CORRELATION BETWEEN SERUM IRREGULAR CHEMOKINE FRACTALKINE AND HS-CRP, ET-1, ADMA LEVELS IN PATIENTS WITH ESSENTIAL HYPERTENSION

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ABSTRACT

Objective: *To study the correlation between the serum irregular chemokine fractalkine (FKN) and hypersensitive C-reactive protein (hs-CRP), endothelin-1 (ET-1), and dimethylarginine (ADMA) in patients with essential hypertension.*

Methods: *From July 2018 to July 2019, 98 patients with essential hypertension who were treated in the cardiovascular department of our hospital were selected as the study group. Forty healthy people who were examined in the physical examination center of our hospital were selected as the control group. The levels of FKN, hs-CRP, ET-1, and ADMA were detected using an enzyme-linked immunosorbent assay (ELISA) and high-performance liquid chromatography (HPLC), respectively. The levels of FKN, hs-CRP, ET-1, and ADMA at admission were compared between the two groups; the differences of blood pressure between the two groups were compared; the relation between FKN and systolic blood pressure, diastolic blood pressure, hs-CRP, ET-1, and ADMA was analyzed by a Pearson correlation.*

Results: *FKN, hs-CRP, ET-1, and ADMA in the study group were significantly higher than those in the control group ($P<0.01$). The mean systolic pressure and diastolic pressure in the study group were higher compared to the control group ($P<0.01$). Pearson correlation analysis showed that FKN was positively correlated with systolic ($r = 0.705$, $P < 0.01$) and diastolic ($r = 0.425$, $P<0.01$) blood pressure. FKN was positively correlated with hs-CRP ($r=0.341$, $P<0.01$), ET-1 ($r=0.468$, $P<0.01$), and ADMA ($r=0.442$, $P<0.01$).*

Conclusion: *The serum FKN level of patients with essential hypertension was higher than that of healthy people and was positively correlated with systolic blood pressure, diastolic blood pressure, hs-CRP, ET-1, and ADMA levels. FKN can be used as an effective index for the detection, evaluation, and treatment of essential hypertension.*

Keywords: *Essential hypertension, fractalkine, hs-CRP, ET-1, ADMA, correlation.*

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Introduction

Hypertension is a progressive cardiovascular syndrome caused by a variety of factors and can lead to changes in blood vessels and heart function structure[(1)]. Essential hypertension is a kind of hypertension disease caused by many factors such as heredity, living habits, and environment. It is the most common hypertension observed in clinics. The proportion of essential hypertension is 90–95% of the hypertension population[(2)]. Essential hypertension is more common in middle-aged and elderly people, its onset is insidious, and progress is slow. The course of the disease is more than ten years to decades. It can cause headache, dizziness, head swelling, insomnia, forgetfulness, dazzling, fatigue, excitement, and other neurological symptoms[(3)]. Long-term serious complications such as heart disease, arrhythmia, chronic renal failure, cerebral hemorrhage, and cerebral infarction can occur[(4)]. In recent years, the prevalence of essential hypertension has been increasing yearly, and the

disability rate and mortality rate are high, which brings grief and heavy economic burden to countless families. Therefore, the main purpose of treating essential hypertension is to minimize the total risk of cardiovascular death and disability[5]. FKN is a kind of macromolecular protein comprising 373 amino acids, which contain many domains. Studies have shown that FKN is highly expressed in patients with essential hypertension[6].

Hypersensitive C-reactive protein (hs-CRP), also referred to as hypersensitive C-reactive protein, is a non-specific marker of the acute phase of systemic inflammatory response. It is mainly synthesized by the liver and is one of the most powerful predictors of cardiovascular event risk[7]. Endothelin (ET) is widely found in various vascular endothelia, tissues, and cells, can maintain basic vascular tension and cardiovascular system homeostasis, and is an important factor regulating cardiovascular function[8]. Dimethylarginine (ADMA) is a newly recognized risk factor of cardiovascular disease and can induce various cardiovascular diseases through a number of mechanisms[9]. We studied the correlation between serum FKN and hs-CRP, ET-1, and ADMA in patients with essential hypertension.

Materials and methods

General information

From July 2018 to July 2019, 98 patients with essential hypertension treated in the cardiovascular department of our hospital were selected as the study group.

Inclusion criteria:

• All patients with essential hypertension met the guidelines for prevention and treatment of hypertension in China issued in 2010;

• Three measurements of systolic blood pressure ≥ 140mmHg and diastolic blood pressure ≥90mmHg without taking antihypertensive drugs within 2 months;

• Age between 20-85 years;

• Patients and their families were informed and signed informed consent;

• No symptoms of heart failure.

Exclusion criteria:

• Secondary hypertension;

• Patients with diabetes mellitus;

• Pregnant women;

• Patients with serious liver and kidney dysfunction;

• Patients with abnormal thyroid function;

• Patients with malignant tumors;

• Patients with serious blood diseases;

• Patients who received antihypertensive drugs within one month;

• Patients who did not cooperate with the test.

The participants comprised 50 males and 48 females, with an average age of 55.45±6.25 years, an average BMI of 20.12±1.26 kg/m^2, a fasting blood glucose of 5.26±0.46 mmol/L, and a blood glucose concentration of 7.49±0.68 mmol/L for two hours after a meal. At the same time, 40 healthy people were selected as the control group, including 22 males and 18 females, with an average age of 54.9±7.05 years, an average BMI of 20.15±1.43 kg/m^2, a fasting blood glucose concentration of 5.30±0.54 mmol/L, and a two-hour postprandial blood glucose concentration of 7.53±0.71 mmol/L. There was no significant difference in age, gender, and BMI between the two groups (P>0.05). See Table 1.

Group	Age (years)	Gender (cases)		BMI value (kg/m^2)	Fasting blood glucose (mmol/L)	Two-hour postprandial blood glucose (mmol/L)
		Male	Female			
Control group (n=40)	54.95± 7.05	22	18	20.15± 1.43	5.30± 0.54	7.53± 0.71
Study group (n=98)	55.45± 6.25	50	48	20.12± 1.26	5.26± 0.46	7.49± 0.68
t/χ^2	0.411	0.182		0.122	0.440	0.310
P	>0.05	>0.05		>0.05	>0.05	>0.05

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

Observation indicators

Five ml of fasting venous blood was collected in the study group before and after treatment, and 5 ml of fasting venous blood was collected in the control group during physical examination. The blood was centrifuged at 4000 r/min for 10 minutes, and the serum was carefully separated and stored at -20 °C to avoid repeated freezing and thawing. An enzyme-linked immunosorbent assay (ELISA) was used to detect the levels of FKN, hs-CRP, and ET-1 in each group of subjects, and high-performance liquid chromatography (HPLC) was used to determine ADMA concentrations in each group of subjects. The mean blood pressure was measured three times without antihypertensive drugs over the course of two months.

FKN, hs-CRP, ET-1, and ADMA levels were compared between the two groups. The differences in systolic and diastolic blood pressure between the two groups were compared. The correlation of FKN with systolic and diastolic blood pressure was

studied by a Pearson correlation analysis, which was also used to analyze the correlation between FKN and hs-CRP, ET-1, and ADMA.

Statistical methods

The SPSS 20.0 software package was used for statistical data analysis, and a single-factor analysis of variance and LSD t-test were used for data comparisons. A χ^2 test was used for counting data comparisons. Pearson correlation was used to analyze the correlation between FKN and systolic, diastolic, hs-CRP, ET-1, and ADMA levels in patients with essential hypertension. Results with P<0.05 were statistically significant.

Results

Comparison of serum FKN, hs-CRP, ET-1, and ADMA levels between the two groups

The levels of FKN, hs-CRP, ET-1, and ADMA in the study group were significantly higher than those in the control group (P<0.01). See Table 2.

Group	FKN (pg/mL)	hs-CRP (mg/L)	ET-1 (pg/mL)	ADMA (μmol/L)
Control group (n=40)	143.25±74.36	3.11±0.84	42.58±5.21	0.24±0.08
Study group (n=98)	432.51±83.21[a]	8.51±0.59[a]	93.36±11.98[a]	0.51±0.21[a]
t	19.087	42.874	25.787	7.887
P	<0.01	<0.01	<0.01	<0.01

Table 2: Comparison of serum FKN, hs-CRP, ET-1, and ADMA levels between the two groups at admission ($\bar{x}\pm s$). *Note: a indicates the comparison with the control group, [a]P<0.01.*

Comparison of systolic and diastolic blood pressure between both groups

The mean systolic pressure and diastolic pressure in the study group were higher than those in the control group (P<0.01). See Table 3.

Group	Blood pressure (mmHg)	
	Systolic pressure	Systolic pressure
Control group (n=40)	115.36±11.69	115.36±11.69
Study group (n=98)	175.26±14.21[a]	175.26±14.21[a]
t	23.586	23.586
P	<0.01	<0.01

Table 3: Comparison of blood pressure between the two groups ($\bar{x}\pm s$).
Note: a indicates the comparison with the control group, [a]P<0.01.

Pearson correlation of FKN and systolic and diastolic blood pressure

Pearson correlation analysis showed that FKN was positively correlated with systolic (r=0.705, p<0.01) and diastolic (r=0.425, p<0.01) blood pressure. See Table 4.

Indicators	Systolic blood pressure		Diastolic blood pressure	
	r	*P*	r	*P*
FKN	0.705	<0.01	0.425	<0.01

Table 4: Pearson correlation analysis of FKN and systolic and diastolic blood pressure.

Pearson correlation of FKN and hs-CRP, ET-1, and ADMA levels

Pearson correlation analysis demonstrated that FKN was positively correlated with hs-CRP (r = 0.341, p <0.01), ET-1 (r = 0.468, p <0.01), and ADMA (r = 0.442, p <0.01). See Table 5.

Indicators	hs-CRP		ET-1		ADMA	
	r	*P*	r	*P*	r	*P*
FKN	0.341	<0.01	0.468	<0.01	0.442	<0.01

Table 5: Pearson correlation analysis of FKN and hs-CRP, ET-1, and ADMA.

Discussion

Essential hypertension is a multifactorial disease caused by the interaction of some congenital genetic genes, multiple pathogenic supercharging factors, and physiological decompression factors. The pathogenesis of the disease is not clear. The clinical treatment mainly depends on life-long treatment with drugs, which do not effectively cure the disease. The vascular endothelium is an important factor for maintaining the dynamic balance of the vascular wall. Under the stimulation of various harmful factors, the endothelium will adjust to the non-adaptive state, resulting in the increased expression of adhesion and pro-inflammatory factors, thromboxane, higher oxidative stress response, and the abnormal adjustment of vascular tension, leading to vascular endothelial dysfunction. Recent studies have found that vascular endothelial dysfunction, such as abnormal vasoconstriction, platelet aggregation, and increased vascular resistance, can induce the occurrence and progress of essential hypertension[10]. Therefore, the evaluation and regulation of vascular endothelial function is

of significance in the prevention and treatment of essential hypertension.

hs-CRP is a C-reactive protein that exists in plasma and mainly plays a role in cardiovascular diseases, neonatal bacterial infections, and kidney transplantation. Many studies have shown that low-level hs-CRP is closely associated with cardiovascular diseases such as hypertension and hyperlipidemia. People with elevated hs-CRP have a higher incidence of hypertension. hs-CRP is a pro-inflammatory factor that affects the occurrence, evolution, and development of hypertension[11]. The European Guidelines for the Prevention and Treatment of Hypertension in 2003 formally recommended that patients with hypertension should be tested for hs-CRP levels[12]. ET is an endogenous long-acting vasoconstrictor regulator-the strongest vasoconstrictor substance known to date-and ET-1 plays a major role in cardiovascular disease. ET-1 is mainly secreted by stimulated endothelial cells.

It can regulate gene transcription level to a certain extent and plays a positive role in muscle strength. It can cause heart rate inhibition through vasoconstriction and a blood pressure rise effect, resulting in insufficient myocardial blood supply, and it can also induce myocardial cell sugar overload, arrhythmia, and myocardial energy metabolism disorder, etc.[13]. ADMA can reduce the content of nitric oxide and inhibit the proliferation of endothelial progenitor cells, thereby destroying the structure of blood vessels, leading to vascular endothelial dysfunction. The clinical detection of ADMA predicts the occurrence and prognosis of various cardiovascular clinical events. Studies have found that ADMA is closely related to essential hypertension, coronary heart disease, hyperlipidemia, diabetes, and pulmonary hypertension[14].

FKN has a specific chemotaxis function. It can participate in the migration and activation of leukocytes, such as phagocytes and lymphocytes, and it can also mediate immune damage. In recent years, many studies have shown that FKN can reduce the bioavailability of NO by activating vasoactive oxygen clusters, leading to vascular dysfunction, indicating that FKN may be related to vascular dysfunction or cardiovascular disease[15]. In this study, the mean systolic and diastolic blood pressures in the study group were higher than those in the control group, and the difference was statistically significant ($P < 0.01$). The levels of serum FKN, hs-CRP, ET-1, and ADMA were higher than those of healthy people, and the difference was statistically significant ($P<0.01$). These results suggested that serum FKN levels in patients with essential hypertension are significantly increased, and FKN levels are related to blood pressure and vascular endothelial dysfunction.

Pearson correlation analysis showed that FKN was positively correlated with systolic ($r = 0.705$, $P<0.01$) and diastolic ($r = 0.425$, $P<0.01$) blood pressure. FKN was positively correlated with hs-CRP ($r = 0.341$, $P<0.01$); ET-1 ($r = 0.468$, $P<0.01$); ADMA ($r = 0.442$, $P<0.01$). FKN can reflect the severity of essential hypertension. Combined with systolic blood pressure, diastolic blood pressure, hs-CRP, ET-1, and ADMA, FKN can be used to evaluate the degree of vascular endothelial damage in essential hypertension and plays a role in the prevention and treatment of essential hypertension.

In conclusion, FKN, hs-CRP, ET-1, and ADMA in the serum of patients with essential hypertension were highly expressed and increased with the increase of blood pressure. FKN was positively correlated with systolic pressure, diastolic pressure, hs-CRP, ET-1, and ADMA, which could effectively reflect the degree of vascular endothelial dysfunction in patients with essential hypertension and play an important role in clinical evaluation, judgment, and treatment of essential hypertension.

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