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Effect of combination of amlodipine and ziyin huoxue fang on hypertension patients with coronary heart disease and omentin-1, MMP-3, and TIMP-1 in blood.

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Abstract

Objective: To observe the clinical efficacy of combination of amlodipine and Ziyin Huoxue Fang on hypertension patients with coronary heart disease.

Methods: A total of 80 cases of hypertension patients with coronary heart disease were retrospectively collected and sorted into control group and observation group based on various medications, 40 a group. The observation group was given amlodipine and Ziyin Huoxue Fang, while the other group amlodipine only, with a treatment course of eight weeks. All patients were watched for curative effect involving the improvements of blood pressure, angina pectoris, blood fat, serum biochemical indexes, and adverse reaction.

Results: The total effective rate and the marked effective rate of lowering blood pressure and improving angina pectoris in the observation group was significantly better than that of the control group (P<0.05); before treatment, there was no significant difference in blood lipid (TG, TC, HDL-C, and LDL-C), serum Nitric Oxide (NO), Homocysteine (HCY), C Reactive Protein (CRP), omentin-1, MMP-3, and TIMP-1 between two groups (P>0.05). However, after treatment, blood fat (TG, TC, HDL-C, and LDL-C), serum HCY, CRP of all patients were greatly decreased and serum NO was significantly increased, and the efficacy of the observation group was better than that of the control group, with a statistical difference (P<0.05). Besides, omentin-1 and TIMP saw a growth but MMP-3 was reduced, and the difference was significant (P<0.05), and compared the control group and observation group, there was statistical difference (P<0.05). About the safety, there was no difference in adverse reactions between two groups (P>0.05).

Conclusion: The combination of amlodipine and Ziyin Huoxue Fang plays a positive role in the treatment of hypertension patients with coronary heart disease, deserving to spread.

Keywords: Amlodipine, Ziyin Huoxue Fang, Hypertension combining with coronary heart disease, Clinical efficacy.

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Introduction

As a common chronic disease in clinic, persistent hypertension may give rise to endothelial damage, myocardial ischemia, and decrease of heart function, thereby contributing to the onset of Coronary Heart Disease (CHD) [1]. A study claims that the incidence of hypertension combining with CHD has seen a growth with exacerbation of aged society year by year which greatly augments treatment difficulties, badly impacting on the elderly individuals' health and quality of life [2]. Therefore, it is essential to explore and develop a therapeutic method with excellent efficacy and safety. In the study, we analyse the effect of the combination of amlodipine and Ziyin Huoxue Fang on the hypertension patients with CHD and its biochemical factors, aiming to provide references for clinical practice.

Data and Methods

Data

A total of 80 hypertension patients with CHD admitted in our hospital from April 2014 to April 2016 were collected retrospectively for the study and divided randomly into observation group and control groups, 40 a group. In the observation group, there were 21 males, 19 females, aged from 40 to 75 y, (61.34 ± 3.26 y) in average, with a course from 1 to 10 y, (5.19 ± 2.21 y) in average. And in the control group, there were 23 males, 17 females, aged from 42 to 79 y, (59.63 ± 4.39 y) in average, with a course from 2~9 y, (5.69 ± 2.08 y) in average. Compared the general data of two groups, there was no statistical difference (P>0.05). With the approval from the ethnic committee of our hospital, all patients signed the informed consent.

Inclusion and exclusion

Inclusion criteria: The patients in accordance with the diagnosis criteria of hypertension combining with CHD drafted by WHO, aged from 40 to 80 y, were eligible. Inclusion criteria: the patients with secondary hypertension, non-CDH, liver dysfunction, mental disorder, or allergy to Amlodipine and Ziyin Huoxue Fang were ineligible for the study.

Treatment methods

The control group: All patients took amlodipine besylate (Shihuida Pharmaceutical Group, Guoyaozhunzi H19991083), 20 mg a time after dinner, once a day. The observation group: apart from amlodipine besylate, the patients also took Ziyin Huoxue Fang, consisted of 12 g Hanliancao (Eclipta Prostrata), 12 g Nvzhenzi (Fructus Ligustri Lucidi), 12 g Gouteng (Ramulus Uncariae Cum Uncis) (put later),12 g Tianma (Rhizoma Gastrodiae), 12 g Shangjisheng (Ramulus Taxilli), 12 g Gegeng (Radix Puerariae), 12 g Chuanniuxi (Radix Cyathulae Chuan),12 g Danshen (Radix Salviae Miltiorrhizae), 10 g Shuizhi (Hirudo), Chuanxiong (Rhizoma Chuanxiong), 10 g Chaomaiya (Fried Fructus Hordei Germinatus), 9 g Zhike (Fructus Aurantil), and 6 g Fuling (Poria) [3,4]. The formula and 500 pure water were cooked into 300 decoction and the patients took half of the decoction a time, twice a day, one formula a day. All patients in the study were treated for eight week.

Criteria and methods on efficacy assessment: (1) The curative effect of hypertension: all patients were measured for their blood pressure before and after treatment, recording Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP). Marked effect: DBP was decreased more than 20 mmHg before treatment, and the clinical symptoms were improved completely; effect: DBP was decreased with a range of 10~20 mmHg before treatment, and the clinical symptoms greatly subsided; ineffectiveness: DBP was decreased less than 20 mmHg before treatment, and the clinical symptoms weren't improved or even aggravated. Total effective rate=(number of marked effect+ number of effect) total number × 100% [5].

(2) The curative effect of angina pectoris: The occurrence of angina pectoris in the patients of two groups before and after treatment was recorded. Marked effect: the incidence of angina pectoris after treatment was decreased by over 80%; DBP was reduced more than 20 mmHg; or angina pectoris didn't occur in the same condition. Effect: the incidence of angina pectoris after treatment was decreased with a range of 50~80%; DBP was reduced with a range of 0~19 mmHg. Ineffectiveness: the incidence of angina pectoris after treatment was decreased less than 50% or wasn't; DBP had no changes. Total effective rate=(number of marked effect+number of effect)/total number × 100% [6].

(3) Changes of blood fat before and after treatment: The serums of two groups were collected before and after treatment to detect the contents of Triglyceride (TG), Total Cholesterol (TC), High Density Lipoprotein (HDL-C) and Low Density Lipoprotein (LDL-C).

(4) Determination of blood biochemical indexes before and after treatment: The serums of two groups was collected before and after treatment which were assayed for NO with nitrate reductase assay and HCY, CRP, omentin-1, and matrix Metalloproteinase-3 (MMP-3) with ELISA.

(5) Adverse reactions: We observed all patients and recorded the adverse reactions occurring during treatment or three months after treatment, calculating them.

Statistical analysis

All data were analysed by software SPSS17.0. The measurement data were expressed by mean ± SM ($\bar{x} \pm s$) and analysed by t-test; the enumeration data were expressed by ratio (n, %) and analysed by chi-square test (χ^2). When P was less than 0.05, the difference was statistically significant [5].

Results

Comparison on the curative effect of hypertension patients of two groups

The total effective rate and obvious effect rate of hypertension in the control group was 92.50% and 47.50% separately, higher than 82.50% and 40.00% of the control group, and the difference was statistically significant (P<0.05, Table 1).

Table 1. Comparison on the curative effect of hypertension patients in two groups (n (%)).

Group	n	Marked effect	Effect	Ineffectiveness	Total effective rate (%)
Control group	40	16 (40.00)	17 (42.50)	7 (17.50)	82.5
Observation group	40	19 (47.50)[a]	18 (45.00)	3 (7.50)	92.5[a]

Notes: compared with the control group, [a]P<0.05

Comparison on the curative effect of angina pectoris of two groups

The total effective rate and obvious effective rate of the observation group was 95.00% and 52.50% in respective, higher than 85.00% and 45.00% of the control group, with a statistical difference (P<0.05, Table 2).

Table 2. *Comparison on the curative effect of angina pectoris of two groups (n (%)).*

Group	n	Marked effect	Effect	Ineffectiveness	Total effective rate (%)
Control group	40	18 (45.00)	16 (40.00)	6 (15.00)	85.00
Observation group	40	21 (52.50)[a]	17 (42.50)	2 (5.00)	95.00[a]

Notes: compared with the control group, [a]P<0.05

Comparison on changes of blood lipid

There was no significant difference in TG, TC, HDL-C, LDL-C of two groups before treatment (P>0.05), while the lipid of both groups was largely reduced after treatment, and TG, TC, HDL-C and LDL-C of the observation group were decreased much more than that of the control group, with a statistical difference (P<0.05, Table 3).

Table 3. *Comparison on changes of lipid of two groups ($\bar{x}$ ± s, g/L).*

Group	n	Time	TG	TC	HDL-C	LDL-C
Control group	40	Before treatment	5.98 ± 1.18	2.32 ± 1.23	1.89 ± 0.54	2.23 ± 2.19
		After treatment	4.92 ± 1.11[a]	1.89 ± 0.69[a]	1.58 ± 0.39[a]	1.53 ± 1.23[a]
Observation group	40	Before treatment	5.87 ± 2.04	2.48 ± 1.49	2.04 ± 0.36	2.19 ± 2.46
		After treatment	4.79 ± 0.95[ab]	1.63 ± 0.58[ab]	1.46 ± 0.21[ab]	1.23 ± 1.31[ab]

Comparison on biochemical indexes

Compared two groups, there was no statistical difference in No, CRP and HCY before treatment (P>0.05). However, CRP and HCY in serum of two groups greatly declined after treatment, NO largely raised, and the decrease of CRP and HCY and the increase of NO in the observation group were much more than that of the control group, with a statistical difference (P<0.05, Table 4).

Table 4. *Comparison on biochemical index changes of two groups ($\bar{x}$ ± s).*

Group	n	Time	NO (μmol/L)	CRP (mg/L)	HCY (μmol/L)
Control group	40	Before treatment	40.37 ± 10.25	6.98 ± 2.49	39.18 ± 6.29
		After treatment	51.57 ± 12.39[a]	5.27 ± 3.48[a]	24.19 ± 5.29[a]
Observation group	40	Before treatment	41.68 ± 11.98	7.03 ± 4.91	40.29 ± 4.03
		After treatment	59.29 ± 13.27[ab]	4.79 ± 2.37ab	20.58 ± 3.95[ab]

Notes: compared with the pretreatment, [a]P <0.0; compared with the control group, [b]P<0.05

Comparison on omentin-1, MMP-3, and TIMP-1

Compared two groups, there was no statistical difference in omentin-1, MMP-3, and TIMP-1 before treatment (P>0.05). While, omentin-1 and TIMP-1 were increased and MMP-3 was decreased after treatment, and the difference was statistically significant (P<0.05). What's more, compared two groups, the difference was significant after treatment (P<0.05, Table 5).

Table 5. *Comparison on omentin-1, MMP-3, and TIMP-1 of two groups before and after treatment.*

Group	Omentin-1 (ng/ml)		MMP-3 (μg/ml)		TIMP-1 (μg/ml)	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observation group (n=40)	12.42 ± 1.68	20.01 ± 1.34*	0.137 ± 0.021	0.113 ± 0.016*	22.59 ± 2.08	26.10 ± 0.06*
Control group (n=40)	12.36 ± 1.69	15.58 ± 1.43*	0.133 ± 0.023	0.121 ± 0.019*	22.57 ± 2.27	24.21 ± 0.07*

t	0.178	2.057	0.161	0.695	1.174	8.437
P	0.859	0.042	0.872	0.488	0.243	0.001

Notes: *compared with the pretreatment, P<0.05

Adverse reactions

During treatment, there was one patients with dizziness and headache and one with slight diarrhea in the control group, with an incidence of adverse reaction of 5%; one with skeletal muscle ache and one with mild diarrhea in the observation group, with an incidence of adverse reaction of 5%. Compared two groups, there was no significant difference in the incidence of adverse reaction.

Discussion

With the exacerbation of aged society in China, the incidence of hypertension has raised gradually year by year. As a chronic disease with high incidence and mortality, it seriously impacts on human's health. Besides, persistent hypertension can change hemodynamics, activate platelets, and then give rise to atherosclerotic lesions, whose further development will lead to serious consequences like ischemia, hypoxia or angionecrosis, badly threatening the health of patients. Coronary Heart Disease (CHD) is a disorder whose common symptom is chest pain induced by rapid, severe, and temporary myocardial ischemia and hypoxia due to coronary insufficiency [5]. And the patients with persistent hypertension are vulnerable to CHD so that when treating the hypertension patients with CHD, doctors should focus on not only their blood pressure but also their blood fat, so as to get a good therapeutic effect and improve their quality of life.

Currently, medication is still the major therapy for hypertension complicated with CHD. As a calcium antagonists, amlodipine is a perfect vasodilator that has good effect on dilating arteries to greatly improve angina pectoris [6,7]. In Ziyin Huoxue Fang, Nuzhenzi, Hanliancao and Sangjisheng can nourish yin and supplement the liver; Tianma and Gouteng pacify the liver and subdue yang; Chuanniuxi is a good herb medicine for activating blood and resolving stasis which can promote blood circulation and improve myocardial ischemia; Shuizhi can break up blood and expel stasis but also anti-coagulate; Chuanxiong can activate blood and resolve stasis, move qi and open depression; Danshen can activate blood and dispel blood stasis, dredge channels and relieve pain, clear heart and eliminate irritability, and cool the blood and disperse abscess; Fuling can calm heart and spirit; Chaomaiya can reinforce kidney qi. They work together to activate blood and resolve stasis, reinforce the healthy qi to eliminate the pathogenic factors, decrease blood pressure and dredge collaterals, and nourish yin and supplement the liver [8,9].

At present, the medication for hypertension complicated with CHD mainly refers to western medicine which has such shortages as taking a variety of drugs, severe adverse reactions, high costs, and poor patient compliance. While Chinese medicine plays a positive role in treating hypertension complicated with CHD but also can reduce a series of adverse reactions of western medicine greatly. The findings of the study suggest that the blood pressure of the patients in the observation group who are given amlodipine and Ziyin Huoxue Fang is improved more than that of the patients in the control group who are only given amlodipine, with a total effective rate up to 92.5%; and the total effective rate of angina pectoris is also up to 95%, which prompts that drug combination, especially Chinese and western medicines combination, may be an effective mean for the treatment of hypertension complicated with CHD. In addition, we find that compared two groups, there is no big difference in blood lipid (TG, TC, HDL-C, and LDL-C) and serum NO, HCY, and CRP before treatment. But after treatment, blood lipid (TG, TC, HDL-C, and LDL-C) and serum CRP and HCY of the patients in two groups have declined significantly and serum NO has seen a great growth, and the efficacy of the observation group is much better than that of the control group. CRP is regard as a high-sensitive index of atherosclerosis and the concentration of HCY in serum is closely related to the occurrence of cerebrovascular disease [10,11]. Moreover, the increase of NO can restrain the development of atherosclerotic plaque and blood lipid is a key index reflecting blood level. Therefore, the outcomes of the study show that the combination of amlodipine and Ziyin Huoxue Fang is able to restore vascular endothelial cells and improve atherosclerosis. Omentin-1 and TIMP-1, protective factors when body metabolic imbalance happens, are in a low expression state in the patients with metabolic syndrome or diabetes, and MMP-3 is involved in the formation and aggravation of atherosclerosis. The levels of these three factors in both groups are improved after treatment, and that of the observation group are improved more than that of the control group. That's to say, the combination of amlodipine and Ziyin Huoxue Fang is able to enhance the protective factors and reduce the risk factor, which plays a role in inhibiting the disease. And the combination did not increase the incidence of adverse reactions, indicating that the patients have a better tolerance to it.

To sum up, the combination of amlodipine and Ziyin Huoxue Fang has a good effect on treating hypertension combined with CHD, deserving to spread. We should positively dig the value of Chinese materia medica and manufacture more formulas. For complex diseases like hypertension combined with CHD, multi-target and path therapies should be used, treating both manifestation and root cause of disease simultaneously, which provides a new idea for the treatment of hypertension combined with CHD in clinic.

References

1. Liu Y. Clinical observation on combination of rosuvastatain with amlodipine in treating senile hypertension patients with coronary heart disease. Cardiovascular Dis J Integ Trad China West Med 2015; 3: 111-112.
2. Hao Z. Efficacy of combination of rosuvastatain with amlodipine in treating senile hypertension and arteriosclerosis. Chongqing Med 2014; 43: 2061-2062.
3. Li YM. Clinical effect of Xuezhikang capsule combined with amlodipine atorvastatin calcium tablet in treating hypertension patients complicated with coronary heart disease and the impact on blood lipids, vascular endothelial function and inflammation. Pract J Cardiac Cerebr Pneum Vasc Dis 2016; 24: 90-93.
4. He HT, Guo LF, Duang HJ. Clinical study on Ziyinhuoxue Fang in treating coronary heart disease with hypertension. J New Chin Med 2011; 43: 17-18.
5. Yin XQ. Clinical observation of amlodipine combined with atorvastatin calcium for the treatment of hypertension complicated with coronary heart disease. Chin J Clin Ration Drug Use 2017; 10: 26-27.
6. Yang ZL, Jia XY, Luo. Effect of benazepril combined with Tongxinluo capsule in treating hypertension complicated with coronary heart disease. Anhui Med Pharm J 2014; 18: 556-558.
7. Li GH. Observation on the effect of benazepril combined with ctorvastatin calcium in treating hypertension complicated by coronary heart disease. Med Recap 2015; 21: 1867-1869.
8. Yu L, Jin XE. Study on Yiqiziyin Tongyangfumai method for the intervention of coronary heart disease-induced arrhythmia and heart rate variability. Med Innov China 2013; 95.
9. Du WT, Ming G, Liu P. Treatment of Chronic heart failure with carotid plaque patients by Yiqi Huoxue Tongyang Xezhuo Recipe. Chinese J Integ Trad West Med 2015; 35: 1322.
10. Chen YH, Lu KF, Jiang Z. Analysis on the levels of Hcy and hs-CRP in the patients with coronary heart disease and hypertension. Lab Med Clin 2010; 7: 2350-2351.
11. Dai XY, Bin YU. Significance of detection of serum Hcy and hs-CRP in patients with H type hypertension and coronary heart disease. China Mod Med 2017.

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