Original Article

Effect of captopril on hypertension complicated with coronary heart disease and angina pectoris

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Abstract: Objective: To investigate how captopril affects hypertension complicated with coronary heart disease (CHD) and angina pectoris. Methods: We selected 617 patients with hypertension complicated with CHD for inclusion in this randomized controlled study. Of these patients, 327 received daily administration of captopril (treatment group) and the remaining 290 received regular medication with nitrrendipine and isosorbide dinitrate (control group). We compared the pre- and post-treatment blood pressure measurements, treatment effectiveness rate, adverse reaction rate, and blood lipid level. Results: Before treatment (T1), the systolic blood pressure (SBP) and diastolic blood pressure (DBP) showed no statistically significant differences between the treatment and control groups (P > 0.050). After treatment, the SBP and DBP in the treatment group both decreased compared with those in the control group (P < 0.001). The treatment effectiveness rates against high blood pressure and CHD were higher in the treatment group than those in the control group (P < 0.001). In the treatment group, the incidence of adverse reactions was 7.34%, which was significantly lower than the rate of 16.21% in the control group (P < 0.006). The difference in blood lipid level at T1 between the 2 groups showed no statistical significance (P > 0.050). At 3 weeks (T2) and 6 weeks (T3) after treatment, the blood lipid level in the treatment group was much improved compared with that in the control group (P < 0.001). Conclusion: In patients with hypertension complicated with CHD, captopril can ameliorate blood pressure control to decrease the incidence of angina, with fewer adverse reactions. Thus, captopril shows promising value in the treatment of hypertension complicated with CHD.

Keywords: Captopril, hypertension, coronary heart disease, SBP, DBP

Introduction

For several decades, hypertension is widely recognized as a highly ranked disease threatening health of middle-aged and elderly persons, and increasing efforts have been placed into clinical studies on the treatment of hypertension [1]. Despite the tremendous efforts, hypertension remains clinically as a lifelong disease without any effective cure [2]. Moreover, hypertension mainly occurs concomitant to disorders of lipid metabolism and glycometabolism, or organic variations of the heart, brain, or vessels [3]. It has been found that among the complications of hypertension, coronary heart disease is the most common, occurring in almost 40% or more of all patients with hypertension [4]. In patients with hypertension complicated with coronary heart disease, the blood pressure is much higher than that in patients with simple hypertension due to stenosis of the coronary artery [5]. In clinical practice, hypertension complicated with coronary heart disease is classified as a high-risk disease for secondary sudden myocardial infarction or cardiac arrest [6]. It has been reported that in patients with hypertension complicated with coronary heart disease, the 5-year survival rate is only 40-60% [7]. Currently, the clinical treatment for hypertension complicated with coronary heart disease is mainly medication, although the varying efficacy of multiple drugs makes it difficult to identify the optimal treatment. Captopril is an enzyme inhibitor transformed from angiotensin. It has been shown to have promising efficacy in the treatment of hypertension, with relevance to improving cardiovascular function [8, 9].

At present, few studies have reported on the use of captopril for hypertension complicated with coronary heart disease. Since 2016, we
have used captopril for this purpose and shown the promising efficacy of this treatment. Thus, we performed this retrospective study to review the clinical efficacy of captopril for hypertension complicated with coronary heart disease, to provide evidence for the clinical treatment of hypertension.

**Materials and methods**

**General data**

We selected patients with hypertension complicated with coronary heart disease and angina pectoris for inclusion in this randomized controlled study. Inclusion criteria were as follows: systolic blood pressure (SBP) ≥140 mmHg or diastolic blood pressure (DBP) ≥90 mmHg, clinical manifestations according to the Guidelines for Diagnosis and Treatment of Coronary Heart Disease (2015 edition) that were confirmed using echocardiography, angina of varying degrees, age <70 years and cooperation with the treating medical personnel [10]. A total of 724 patients met the criteria and were enrolled. Exclusion criteria were as follows: tumor as a complication, other cardiovascular or cerebrovascular diseases as complications, severe organ failure, renal or hepatic dysfunction, infectious diseases, mental diseases, physical disability, pregnancy, bedridden status, and allergy to the study drugs. After excluding patients, we finally enrolled a total of 617 patients. Among them, 384 were men and 233 were women, aged between 47 and 66 years (average age, 54.23 ± 10.74 years). All patients provided signed written informed consent. The study was approved by the Committee on the Ethics of Panyu Central Hospital.

**Methods**

617 patients were randomly divided into a treatment group and control group. Among the 617 patients, 327 were assigned to receive captopril (treatment group) and the remaining 290 patients were assigned to receive regular treatment with nitrendipine and isosorbide dinitrate (control group). Patients in the treatment group took 25.00 mg captopril (Bristol-Myers Squibb) twice a day, every 8 h. Patients in the control group took 10.00 mg nitrendipine (Guangxi Medictop Pharma Co., Ltd.) 3 times a day, every 6 h. In both groups, the treatment lasted for 7 weeks [11, 12]. Fasting venous blood (4 mL) was drawn from patients before treatment (T1) and at 3 (T2) and 6 weeks (T3) after treatment, and centrifuged at 4000 rpm/min for 5 min. Then, the supernatant was preserved at -80°C for later use.

**Outcome measures**

The clinical data of patients in the 2 groups, including sex, age, disease course, and weight, were obtained. Blood pressure (SBP and DBP) of patients in the 2 groups was measured before and after treatment. The effectiveness of treatment for blood pressure control in the 2 groups was graded as follows: excellent (decrease in SBP by 20 mmHg or more, or decrease in DBP by 10 mmHg or more), improved (decrease in SBP by 20 mmHg or less, or decrease in DBP by 10 mmHg or less), and failure (no amelioration, or even deterioration in SBP or DBP). The treatment effectiveness rate for blood pressure was calculated as (excellent + improved)/total × 100%. The effectiveness rate of treatment for coronary heart disease was based on Rehabilitation Training for Coronary Heart Disease (2015 edition) and graded as follows [13]: excellent (significant improvement in clinical symptoms, without onset of angina), improved (improved signs of clinical symptoms, with a decrease in angina attacks), and failure (no significant improvement, or even deterioration in clinical symptoms or angina). The treatment effectiveness rate for coronary heart disease was calculated as (excellent + improved)/total × 100%. For the measurement of blood lipids in patients of the 2 groups at T1, T2, and T3, the low-density lipoprotein (LDL), high-density lipoprotein (HDL), total glycerol (TG), and total cholesterol (TC) levels were determined using an automatic biochemical analyzer (PU-ZS-300X, Beijing Perlong Co., Ltd.). Additionally, we observed the incidence of nausea, vomiting, diarrhea, dizziness, headache, palpitation, or edema during drug treatment. The incidence rate of adverse reactions was calculated as number of patients with adverse reaction/total × 100%.

**Statistical methods**

SPSS 22.0 software was used to analyze the data. Enumeration data, including sex, treat-
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Results

Comparison of clinical data between the 2 groups

We compared the clinical data of patients between the 2 groups, including age, weight, disease course, sex, smoking history, alcohol use history, and exercise habit, and found no statistically significant difference (P>0.050) (Table 1).

Comparison of blood pressure between the 2 groups

Before treatment, SBP and DBP showed no statistically significant differences between the 2 groups (P>0.050); after treatment, the SBP in the treatment group was 127.86 ± 6.54 mmHg, which was significantly lower than the SBP of 151.27 ± 6.94 mmHg in the control group (p<0.001). A similar change was also observed for DBP. The DBP in the treatment group was 84.37 ± 4.49 mmHg, which was also significantly lower than the DBP of 92.84 ± 5.81 mmHg in the control group (P<0.001). The results showed significant decreases in SBP and DBP in both groups after treatment (P<0.001; Figures 1 and 2).

Comparison of the treatment effectiveness rate for blood pressure between the 2 groups

In the treatment group, the treatment effectiveness rate for blood pressure was 96.33%, which was significantly higher than the rate of the control group.
Comparison of the treatment effectiveness rate for coronary heart disease between the 2 groups

In the treatment group, the treatment effectiveness rate for coronary heart disease was 89.91%, which was significantly higher than the rate of 70.00% in the control group (P<0.001; Table 3).

Comparison of the incidence rate of adverse reactions between the 2 groups

In the treatment group, 7 patients experienced vomiting, 3 had dizziness, 6 had headache, 4 had palpitations, and 4 had diarrhea. In the control group, 12 patients experienced vomiting, 8 had dizziness, 9 had headache, 9 had palpitations, 6 had diarrhea, and 4 had edema. The incidence rate (7.34%) of adverse reactions in the treatment group was significantly lower than that (16.21%) in the control group (P=0.006; Table 4).

Comparison of the blood lipid level between the 2 groups

At T1, we compared the blood lipid levels of patients in the 2 groups, and found no statistically significant difference (P>0.050). At T2, the levels of LDL, TG, and TC in the treatment group were significantly lower than those in the control group; however, the HDL level was higher (P<0.050). Measurements of these indices at T3 were also similar to those at T2 (P>0.050). At T2, the levels of LDL, TG, and TC in the treatment group were lower than those at T1 in the treatment group, with an increase in HDL (P<0.05). From T2 to T3, patients in the treatment group showed decreases in LDL, TG, and TC with an increase in HDL (P<0.001). In the control group, no alteration was identified in the levels of LDL, TG, TC, or HDL from T1 to T2 (P>0.05), and from T2 to T3 (P>0.05); however, at T3, the levels of LDL, TG, and TC were all lower than those at T1, with an elevated HDL (P<0.05; Figures 3-6).

Discussion

Hypertension and coronary heart disease are frequent in the middle-aged and elderly populations, and usually occur with complications [14]. However, the incidence rate of hypertension complicated with coronary heart disease is increasing together with the improvements in the standard of living [15]. Patients with hypertension complicated with coronary heart disease usually experience contractile pains or suppression of the sternum to varying degrees, which severely affects their quality of life [16]. In addition, long-term hypertension generates irreversible damages to the affected organs [17]. It has been reported that hypertension complicated with coronary heart disease is a kind of mutually interacting chronic disease. Hypertension results in an increase in blood pressure, largely injuring the vascular endothelium and facilitating progression of coronary heart disease, whereas the resultant progression of coronary heart disease causes blocking of vessels, leading to further increases in the blood pressure level [18]. The lack of an appropriate, timely treatment at the early stage of disease can directly induce organ failure, heart failure, or vascular necrosis, severely threatening health and life of patients [19].

The clinical treatment for hypertension complicated with coronary heart disease mainly focuses on decreasing the blood pressure level with vasodilators, calcium antagonists, or diuretics [20]. Among these drugs, captopril is a kind of angiotensin-converting enzyme inhibitor that can inhibit contractility and peripheral...
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Table 2. Comparison of effectiveness of blood pressure treatment between the 2 groups, n (%)

<table>
<thead>
<tr>
<th></th>
<th>Therapy group (n=327)</th>
<th>Regular group (n=290)</th>
<th>X²</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Excellent</td>
<td>263 (80.43)</td>
<td>174 (60.00)</td>
<td></td>
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<tr>
<td>Effective</td>
<td>52 (15.90)</td>
<td>79 (27.24)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Invalid</td>
<td>12 (3.67)</td>
<td>37 (12.76)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Effectiveness rate (%)</td>
<td>96.33</td>
<td>87.24</td>
<td>17.372</td>
<td>&lt;0.001</td>
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</table>

Table 3. Comparison of the treatment effectiveness rate for coronary heart disease between the 2 groups, n (%)

<table>
<thead>
<tr>
<th></th>
<th>Therapy group (n=327)</th>
<th>Regular group (n=290)</th>
<th>X²</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Excellent</td>
<td>157 (48.01)</td>
<td>69 (23.79)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Effective</td>
<td>137 (41.90)</td>
<td>134 (46.21)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Invalid</td>
<td>33 (10.09)</td>
<td>87 (30.00)</td>
<td></td>
<td></td>
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<tr>
<td>Effectiveness rate (%)</td>
<td>89.91</td>
<td>70.00</td>
<td>38.884</td>
<td>&lt;0.001</td>
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</table>

Table 4. Comparison of the incidence of adverse reactions between the 2 groups, n (%)

<table>
<thead>
<tr>
<th></th>
<th>Therapy group (n=327)</th>
<th>Regular group (n=290)</th>
<th>X²</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vomiting</td>
<td>7 (2.14)</td>
<td>12 (4.14)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dizziness</td>
<td>3 (0.92)</td>
<td>8 (2.76)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>6 (1.83)</td>
<td>9 (3.10)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Palpitations</td>
<td>4 (1.22)</td>
<td>9 (3.10)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diarrhea</td>
<td>4 (1.22)</td>
<td>6 (2.07)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adverse reaction rate (%)</td>
<td>7.34</td>
<td>16.21</td>
<td>11.872</td>
<td>0.006</td>
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</table>

The higher treatment effectiveness rates for blood pressure and coronary heart disease suggest that captopril is superior to the traditional drugs in the treatment of hypertension complicated with coronary heart disease. Mainly targeting the renin-angiotensin-aldosterone system, captopril can effectively inhibit the transition of angiotensin I to II, thereby curbing the secretion of aldosterone and reducing the retention of water and sodium [21]. In addition to the effect of lowering blood pressure, captopril can simultaneously maintain the heart rates, which can improve heart-related diseases by increasing the hemodynamics and blood flow. It has been shown that captopril can dilate the coronary artery and small artery to increase the oxygen supply to the myocardium of patients with coronary artery diseases [22]. Acting as a vasodilator, captopril can augment the stroke volume and blood flow in the kidney, decrease ventricular remodeling and proteinuria formation, and protect the integrity and regular functions of the heart, thereby decreasing the incidence of angina and increasing the effectiveness rate of treatment for coronary heart disease, as previously reported by Sepehri et al [23].

As the abnormal metabolism of blood lipids is the major cause of atherosclerosis of the coronary artery, the considerable amelioration of
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Figure 3. Low-density lipoprotein (LDL) levels during the 2 treatments. There was no significant difference in LDL between the 2 groups before treatment (T1). At T2, the treatment group showed significantly lower LDL than the control group. At 6 weeks after treatment (T3), the treatment group showed significantly lower LDL than the control group. In the treatment group, LDL was significantly lower at 3 weeks after treatment (T2) than at T1, and at T3 than at T2. There was no significant difference in LDL in the control group between T1 and T2, and LDL was lower at T1 than at T1. *, P<0.050 compared with LDL in the treatment group; #, P<0.050 compared with LDL in the same group at T1; Δ, P<0.050 compared with LDL in the same group at T2.

Figure 4. High-density lipoprotein (HDL) during the 2 treatments. There was no significant difference in HDL between the 2 groups before treatment (T1). The HDL in the treatment group was significantly higher than that in the control group at T2. The HDL in the treatment group at 6 weeks after treatment (T3) was significantly higher than that in the control group. The HDL in the treatment group was significantly higher than that in the control group at T1, and HDL at T3 was significantly higher than that at 3 weeks after treatment (T2). There was no significant difference in HDL between T1 and T2 in the control group, and HDL was higher at T3 than at T1. *, P<0.050 compared with HDL in the treatment group; #, P<0.050 compared with HDL in the same group at T1; Δ, P<0.050 compared with HDL in the same group at T2.

Figure 5. Total glycerol (TG) during the 2 treatments. There was no significant difference in TG between the 2 groups before treatment (T1). The treatment group showed significantly lower TG than the control group at T2. At 6 weeks after treatment (T3), the treatment group showed significantly lower TG than the control group. The TG of the treatment group was significantly lower at 3 weeks after treatment (T2) than at T1, and at T3 than at T2. There was no significant difference in TG between T1 and T2 in the control group, and TG was lower at T3 than at T1. *, P<0.050 compared with TG in the treatment group; #, P<0.050 compared with TG in the same group at T1; Δ, P<0.050 compared with TG in the same group at T2.

Figure 6. Total cholesterol (TC) during the 2 treatments. There was no significant difference in TC between the 2 groups before treatment (T1). The treatment group showed significantly lower TC than the control group at T2. At 6 weeks after treatment (T3), the treatment group showed significantly lower TC than the control group. The TC at T2 was significantly lower than that at T1, and TC at T3 was significantly lower than that at T2. There was no significant difference in TC between T1 and T2 in the control group, and TC was lower at T3 than at T1. *, P<0.050 compared with TC in the treatment group; #, P<0.050 compared with TC in the same group at T1; Δ, P<0.050 compared with TC in the same group at T2.
blood lipids in patients who received captopril medication suggests that captopril can improve the blood lipid levels [24]. Some papers show that captopril can lead to reduced plasma hepatic triglycerides [25]. Erik argued that both short- and long-term treatments with captopril significantly improved insulin-stimulated glucose transport activity in skeletal muscle of the obese Zucker rat, and that this improvement involved bradykinin metabolism [26]. However, the specific mechanism requires further investigation [27].

In addition, the lower incidence of adverse reactions in the treatment group than in the control group suggests that, in the treatment of hypertension complicated with coronary heart disease, captopril confers a protective effect to the key human organs such as the heart and kidneys.

Nonetheless, this study has some limitations, including the simple constitution of the sample population, a strong regional focus, being too population-specific, or the field being only conducive to incremental findings, and failure in big data analysis. Furthermore, the specific mechanism of action of captopril requires more in-depth studies. To optimize the results, we plan to follow up the patients of this study.

In conclusion, in patients with hypertension complicated with coronary heart disease, captopril can ameliorate blood pressure, thus decreasing the incidence of angina, with fewer adverse reactions. Therefore, captopril shows promising value in the treatment of hypertension complicated with coronary heart disease.

**Disclosure of conflict of interest**

None.

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