, and factors induced by disease were excluded. Patients were asked to take adequate rest, limited amount of water, vasodilators, diuretic and *digitalis*.

The observation group: On the basis of the conventional treatment, patients were treated with meglumine adenosine cyclophosphate in combination with perindopril. Nighty to one hundred and twenty mg of meglumine adenosine cyclophosphate (Shandong Rui Yang Pharmaceutical Co., Ltd., China, batch number: H20131212) and 250 ml of glucose injection were given to the patients once a day, and 2 mg of perindopril (Servier Pharmaceutical Co., Ltd., China, the batch number: H20131210) was taken orally once a day. The treatment lasted for one month and curative effects were observed.

Observation indexes

(1). Electrocardiographic examination: Left Ventricular End Systolic Diameter (LVESD), Left Ventricular End-Diastolic Diameter (LVEDD), Interventricular Septum Thickness (IVST), Left Ventricular Posterior Wall Thickness (LVPWT) and High Left Ventricular Ejection Fraction (LVEF) were respectively measured by the same physician and the same color doppler ultrasound. (2). Movement ability: Walking distance within 6 minutes was determined. (3). Cytokines expressions: N-Terminal pro-Brain Natriuretic Peptide (NT-pro BNP) was measured by electrochemiluminescence immunoassay, Insulin-Like Growth Factor 1 (IGF 1) was measured by enzyme linked immunosorbent assay, and Homocysteine (Hcy) was detected by BS-330 Mindray fully automatic biochemical analyser (Mindray Inc., Shenzhen, China).

Criteria for therapeutic effects

Cardiac function before and after treatment was evaluated by the New York Heart Association (NYHA) classification standard. Treatment was considered as significantly effective if the improvement of cardiac function was equal to or higher than level II, reflecting as the disappearance or significantly relieved palpitation and anhelation, the disappearance or significantly reduced lung rale, normal heart rate and the improved electrocardiogram. Treatment was considered as effective if the improvement of cardiac function was equal to or higher than level I, reflecting as the disappearance of palpitation and anhelation or reduced lung rale. Treatment was determined as ineffective if the improvement of cardiac function was lower than level I, disease condition aggravated or patients died. The calculation formula of overall effective rate was as follows: overall effective rate (%) = significantly effective rate+effective rate.

Statistical analysis

Data were analysed by SPSS ver. 20.0. Measurement data were expressed as mean ± SD and processed by t-test; enumeration data were processed by chi-square test, and P<0.05 meant that difference was statistically significant.

Results

Comparison of clinical effects between the two groups

Compared with the effective rate in the control group, the effective rate in the observation group significantly increased

after the treatment; the difference was statistically significant (P<0.05). Details are shown in as shown in Table 1.

Table 1. *Comparison of clinical effects between the two groups (n (%)).*

Group	Significantly effective	Effective	Ineffective	Total effective rate
Control group	32 (20.5)	82 (52.6)	42 (26.9)	114 (73.1)
Observation group	47 (30.1)	98 (62.8)	11 (7.1)	145 (92.9)
X^2				14.93
P				0.019

Comparison of improvements in cardiac function and movement ability between the two groups

LVEDD, LVESD, IVST and LVPWT of the patients significantly decreased in the observation group, compared with those before treatment (P<0.05); but LVEF and walking distance within 6 minutes increased significantly (P<0.05). All indexes improved after treatment in the observation group, compared to the control group; the difference was statistically significant (P<0.05). Details are shown in as shown in Table 2.

Comparison of NT-pro BNP, IGF 1 and Hcy of the two groups before and after treatment

Differences between the two groups in cytokines NT-pro BNP, IGF 1 and Hcy expression before treatment had no statistical significance (P>0.05); cytokine expression in the control group and the observation group were better after treatment than before treatment (P<0.05), and cytokine expression in the observation group was better than that of the control group after treatment; the difference has statistical significance (P<0.05). Details are shown in as shown in Table 3.

Table 2. Comparison of cardiac function and movement ability between the two groups.

Groups	LVEDD (mm)	LVESD (mm)	LVEF (%)	IVST (mm)	LVPWT (mm)	Walking distance within 6 minutes (m)
Control group						
Before treatment	57.16 ± 5.31	45.83 ± 3.76	38.72 ± 5.02	14.53 ± 1.02	13.32 ± 1.36	311.88 ± 36.86
After treatment	55.28 ± 4.52	40.04 ± 4.22*	44.97 ± 4.72*	12.13 ± 0. 79*	11.26 ± 1.12*	391.81 ± 42.31*
Observation group						
Before treatment	56.86 ± 4.77	45.36 ± 4.09	39.10 ± 4.91	14.63 ± 1.01	13.31 ± 1.43	309.56 ± 35.37
After treatment	48.52 ± 3.56*#	33.51 ± 5.04*#	51.24 ± 5.00*#	7.55 ± 0.62*#	7.41 ± 0.62*#	498.23 ± 79.17*#

Note: *Means P<0.05, compared with before treatment; #means P<0.05, compared with the control group.

Table 3. *Comparison of NT-pro BNP, IGF 1 and Hcy of the two groups.*

Groups	NT-pro BNP (pg/m L)	IGF-1 (ng/m L)	Hcy (μmol/L)
Control group			
Before treatment	610.92 ± 67.36	105.62 ± 10.14	22.82 ± 2.61
After treatment	345.02 ± 58.07*	106.43 ± 10.95	18.81 ± 2.23*
Observation group			
Before treatment	612.46 ± 69.27	106.97 ± 10.93	23.03 ± 2.72
After treatment	287.36 ± 51. 23*#	128.72 ± 13.17*#	15.11 ± 1.58*#

Note: *Means P<0.05, compared with before treatment; #means P<0.05, compared with the control group.

Discussion

Chronic heart failure is the serious stage of different types of heart diseases. It has high incidence and complex clinical symptoms, which is a serious threat to the physical and mental health and life security of patients [11]. The current study found that the reason why the development of heart failure is progressive is the excessive activation of neurohormone after the occurrence of myocardial injury. Long-term chronic activation of neuroendocrine hormone results in the occurrence of myocardial remodelling, which further aggravates heart function deterioration and myocardial damage; heart function deterioration and myocardial damage, in return, further activates neuroendocrine hormone [12].

This study divided 312 confirmed cases of chronic heart failure into an observation group and a control group according to different treatment methods. Patients in the control group received conventional treatment and the patients in the observation group were treated with meglumine adenosine cyclophosphate in combination with perindopril. The results indicated that, the observation group had significant curative effect compared to the control group. LVEDD and LVESD decreased obviously, and LVEF increased, which suggested that cardiac function was significantly enhanced. IVST, LVPWT obviously decreased, which showed that left ventricular morphology improved, movement ability enhanced, and walking distance within 6 minutes prolonged significantly.

BNP, a hormone secreted by left ventricular heart, has compensatory effects on the neuroendocrine system of patients with heart failure, and it can produce natriuretic effects, relaxed blood vessels, inhibit the secretion of renin activity and aldosterone, and adjust blood pressure, humoral level and electrolyte balance [13,14]. Increased NT-pro BNP level represents neurohormonal activation, which is one of the most specific and sensitive biological indexes of heart failure [15]. The NT-pro BNP level of patients in the observation group significantly decreased, which indicated the combined therapy had significant effect. IGF 1 is also a kind of hormones secreted by heart, which can strengthen cardiac ejection function. IGF 1 concentration in the observation group increased more significantly than that of the control group, which showed that cardiac ejection function of the patients in the observation group improved significantly. Hcy, a non-essential amino acid containing sulfonium, is not involved in the synthesis of protein, and it is generated from hypo methylated methionine [16]. Elevated homocysteine concentration in blood can produce superoxide, peroxide and other strong oxidizing substances, which will bring damages to heart and blood vessel, smooth muscle, and cardiovascular endothelial cells and increase the risk of thrombosis [17]. Okuyan et al. [18] found that, Hcy level of patients with cardiac failure was much higher than patients with coronary heart disease ($P<0.05$), by comparing 68 cases of confirmed heart failure and 40 cases of confirmed coronary heart disease whose age and other dangerous factors had no significant differences. This study results displayed that the Hcy level of the two groups significantly reduced after the treatment, but the decline was more obvious in the observation group, suggesting meglumine adenosine cyclophosphate in combination with perindopril could significantly decrease Hcy level and reduce the severity of heart failure.

Conclusion

Above all, meglumine adenosine cyclophosphate in combination with perindopril in the treatment of chronic heart failure patients produces great coordination effect. The therapy can further improve clinical curative effect, significantly improve cardiac function, increase IGF 1 concentration and reduce BNP and Hcy concentrations. The conclusion is of important guidance significance for future clinical medication.

Declaration of Interest

All authors declared there was no conflict interests involved.

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