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Plasma vaspin concentrations are decreased in acute coronary syndrome, but unchanged in patients without coronary lesions

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ABSTRACT

Objective: Previous studies suggested that decreased serum vaspin levels were associated with coronary artery disease (CAD). The present study aimed to investigate the association between plasma vaspin levels and different states of CAD.

Design and methods: A total of 162 patients with coronary angiography (CAG) proved that CAD was enrolled. Additional 103 patients complained with "chest discomfort" with negative CAG, and 60 normal subjects were enrolled in this study. The levels of plasma vaspin, adiponectin, clinical parameters, lipid profile and C reactive protein (CRP) were measured.

Results: The levels of plasma vaspin were significantly lower in the CAD group (0.47 ± 0.63 μg/L) than those in the healthy group and CAG (−) group (all $p < 0.001$). In CAD group, the pos hoc analysis showed that serum vaspin concentration in acute myocardial infarction group (0.21 ± 0.19 μg/L) was significantly lower than that in the unstable angina pectoris group (0.40 ± 0.37 μg/L) ($p = 0.012$), and serum vaspin concentration in unstable angina pectoris was significantly lower than that in stable angina pectoris group (0.92 ± 0.94 μg/L) ($p = 0.013$). The plasma vaspin concentration was also negatively correlated with the severity of CAD (1-vessel: 0.86 ± 0.90 μg/L; 2-vessel: 0.36 ± 0.39 μg/L; 3-vessel: 0.21 ± 0.16 μg/L). The plasma vaspin concentration in CAG (−) group with "chest discomfort" (1.93 ± 2.57 μg/L) was similar to the healthy control group (2.18 ± 3.49 μg/L).

Conclusions: The plasma vaspin concentration correlated to the severity of CAD. Furthermore, plasma vaspin has a value of avoiding patients without CAD from unnecessary CAG.

Introduction

Adipose tissue, previously perceived to be a storage reservoir of fat, is now recognized as an active endocrine organ [1]. It secretes a number of adipocyte-specific cytokines (adipokines), which played important roles in the process of the metabolism, inflammation, cell proliferation and so on [2,3].

Visceral adipose tissue-derived serine protease inhibitor (vaspin) is a new adipokine indentified from visceral adipose tissue in a rat model of type 2 diabetes [4]. Prior studies found that it had little effect on serine protease activity, but had multiple effects on metabolism, including improving insulin resistance, reducing food intakes and lowering blood glucose [5]. In human beings, accumulating data confirmed that there was a tight relationship between vaspin and the parameters of metabolism syndrome [6]. Moreover, recent studies revealed that vaspin could target vascular cells, exerting anti-inflammation and anti-apoptotic effects as well as improving insulin resistance [7]. Vaspin could inhibit inflammatory factor secretion from vascular smooth muscle cells and antagonize endothelial cell apoptosis induced by free fatty acid [8,9].

Coronary artery disease (CAD) is the leading cause of death worldwide. Though the symptoms and signs of CAD are noted in the advanced state of disease, a majority of CAD patients remain asymptomatic for decades prior to any overt signs of diseases. On the other side, some patients often have atypical chest pain, which often confounds the diagnosis, and leads to inappropriate examination, such as coronary angiography and unnecessary medical treatment.

Abbreviations: CAD, coronary artery disease; SAP, stable angina pectoris; UAP, unstable angina pectoris; AMI, acute myocardial infarction; CAG, coronary angiography; CRP, c reactive protein; WBC, white blood cell count; HbA1c, glycosylated hemoglobin; HC, healthy control; ROC, receiver operating characteristic; BMI, body mass index; TC, total cholesterol; TG, triglyceride; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; FPG, fasting plasma glucose; PG2h, 2-hour post-load plasma glucose; ALT, alanine aminotransferase; LVEF, left ventricular ejection fraction; TnT, troponin T; OR, odd risk; SD, standard deviation.

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In a clinical study, decreased serum vaspin levels were observed in asymptomatic CAD patients and the vaspin concentration was correlated with the severity of CAD [10]. Another study showed that the symptomatic patients with carotid stenosis had a lower vaspin serum concentration than the asymptomatic individuals [11]. Our previous study showed that circulating vaspin levels were lower in patients with unstable angina compared with those with stable angina [12]. All these studies showed that there might be associations between plasma vaspin levels and the severity of symptoms in CAD patients.

In view of the possible relationship between vaspin and symptoms or the severity of vessel injury in patients with CAD, the first goal of the present study was to explore the hypothesis that plasma vaspin concentration was inversely associated with severity of CAD and was lowest in patients with acute myocardial infarction (AMI). For this purpose, we analyzed plasma levels of vaspin in patients with stable angina pectoris (SAP), unstable angina pectoris (UAP) and AMI. Furthermore, we measured plasma vaspin concentration in normal group as well as in negative CAG with "chest discomfort" group.

Patients and methods

Study population

All participants gave written informed consent and the protocol was approved by the Shanghai Tenth Hospital's Ethics Committee. This study included 265 patients complained with "chest discomfort" who underwent coronary angiography or/and intervention in the Department of Cardiology, Shanghai Tenth People's Hospital (China) from December 2010 to May 2011. SAP, UAP, AMI and acute coronary syndrome (ACS) were diagnosed according to the American College of Cardiology/American Heart Association (ACC/AHA) 2007 guidelines [13]. Another 60 subjects without any health problem were enrolled as the healthy control (HC) group. HC individuals were selected from subjects who had visited medical examination center of Shanghai Tenth People's Hospital for check-up and had no history of any chronic disease, cardiovascular disease or overt cardiac origin symptoms. The absence of cardiovascular disease was based on the findings from complete medical history, comprehensive physical examination, electrocardiogram, and echocardiography. None of them was receiving any long-term medication or was suffering from an acute infection.

Exclusion criteria for all the participants included previous myocardial infarction, acute or chronic heart failure, valvular heart disease, acute infection, acute state of chronic infections or inflammatory diseases, severe liver or renal disease, neoplasm and hematologic disorders.

Based upon the clinical manifestations and the results of electrocardiography, cardiac enzyme assessment and coronary angiography (CAG), patients were divided into HC group ($n = 60$, healthy subjects), CAG (−) group ($n = 103$, 45 patients with normal coronary artery, 35 patients with myocardial bridge, and 23 patients with non-significant coronary artery disease [luminal diameter stenosis ≤ 30%]), and CAD group ($n = 162$, including 47 patients with SAP, 49 patients with UAP, and 66 patients with AMI).

Coronary angiography

Coronary angiography was performed through radial or femoral artery approach. Significant CAD was diagnosed visually if luminal diameter stenosis ≥50% was present at a major epicardial coronary artery, and left main trunk stenosis ≥50% was considered as a 2-vessel disease. The severity of coronary atherosclerosis was categorized according to the number of diseased vessels as 1-, 2- or ≥3-vessel disease [14].

Biochemical investigation

Blood samples were collected and investigated as before [15]. To put it brief, plasma were taken after an overnight fasting. Plasma specimens were stored at −80 °C until analysis. White blood cell count, C reactive protein (CRP), serum glucose, glycosylated hemoglobin (HbA1c), creatinine, uric acid, and lipid profiles were measured by colorimetric enzymatic assay systems (Roche Modular P-800, Switzerland). Human vaspin (Adipogen, Seoul, South Korea) and human adiponectin (R&D Systems, Minnerapolis, MN, USA) plasma levels were measured with commercially available ELISA according to the manufactures' instructions.

Statistical analysis

Continuous variables were presented as mean ± SD, and categorical data were summarized as frequencies or percentages. For continuous variables, normal distribution was evaluated with Kolmogorov–Smirnov test. The continuous variables were compared using the Student's t test (if homogeneity of variances was assumed) or the Mann–Whitney test (if homogeneity of variances was not met). For categorical clinical variables, differences between groups were evaluated with the X^2 or Fisher exact test when appropriate. Receiver operating characteristic (ROC) curves were performed to investigate the value of vaspin plasma concentration in differentiating ACS and AMI patients. Spearman correlation coefficients were used to evaluate correlations between vaspin plasma concentration and other variables. Subsequently, analysis was undertaken through multiple linear regressions to investigate a set of independent variable predictors of vaspin plasma concentration. A p value of ≤0.05 was taken as significance and ≤0.016 was taken as significance for post-hoc analysis. All analyses were done with SPSS for Windows 13.0 (SPSS Inc., Chicago, IL, USA).

Results

Baseline clinical characteristics and biochemical measurements

The basic characteristics of the participants are shown in Table 1. The CAD group had a male predominance over the CAG (−) group. The patients in the CAD group had older age, more cigarette smokers, and higher incidence of diabetes. The patients in the CAD group had higher levels of fasting plasma glucose, HbA1c and PG2h. Additionally, inflammatory factors such as white blood cell count were significantly higher in the CAD group than those in the HC or CAG (−) group ($p < 0.01$). CAD patients had worse cardiac and renal functions.

Vaspin plasma concentration in different groups

The concentration of vaspin was significantly lower in the CAD group (0.47 ± 0.63 μg/L) than that in the HC group (2.18 ± 3.49 μg/L) ($p < 0.001$) and CAG (−) group (1.93 ± 2.57 μg/L) ($p < 0.001$). The level of CRP in the CAD group (18.66 ± 18.96 mg/L) was significantly higher than that in the HC group (5.90 ± 3.76 mg/L) and CAG (−) group (5.87 ± 4.08 mg/L) ($p < 0.001$). The difference of plasma vaspin and CRP concentration between the HC group and the CAG (−) group was not significant (Fig. 1). CAD patients can be distinguished by the construction of receiver operating characteristic (ROC) curves of vaspin plasma concentration [area under the curve (AUC) = 0.775, $p < 0.001$ for the significant AUC] (Fig. 2A).

Vaspin plasma concentration in sub-groups of CAD

The CAD group was further divided into three sub-groups (SAP, UAP and AMI) according to the diagnostic standard [13,16]. Circulating vaspin concentration was significantly lower in the AMI sub-group (0.21 ± 0.19 μg/L) than that in the UAP sub-group (0.40 ± 0.37 μg/L) ($p = 0.012$) and SAP sub-group (0.92 ± 0.94 μg/L) ($p < 0.001$). The