EFFICACY OF BENAZEPRIL COMBINED WITH AMLODIPINE IN THE TREATMENT OF PATIENTS WITH HYPERTENSION AND HEART FAILURE AND ITS EFFECTS ON SERUM ADRENOMEDULLIN, ANGIOTENSIN AND PENTRAXIN 3

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ABSTRACT

Objective*: To observe the efficacy of benazepril combined with amlodipine in the treatment of hypertension with heart failure and its effects on serum adrenomedullin, angiotensin, and pentraxin 3.*

Methods*: Eighty patients with hypertension and heart failure were selected in our hospital from March 2015 to November 2016 and were divided into an observation group (n=40) and a control group (n=40). Patients were treated with benazepril, 10 mg orally, once a day in the control group. In the observation group, patients were treated with benazepril combined with amlodipine, 10 mg orally, once a day. Treatment was continued for 6 months in both groups. The changes in systolic blood pressure, diastolic blood pressure and heart rate were observed before and after treatment. The effects of the treatments on serum adrenomedullin, angiotensin and pentraxin 3 were compared.*

Results*: After treatment, the systolic blood pressure, diastolic blood pressure and heart rate decreased in both groups, showing a statistically significant difference (P<0.05). The blood pressure and heart rate measurements of patients in the observation group were significantly different from those of the control group (P<0.05). The total effective rate of the observation group was 95%, which was higher than that of the control group (77.5%), and this was a statistically significant difference (P<0.05). The levels of serum adrenomedullin, angiotensin and pentraxin 3 in the two groups were significantly lower than those before treatment in the same group (P<0.05). The levels of serum adrenomedullin, angiotensin and pentraxin 3 in the control group were lower than those in the observation group, and the difference was statistically significant (P<0.05).*

Conclusion*: Benazepril combined with amlodipine is effective for reducing the blood pressure of patients with hypertension and heart failure. Simultaneous lowering of serum adrenomedullin, angiotensin and pentraxin 3 levels could improve cardiac function and be worthy of clinical promotion.*

Keywords*: Benazepril, Amlodipine, Hypertension with heart failure, Adrenomedullin, Angiotensin, Pentraxin 3.*

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Introduction

Hypertension (HTN) is one of the most common chronic diseases. It can cause functional changes in the heart, brain and kidneys, leading to chronic kidney disease, myocardial infarction, heart failure, cerebral thrombosis and cerebral hemorrhage. Symptoms pose a serious threat to the lives and property of patients[(1)]. According to relevant statistics, the incidence of hypertension in the middle-aged and elderly in China has recently exceeded 40%, showing an upward trend[(2)], and the incidence of heart failure has also increased. Hypertension with heart failure refers to myocardial compensatory dysfunction, impaired ventricular function and pulmonary congestion caused by long-term hypertension; these symptoms are seen in the C or D stages of heart failure development. At present, the main treatment of hypertension with heart failure is to improve neurohormonal abnormalities and prevent myocardial remodeling. The therapeutic drugs are mainly diuretics, angiotensin-converting enzyme inhibitors (ACEI) and β-blockers.

This study enrolled 80 patients with hypertension and heart failure in our hospital. These patients were treated with benazepril or benazepril combined with amlodipine in order to investigate the combination of benazepril and amlodipine in the treatment of hypertension with heart failure. The efficacy and effects of the treatment on serum adrenal dysfunction (ADM), angiotensin (adrenotenin, ADT), and pentraxin-3 (PTX-3) were also studied.

Data and methods

General information

The study subjects included 80 patients with hypertension and heart failure who were admitted to our hospital from March 2015 to November 2016. The diagnosis of hypertension is based on the "China Guidelines for the Prevention and Treatment of Hypertension 2010"[3], and the diagnosis of heart failure is based on the 2014 Guidelines for the Diagnosis and Treatment of Heart Failure in China[4].

Inclusion criteria were as follows:

- patients clinically diagnosed with hypertension and heart failure;
- patients 55-79 years of age;
- patients who had not taken benazepril or amlodipine within three months.

Exclusion criteria were as follows:

- patients who are allergic to benazepril or amlodipine;
- patients with severe coronary or cerebral arteriosclerosis;
- patients with mental illness.

Group	N (case)	Averaged age (year)	Sex (case)		Diabetes	Smoke	Drink
			Male	Female			
The observation group	40	64.3±11.2	27	13	8	10	12
The control group	40	63.8±11.4	25	15	11	12	11
t / x^2	-	1.583	0.22		0.693	0.287	0.071
P	-	0.118	0.639		0.405	0.592	0.791

Table 1: Analysis of general clinical data of patients.

All patients were randomly divided into an observation group and a control group, with 40 cases in each group. There were 27 males and 13 females in the observation group, aged 56-79 years old, with an average age of 64.3±11.2 years. In the control group, there were 25 males and 15 females, aged 55-78 years, with an average age of 63.8±11.4 years.

There was no significant difference in the general data between the two groups (P>0.05), therefore, the two groups were comparable. This study was approved by the local ethics committee (Table 1)

Treatment methods

Patients were treated with benazepril (Beijing Novartis Pharmaceutical Co., Ltd., Guoji Zhunzi H20030514) 10 mg orally, once a day for 6 months in the control group. In the observation group, the benazepril treatment was combined with amlodipine (Pfizer Pharmaceutical Co., Ltd., National Pharmaceutical Standard H10950224), 10 mg orally, once a day for 6 months.

Test indicators and efficacy standards

General indicators

Blood pressure, electrocardiogram and blood routine examination were performed before and after treatment, and systolic blood pressure, diastolic blood pressure and heart rate were also measured.

Determination of serum ADM, ADT, PTX-3

A 5.0 mL quantity of fasting venous blood was drawn from the patients in the morning, and the specimens were separated by TD5K-III medical centrifuge, 3500 r/min for 10 min, and the supernatant was taken for detection. The ELISA method was used for uniform detection, and ADM, ADT, and PTX-3 were measured according to the kit (manufactured by Shanghai Guangrui Biotechnology Co., Ltd.).

Efficacy criteria

According to the *Guidelines for Clinical Research of Drugs*[5], the blood pressure judgment standard is divided into ①markedly effective: diastolic blood pressure decreased by 20 mmHg or 10 mmHg and decreased to normal; ②effective: diastolic blood pressure decreased by less than 10 mmHg and decreased to normal or decreased by 10-19 mmHg and not decreased to normal; and ③invalid: none of the above conditions are reached. Total efficiency = (significant + effective) / total × 100%.

Statistical methods

The data in this study were collected by the researchers and completely entered into the research database. The data were statistically

analyzed by SPSS21.0 software, and the count data were expressed as a percentage. The comparison was performed using the χ^2 test, and the measurement data were indicated by "$\bar{x}\pm s$". The t test was used for comparison. The test level was P<0.05, indicating that the data comparison results were statistically significant.

Results

Blood pressure and heart rate in the two groups

Before treatment, there was no significant difference in systolic blood pressure, diastolic blood pressure and heart rate between the observation group and the control group (P>0.05). After treatment, the blood pressure and heart rate of patients in both groups were lower, and the decrease was a statistically significant difference (P<0.05). The decrease in the observation group was greater than that of the control group, and it was a statistically significant difference (P<0.05) (Table 2).

Group	Systolic blood pressure (mmHg)		Diastolic blood pressure (mmHg)		Heart rate (time/min)	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
The observation group (n=40)	169.20 ± 17.59	133.43 ± 7.58	112.67 ± 10.53	81.52 ± 9.03	102.45 ± 11.56	71.56 ± 7.84
The control group (n=40)	166.45 ± 18.89	141.67 ± 14.36	110.61 ± 11.34	90.53 ± 11.64	103.98 ± 11.52	98.23 ± 8.74
t	0.67	3.21	0.84	3.87	0.60	14.37
P	0.50	0.02	0.40	0.002	0.55	0.001

Table 2: Comparison of blood pressure and heart rate before and after treatment in two groups ($\bar{x}\pm s$).

Comparison of treatment effects between the two groups

In the observation group, 22 cases were markedly effective (55%), 16 cases were effective (40%), 2 cases were invalid (5%), and the total effective rate was 95%. In the control group, 14 cases (35%) were markedly effective, 17 cases (42.5%) were effective, 9 cases were invalid (22.5%), and the total effective rate was 77.5%. The total effective rate of the observation group was higher than that of the control group, and it was a statistically significant difference (P<0.05) (Table 3).

Group	Markedly effective	Effective	Invalid	The total effective rate
The control group (n=40)	22 (55%)	16 (40%)	2 (5%)	38 (95%)
The observation group (n=40)	14 (35%)	17 (42.5%)	9 (22.5%)	31 (77.5%)
χ^2	3.232	0.052	5.165	5.165
P	0.072	0.820	0.023	0.023

Table 3: Comparison of treatment effects between the two groups of patients [n (%)].

Comparison of ADM, ADT and PTX-3 levels in the two groups

Group	ADM (ng/L)		ADT (ng/L)		PTX-3 (ng/mL)	
	Before treatment	After treatment	Befor treatment	After treatment	Before treatment	After treatment
The control group (n=40)	74.69 ± 8.91	36.71 ± 5.23	164.27 ± 11.06	111.36 ± 12.69	4.57 ± 0.52	2.13 ± 0.11
The observation group (n=40)	76.28 ± 10.32	41.14 ± 4.57	167.76 ± 12.63	117.82 ± 13.74	4.55 ± 0.51	3.07 ± 0.26
t	0.74	2.21	1.31	2.18	0.17	21.45
P	0.46	0.03	0.19	0.03	0.86	0.001

Table 4: Comparison of ADM, ADT, PTX-3 before and after treatment ($\bar{x}\pm s$).

Before treatment, there were no significant differences in the levels of ADM, ADT and PTX-3 between the two groups (P>0.05). After treatment, the levels of ADM, ADT and PTX-3 in the two groups were significantly lower than those before treatment in the same group (P<0.05). The differences in ADM, ADT and PTX-3 levels between the observation group and the control group were statistically significant (P<0.05) (Table 4).

Discussion

Hypertension is a cardiovascular disease characterized by an increase in systemic arterial blood pressure, which in turn increases cardiac load and leads to an early adaptive response. This results in cardiac hypertrophy and remodeling, which eventually leads to heart failure. In China, high blood pressure is a common and frequently occurring disease. Epidemiological studies have shown that heart failure caused by high blood pressure is six times that of non-hypertensive people[6]. The main goal of treatment for hypertension with heart failure is to keep blood pressure within the ideal range, reduce cardiac load and improve heart function.

Amlodipine is a third-generation calcium channel blocker (CCB) that reduces blood pressure by selectively inhibiting calcium ion transmembrane into vascular smooth muscle, reducing intracellular calcium ion concentration, dilating peripheral arterioles, and reducing peripheral vascular resistance[7]. Amlodipine can inhibit collagen synthesis, protect the vascular endothelium, and has an anti-atherosclerosis effect[8]. Compared with early CCBs, the drug has mild adverse reactions and a more stable antihypertensive effect. Long-term treatment with amlodipine can not only improve the blood pressure of patients but also reduce the incidence of cardiovascular events.

Benazepril is a third-generation ACEI drug that provides long-term antihypertensive protection of the cardiovascular system, improves clinical symptoms of heart failure, and restores heart function[9]. The drug can inhibit systemic circulation and reduce ADT content in the blood, reverse the symptoms of ventricular hypertrophy, and delay myocardial remodeling, thus improving cardiac function. ADT is associated with the release of adrenaline, which promotes sympathetic transmission and aggravates myocardial load. Benazepril inhibits sympathetic nerve activity by reducing ADT secretion[10], reducing the contractile effect of ADT on blood vessels, expanding blood vessels, and relieving cardiac load.

The results showed that after 6 months of treatment, the total effective rate of the observation group was 95%, which was significantly higher than that of the control group at 77.5% ($P<0.05$). This indicates that benazepril combined with amlodipine has a significant antihypertensive effect, which is better than amlodipine alone. The blood pressure and heart rate of patients in the two groups were significantly lower than those of the same group before treatment ($P<0.05$). After treatment, the systolic blood pressure, diastolic blood pressure and heart rate of patients in the observation group were significantly different from those of the control group ($P<0.05$), which indicates that benazepril combined with amlodipine can effectively control blood pressure and improve heart function.

ADM and ADT are a pair of hormones related to vasoconstriction. ADM has the effect of reducing blood pressure, mainly in vascular endothelium and smooth muscle cells. The study found that[11-13] ADM levels in patients with hypertension and heart failure were higher than normal, and the compensatory secretion of ADT was also significantly increased. Therefore, the regulation of ADM and ADT is important for the treatment of hypertension with heart failure. PTX-3 is an acute phase protein that binds to soluble receptors involved in body tissue remodeling[14-15]. PTX-3 can accelerate cell proliferation, stimulate the secretion of cellular proteases, and thus improve arteriosclerosis. After treatment, the levels of ADM, ADT and PTX-3 in the two groups significantly decreased, and the levels in the observation group were significantly lower than those in the control group ($P<0.05$). After treatment, the PTX-3 levels in the observation group were significantly lower than those in the control group, indicating that benazepril combined with amlodipine can effectively improve blood circulation and improve myocardial ischemia.

In summary, blood pressure, heart rate, and serum adrenomedullin, angiotensin and pentraxin 3 levels in patients treated with benazepril and amlodipine were significantly lower than those in patients treated with benazepril alone. This study provides a certain reference experience in the treatment of patients with hypertension and heart failure.

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