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Original Article

Efficacy of Huanglian lipid-lowering mixture on blood lipids in hypertension patients

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Abstract: Objective: The aim of the current study was to evaluate efficacy and safety levels of huanglian lipid-lowering mixture for treatment of hypertension patients with complicated with hyperlipidemia, exploring the effects on biochemical and related indexes. Methods: Ninety patients diagnosed with hypertension complicated with hyperlipidemia were selected and randomized into the experimental group (EXP group), ACEI group, and FVT group (n=30). Based on conventional treatment, patients in EXP, ACEI, and FVT groups were orally administrated the huanglian lipid-lowering mixture, captopril capsules, and fluvastatin capsules, respectively. Results: Before treatment, there were no significant differences in serum triglycerides (TG), total cholesterol (TC), low density lipoprotein (LDL), high density lipoprotein (HDL) and mean arterial pressure (MAP) between the three groups (all P>0.05). In EXP and FVT groups, TG, TC, and LDL levels after 1, 2, and 3 courses of treatment were significantly lower than those before treatment. HDL levels were higher (both P<0.001). In the ACEI group, there were no significant differences before treatment and after 1, 2, and 3 courses of treatment in TG, TC, LDL, and HDL levels (P>0.05). After 1, 2, and 3 courses of treatment, MAP levels in the ACEI group were lower than those in the FVT group. Levels in the EXP group were significantly lower than those in the FVT group (both P<0.001). In the FVT group, there were no statistically significant differences in MAP levels before treatment and after 1, 2, and 3 courses of treatment (P>0.05). In EXP and ACEI groups, MAP levels after 1, 2, and 3 courses of treatment were lower than those before treatment (both P<0.001). Conclusion: Huanglian lipid-lowering mixture can effectively reduce TG, TC, LDL, and MAP levels, as well as improve HDL levels, providing a basis for clinical treatment of hypertension complicated with hyperlipidemia.

Keywords: Hypertension, hyperlipidemia, huanglian lipid-lowering mixture, efficacy

Introduction

With recent improvements in living standards, more people are suffering from hyperlipidemia. This disease causes obesity and accumulation of large amounts of fat in the organs, affecting organ function [1]. Hyperlipidemia is usually complicated with hypertension, both of which are the cause and effect of each other [2]. The current prevalence rate of hypertension complicated with hyperlipidemia is 14.5% [3]. Thus, finding effective antihypertensive and lipid-lowering drugs is of great significance for treatment of the disease. Clinical lipid-lowering drugs mainly include statins, which have different effects on different blood lipids [4]. However, statins have no antihypertensive effects. Commonly used antihypertensive drugs include diuretics, angiotensin converting enzyme inhibitors (ACEI), β-receptor blockers, and calcium channel blockers. Each have different effects on hypertension caused by different reasons. However, these antihypertensive drugs have no lipid-lowering effects. Therefore, it is necessary to find a therapy that reduces blood lipids and blood pressure at the same time [5].

Huanglian lipid-lowering mixture, a traditional formula of Traditional Chinese Medicine, mainly includes Rhizoma Coptidis, Panax Notoginseng, Pueraria lobata, dried tangerine or orange peels, Gastrodia elata, and Rhizoma Pinelliae Preparata. It plays a role in relieving coronary heart disease with unstable angina pectoris, chronic heart failure, and atherosclerosis [6, 7]. However, there are few studies concerning its

efficacy on hypertension complicated with hyperlipidemia. Therefore, in the current study, the efficacy of huanglian lipid-lowering mixture was compared with that of statins in the treatment of hypertension complicated with hyperlipidemia, aiming to provide a basis for clinical treatment.

Materials and methods

Information and grouping

Ninety patients, diagnosed with hypertension complicated with hyperlipidemia, in the Department of Traditional Chinese Medicine of Maternity and Child Health Care of Zaozhuang, from January 2015 to January 2018, were selected and divided into the experimental group (EXP group), captopril group (ACEI group), and fluvastatin group (FVT group) (n=30), according to random number sequence. Based on conventional treatment, patients in the EXP group were orally administrated the huanglian lipid-lowering mixture. The ACEI group was orally administrated captopril capsules. The FVT group was orally administrated fluvastatin capsules. Before treatment, all patients and their families provided informed consent. This clinical study was approved by the Ethics Committee of Maternity and Child Health Care of Zaozhuang.

Inclusion criteria: Patients newly diagnosed with hypertension complicated with hyperlipidemia; Patients that met the diagnostic criteria for hypertension and hyperlipidemia, according to the 2016 *Chinese Guideline for the Management of Dyslipidemia in Adults (2016 Revision)* [8].

Exclusion criteria: Patients that had taken anticoagulants in the past half-year; Patients with previous acute myocardial infarction and cerebrovascular accidents; Patients with secondary hypertension and hypertensive crisis; Patients with severe heart, liver and lung failure; Patients complicated with malignant tumors; Pregnant women.

Treatment methods

Patients in the EXP group were orally administrated the huanglian lipid-lowering mixture. It was uniformly prepared and decocted by Maternity and Child Health Care of Zaozhuang. The huanglian lipid-lowering mixture included 20 g of Rhizoma Coptidis, 8 g of Gastrodia elata, 16 g of Pueraria lobata, 12 g of dried tangerine or orange peels, 10 g of Rhizoma Pinelliae Preparata, and 10 g of Panax Notoginseng (Traditional Chinese Medicines were purchased from Nanjing Haichang Chinese Medicine Group Corporation). Each dose was decocted twice and filtered with a final volume for oral administration of 100 mL, once daily. One course of treatment was 2 months.

Patients in the FVT group were orally administrated 40 mg of fluvastatin capsules (Lescol, Beijing Novartis Pharma Co., Ltd.), once daily in the morning. One course of treatment was 2 months.

Patients in the ACEI group were orally administrated 12.5 mg of captopril 2 (Sino-US Shanghai Bristol-Myers Squibb Pharmaceutical Co., Ltd.), once daily in the morning. One course of treatment was 2 months.

Fasting venous blood before treatment (T0) and after 1 (T1), 2 (T2), and 3 (T3) courses of treatment was extracted. The blood was allowed to stand in sodium citrate tubes for anticoagulation for 2 hours. Afterward, the blood was centrifuged and serum was collected, detecting serum triglycerides (TG), total cholesterol (TC), low density lipoprotein (LDL), and high density lipoprotein (HDL) (operations were carried out in strict accordance with kit instructions of kits; Kits were purchased from Shanghai Westang Bio-Tech Co., Ltd.) using enzyme-linked immunosorbent assays (ELISA).

Outcome measures

Main outcome measures included fasting TG, TC, LDL, HDL, and mean arterial pressure (MAP) before treatment and after 1, 2, and 3 courses of treatment.

Secondary outcome measures included general information and adverse reactions.

Statistical methods

SPSS19.0 was used to analyze data. Measurement data are expressed as mean ± standard deviation ($\bar{x}$±sd) and one-way analysis of variance (ANOVA) was used for comparisons between groups. Paired t-tests were used for comparisons within groups. After ANOVA, LSD-post-hoc-t tests were used for comparisons between the three groups if results were signifi-

Table 1. Comparison of general information

	FVT group (n=30)	EXP group (n=30)	ACEI group (n=30)	F/χ^2	P
Gender (male/female)	19/11	18/12	14/16	0.071	0.791
Age (year)	45.2±4.5	43.7±4.8	44.2±4.4	1.249	0.217
BMI (kg/m^2)	30.4±3.10	31.2±2.75	29.8±3.52	1.067	0.294
Complication (n)					
Cerebral infarction	2	4	3	0.741	0.389
Coronary heart disease	6	5	4	0.111	0.739
Fatty liver	15	12	16	0.606	0.436
Liver cirrhosis	4	5	5	0.131	0.718

Note: BMI, body mass index = weight (kg)/height (m^2).

Table 2. Comparison of triglycerides

	FVT group (n=30)	ACEI group (n=30)	EXP group (n=30)	F	P
T0	13.45±2.33	13.56±2.51	14.32±2.81	4.92	0.861
T1	9.32±1.42$^{\Delta\Delta\Delta,***}$	12.43±2.41	9.25±1.52$^{\Phi\Phi\Phi,\#\#\#}$	62.48	<0.001
T2	5.21±1.13$^{\Delta\Delta\Delta,***}$	13.25±2.32	5.53±1.42$^{\Phi\Phi\Phi,\#\#\#}$	307.4	<0.001
T3	2.09±0.44$^{\Delta\Delta\Delta,***}$	12.35±2.04	2.14±0.73$^{\Phi\Phi\Phi,\#\#\#}$	304.2	<0.001
F	328.500	1.998	256.500		
P	<0.001	0.723	<0.001		

Note: Compared with T0 in FVT group, $^{\Delta\Delta\Delta}$P<0.001; compared with T0 in EXP group, $^{\Phi\Phi\Phi}$P<0.001; ***P<0.001: FVT group vs. ACEI group; $^{\#\#\#}$P<0.001: EXP group vs. ACEI group. T0, before the treatment; T1, after 1 course of treatment; T2, after 2 courses of treatment; T3, after 3 courses of treatment.

Table 3. Comparison of total cholesterol

	FVT group (n=30)	ACEI group (n=30)	EXP group (n=30)	F	P
T0	25.44±5.40	25.32±3.44	24.62±5.22	4.72	0.611
T1	20.43±4.51$^{\Delta\Delta\Delta,***}$	24.33±3.32	21.53±4.36$^{\Phi\Phi\Phi,\#\#\#}$	32.75	<0.001
T2	12.44±3.21$^{\Delta\Delta\Delta,***}$	23.21±3.31	13.62±3.15$^{\Phi\Phi\Phi,\#\#\#}$	283.0	<0.001
T3	5.32±1.32$^{\Delta\Delta\Delta,***}$	20.34±2.34	5.92±1.29$^{\Phi\Phi\Phi,\#\#\#}$	154.6	<0.001
F	274.300	1.420	146.200		
P	<0.001	0.632	<0.001		

Note: Compared with T0 in FVT group, $^{\Delta\Delta\Delta}$P<0.001; compared with T0 in EXP group, $^{\Phi\Phi\Phi}$P<0.001; ***P<0.001: FVT group vs. ACEI group; $^{\#\#\#}$P<0.001: EXP group vs. ACEI group. T0, before the treatment; T1, after 1 course of treatment; T2, after 2 courses of treatment; T3, after 3 courses of treatment.

cant. Count data are expressed as the number of cases/percentage (n/%) and were tested with Chi-square tests. P<0.05 indicates statistically significant differences.

Results

No significant differences in the general data between the two groups

There were no significant differences in general information between the three groups (all P>0.05). Details are shown in **Table 1**.

Huanglian lipid-lowering mixture can reduce the content of TG and TC

Before treatment, there were no significant differences in TG and TC levels between the three groups (all P>0.05). After 1, 2, and 3 courses of treatment, there were no significant differences between EXP and FVT groups in TG and TC levels (all P>0.05). Levels in the FVI group were significantly lower than those in the ACEI group (P< 0.001). Levels in the EXP group were significantly lower than those in the ACEI group (P<0.001). In EXP and FVT groups, TG and TC levels after 1, 2, and 3 courses of treatment were lower than those before treatment (P<0.001). In the ACEI group, there were no significant differences in TG and TC levels at each time point (P>0.05). Details are shown in **Tables 2**, **3** and **Figure 1**.

Huanglian lipid-lowering mixture can reduce the content of LDL and HDL

Before treatment, there were no significant differences in LDL and HDL levels between the three groups (P>0.05). After 1, 2, and 3 courses of treatment, LDL levels in the EXP group were significantly lower than those in the ACEI group. HDL levels were significantly higher than those in the ACEI group (P<0.001). LDL levels in the FVT group were significantly lower than those in the ACEI group. HDL levels were significantly higher than those in the ACEI group (P<0.001). There were no significant differences in LDL and HDL levels between FVT and EXP

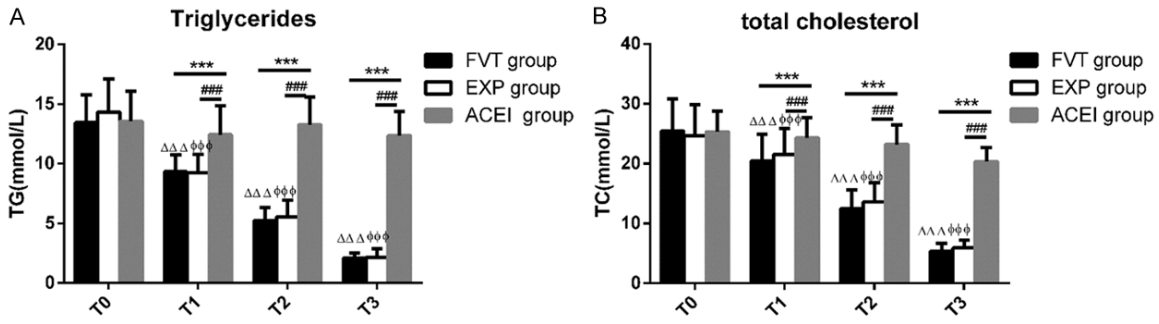

Figure 1. Comparison of triglycerides and total cholesterol. Compared with T0 in FVT group, $^{\Delta\Delta\Delta}P<0.001$; compared with T0 in EXP group, $^{\Phi\Phi\Phi}P<0.001$; $^{***}P<0.001$: FVT group vs. ACEI group; $^{\#\#\#}P<0.001$: EXP group vs. ACEI group. T0, before the treatment; T1, after 1 course of treatment; T2, after 2 courses of treatment; T3, after 3 courses of treatment.

Table 4. Comparison of low density lipoprotein

	FVT group (n=30)	ACEI group (n=30)	EXP group (n=30)	F	P
T0	14.55±2.32	13.43±2.03	15.22±2.62	3.07	0.178
T1	$10.32\pm2.11^{\Delta\Delta\Delta,***}$	13.24±2.34	$11.43\pm2.03^{\Phi\Phi\Phi,\#\#\#}$	61.10	<0.001
T2	$6.33\pm1.23^{\Delta\Delta\Delta,***}$	12.45±1.87	$6.76\pm0.82^{\Phi\Phi\Phi,\#\#\#}$	321.50	<0.001
T3	$3.54\pm0.45^{\Delta\Delta\Delta,***}$	12.52±2.13	$3.35\pm0.25^{\Phi\Phi\Phi,\#\#\#}$	187.40	<0.001
F	239.300	1.686	277.800		
P	<0.001	0.174	<0.001		

Note: Compared with T0 in FVT group, $^{\Delta\Delta\Delta}P<0.001$; compared with T0 in EXP group, $^{\Phi\Phi\Phi}P<0.001$; $^{***}P<0.001$: FVT group vs. ACEI group; $^{\#\#\#}P<0.001$: EXP group vs. ACEI group. T0, before the treatment; T1, after 1 course of treatment; T2, after 2 courses of treatment; T3, after 3 courses of treatment.

Table 5. Comparison of high density lipoprotein

	FVT group (n=30)	ACEI group (n=30)	EXP group (n=30)	F	P
T0	0.24±0.02	0.23±0.01	0.34±0.04	3.546	0.156
T1	$0.32\pm0.03^{\Delta\Delta\Delta,***}$	0.25±0.02	$0.45\pm0.05^{\Phi\Phi\Phi,\#\#\#}$	314.6	<0.001
T2	$0.52\pm0.04^{\Delta\Delta\Delta,***}$	0.23±0.03	$0.68\pm0.06^{\Phi\Phi\Phi,\#\#\#}$	1435.22	<0.001
T3	$1.25\pm0.10^{\Delta\Delta\Delta,***}$	0.28±0.04	$1.34\pm0.22^{\Phi\Phi\Phi,\#\#\#}$	1116.34	<0.001
F	1967.00	22.33	429.300		
P	<0.001	0.079	<0.001		

Note: Compared with T0 in FVT group, $^{\Delta\Delta\Delta}P<0.001$; compared with T0 in EXP group, $^{\Phi\Phi\Phi}P<0.001$; $^{***}P<0.001$: FVT group vs. ACEI group; $^{\#\#\#}P<0.001$: EXP group vs. ACEI group. T0, before the treatment; T1, after 1 course of treatment; T2, after 2 courses of treatment; T3, after 3 courses of treatment.

groups (P>0.05). In EXP and FVT groups, LDL levels after 1, 2, and 3 courses of treatment were lower than those before treatment. HDL levels were significantly higher than those before treatment (P<0.001). In the ACEI group, there were no significant differences in LDL and HDL levels at each time point (P>0.05). Details are shown in **Tables 4**, **5** and **Figure 2**.

Huanglian lipid-lowering mixture can reduce blood pressure

Before treatment, there were no significant differences in MAP levels between the three groups (P>0.05). After 1, 2, and 3 courses of treatment, MAP levels in the ACEI group was lower than those in the FVT group. Levels in the EXP group were significantly lower than those in the FVT group (P<0.001). In the FVT group, there were no statistically significant differences in MAP levels before treatment and after 1, 2, and 3 courses of treatment (P>0.05). In EXP and ACEI groups, MAP levels after 1, 2, and 3 courses of treatment were lower than those before treatment (P< 0.001). Details are shown in **Table 6** and **Figure 3**.

Huanglian lipid-lowering mixture will not increase adverse reactions

There were no statistically significant differences in total adverse reactions between the three groups (P=0.954). Details are shown in **Table 7**.

Discussion

Previous studies have shown that hyperlipidemia complicated with hypertension is more

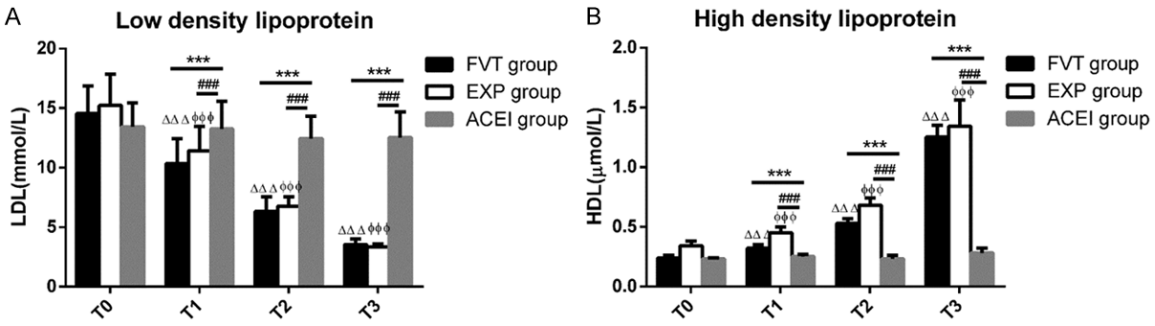

Figure 2. Comparison of low density lipoprotein and high density lipoprotein. Compared with T0 in FVT group, $^{\Delta\Delta\Delta}$P<0.001; compared with T0 in EXP group, $^{\Phi\Phi\Phi}$P<0.001; ***P<0.001: FVT group vs. ACEI group; $^{###}$P<0.001: EXP group vs. ACEI group. T0, before the treatment; T1, after 1 course of treatment; T2, after 2 courses of treatment; T3, after 3 courses of treatment.

Table 6. Comparison of mean arterial pressure

	FVT group (n=30)	ACEI group (n=30)	EXP group (n=30)	F	P
T0	185.22±12.23	178.35±13.21	183.35±10.22	77.54	0.071
T1	162.32±10.41	134.43±12.34^{bbb,***}	140.62±9.34$^{\Phi\Phi\Phi,\&\&\&}$	88.92	<0.001
T2	155.31±7.33	95.42±5.42^{bbb,***}	100.35±8.12$^{\Phi\Phi\Phi,\&\&\&}$	1420.20	<0.001
T3	140.34±4.35	75.56±4.44^{bbb,***}	83.32±5.32$^{\Phi\Phi\Phi,\&\&\&}$	670.50	<0.001
F	12.670	658.600	836.400		
P	0.063	<0.001	<0.001		

Note: Compared with T0 in EXP group, $^{\Phi\Phi\Phi}$P<0.001; compared with T0 in ACEI group, ^{bbb}P<0.001; ***P<0.001: FVT group vs. ACEI group; $^{\&\&\&}$P<0.001: EXP group vs. FVT group. T0, before the treatment; T1, after 1 course of treatment; T2, after 2 courses of treatment; T3, after 3 courses of treatment.

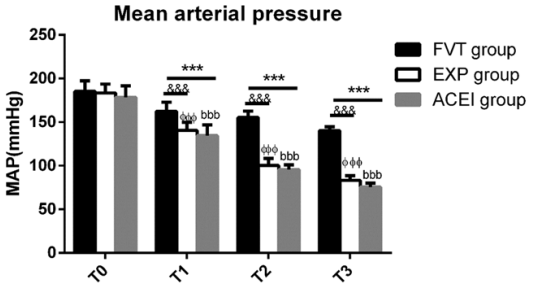

Figure 3. Comparison of mean arterial pressure. Compared with T0 in EXP group, $^{\Phi\Phi\Phi}$P<0.001; compared with T0 in ACEI group, ^{bbb}P<0.001; ***P<0.001: FVT group vs. ACEI group; $^{\&\&\&}$P<0.001: EXP group vs. FVT group. T0, before the treatment; T1, after 1 course of treatment; T2, after 2 courses of treatment; T3, after 3 courses of treatment.

and more common and that the two diseases are closely related [9]. Patients with hypertension are often accompanied by disorders of lipid metabolism. Cholesterol and TG in the blood are significantly increased. Patients with hyperlipidemia are often accompanied by significant increases in blood pressure caused by atherosclerosis [10]. Abnormal lipid metabolism accelerates atherosclerosis, narrows lumen of the blood vessels, and increases MAP significantly [11]. Therefore, patients diagnosed with hyperlipidemia should pay attention to the management of cholesterol. They should regularly test blood lipids and adjust diets. If necessary, drugs should be used to prevent hypertension caused by blood lipids from the source [12].

Huanglian lipid-lowering mixture, a Traditional Chinese Medicine formula, clears away heat and toxic materials, promotes blood circulation, and removes blood stasis. Rhizoma Coptidis, with the largest content in the mixture, is the main component for lowering blood lipids. According to previous studies, Rhizoma Coptidis improves the sensitivity of LDL receptors and improves the lipid-lowering function. Gastrodia elata dispels internal wind, enters the liver meridian, and strengthens the lipid-lowering function. Gastrodin inhibits the absorption of exogenous blood lipids and reduces TG and cholesterol [13, 14]. Rhizoma Pinelliae Preparata and dried tangerine or orange peels enter the lungs and spleen meridian. They regulate qi, eliminate dampness, and significantly lower blood lipids of patients with arteriosclerosis via strengthening cholesterol metabolism and pro-

Table 7. Comparison of adverse reactions

Adverse reactions (n)	FVT group (n=30)	EXP group (n=30)	ACEI group (n=30)	t/χ^2	P
Gastrointestinal reaction	6	5	4	0.111	0.739
Elevated cereal third transaminase	5	3	3	0.577	0.448
Elevated aspartate aminotransferase	3	4	5	0.162	0.688
Nervous system	2	4	5	0.741	0.389
Rash	3	2	2	0.218	0.640
Total	19	18	19	0.095	0.954

moting cholesterol to be converted into bile acids [15-17]. Panax Notoginseng, which has significant regulatory function effects in patients with coagulation disorders and hypertension, relieves atherosclerosis because it reduces blood pressure, dilates blood vessels, and inhibits thrombosis through dilating peripheral arteries [18-20].

Hyperlipidemia complicated with hypertension is currently treated by statins. These inhibit the synthesis of methylglutaryl coenzyme A and endogenous cholesterol, reducing cholesterol in liver cells, concentrations of plasma TC, and serum lipid levels, according to pharmacological studies [21, 22]. However, statins do not affect blood pressure. In studies by Xia A and Herd JA et al., fluvastatin reduced TC and LDL levels and relieved atherosclerosis in patients with atherosclerosis [23, 24]. In this study, fluvastatin reduced LDL levels but increased HDL levels in patients with hyperlipidemia. However, statins cause adverse reactions, including gastrointestinal reactions, abnormal liver function, and rashes, while lowering blood pressure. According to Fei L and Jick H et al., long-term use of statins leads to abnormal liver function, possibly because metabolic products of statins after hepatic biotransformation have a significant regulatory function on excessive TG and LDL after blood circulation. In addition, the release of liver enzymes results in significant increases in glutamic pyruvic transaminase and glutamic oxaloacetic transaminase in the blood circulation [25, 26]. In the current study, patients with abnormal liver function were 10% after taking statins for 3 courses of treatment. There were no significant differences in adverse reactions caused by huanglian lipid-lowering mixture and statins. This is possibly because huanglian lipid-lowering mixture after liver metabolism greatly affects liver function [27]. Therefore, huanglian lipid-lowering mixture effectively reduces TG, TC, LDL, and MAP levels and increases HDL levels in patients with hypertension complicated with hyperlipidemia. Thus, it is an effective treatment worthy of promotion.

Disclosure of conflict of interest

None.

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