CORRELATION BETWEEN SERUM CTRP9 LEVEL AND BLOOD PRESSURE, BLOOD GLUCOSE, LDL AND INSULIN RESISTANCE IN PATIENTS WITH PRIMARY HYPERTENSION

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ABSTRACT

Objective: *To study the correlation between serum CTRP9 level and blood pressure, blood glucose, LDL and insulin resistance in patients with primary hypertension.*

Methods: *A test group enrolled 120 patients with primary hypertension who underwent cardiovascular medicine in our hospital from August 2018 to August 2019. Sixty healthy people in the physical examination centre of our hospital were selected as the control group in the same period. The venous blood samples from the two groups were taken, and the differences of serum C1q/TNF-related protein 9 (CTRP9), blood pressure, blood glucose, LDL and insulin resistance between the two groups were detected and compared. The correlation between serum CTRP9 level and blood pressure, blood glucose, LDL and insulin resistance in patients with primary hypertension was studied.*

Results: *The systolic blood pressure, diastolic blood pressure, mean arterial pressure, insulin resistance index, fasting plasma glucose (FPG), LDL and serum hs-CRP levels in the test group were higher than those in the control group (P<0.05 or <0.01). The serum level of CTRP9 in patients in the test group was lower than that in the control group (P<0.01). There was no significant difference in serum HDL levels between the two groups (P>0.05). The levels of the insulin resistance index (HOMA-IR) and serum hs-CRP in hypertension grade 1 group were lower than those in the hypertension grade 2, and the levels in the hypertension grade 2 group were lower than in the hypertension grade 3 group (P<0.05 or <0.01). The level of serum CTRP9 in patients with hypertension grade 1 was higher than that in hypertension grade 2 group, the level in the hypertension grade 2 group was higher than the hypertension grade 3 group, (P<0.01). Pearson correlation analysis showed that serum CTRP9 was negatively correlated with mean arterial pressure, fasting blood glucose, LDL, HOMA-IR, and hs-CRP (P<0.05 or 0.01).*

Conclusion: *Serum CTRP9 levels in patients with primary hypertension are lower than those in healthy people and negatively correlated with blood pressure, blood glucose, LDL and insulin resistance.*

Keywords: *Primary hypertension, CTRP9, blood pressure, blood glucose, LDL, insulin resistance.*

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Introduction

Primary hypertension is a hypertensive disease caused by a combination of factors such as heredity, living habits and environment and is the most common type of hypertension in the clinic[(1)]. Most primary hypertension has characteristic pathological manifestations such as remodelling of vascular structure, hypertrophy and atheromatous plaques, which can cause serious damage to target organs such as heart, brain blood vessels, blood vessels, kidneys and fundus. Studies have shown that more than half of cardiovascular diseases are caused by high blood pressure, and hypertension has become an independent risk factor for atherosclerosis[(2)]. In recent years, China's economy has developed rapidly and the people's living standards have improved substantially.

The prevalence of primary hypertension has also increased year by year, which brings grief and a heavy financial burden to many families and has aroused widespread concern in the medical community[(3)]. C1q/TNF-related protein 9 (CRP/9) is a novel adipocytokine that is homologous to

adiponectin and is mainly secreted by adipose tissue and vascular basal cells[4]. Some research has found that CTRP9 is highly expressed in the cardiovascular system and is closely related to primary hypertension[5]. This study was conducted to explore the correlation between the expression of serum CTRP9 and blood pressure, blood glucose, LDL and insulin resistance in patients with primary hypertension.

Materials and methods

General data

A test group enrolled 120 patients with primary hypertension who were treated in our Department of Cardiology from August 2018 to August 2019.

Inclusion criteria:

• All patients with primary hypertension met the diagnostic criteria of the Chinese Guidelines for the Prevention and Treatment of Hypertension;

• Patients who had systolic blood pressure ≥140mm Hg and or a diastolic blood pressure ≥90mm Hg when their upper arm radial artery blood pressure was measured twice in a quiet environment;

• Patients and their families have been informed and signed informed consent.

Exclusion criteria:

• Those who has previous cerebral infarction or cerebral haemorrhage;

• Patients with diabetes;

• Patients with secondary hypertension;

• Those with severe liver and kidney dysfunction;

• Those with severe blood disease; patients who received blood-pressure-lowering medication within one month;

• Those with thyroid dysfunction;

• Those with severe arrhythmia, congenital viscera and heart failure;

• Those with malignant tumours;

• Pregnant women.

The study group comprised 64 males and 56 females with an average age of 62.25±10.45 years and an average BMI of 20.12±1.31 Kg/m^2.

In the same period, 60 healthy people in the physical examination centre of our hospital were selected as the control group, including 32 males and 28 females.

The average age was 61.95±11.15 years old, and the average BMI was 20.34±1.08 Kg/m^2. There were no significant differences in the general data of age, gender and BMI between the two groups (P>0.05). See Table 1.

Groups	Age (years)	Gender (cases)		BMI value (kg/m^2)
		Male	Female	
Control group (n = 60)	61.95±11.15	32	28	20.34±1.08
Test group (n = 120)	62.25±10.45	64	56	20.12±1.31
t/χ^2	0.178	0.281		1.124
P	0.861	0.597		0.260

Table 1: Comparison of general data between the two groups ($\bar{x}\pm s$).

Observation indicators

A sample of 5 ml of fasting venous blood was collected from each subject admitted to our hospital for at least 24 hours. The sample was allowed to stand at room temperature for 2 h, then centrifuged at 1000 r/min for 15 min. The upper serum was taken carefully and refrigerated at –80 °C to avoid repeated freezing and thawing. Serum CTRP9 levels were detected by enzyme-linked immunosorbent assay (ELISA), fasting insulin (FINS) was detected by radioimmunoassay, and low-density lipoprotein (LDL), fasting blood glucose (FPG), hypersensitive C-reactive protein (hs-CRP) and high-density lipoprotein cholesterol (HDL) were measured by an automatic biochemical analyzer.

Blood pressure

The subject was placed in a supine position, lying flat and resting for 30 min. The upper arm radial artery blood pressure was measured twice with an interval of 5 min, and the average value was taken as the final blood pressure value. The mean arterial pressure was calculated using the formula:

Mean arterial pressure = [systolic blood pressure + 2 × diastolic blood pressure]/3.

Insulin resistance

Insulin resistance was measured by the insulin resistance index (HOMA-IR), in which HOMA-IR = FPG × FINS/22.5. The differences of serum CTRP9, blood pressure, blood glucose, LDL and insulin resistance between the two groups were compared. The differences of serum CTRP9, hs-CRP and HOMA-IR in patients with different grades of hypertension were studied. Correlations between serum CTRP9 and blood pressure, blood sugar, LDL, and insulin resistance in patients with primary hypertension were studied.

Statistical methods

Statistical data analysis was performed using the SPSS 20.0 software package. One-way ANOVA

and t-tests were used to compare the measurement data. The χ^2 test was used to compare the count data.

Pearson correlation analysis was used to study the correlation between serum CTRP9 levels and blood pressure, blood glucose, LDL, and insulin resistance. The statistical results were statistically significant at P<0.05.

Results

Comparison of serum CTRP9, blood glucose, LDL, blood pressure and HOMA-IR between the two groups

The systolic blood pressure, diastolic blood pressure, mean arterial pressure, HOMA-IR, FPG, LDL and serum hs-CRP levels in the test group were higher than those in the control group, and the difference was statistically significant (P<0.05 or <0.01). The serum level of CTRP9 in patients with primary hypertension in the test group was lower than that of patients in the control group, and the difference was statistically significant (P<0.01). There was no significant difference in serum HDL levels between the two groups (P>0.05). See Tables 2 and 3.

Groups	Blood pressure (mmHg)			CTRP9 (ng/mL)
	Systolic pressure	Diastolic pressure	Mean arterial pressure	
Control group (n = 60)	116.26±10.51	81.98±9.58	93.41±9.85	148.36±30.15
Test group (n = 120)	176.39±11.52	98.37±10.28	124.38±10.69	121.78±18.49
t	33.969	10.311	18.799	7.303
P	< 0.001	< 0.001	< 0.001	< 0.001

Table 2: Comparison of blood pressure and serum CTRP9 between the two groups ($\bar{x}\pm s$).

Groups	HOMA-IR	LDL (mol/L)	HDL (mol/L)	hs-CRP (mg/L)	FPG (mmol/L)
Control group (n = 60)	0.91±0.31	1.85±0.28	1.08±0.21	0.95±0.29	5.01±0.59
Test group (n = 120)	2.18±0.48	2.18±0.19	1.11±0.19	1.33±0.31	5.26±0.56
t	18.63	9.322	0.964	7.918	2.773
P	< 0.001	< 0.001	0.347	< 0.001	0.006

Table 3: Comparison of other test indicators between the two groups ($\bar{x}\pm s$).

Comparison of serum CTRP9, hs-CRP and HOMA-IR in patients with different grades of hypertension

Patients with primary hypertension were divided into three subgroups according to their grade of hypertension: hypertension grade 1 group (n = 42), hypertension grade 2 group (n = 41), and hypertension grade 3 group (n = 37). The differences of serum CTRP9, insulin resistance and HOMA-IR were compared between the three subgroups of hypertensive patients. The levels of HOMA-IR and serum hs-CRP in patients in the hypertension grade 1 group were lower than those in the grade 2 and grade 3 groups. The levels in patients in the hypertension grade 2 group were lower than those in the grade 3 group, and the difference was statistically significant (P<0.05 or <0.01). The level of serum CTRP9 in patients in the hypertension grade 1 group was higher than in the hypertension grade 2 and grade 3 groups. The level in patients in the grade 2 group was higher than in grade 3 group, and the difference was statistically significant (P<0.01). See Table 4.

Groups	HOMA-IR	CTRP9	hs-CRP
Hypertension grade 1 group (n = 42)	1.85±0.39	141.36±30.95	1.13±0.34
Hypertension grade 2 group (n = 41)	2.11±0.41[a]	128.74±30.78[a]	1.31±0.28[a]
Hypertension grade 3 group (n = 37)	2.56±0.45[ab]	109.85±26.6[ab]	1.47±0.38[ab]
F	29.06	11.19	10.23
P	< 0.001	< 0.001	0.001

Table 4: Comparison of serum CTRP9, hs-CRP and HOMA-IR in hypertensive patients with different blood pressure grading ($\bar{x}\pm s$).

Note: a indicates that compared with the hypertension grade 1 group, [a]P<0.05 and b indicates compared with the hypertension grade 2 group, [b]P<0.05.

Correlation analysis between serum CTRP9 and mean arterial blood pressure, fasting blood glucose, LDL and HOMA-IR

Pearson correlation analysis showed that CTRP9 was negatively correlated with mean arterial pressure, fasting blood glucose, LDL, HOMA-IR, and hs-CRP (P<0.05 or 0.01). See Table 5.

Indicators		HOMA-IR	hs-CRP	Mean arterial pressure	Fasting blood glucose	LDL
CTRP9	*r*	– 0.259	– 0.369	– 0.358	– 0.241	– 0.261
	P	0.003	< 0.001	0.023	0.043	0.012

Table 5: Correlation analysis between serum CTRP9 and mean arterial blood pressure, fasting blood glucose, LDL and HOMA-IR.

Discussion

LDL is a lipoprotein particle that carries cholesterol into peripheral tissue cells and can be oxidized to oxidized low-density lipoprotein. An LDL level that is too high can lead to hypertension, arteriosclerosis, coronary heart disease, stroke and peripheral

arterial disease and can also increase the risk of the heart[6]. Insulin resistance refers to the lack of factors that promote the uptake and utilization of glucose so that patients can compensate for excessive insulin to maintain blood sugar stability, leading to hyperinsulinemia. Insulin resistance easily leads to metabolic diseases, such as hypertension[7]. More studies have shown that serum hs-CRP levels are independent predictive risk factors for primary hypertension, stroke, peripheral arterial disease in patients with no significant cardiovascular disease and in coronary artery disease (CAD) patients[8, 9].

CTRP9 is located on chromosome 13 and is a core member of the C1q/tumour necrosis factor-related protein family. CTRP9 also an independent protective factor for hypertension, coronary heart disease and obesity-related diseases[10, 11], has a positive effect on the body, can reduce the expression of macrophage pro-inflammatory factors and inhibit the inflammatory response, which has a certain improvement function on vascular endothelial cell function. CTRP9 can relax blood vessels, improve vascular remodelling, inhibit apoptosis and reduce the ischemic injury of the body, thereby improving cardiac function, which plays an important role in regulating lipid metabolism and insulin resistance[12–14]. Studies have found that CTRP can induce endothelial cell type nitric oxide synthase phosphorylation, induce endothelial cells to produce nitric oxide, induce a relaxation effect on vascular smooth muscle, and improve the vascular oxidative stress state of the body[15].

In this study, the levels of HOMA-IR, FPG, LDL, and serum hs-CRP in patients with primary hypertension were higher than those in healthy subjects, and the difference was statistically significant ($P<0.05$ or <0.01). The levels of serum CTRP9 in primary hypertension patients were lower than those in the control group, and the difference was statistically significant ($P<0.01$). The level of serum CTRP9 in patients with hypertension grade 1 was higher than that in grade 2 and grade 3. The level in patients with grade 2 was higher than that of patients with grade 3, and the difference was statistically significant ($P<0.01$). These findings suggest that patients with primary hypertension have a certain inflammatory reaction, insulin resistance is decreased, and there is a certain degree of arteriosclerosis. CTRP9 can regulate the vasomotor activity of the body and affect blood pressure to a certain extent. Pearson correlation analysis conducted in this study indicated that serum CTRP9 was negatively correlated with mean arterial pressure, fasting blood glucose, LDL, HOMA-IR, and hs-CRP ($P<0.05$ or 0.01). The negative correlation suggests that CTRP9 can inhibit the inflammatory response to increase the body's sensitivity to insulin, lower blood sugar levels, improve insulin resistance, reduce blood pressure and slow the occurrence and progression of hypertension.

In summary, the serum levels of CTRP9 in patients with primary hypertension was lower and decreased with higher blood pressure levels. The serum levels of CTRP9 are negatively correlated with blood pressure, blood glucose, LDL, and insulin resistance. CTRP9 can improve insulin resistance, decrease the LDL level and slow down the body's inflammatory response and regulate blood pressure by decreasing blood glucose. Lower blood glucose can lead to lower blood pressure and a better classification of primary hypertension and play an important role in the evaluation and treatment of primary hypertension.

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