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Research Article

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Research on the Clinical Phenotype of Coronary Heart Disease with Retinol Binding Protein 4, Lipoprotein-related Phospholipase A2, and the Severity of Coronary Artery Lesion

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ABSTRACT

This study has been done to investigate the correlation between retinol binding protein 4 (RBP4), lipoprotein associated phospholipase A2 (Lp-PLA2) and the clinical phenotype of coronary heart disease (CHD) and the severity of coronary artery disease. 160 cases of patients were suspected with coronary heart disease underwent coronary angiography, 112 cases of patients with coronary heart as treatment group, and 48 cases of patients with non CHD as control group. According to the clinical characteristics, the coronary heart disease group was divided into acute myocardial infarction (AMI) group with 15 cases, unstable angina pectoris (UAP) group with 71 cases, and stable angina pectoris (SAP) group with 26 cases; according to the results of coronary angiography, it was divided into single-branch lesion group with 42 cases, double-branch lesion group with 47 cases, and three-branch lesion group with 23 cases. Fasting serum RBP4 and LP-PLA2 levels were detected. (1) Serum RBP4 concentrations and the clinical phenotype of coronary artery disease: AMI group and UAP group were significantly higher than those in SAP and control group ($P<0.05$); the difference was not statistically significant between the comparison of AMI, UAP group, SAP and control group ($P>0.05$). (2) Serum LP-PLA2 concentration in patients with coronary heart disease were significantly higher than those in the control group ($P<0.01$), in LP-PLA2 concentration comparison between subgroup, AMI group was significantly higher than UAP and SAP group ($P<0.01$), UAP group was higher than SAP group ($P<0.05$). (3) RBP4, LP-PLA2 concentration and coronary angiography results: three groups of lesions, RBP4, LP-PLA2 concentration of the three groups pf lesions were significantly higher than the control group, the differences were statistically significant ($P<0.05$), the group comparison in three groups, differences in RBP4 concentration have no statistical significance ($P>0.05$); differences in LP-PLA2 concentration have statistical significance ($P<0.05$). The changes of retinol binding protein 4, LP-PLA2of serum concentration has relation with the severity of coronary artery disease progression, but no clear relationship with the degree of coronary artery lesion and count, LP-PLA2 concentration increases with the increase of the severity of coronary artery disease and the number of disease.

Keywords: *Retinol Binding Protein 4; Lipoprotein Associated Phospholipase A2; Coronary Heart Disease; Coronary Artery Lesion Degree*

INTRODUCTION

Coronary heart disease is one of the common diseases in cardiology. Many risk factors and chronic inflammatory reaction can lead to the formation of coronary heart disease. One of the common risk factors is dyslipidemia. Lipid deposition in the vascular wall, causing atherosclerosis and plaque formation lumen narrowing, results in loss of oxygen and oxygen consumption out of balance. Plaque rupture, can lead to a series of coronary events, in which of inflammatory reaction in the arteriosclerosis process plays a certain role in triggering. RBP4 is a novel adipocyte-derived cytokine that mediates chronic inflammatory response and promotes insulin resistance (IR), leading to further metabolic disorders of glucose and lipid [1-2]. These metabolic disorders are the major risk factors for coronary heart disease. LP-PLA2 is a newly discovered inflammatory factor, and has shown an important role in the promotion of atherosclerosis formation and development process [3][6]. In this paper, the concentrations of RBP4 and LP-PLA2 in different populations were evaluated, and the values of RBP4 and LP-PLA2 in predicting the different types of coronary artery disease and the degree of coronary artery disease were assessed.

MATERIALS AND METHODS

From September 2013 to March 2014, 160 patients with coronary heart disease were selected from our hospital, including 102 males and 58 females with an average age of (65.37 ± 7.52) years [4-5], [7-8]. Selection criteria: refer to the 2012 Chinese Medical Association coronary atherosclerotic heart disease diagnosis and classification criteria [9-10]. All the selected patients underwent coronary angiography. According to the results of coronary angiography, 112 patients were divided into two groups: the coronary artery disease group (treatment group), the coronary artery disease group, and the control group of 48 cases. Exclusion criteria: primary and secondary cardiomyopathy, rheumatic heart disease, senile valve disease, infectious diseases, severe hepatitis, severe renal insufficiency and so on. There was no significant difference between the two groups in age, gender differences, duration of disease, history of smoking, blood pressure and body mass ratio ($P > 0.05$).

Coronary angiography and coronary heart disease diagnostic criteria and the determination of the number of coronary artery disease

Coronary angiography was done using Judkins method, the radial artery approach; in the DSA room (catheter room) coronary angiography, there are at least two qualified physicians in our division of our hospital to complete the acquisition of orthotopic, liver, right shoulder position, head bit, left shoulder position, spider bit irradiation image. Acute myocardial infarction, unstable angina, stable angina diagnosis consistent with the 2012 Chinese Medical Association of coronary atherosclerotic heart disease diagnosis and classification criteria was done [5]. Criteria for determining the number of lesions: single branch disease: refers to the anterior descending artery, circumflex artery, right coronary artery in any one involvement, diameter stenosis greater than 50%; double-vessel disease: refers to the anterior descending artery, circumflex artery, right coronary artery in the Diameter stenosis greater than 50%; three lesions: anterior descending artery, circumflex artery, right coronary artery involvement at the same time, the diameter stenosis greater than 50%, or the degree of stenosis is greater than 50%; left main plus any one of the vessels, the diameter stenosis greater than 50%.

Specimen collection and testing methods

Specimen collection: Before coronary angiography, early morning fasting venous blood 5ml, 1000r / min Centrifuge 5min, collected serum, stored in -70 ℃ refrigerator, to be measured. Detection methods: The enzyme-linked immunosorbent assay (ELISA) quantitative determination of RBP4, LP-PLA2 concentration levels, kit were provided by Wuhan Huamei Biotechnology Co., Ltd., and microplate reader was provided by Beijing Tianshi Technology Co.

Statistical methods

Statistical analysis was performed with SPSS 16.0 software. Paired t-test was used to measure the data, and$\chi 2$ test was used for the count data. The difference was statistically significant (P <0.05), P <0.01 was significant difference (χx ± S) and had statistical significance.

RESULT Results & Discussion

There are four groups of serum retinol binding protein 4 as seen in Table 1, lipoprotein-related phospholipase A2 concentration comparison. RBP4 concentration in AMI group and UAP group was significantly higher and in the SAP group and the control group was low, the difference was statistically significant (P <0.05), there was no statistically significant difference between AMI group and UAP group (P (P> 0.05). There was no significant difference between the SAP group and the control group (P> 0.05). The LP-PLA2 concentration in the clinical type of coronary heart disease was significantly higher than that in the control group (P <0.01) (P <0.01). There was significant difference between UAP group and SAP group (P <0.05). There was significant difference between AMI group and UAP group and SAP group (P <0.01).

Table 1 Four groups of serum retinol binding protein 4, lipoprotein-related phospholipase A2 concentration comparison. （ $\bar{x}$ ±S）

Group	Case	RBP4	LP-PLA2
Control Group	48	14.17±2.81	150.63±32.81
Acute Myocardial infraction	15	25.36±8.63*	483.38±54.71▲△
Unstable angina pectoris	71	19.72±5.27* #	432.04±49.68▲
Stable angina pectoris	26	16.63±4.53	395.27±32.90▲

Note: Compared with the control group and stable angina p <0.05; compared with the control group ▲ p <0.01; unstable angina, stable angina p <0.01; compared with stable angina p <0.05;

According to coronary angiography results, patients with different coronary artery disease and control group serum RBP4, LP-PLA2 concentration comparison are seen in Table 2. The levels of RBP4 and LP-PLA2 in the three groups were significantly higher than those in the control group (P <0.05). There was no significant difference between the three groups (P> 0.05). LP-PLA2 concentration difference was statistically significant (P <0.05).

Table 2 Different coronary artery disease and control group serum RBP4, LP-PLA2 concentration comparison (x ±S)

Group	Case	RBP4	LP-PLA2
Control	48	15.83±7.85	150.63±32.81
Single-vessel	42	19.84±6.25 *	367.52±45.54*
Double-vessel	47	23.26±5.61*	446.37±32.54* #
Triple-vessel	23	25.76±6.73*	483.75±51.23* # ▲

Note: Compared with the control group * p <0.05; compared with single-vessel disease group # p <0.05; and double-vessel disease group ▲ p <0.05;

Discussion

Abnormal lipid metabolism and inflammatory response is the main risk factor of coronary atherosclerosis and one of the trigger factors. RBP4 as a vitamin A carrier protein, is a newly discovered fat cell factor, the relative molecular mass of 21KU. Numbers of animal and human studies have shown that when its level rises, it is closely related to the changes in insulin resistance, diabetes, central obesity, primary hypertension, lipid metabolism, such as changes in lipid profile and so on [1, 9], and it is a cardiovascular disease risk factor which may occur directly or indirectly through a variety of ways involved in the occurrence and development of coronary heart disease, but the specific mechanism of action has not yet elucidated. It May be associated with its relatedness to metabolic signals, inflammation and atherosclerosis of the link [10]. LP-PLA2, also known as platelet activating factor acetychydrocase (PAF-AH), contains 441 amino acids and has a relative molecular mass of 50,000 and is secreted by monocytes, macrophages, T lymphocytes and mast cells [11]. About 80% of LP-PLA2 in blood binds to LDL-C and 15-20% binds to HDL-C [7]. LP-PLA2 hydrolyzes oxidized phospholipids derived from LDL-C into fatty acids, releasing both lysophosphatidylcholine and oxidized non-esterified fatty acids, both of which have significant pro inflammatory effects and contribute to the formation of atheromatous plaques [12]. LP-PLA2 is an inflammatory marker associated with coronary artery disease. It is an independent risk predictor of coronary artery disease [13-14].

The results showed that RBP4 concentration in AMI group and UAP group was significantly higher than that in SAP group and control group (P <0.05). There was no significant difference between each group (P> 0.05), indicating that coronary artery plaque block stability is associated with RBP4 concentration; abnormal concentration may represent coronary plaque stability changes, leading to the instability of development, which also may lead to coronary artery endothelial injury, plaque rupture, leading to acute thrombosis, that is, stable angina pectoris may be transferred to unstable angina pectoris, myocardial infarction development, or even sudden death. The RBP4 concentration in coronary artery disease group was significantly higher than that in the control group (P <0.05). There was no significant difference in the RBP4 concentration among the subgroups of CHD group (P> 0.05). The results of this study is similar to the study of the domestic scholars Liu Hailiang et al. [15], indicating that RBP4 cannot reflect the degree and extent of coronary artery stenosis, but may become a risk of stratification basis for further study.

The results showed that LP-PLA2 concentration in coronary heart disease was significantly higher than that in control group (P <0.01), indicating that LP-PLA2 may be a new inflammation marker associated with coronary heart disease, and may be directly involved in atherosclerosis and independently predict coronary event risk [16-17]. There were significant differences among the subgroups, and the concentration of LP-PLA2 in the two groups was significantly higher than that in the control group and the three-vessel disease group (P <0.05). The concentration of LP-PLA2 in the two groups was significantly higher than that in the control group (P <0.01). There was a significant difference between the groups (P <0.05), indicating that LP-PLA2 could be used in the patients with severe coronary heart disease (CHD), the difference was statistically significant (P <0.05), and the difference was statistically significant to a certain

extent, that can reflect the extent of coronary lesions or stenosis [18]. The study of the domestic scholars Pan Chenliang et al. [19] has shown that plasma LP-PLA2 levels can be used to indirectly assess the scope of coronary lesions.

CONCLUSION

In summary, the level of RBP4 is associated with the progression of coronary artery disease, and has nothing to do with the severity of coronary artery disease. The level of LP-PLA2 in patients with coronary heart disease increases with the progression and severity of coronary lesion. So, the changes in LP-PLA2 levels can determine the deterioration of coronary heart disease, progress and degree of severity of coronary artery disease. Due to the small sample size of this study, the future studies still are needed to increase the sample size and more clinical centers to participate in further studies to confirm the value from the response to the clinical phenotype of coronary heart disease and coronary lesions[20].

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