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Original Article

Effect of captopril on angina relief, blood pressure and electrocardiographic abnormality changes in patients with hypertension and coronary artery disease

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Abstract: Objective: To investigate clinical effectiveness and safety of captopril in patients with hypertension and coronary artery disease (CAD). Methods: A total of 96 patients with hypertension and CAD admitted to The Second Affiliated Hospital of Xingtai Medical College during the time between September 2015 and March 2017 were chosen as objects of this study and were divided by random number table into two groups: observation group and control group, each consisting of 48 patients. Patients in both groups were advised to lie down and rest and diet scientifically. They were also given anticoagulant of aspirin and statins which could draw down blood lipids. What's more, the control group was given oral nitrendipine tablets (10 mg at a time, 1 time/day); the observation group was given oral captopril tablets (12.5 mg at a time, 3 times/day). The treatment course was 2 weeks. After that, we compared angina, blood pressure, electrocardiogram (ECG) changes and adverse drug reactions (ADRs) of the two groups. Results: After 2 weeks of treatment, patients of the two groups showed distinctly lower systolic pressure and diastolic blood pressure than those before treatment, and the observation group was much lower than the control group (122.72 ± 11.90 mmHg vs. 132.56 ± 13.72 mmHg; 81.52 ± 9.43 mmHg vs. 89.21 ± 8.15 mmHg), with statistical difference (both $P < 0.05$). The observation group's overall response rate (ORR) of angina effectiveness was up to 89.58%, while the control group was only 77.08%, difference between which was of statistical significance ($P < 0.05$). The observation group's ORR of ECG effectiveness was up to 87.50%, while the control group was only 72.92%, difference between which was of statistical significance ($P < 0.05$). There was no treatment withdrawal due to severe ADRs. All the ADRs were relieved after symptomatic treatment. The observation group's incidence rate of ADRs was 10.42%, and the control group's 8.33%, difference between which was of no statistical significance ($P > 0.05$). Conclusion: The adjuvant treatment of captopril for primary hypertension complicated with CAD shows better effect than nitrendipine in lowering blood pressure, and can relieve angina obviously, correct abnormal electrocardiogram effectively, slow down the progress of the disease and improve the quality of life. It is safe and worthy of widely clinical promotion and application.

Keywords: Hypertension with coronary artery disease, captopril, angiotensin converting enzyme inhibitors, electrocardiogram

Introduction

Hypertension is one of the most common chronic diseases. Epidemiology research shows that hypertension prevalence among adults aged over 18 in 2016 in northern China was up to 25.2% [1]. Sustained increase in arterial pressure leads to arteriolosclerosis all over the body and gradually cardio-cerebrovascular complications such as angina, cardiac failure, brain stroke, coronary heart disease (CAD), myocardial infarction which are all severe consequences and coronary heart disease occurs the most. Experience home and abroad indicates that, risk of mortality from CAD increases by more than 1/4 per 10 mmHg increase in systolic pressure [2]. For patients with hypertension and CAD, lowering blood pressure with just vasodilator, calcium channel blockers, or diuretics are far from enough. Besides, long-term medication on nitroglycerin could result in drug tolerance, let alone to effectively relieve patients' angina [3]. Michishita et al. insisted that it is necessary to take opti-

Table 1. Baseline data

	Observation group (n = 48)	Control group (n = 48)	χ^2/t	P
Gender (male/female)	27/21	25/23	0.338※	0.551
Age (year)	63.21 ± 9.23	62.78 ± 8.56	0.235#	0.664
Angina pectoris attack frequency (time/week)	3.55 ± 1.76	3.60 ± 1.56	0.452#	0.448
Course of hypertension (year)	6.24 ± 2.84	6.57 ± 2.69	0.121#	0.785
Course of coronary heart disease (year)	4.03 ± 1.62	3.86 ± 1.55	0.103#	0.886
Hypertension risk classification			0.421※	0.307
Grade I	25	28		
Grade II	23	20		

Note: ※tested by χ^2; #tested by t test.

mized treatment of "protecting heart by lowering blood pressure" and attach importance to drugs that are proven to have effect on protecting cardiovascular system and improving quality of life, at the same time, managing risks of cardiovascular and angina while lowering blood pressure is standard [4]. Wang et al. performed a meta-analysis and found out that angiotensin converting enzyme inhibitor (ACE-I) could prominently decrease diabetes patients' all-cause mortality, cardiovascular mortality, main cardiovascular mortality and incidence of main cardiovascular events (such as myocardial infarction and cardiac failure) [5]. The ACE-I drugs' effect on relieving angina has been proved aboard, whereas in China, there's just few studies on effectiveness of ACE-I application on hypertension and CAD [6]. Therefore, this study aims to discuss captopril's effect on angina relief, blood pressure and electrocardiogram (ECG) abnormality changes in patients with hypertension and coronary artery disease, and provide reference to clinical practice.

Materials and methods

General data

Objects of this study were ninety-six patients with hypertension and coronary artery disease admitted to The Second Affiliated Hospital of Xingtai Medical College between September 2015 and March 2017.

Diagnosis criterion: *American Heart Association Hypertension (2012)* and *World Health Organization Diagnosis Criteria for Coronary Heart Disease* [7].

Inclusion criteria: In conformity with the above guidelines; 18-78 years of age; capable of thinking clearly and communicating fluently; with no interventional therapy history; patients and their families knew about the research and volunteered to participate and signed the informed consent.

Exclusion criteria: There were other heart diseases like secondary hypertension, congenital heart disease, and severe atrioventricular block, myocardial infarction; pregnancy-induced hypertension; acute and chronic infectious diseases; severe hepatic and renal dysfunction; malignant tumor patients; patients taking captopril or other drugs working similarly; captopril contraindication; patients had acute attack by CAD and needed emergent percutaneous coronary intervention patients allergic to drugs used in the study [8].

This research was performed with the approval by the Ethics Committee of The Second Affiliated Hospital of Xingtai Medical College. Patients were divided by random number table into two groups: the observation group and the control group, each consisting of 48 patients.

Methods

Patients in both the two groups were advised to lie down, rest and diet scientifically. They were also given aspirin anticoagulants and statins which could draw down blood lipids. What's more, the control group was given oral nitrendipine tablets (10 mg at a time, 1 time/day; Tianjin Pacific Pharmacy Co., Ltd., China); the observation group was given oral captopril tablets (12.5 mg at a time, 3 times/day; Changzhou Pharmacy Co., Ltd., China). ADRs of patients were monitored during medication, of which if patients could not tolerate, the corresponding

Table 2. Comparison of systolic blood pressure between two groups ($\bar{x}$ ± sd, mmHg)

Group	Observation group (n = 48)	Control group (n = 48)	t	P
Before treatment	153.06 ± 14.55	152.58 ± 13.39	0.171	0.834
After treatment	122.72 ± 11.90	132.56 ± 13.72	3.527	0.031
t	5.113	4.878		
P	0.000	0.012		

Table 3. Comparison of diastolic blood pressure between two groups ($\bar{x}$ ± sd, mmHg)

Group	Observation group (n = 48)	Control group (n = 48)	t	P
Before treatment	102.82 ± 8.23	101.25 ± 7.96	0.203	0.758
After treatment	81.52 ± 9.43	89.21 ± 8.15	2.731	0.041
t	4.908	3.653		
P	0.009	0.035		

medicine should be halved or discontinued. The treatment course was 2 weeks.

Observation indicators

Baseline data of two groups was compared. Primary indicators: Observing the patients' weekly angina times before and two weeks after the medication and monitoring ECG every day. At the same time, patients' systolic pressure and diastolic blood pressure were measured 3 times respectively before and two weeks after the medication, calculating the mean values. Patients' ADRs like rash, palpitation, dizziness, and cough were also recorded.

Effectiveness evaluation criteria

Effectiveness evaluation criteria for CAD were as follows. Remarkably effective: Spontaneous angina was controlled with lifestyle unchanged, exertional angina improved by more than grade 2. Effective: Spontaneous angina frequency dropped down to 1/3 of that before, duration shortened prominently and exertional angina improved by grade 1. Ineffective: Patients' angina was not effectively controlled or even tended to be worsened [9].

Effectiveness evaluation criteria for ECG were as follows. Remarkably effective: ECG back to normal or mostly normal at rest. Effective: ST segment declined at rest rose back by 0.5 mV after treatment yet not back to normal and main inverted T wave returned to normal or shallowed more than 50%. Ineffective: ST segment and T wave not changed much compared with pre-treatment. Aggravated: ST segment declined at rest dropped by 0.5 mV or more, compared with pre-treatment, main T wave inversion went deeper by more than 50% [10].

The overall response rate (ORR) was calculated in the 15th day of treatment. ORR = (remarkably effective cases + effective cases)/total cases * 100%.

Statistical processing

All the clinical data collected in this research were entered into Excel database and analyzed by two professional medical statistical researchers independently with SPSS 21.0. Measurement data tallied with normal distribution was expressed as mean ± standard deviation ($\bar{x}$ ± sd). Independent t test was used for inter-group comparison; paired t test was used for intra-group comparison. Enumeration data was examined by chi-square test and expressed by rate (%). $P < 0.05$ means the differences is of statistical significance.

Results

Comparison of baseline data of the two groups

Statistical analysis showed differences of baseline data such as gender, age, hypertension risk classification, angina attack frequency, course of hypertension, course of CAD of the two groups were of no statistical significance (all $P > 0.05$). See **Table 1**.

Blood pressure parameters of the two groups before and after treatment

Systolic and diastolic pressure levels of the two groups were about the same before the treatment. Their differences were of no statistical significance (both $P > 0.05$). Two weeks after the treatment, systolic pressure and diastolic pressure of two groups declined remarkably and that of observation group was much lower than that of control group. Differences were of

Table 4. Comparison of effectiveness of coronary heart disease of the two groups (n, %)

Group	Observation group (n = 48)	Control Group (n = 48)	χ^2	P
Remarkably effective	27	21		
Effective	16	16		
Ineffective	5	11		
Total effective rate	43 (89.58)	37 (77.08)	5.134	0.003

Table 5. ECG effectiveness comparison of the two groups (n, %)

Group	Observation group (n = 48)	Control group (n = 48)	χ^2	P
Remarkably effective	22	17		
Effective	20	18		
Ineffective	4	9		
Aggravated	2	4		
Total effective rate	42 (87.50)	35 (72.92)	6.542	0.000

Note: ECG, electrocardiogram.

Table 6. Adverse drug reactions (n, %)

Group	Observation group (n = 48)	Control group (n = 48)	χ^2	P
Rash	2	0	8.652	0.000
Dizziness	1	2	0.411	0.625
Palpitation	0	2	8.652	0.000
Cough	2	0	8.652	0.000
Adverse reaction rate	5 (10.42)	4 (8.33)	0.127	0.914

statistical significance (all P < 0.05). See **Tables 2** and **3**.

Angina relief

Two weeks after the treatment, the observation group's ORR of CAD was up to 89.58%, while the control group was only 77.08%, difference between which was of statistical significance (P < 0.05). See **Table 4**.

ECG changes

Two weeks after the treatment, the observation group's ORR of ECG was up to 87.50%, while the control group was only 72.92%, difference between which was of statistical significance (P < 0.05). See **Table 5**.

Adverse drug reactions

There was no withdrawal case due to severe ADRs. All ADRs were relieved after symptomatic treatment. The observation group's ADR incidence was 10.42%, and the control group was 8.33%, difference between which was of no statistical significance (P > 0.05). See **Table 6**.

Discussion

Captopril, as one of the effective and competitive ACE-I, can decrease synthesis of Ang II by antagonizing angiotensin converting enzyme in plasma, tissue and atherosclerotic plaque, decrease water-sodium retention, interrupt degradation of bradykinin and dilate coronary and peripheral arterial by inhibiting aldosterone secretion and thereby control blood pressure level [11, 12]. In this study, two weeks after the treatment, systolic and diastolic pressure of both the two groups declined remarkably and those in observation group was much lower than the control group. Differences were of statistical significance, which is close to research results in the past, and proves that captopril is especially effective at decreasing blood pressure in treating primary hypertension and coronary artery disease [13].

Treatment of hypertension by far has turned from merely lowering pressure to maintaining target organ functions [14]. Lipid peroxidation refers to a series of free radical reactions happened in polyunsaturated fatty acids. It is a critical pathogenesis of cellular damage and is closely associated with incidence and progression of atherosclerosis and CAD. Too much serum lipid hyperoxides could oxidize low density lipoprotein, resulting in increase in Malondialdehyde-like aldehydes and higher cytotoxicity; what's worse, new receptor binding sites would be produced and recognized by scavenger receptor or other receptors and form foam cells, which leads to cholesterol buildup and then atherosclerosis [15]. Angina pathogenesis is that the increase of myocardial oxygen consumption based on fixed coronary

artery stenosis leads to activation of regional intracardiac renin-angiotensin system and decrease of Ang II production, thereby aggregating myocardium ischemia. Ang II induces vascular endothelial cell and smooth muscle cell to express various cytokines, which exacerbates coronary inflammation, damages vascular endothelial function, participates in vascular and myocardial reconstruction, and oxidative modification of low density lipoprotein, thus inducing coronary artery spasm and lowering stability of artery atherosclerotic plaque [16].

In this study, two weeks after the treatment, the observation group's ORR of CAD was up to 89.58%, while the control group was only 77.08%. The observation group's ORR of ECG was up to 87.50%, while the control group was only 72.92%. These results proved that captopril could effectively protect myocardial cellular functions and improve myocardium ischemia. The mechanism thereof might be as follows. Firstly, increase in intracardiac regional bradykinin concentration could increase intracardiac regional NO volume and have vascular protection effect and improve vascular endothelial dysfunction. ACE-I decreases stimulus to Ang II receptor by reducing generation of Ang II, thereby inhibiting secretion of catecholamine, decreasing heart rate and myocardial oxygen consumption and achieving myocardial oxygen supply-demand balance [17]. Secondly, slow atherosclerosis progression to stabilize artery and make it hard to rupture [18]. Thirdly, induce antiplatelet effect with bradykinin and probably improve balance between plasminogen activator inhibitor-1 and tissue-type plasminogen activator and improve fibrinolytic function [19]. Research reported that captopril, by lowering blood viscosity and improving deformability of erythrocyte, relieves angina degree, shortens its duration and improves cardiac blood supply [20].

Irritated dry cough is the most common ADR of ACE-I. Medication with ACE-I drugs not only reduces degradation of substance P through inhibiting ACE activity but also increases production of substance P with bradykinin accumulation, which augments airway reactivity and induces incidence of cough in allergic individuals. But when patients stop medication on captopril, coughing disappeared [21]. Therefore, for patients with severe respiratory disease, captopril should be used with caution. In this study, there were 2 patients suffered from dry cough but it could be tolerated; 2 patients felt itchy 2 days after taking captopril and had tip-like rash on skin, and the rash disappeared and pruritus was relieved by treating with calamine lotion after 3 days. Meanwhile, in this study, difference of ADRs incidence of the two groups was of no statistical significance, suggesting that using captopril for treatment of primary hypertension and CAD didn't increase ADRs incidence, thus it is relatively safe.

Notwithstanding, this study is sample limited and it is a retrospective study. We still need large-scale prospective randomized controlled trial to verify the results.

In summary, the adjuvant treatment of captopril for primary hypertension complicated with CAD shows good effect on lowering blood pressure, relieving angina obviously, correcting abnormal electrocardiogram effectively, slowing down the progress of the disease and improving the quality of life. It is safe and worthy of widely clinical promotion and application.

Disclosure of conflict of interest

None.

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