CHANGES AND CORRELATION OF SERUM SFRP5, HN, AND SCD40L EXPRESSION IN PATIENTS WITH CORONARY HEART DISEASE

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ABSTRACT

Objective: *To analyze the changes and correlation of serum secreted frizzled-related protein 5 (SFRP5), Humanin (HN), and soluble CD40L (sCD40L) expression in patients with coronary heart disease (CHD).*

Methods: *From March 2017 to December 2018, 157 patients who underwent coronary angiography in our hospital were divided into 73 patients with acute coronary syndrome, 40 patients with stable angina pectoris, and 44 patients with normal coronary angiography or coronary artery stenosis less than 50% as a control group. General data of all subjects were collected, and all patients were detected by ELISA. The serum levels of SFRP5, HN, and sCD40L were measured, the risk factors of coronary heart disease were analyzed by multivariate logistic regression, and the correlation between serum SFRP5, HN, and sCD40L and blood lipid was analyzed by Kendall test.*

Results: *Compared with the control group, the levels of serum SFRP5, HN, and sCD40L in the acute coronary syndrome group and the stable angina pectoris group were significantly lower, and the levels of sCD40L were significantly higher (P< 0.01), and the levels of SFRP5, HN and sCD40L in the acute coronary syndrome group and the stable angina pectoris group were significantly different (P<0.05). The results showed that serum SFRP5, HN, and sCD40L were independent risk factors for coronary heart disease (P<0.05); serum SFRP5 was positively correlated with HN, negatively correlated with sCD40L, TC, and HDL (P<0.05) but not with other indicators (P>0.05); HN was negatively correlated with sCD40L and positively correlated with TG, TC, HDL, and LDL (P<0.05).*

Conclusion: *The changes of serum SFRP5, HN, and sCD40L levels may be one of the mechanisms of the occurrence and development of coronary heart disease, and the three indicators are expected to become new targets of drug therapy for clinical prevention and treatment of coronary heart disease.*

Keywords: *Coronary heart disease, serum SFRP5, anti-apoptotic polypeptide, humanin, sCD40L, correlation.*

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Introduction

Coronary heart disease (CHD) is short for coronary atherosclerotic heart disease (CAHD). It refers to abnormal lipid metabolism in patients. Some atherosclerotic lipids accumulate on the intima of the artery to form white plaques. These plaques can cause atherosclerosis and then lead to vascular stenosis or obstruction, leading to myocardial ischemia and angina[(1)]. Acute coronary syndromes (ACS) is a serious type of coronary heart disease, which is the main cause of death in patients with atherosclerotic cardiovascular disease. ACS is common in the elderly, men and postmenopausal women, accounting for about 30% to 40% of coronary heart disease, including acute ST-segment elevation myocardial infarction, acute non-ST-segment elevation myocardial infarction, and unstable angina[(2)]. Relevant data show that fat can participate in the occurrence and development of atherosclerosis by secreting pro-inflammatory and anti-inflammatory factors and plays an important role in many pathophysiological processes such as type 2 diabetes mellitus and metabolic syndrome[(3)]. Secreted frizzled-related protein 5 (SFRP5) is a confirmed anti-inflammatory adipocytokine, which is related to abnormal glucose metabolism and obesity. It can increase insulin sensitivity and resist inflammation. Humanin (HN)

is an endogenous anti-apoptotic polypeptide. Some clinical scholars have found through animal experiments that[4], HN can reduce the area of myocardial infarction in a dose-dependent manner and play a protective role on the heart of mice with myocardial ischemia. SolubleCD 40 ligand (sCD40L) mainly comes from platelets and T lymphocytes and mainly participates in the immune response in the process of atherosclerosis[5]. This study analyzed the changes of serum SFRP5, HN, and sCD40L levels in patients with coronary heart disease and further explored the correlation between inflammatory factors and coronary heart disease.

Materials and methods

Research subjects

A retrospective analysis was made of 157 patients who underwent coronary angiography in our hospital from March 2017 to December 2018. According to the results of coronary angiography and clinical manifestations, they were divided into 73 patients with acute coronary syndrome, 40 patients with stable angina and 44 patients with normal coronary angiography or coronary artery stenosis less than 50% as the control group.

The criteria for admission were as follows:

• Stable angina pectoris patients accorded with the following criteria: positive exercise test, labor angina lasting for more than 3 months; acute coronary syndrome accorded with the relevant diagnostic criteria formulated by the International Heart Association and WHO clinically;

• No previous history of coronary intervention or bypass surgery;

• Age <80 years old;

• The condition of angina pectoris patients was stable >3 days, and the course of acute coronary syndrome patients was >3 weeks;

• The patients and their families had informed consent and cooperated with the treatment, which was approved by the ethical committee of the hospital.

Exclusion criteria:

• Severe heart disease, severe liver and kidney dysfunction;

• Patients with infectious diseases, autoimmune diseases and tumors;

• Patients with major surgical history in recent three months;

• Healthy control group excluded cerebrovascular or peripheral vascular diseases;

• Pregnant and lactating women.

Sample collection

The fasting venous blood of all patients was collected and placed in heparin anticoagulant tubes at room temperature for 20 minutes. After centrifugation for 10 minutes at 3000 r/min, the supernatant was stored in the refrigerator at –80° C for reserve.

Index detection

The levels of serum SFRP5, HN, and sCD40L were detected by enzyme-linked immunosorbent assay (ELISA). The kit was purchased from the R&D Company of the United States. The procedure was carried out in strict accordance with the instructions of the ELISA kit. The blood lipid levels of all subjects were measured by an automatic biochemical analyzer.

Statistical method

All data of this study were analyzed by SPSS 20.0 software. Quantitative variables were analyzed by single-factor analysis of variance, LSD-T test, multivariate logistic regression analysis, and Kendall test. The risk factors of coronary heart disease were analyzed. The Kendall test was used to analyze the correlation between serum SFRP5, HN, and sCD40L and blood lipids; P<0.05 had statistical significance.

Results

Comparison of the general situation of the subjects in each group

There were significant differences in LDL, CRP, Gensini, and WBC between the acute coronary syndrome group, the stable angina pectoris group, and the control group (P<0.05), but there was no significant difference between them (P>0.05). See Table 1.

Index	Control group (n=44)	Stable angina pectoris group (n=40)	Acute coronary syndrome group (n=73)	*P*
Age (years)	59.76±7.21	59.63±6.04	61.73±8.63	0.493
Gender	23/21	21/19	53/20	0.211
BMI (kg/m2)	22.02±2.36	21.28±2.44	21.39±1.87	0.153
Smoking	21	20	43	0.389
Hypertension	25	23	50	0.337
Diabetes	6	7	18	0.424
TG (mmol/L)	2.19 (1.69, 3.50)	2.38 (1.47, 3.82)	1.83 (1.37, 2.69)	0.142
TC (mmol/L)	4.12±1.25	3.97±1.25	4.17±1.12	0.282
HDL (mmol/L)	1.27±0.33	1.20±0.37	1.37±0.19	0.215
LDL (mmol/L)	1.75±0.48	1.58±0.39	2.20±0.47	0.016
GGT (U/L)	34.9 (23.8, 54.4)	43.8 (17.9, 95.7)	76.8 (24.0, 75.7)	0.052
TB (μmol/L)	8.49 (6.64, 10.24)	8.02 (5.69, 9.87)	8.57 (7.09, 14.65)	0.410
FBG (mmol/L)	5.58±1.41	5.71±1.51	6.30±1.68	0.116
Uric acid (μmol/L)	302.59±79.04	305.37±78.34	297..02±73.45	0.451
Leukocyte (×10^9/L)	6.87±1.52	7.17±1.98	8.63±2.56	0.003
CRP (mg/L)	4.19±2.05	4.13±1.57	11.53±3.27	<0.001
FG (g/L)	3.12±0.58	3.25±1.46	3.28±1.14	0.210
Gensini integral	3.01±1.68	20.11±21.89	43.51±22.67	<0.001

Table. 1: General comparison of the subjects in each group.

Changes of serum SFRP5, HN, and sCD40L levels in each group

Compared with the control group, the levels of serum SFRP5, HN, and sCD40L in the acute coronary syndrome group and the stable angina pectoris group were significantly lower, the levels of sCD40L were significantly higher (P<0.01), and the levels of serum SFRP5, HN, and sCD40L in the acute coronary syndrome group and the stable angina pectoris group were significantly different (P<0.05). See Table 2.

Group	Cases	SFRP5 (ng/ml)	HN (ng/ml)	sCD40L
Acute coronary syndrome group	73	32.78±5.70	1.58±0.22	2.34±0.78
Stable angina pectoris group	40	40.05±4.12	2.51±0.13	1.87±0.73
Control group	44	49.34±4.14	3.57±0.21	1.19±0.65
F		155.74	1398.45	33.82
P		<0.001	<0.001	<0.001

Table. 2: Changes of serum SFRP5, HN, and sCD40L levels in each group.

Logistic regression analysis of risk factors of coronary heart disease

Logistic regression analysis showed that serum SFRP5, HN, and sCD40L were independent risk factors for coronary heart disease (P<0.05), as shown in Table 3.

Index	B	*SE*	*OR*	95%CI	*P*
Age	0.148	0.024	1.140	1.017~1.129	0.020
Family history of coronary heart disease	1.165	0.423	1.746	1.230~4.430	0.011
History of smoking	1.768	0.752	4.650	3.038~9.043	0.008
SFRP5	1.225	0.184	0.855	0.824~1.012	0.024
HN	1.157	0.264	1.001	1.000~1.025	0.019
sCD40L	1.789	0.378	2.457	1.569~7.549	0.001

Table. 3: Logistic regression analysis of risk factors for coronary heart disease.

The correlation between serum levels of SFRP5, HN and sCD40L and blood lipids

Serum SFRP5 was positively correlated with HN, negatively correlated with sCD40L, TC, and HDL (P<0.05), but not with other indicators (P>0.05); serum SFRP5 was negatively correlated with sCD40L and positively correlated with TG, TC, HDL, and LDL (P<0.05). See Table 4.

	HN	sCD40L	TG	LDL	TC	HDL
SFRP5	0.282	-0.157	0.287	0.029	-0.356	-0.282
HN	-	-0.324	0.125	0.071	0.011	0.172
sCD40L	-	-	0.143	0.039	0.030	-0.245
TG	-	-	-	0.105	0.429	-0.277
LDL	-	-	-	-	0.761	-0.162
TC	-	-	-	-	-	0.081

Table. 4: The correlation between serum levels of SFRP5, HN, and sCD40L and blood lipids.

Discussion

Atherosclerosis is the leading destroyer of human health. The rupture of atherosclerotic plaque and thrombosis are closely related to the regulation of inflammation and immune mechanism[7-8]. Many studies have found that the incidence of diabetes, hyperlipidemia and other diseases is closely related to the occurrence of acute coronary events. Plaque instability plays an important role in the occurrence of ACS. Its pathophysiological links are complex. Its clinical features are mainly inflammatory reaction, plaque rupture, and local thrombosis. Relevant data show that the natural course of the disease is the process of occurrence and development of atherosclerosis, and the degree of plaque sclerosis is the main factor determining the severity of coronary artery disease. Therefore, early detection of the stability of coronary atherosclerotic plaque is the key to reducing adverse events of coronary heart disease[9].

SFRP5 is one of the members of the SFRP family. SFRP5 can be expressed in adipose tissue, pancreatic tissue and retinal epithelial cells. The CRD region of SFRP5 family members contains the Wnt receptor frizzled protein, which is homologous to a homologous convoluted cysteine-rich region[10]. SFRP5 has been proved to be an anti-inflammatory adipocytokine that can compete with Wnt. The biological function of SFRP5 is mainly mediated by the Wnt signaling pathway. Wnt is a member of the secretory glycoprotein family. It can activate the typical or the independent Wnt signaling pathway of β-catenin. The atypical Wnt signaling pathway is an important promoter of an inflammatory response and destroying the insulin signaling system, while the typical Wnt signaling pathway is an important promoter of inflammatory response and insulin signaling system. The signaling pathway can regulate mesenchymal cells. The activation of the Wnt signaling pathway is the source of a series of

inflammatory factors and inflammation. Therefore, the SFRP protein can compete with the frizzled protein through a non-classical pathway to inhibit the Wnt signaling pathway, thus delaying the occurrence of inflammation[11].

HN is a linear neuroprotective peptide. It was first found in the occipital DNA of patients with Alzheimer's disease. It was initially found that HN can resist apoptotic neurons induced by β-amyloid peptide and mutations in various family AD genes[12]. Relevant data show that[13], HN not only plays a role in neuroprotection, antioxidant, anti-inflammatory and other aspects, but it also plays an anti-apoptotic and wider role in various stresses and diseases. Some scholars have found that[14], the elevation of the serum HN level is related to normal coronary endothelial function, and its expression content can improve vascular endothelial function and reduce the occurrence and development of coronary atherosclerosis. Other scholars have found through animal experiments that[15], HN can reduce the size of myocardial infarction in mice and has a therapeutic effect on myocardial ischemia and reperfusion injury. In the process of atherosclerotic plaque formation, a large number of platelets are activated and release SCD40L, which is widely distributed in atherosclerotic plaques, vascular endothelial cells, macrophages and platelets. HN has strong biological activity. It can produce interleukin, metalloproteinase, tissue factor and other active substances by activating lymphocytes, which can cause endothelial cell inflammation. Some scholars believe that the application of the anti-sCD40L antibody can slow the progression of atherosclerosis and plaque rupture and increase plaque stability[16].

The results showed that the levels of serum SFRP5 and HN in the acute coronary syndrome group and the stable angina pectoris group were significantly lower than those in the control group, and the levels of sCD40L were significantly higher than those in the control group ($P<0.01$). Logistic regression analysis showed that serum SFRP5, HN, and sCD40L were independent risk factors for coronary heart disease ($P<0.05$), suggesting that the changes of serum SFRP5, HN, and sCD40L levels may be independent predictors of the severity of coronary artery disease independent of age and blood lipids. The results of the Kendall test showed that serum SFRP5 was positively correlated with HN, negatively correlated with sCD40L, TC, and HDL ($P<0.05$), negatively correlated with sCD40L, and positively correlated with TG, TC, HDL, and LDL ($P<0.05$), suggesting that serum SFRP5, HN, and sCD40L could promote the occurrence and development of coronary heart disease, and the effect on blood lipids might be related to them. Participation in inflammation is related.

In summary, changes in serum SFRP5, HN, and sCD40L levels may be one of the mechanisms of the occurrence and development of coronary heart disease. These three indicators are expected to become new targets for clinical treatment of coronary heart disease.

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