Journal of Hainan Medical University

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Effects of telmisartan combined with nifedipine controlled release tablet on inflammatory factors, vascular endothelial function and left ventricular function in patients with coronary heart disease with mild to moderate hypertension

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ARTICLE INFO

Article history:
Received 11 Oct 2017
Received in revised form 15 Oct 2017
Accepted 18 Oct 2017
Available online 28 Oct 2017

Keywords:
Coronary heart disease with mild to moderate hypertension
Telmisartan
Nifedipine Controlled Release Table
Inflammatory factors
Vascular endothelial function
Left ventricular function

ABSTRACT

Objective: To investigate the effect of telmisartan combined with Nifedipine Controlled Release Tablet on inflammatory factors, vascular endothelial function and left ventricular function in patients with coronary heart disease with mild to moderate hypertension. **Methods:** A total of 92 cases of patients with coronary heart disease with mild to moderate hypertension were selected as the object of observation, according to the random data table, they were divided into the control group (n=46) and observation group (n=46), and patients in the control group were treated with Nifedipine Controlled Release Table therapy, on this basis, the observation group patients were given telmisartan treatment, two groups were treated for 6 months. The levels of the blood pressure, inflammatory factors, vascular endothelial function and left ventricular function compared between the two groups before and after treatment. **Results:** There were no significant differences in the levels of SBP, DBP, hs-CRP, TNF-α, NO, ET-1, LVEF, LVEDD and LVESD in the two groups before treatment. After treatment, two groups of SBP, DBP, hs-CRP, TNF-α, ET-1, LVEDD and LVESD levels were significantly lower than those in the same group before treatment, and after treatment, the levels of SBP, DBP, hs-CRP, TNF-α, ET-1 and LVESD in the observation group were significantly lower than those in the control group, while there were no significant difference in the level of LVEDD between the two groups after treatment; Compared with level in the group before treatment, the levels of NO and LVEF in the two groups were significantly increased, and the observation group [(82.13±19.01) μmol/L, (52.83±7.45)%] was significantly higher than the control group [(67.37±13.08) μmol/L, (49.47±6.96)%]. **Conclusion:** Telmisartan combined with Nifedipine Controlled Release Table in treating coronary heart disease with mild to moderate hypertension, can effectively control blood pressure, reduce the inflammatory stress, improve vascular endothelial function and left ventricular function of patients, has an important clinical value.

1. Introduction

Coronary heart disease (CHD) is a common disease in cardiovascular and cerebrovascular diseases. The incidence of coronary heart disease in China is increasing year by year, which causes serious harm to the patient's life safety. Some studies have pointed out that coronary heart diseases related to hypertension closely. As one of the important pathogenic factors, hypertension participates in and promotes the development and progression of coronary atherosclerosis. According to incomplete statistics, 60%-70% patients with coronary heart disease accompany by hypertension. Nearly 69% of hypertensive death patients have severe coronary heart disease[1−3]. Nifedipine Controlled Release Tablets and telmisartan are commonly used antihypertensive drugs in clinic. The combination of these two drugs can effectively control blood pressure and improve left ventricular function[4−5]. At present, there

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Fund Project: Sustentation fund from Beijing Municipal Health Bureau (Num: 201712344)

are relatively few studies on the effects of two drugs on biochemical indexes, hence, the following studies were conducted to investigate the efficacy of combined therapy.

2. Data and methods

2.1. Clinical data

A total of 92 cases of patients with coronary heart disease with mild to moderate hypertension from our hospital were selected as the object of observation. All patients met the relevant criteria in the 2007 guidelines for the diagnosis and treatment of coronary artery disease[6]. It is also consistent with the diagnostic criteria of the diagnosis and treatment of hypertension set by mild and moderate hypertension guidelines in Chinese[7]. The contents and processes involved in this study are in line with the standards of the ethics committee of this hospital, and approved by the committee. According to the random data table, all the patients divided into the control group and observation group (each of 46 cases). In control group, there were 28 males and 18 females, with ages of 42-70 years. In observation group, there were 26 males and 20 females, with ages of 40-70 years. All patients excluded: (1) Patients suffering from severe liver and kidney dysfunction, acute and chronic infection, metabolic diseases and autoimmune diseases; (2) Pregnant or lactating pregnant and lying in women; (3) Patients suffer from mental illness and could complete treat according to doctor's orders; (4) Allergic to the study of active ingredients of drugs; (5) Patients with biliary obstructive diseases; (6) Patients who have been treated with related drugs have been treated; (7) Patients with poor treatment compliance, could not complete the course of treatment of patients; (8) Patients do not want to participate in the study. There was no significant difference between the two groups in terms of age and sex (P>0.05). All patients informed and agreed on the content of the study.

2.2. Therapeutic method

Basic treatment of coronary heart disease and hypertension was given in two groups of patients. Based on this, patients in the control group were treated with Nifedipine Controlled Release Tablets (Adalat, Germany bayer medical care co. LTD., lot number 050109, specification 30 mg/s) 30 mg/time, 1 time/day; Patients in the observation group were treated with telmisartan (micardis, producted by Boehringer Ingelheim, product batch number 050118, specification 80 mg 7 s). The initial dose is 40 mg/time, 1 time/d, under dinner or after meals, According to the patient's blood pressure, the dosage range was 20-80 mg, Nifedipine Tablets were given at the same time as the control group. Two groups of patients were treated by this way for 6 months.

2.3. Observational indexes

The blood pressure [systolic blood pressure (SBP) and diastolic blood pressure (DBP)] were measured before and after treatment. At the same time, 5 mL the fasting peripheral venous blood of patients were extracted and the serum were separated by centrifugation, the related indexes were detected. Serological indicators include inflammatory factors [high sensitivity C reactive protein (hs-CRP), tumor necrosis factor alpha (TNF-)] and vascular endothelial function [nitric oxide (NO), endothelin -1 (ET-1)]. Hs-CRP and ET-1 levels were detected by radioimmunoassay, detection kit from Shanghai Harling Biological Technology Co., TNF- levels were measured by ELISA and NO levels were measured by nitrate reductase assay. TNF- α and NO kits were provided by Shanghai Enzyme Biotechnology Co., ltd. All laboratory procedures strictly followed the kit instructions. Meanwhile, doppler ultrasound were used to recorded and calculated left ventricular ejection fraction (LVEF), left ventricular end systolic diameter (LVESD), left ventricular end diastolic diameter (LVEDD) of patients before and after treatment in two groups.

Table 1.
Comparison of SBP and DBP levels before and after treatment.

Groups	n	Time	SBP (mmHg)	DBP (mmHg)
Control group	46	Before treatment	164.94±13.58	110.22±9.67
		After treatment	140.68±11.19*	84.56±8.01*
Observation group	46	Before treatment	163.68±13.05	110.86±9.55
		After treatment	124.13±9.93*#	78.21±6.78*#

Note：* Compared with that before treatment,# Compared with the control group after treatment, P<0.05.

Table 2.
Comparison of inflammatory factors before and after treatment.

Groups	n	Time	hs-CRP (mg/L)	TNF- α (ng/L)
Control group	46	Before treatment	11.07±2.12	58.79±13.69
		After treatment	8.99±1.27*	51.28±8.37*
Observation group	46	Before treatment	10.84±2.23	59.02±14.38
		After treatment	6.31±0.87*#	39.37±9.84*#

Note：* Compared with that before treatment, # # Compared with the control group after treatment, P<0.05.

Table 3.
Comparison of vascular endothelial function in two groups.

Groups	*n*	Time	NO (μmol/L)	ET-1 (ng/L)
Control group	46	Before treatment	47.44±12.78	101.46±23.74
		After treatment	67.37±13.08*	68.35±14.36*
Observation group	46	Before treatment	47.33±12.70	102.17±23.49
		After treatment	82.13±19.01*#	51.38±12.65*#

Note：* Compared with that before treatment, # Compared with the control group after treatment, $P<0.05$.

Table 4.
Comparison of cardiac function indexes before and after treatment.

Groups	*n*	Time	LVEF (%)	LVEDD (mm)	LVESD (mm)
Control group	46	Before treatment	44.01±6.50	57.68±6.98	51.13±7.64
		After treatment	49.47±6.96*	54.12±5.88*	46.41±6.94*
Observation group	46	Before treatment	43.88±6.37	58.40±6.69	51.58±7.52
		After treatment	52.83±7.45*#	52.42±6.12*	43.12±6.96*#

Note：* Compared with that before treatment, # Compared with the control group after treatment, $P<0.05$.

2.4. Statistical analysis

SPSS 17.0 statistical package was conducted for statistical analysis. The levels of blood pressure, inflammatory factors, vascular endothelial function and cardiac function indexes in this study were in line with the normal distribution, which were described as (Mean ± SD). t test was conducted to comparison the indexes between two groups before and after treatment as well as between the group after treatment, values of $P<0.05$ were considered to be statistically significant.

3. Result

3.1. Comparison of SBP and DBP levels before and after treatment

SBP and DBP levels before and after treatment in two groups are shown in Table 1. As shown in Table 1, before treatment, there was no significant difference in SBP and DBP levels between the two groups ($P>0.05$). The levels of SBP and DBP in control group were (140.68±11.19) mmHg and (84.56±8.01) mmHg, respectively, which were significant lower than these before treatment. The levels of SBP and DBP in observation group were (124.13±9.93) mmHg and (78.21±6.78) mmHg, respectively, which were significant lower than these before treatment as well as in control group. There was significant difference between the two groups ($P<0.05$).

3.2 Comparison of inflammatory factors before and after treatment

hs-CRP and TNF-α levels before and after treatment in two groups are shown in Table 2. Before treatment, there was no significant difference in hs-CRP and TNF-α levels between the two groups ($P>0.05$). After treatment, the levels of hs-CRP and TNF- in control group and observation group were (8.99±1.27) mg/L, (51.28±8.37) ng/L, (6.31±0.87) mg/L and (39.37±9.84) ng/L, respectively, which were significant lower than these before treatment in groups, and the hs-CRP and TNF-α levels in observation group were significant lower than these in control group ($P<0.05$).

3.3 Comparison of vascular endothelial function before and after treatment

NO and ET-1 levels before and after treatment in two groups are shown in Table 3. Before treatment, there was no significant difference in NO and ET-1 levels between the two groups ($P>0.05$). After treatment, the levels of NO in control group and observation group were (67.37±13.08) μmol/L and (82.13±19.01) μmol/L, respectively, which were significant higher than these before treatment in groups. Compared with that before treatment, the ET-1 levels in two group were significant decreased, and the levels after treatment in observation group (51.38±12.65) ng/L were significant lower than that in control group (68.35±14.36) ng/L.

3.4 Comparison of cardiac function indexes before and after treatment

LVEF, LVEDD and LVESD levels before and after treatment in two groups are shown in Table 4. Before treatment, there was no significant difference in LVEF, LVEDD and LVESD levels between the two groups ($P>0.05$). After treatment, the levels of LVEF, in control group and observation group were (49.47±6.96)% and (52.83±7.45)%, respectively, which were significant higher than these before treatment in groups. And the levels of LVEF in observation group were ere significant higher than that in control group. The LVEDD and LVESD levels in two group after treatment were significant lower than that before treatment in groups, and the levels of LVESD in observation group were significant lower than

that in control group (P<0.05). There was no significant difference in LVEDD levels between the two groups after treatment (P> 0.05).

4. Discussion

Coronary heart disease is the world's leading cause of death. Coronary artery stenosis caused by atherosclerosis can lead to myocardial ischemia hypoxia, hypertension, chronic inflammation, endothelial dysfunction and lipid metabolism disorder, which are important risk factors for the onset and development of disease[8,9]. Epidemiological studies have pointed out that the mortality rate of coronary heart disease in hypertensive patients is 5 times as many as persons with normal blood pressure, among which the prevalence rate of elderly patients and men is relatively high[10]. A large number of clinical studies have confirmed that effective blood pressure control in the normal range can prevent the occurrence of coronary heart disease, reduce mortality rate of coronary heart disease [11], hence, the antihypertensive therapy plays an important role in the treatment of coronary heart disease.

Nifedipine Controlled Release Tablets is a long-acting calcium channel antagonist. It is widely used in the treatment of angina pectoris, hypertension and other diseases. It is pointed out that Nifedipine Controlled Release Tablets has a long-lasting hypotensive effect[12]. Telmisartan is a specific angiotensin II receptor antagonist, which can increase the content of serum adiponectin, control pressure for 24 h, regulate metabolism and inhibit of atherosclerosis function [13]. Related studies have pointed out that, compared with the single use of Nifedipine Controlled Release Tablets, combined with telmisartan can further reduce blood pressure, reduce the liver cell growth factor and vascular endothelial growth factor in patients, also pointed out that telmisartan has a protective effect of on vascular endothelial cell function[14,15]. This study pointed out that, compared with the single use of Nifedipine Controlled Release Tablets, combined with telmisartan treatment, the DBP and SBP levels were further reduced, and the blood pressure control effect is significant, which consistent with the previous reports, further confirmed the synergistic antihypertensive effect of two pesticides[16,17]. In addition to blood pressure, this study also analyzed the levels of inflammatory factors, vascular endothelial function and left ventricular function after two treatments, in order to investigate the clinical effect of combined therapy.

A large number of domestic and foreign studies have confirmed that the occurrence and development of coronary heart disease and hypertension were closely related to inflammatory response. Inflammatory factors play an important role in the formation, rupture and abscission of coronary atherosclerotic plaques[18]. The study indicated that the levels of hs-CRP and TNF-α in serum were significantly increased in patients with coronary heart disease, hypertension and diabetes mellitus. As the main markers of inflammation, the levels of CRP and TNF-α were significantly correlated with the severity of the disease. In addition, hs-CRP could predict the stability ofcoronary plaque. TNF-α is mainly involved in vascular structure and function damage mechanism[19,20]. The results of this study indicated that after combined with telmisartan, the level of hs-CRP and TNF- in patients were further decreased, and the extent of reduction were significantly better than that in the control group. The results showed that telmisartan had anti-inflammatory effects, and the reason may be that telmisartan can activate the peroxisome proliferator activated receptor gene, thereby inhibiting the synthesis, release and signal transduction of inflammatory factors, so as to exert its anti-inflammatory effects[21].

NO and ET-1 are important markers of vascular endothelial function, which belong to the important regulating substances of cardiovascular system secreted by vascular endothelial cells. NO can inhibit the synthesis of ET-1, and the main functions of NO are dilation blood vessels, inhibition of monocyte adhesion, platelet aggregation and formation of atherosclerotic plaques; ET-1 is the most potent vasoconstrictor and has the function of maintaining vascular tone and homeostasis of the cardiovascular system. The increase of ET-1 level may cause vasoconstriction, spasticity, and increased blood pressure, which can accelerate hypoxia ischemia[22]. The results of this study indicated that both two treatments can effectively reduce the level of ET-1 and raise the level of NO. But in the group combination with telmisartan, the levels of NO and ET-1 improved more significantly in the patients, which suggested that telmisartan could improve vascular endothelial function in patients, but the cause remains to be explored.

Hypertension is one of the major causes of ventricular dysfunction and myocardial remodeling. The related studies pointed out that the combination of Nifedipine Controlled Release Table with telmisartan can improve left ventricular function in hypertensive patients. The mechanism of Nifedipine Controlled Release Table is to dilate vessels and decrease ventricular filling. The telmisartan could improve left ventricular function by inhibiting myocardial remodeling[23]. The results of this study indicated that the level of left ventricular function in the combined telmisartan group is further improved, compared with the control group. The results of this study were consistent with the previous reports, and further confirmed that combination therapy with Nifedipine Controlled Release Tablets and telmisartan can improve left ventricular function and reverse left ventricular hypertrophy[24].

In conclusion, Telmisartan compared with single use of Nifedipine Controlled Release Table, combined with telmisartan can effectively improve the efficacy in treating coronary heart disease with mild to moderate hypertension, also can control blood pressure, reduce the inflammatory stress, improve vascular endothelial function and left ventricular function of patients, which has an important clinical value.

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