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Orginal article

Study on the correlation between the concentration of plasma lipoprotein-associated phospholipase A2 and coronary heart disease

Jin-Ming Cen [a], Jie Cheng [b], Qing-Yuan Xiong [c], Bai-Qiang Mei [a], Wei-Biao Cai [a], Xi-Li Yang [a,*]

[a] *Department of Cardiology, Foshan Municipal First People's Hospital, Foshan, Guangdong 528000, China*

[b] *Institute of Biochemistry & Molecular Biology, Guangdong Medical College, Dongguan Guangdong 523808, China*

[c] *Department of Clinical Laboratory, The Chancheng District Central Hospital of Foshan, Guangdong 528000, China*

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Abstract

Objective: This study explores the correlation between plasma lipoprotein-associated phospholipase A2 (Lp-PLA2) and coronary heart disease (CHD) by comparing the level of plasma Lp-PLA2 in the plasma of patients with different types of CHD.

Methods: Blood samples were collected from 56 patients diagnosed with CHD by the Department of Cardiology of the First People's Hospital of Foshan and 34 healthy subjects from February 2013 to January 2014. We measured the concentration of plasma Lp-PLA2 and determined the levels of total cholesterol (Tch), triglyceride (TG), apolipoprotein A1 (Apo-A1), apolipoprotein B (Apo-B), high density lipoprotein-cholesterol (HDL-c), low density lipoprotein-cholesterol (LDL-c), lipoprotein a (Lp(a)), glucose (Glu), and high-sensitivity C-reactive protein (hs-CRP). The concentration of plasma Lp-PLA2 in the healthy control group and each subgroup of CHD patients were compared and analyzed for correlations of plasma Lp-PLA2 between the patients in different CHD subgroups and several laboratory indicators.

Results: The concentration of plasma Lp-PLA2 in each subgroup of CHD was significantly higher than in the control group ($P < 0.05$). The concentration of Lp-PLA2 in the unstable angina pectoris (UAP) group and acute myocardial infarction (AMI) group were significantly higher than in the stable angina pectoris (SAP) group ($P < 0.05$), and the concentration of plasma Lp-PLA2 in the AMI group was significantly higher than in the UAP group ($P < 0.05$). The concentration of plasma Lp-PLA2 in the CHD group merely showed a positive correlation ($r = 0.493$, $P < 0.05$) with the hs-CRP group, but the levels of Tch, TG, Apo-A1, Apo-B, HDL-c, LDL-c, Lp(a) and Glu did not.

Conclusions: The concentration of plasma Lp-PLA2 in patients with CHD was higher than that in the control group. The concentration of plasma Lp-PLA2 in the subgroups of CHD patients varied greatly from each other. The inflammatory response of atherosclerosis might be resulted from the synergy of plasma Lp-PLA2 and hs-CRP.

* Corresponding author.

E-mail address: 289124834@qq.com (X.-L. Yang).

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Coronal atherosclerosis heart disease (CHD) is one of the most common cardiovascular diseases and severely endangers human health. In developed country, CHD is one of the major diseases that threaten human health. Recent years the morbidity of CHD in China is increasing, the patients are getting younger.[1] Therefore, it is important and necessary to study factors correlated with CHD.

The mechanism of CHD involves several factors, among which one important pathological factor is atherosclerosis (AS). Inflammatory mediators are involved in the formation, development and even the final rupture of atheromatous plaque and the inflammatory response plays an important role in the occurrence and development of atheromatous plaque.[2] A recent study found that Lipoprotein-associated phospholipase A2 (Lp-PLA2) served as a new inflammation marker associated with CHD, it may directly participate in AS, and it is able to independently forecast coronary events.[3,4] A large number of clinical studies abroad found that Lp-PLA2 had various close associations with CHD.[5−7]

We aim to discuss the relationship of Lp-PLA2 with CHD as well as its correlation with blood lipid levels and high-sensitivity C-reactive protein (hs-CRP) by comparing the levels of Lp-PLA2 in CHD patients and a healthy control group.

Materials and methods

Research subjects

Blood were drawn from 56 patients who were hospitalized and had a coronary angiography (CAG) in the Department of Cardiology of the First People's Hospital of Foshan from February 2013 to January 2014. There are 37 men (66.07%) and 19 women (33.93%), age 45−85 years, with an average age of 62.85 ± 12.42 years. Patients include 10 cases of stable angina pectoris (SAP), 11 of unstable angina pectoris (UAP), and 45 with acute myocardial infarction (AMI). The control group was made up by 34 healthy individuals aging 42−88 years, with an average age of 62.85 ± 12.42 years, selected from the Physical Examination Center of the First People's Hospital of Foshan during the corresponding period. The following conditions were excluded; cardiomyopathy, valvular heart disease, severe hepatic and renal dysfunction, malignant tumor, acute infection, long-term medication with lipid-lowering drugs, taking statins drugs or aspirin before drawing blood.[8,9]

Methods

Specimen collection

Venous blood samples of all subjects were collected from the elbow after overnight fasting after hospitalization and samples were immediately sent for analysis. For biochemical test blood were injected into separation gel tubes while for Lp-PLA2 blood was drawn into an EDTA-Na2 anticoagulant tube. General clinical data were recorded, such as gender and age.

Testing method

The quantitative determination of Lp-PLA2 was measured by enzyme-linked immunosorbent assay (ELISA), while the seven indicators of blood lipids and blood glucose were determined with an automatic biochemical analyzer (Olympus AU5421), hs-CRP was determined with a BN II Immune Turbidimetry.

Statistics process

SPSS17.0 statistical software (SPSS Inc., IL, USA) was applied for data analysis. Measurement data are represented by mean ± standard deviation (SD), samples were compared between subgroups by *t*-tests and the analysis of variance. Correlation analyses are shown by Pearson linear correlation. $P < 0.05$ was considered statistically significant.

Results

Comparison of clinical data

Comparing each CHD subgroup with the control group for age, gender ratio, high blood pressure, and smoking, there was no statistically significant difference, $P > 0.05$ (Table 1).

Table 1
Comparison of clinical data among subgroups.

Factor	Control group ($n = 34$)	SAP group ($n = 10$)	UAP group ($n = 10$)	AMI group ($n = 36$)
Age (years)	62.85 ± 12.42	73.00 ± 8.86	65.60 ± 10.70	66.31 ± 12.15
Male (n, %)	20 (58.82)	6 (6/10)	6 (6/10)	25 (69.44)
Hypertension (n, %)	15 (44.12)	6 (6/10)	4 (4/10)	16 (44.44)
Smoking (n, %)	8 (23.53)	5 (5/10)	5 (5/10)	10 (27.78)

SAP: stable angina pectoris; UAP: unstable angina pectoris; AMI: acute myocardial infarction.

Comparison of the levels of Plasma Lp-PLA2 in subgroups and other laboratory indexes

The concentration of plasma Lp-PLA2 in each CHD subgroup was significantly higher than that in the control group ($P < 0.05$). The concentration of Lp-PLA2 in UAP group and AMI group were higher than SAP group respectively ($P < 0.05$); meanwhile, there was difference between AMI group and UAP group ($P < 0.05$). The level of hs-CRP of AMI group was apparently higher than that in the control group, SAP group as well as USP group ($P < 0.05$). The level of Lp(a) in each subgroup of CHD was higher than that in the control group, among which, there was statistical significance ($P < 0.05$) between AMI group and the control group while no statistical significance between SAP group as well as UAP group and the control group. Regarding to the level of Glu, each CHD subgroup was higher than control group, and the statistical significance ($P < 0.05$) was only shared between AMI group and the control group while there was no statistical significance shown between SAP group as well as UAP group and the control group. For the levels of Tch, TG, Apo-A1, Apo-B, HDL-c, LDL-c, although there was difference between each subgroup of CHD and the control group, the difference failed to show statistical significance ($P > 0.05$) (Table 2).

The correlation between concentrations of Plasma Lp-PLA2 and other laboratory indexes

With bi-variate linear analysis, it can be found that among the whole population of this study, the concentration of plasma Lp-PLA2 was positively correlated with the levels of Glu and hs-CRP ($r = 0.249$, $P < 0.05$; $r = 0.616$, $P < 0.05$), while no correlation with levels of Tch, TG, Apo-A1, Apo-B, HDL-c, LDL-c,LP(a). In CHD group, the concentration of plasma Lp-PLA2 only had positive correlation with hs-CRP ($r = 0.493$, $P < 0.05$), and no correlation with levels of other indexes, like Tch, TG, Apo-A1, Apo-B, HDL-c, LDL-c, LP(a), Glu, was found. In the control group, the concentration of plasma Lp-PLA2 had positive correlation with TG and Glu ($r = 0.410$, $P < 0.05$; $r = 0.397$, $P < 0.05$) (Table 3).

Discussion

At present, CHD is one of severe threat to public health and its morbidity, disability rate and mortality are rising year by year. Though many search on the pathogenesis of CHD, there is no recognized theory yet. Directly related to the occurrence of CHD, atherosclerosis is a disease closely related to inflammation, a dynamic pathologic change when

Table 2
Comparison of laboratory indexes among groups.

Index	Control group ($n = 34$)	SAP group ($n = 10$)	UAP group ($n = 10$)	AMI group ($n = 36$)
Lp-PLA2 (ng/ml)	32.65 ± 37.87	145.00 ± 40.61*	195.55 ± 87.80*#	453.40 ± 272.45*#@
Tch (mmol/L)	4.71 ± 1.01	4.62 ± 0.98	4.84 ± 1.01	4.98 ± 1.25
TG (mmol/L)	1.55 ± 0.70	1.26 ± 0.45	1.61 ± 0.82	1.56 ± 0.56
Apo-A1 (g/L)	1.32 ± 0.30	1.22 ± 0.20	1.29 ± 0.24	1.35 ± 0.30
Apo-B (g/L)	0.98 ± 0.31	0.98 ± 0.27	0.98 ± 0.35	1.06 ± 0.35
HDL-c (mmol/L)	1.26 ± 0.34	1.05 ± 0.15	1.12 ± 0.66	1.10 ± 0.36
LDL-c (mmol/L)	3.11 ± 0.97	3.01 ± 0.82	3.07 ± 0.94	3.08 ± 1.16
Lp(a) (mg/L)	207.18 ± 182.67	370.9 ± 291.09	375.40 ± 230.81	383.94 ± 328.77*
Glu (mmol/L)	6.69 ± 3.03	7.62 ± 3.39	7.72 ± 2.60	8.87 ± 3.44*
hs-CRP (mg/L)	4.41 ± 3.09	7.22 ± 4.80	9.22 ± 5.11	39.16 ± 25.77*#@

* compared with the control group and $P < 0.05$; # compared with SAP group and $P < 0.05$; @ compared with UAP group and $P < 0.05$.
SAP: stable angina pectoris; UAP: unstable angina pectoris; AMI: acute myocardial infarction; Lp-PLA2: plasma lipoprotein-associated phospholipase A2; Tch: total cholesterol; TG: triglyceride; Apo-A1: apolipoprotein A1; Apo-B: apolipoprotein B; HDL-c: high density lipoprotein-cholesterol; LDL-c: low density lipoprotein-cholesterol; LP(a): lipoprotein a; Glu: glucose; Hs-CRP: high-sensitivity C-reactive protein.

Table 3
The Pearson correlation coefficient of Lp-PLA2 and other indexes.

Indices	All subjects ($n = 90$)		Control group ($n = 34$)		CHD group ($n = 56$)	
	r	P	r	P	r	P
Tch	−0.019	0.860	−0.016	0.930	−0.101	0.461
TG	0.022	0.838	0.410	<0.05	0.023	0.868
Apo-A1	0.036	0.734	0.151	0.394	0.048	0.724
Apo-B	−0.002	0.985	0.141	0.426	−0.090	0.511
HDL-c	−0.05	0.642	−0.219	0.212	0.138	0.310
LDL-c	−0.093	0.385	0.307	0.078	−0.146	0.282
LP(a)	0.056	0.602	0.038	0.831	−0.191	0.159
Glu	0.249	<0.05	0.398	<0.05	0.124	0.364
hs-CRP	0.616	<0.05	−0.206	0.427	0.493	<0.05

Tch: total cholesterol; TG: triglyceride; Apo-A1: apolipoprotein A1; Apo-B: apolipoprotein B;HDL-c: high density lipoprotein-cholesterol; LDL-c: low density lipoprotein-cholesterol; LP(a): lipoprotein a; Glu: glucose; hs-CRP: high-sensitivity C-reactive protein; CHD coronary heart disease.

dysfunction of vascular endothelium interacts with inflammatory response. Inflammatory cytokines play an important role in the occurrence, development and rupture of AS plaque.[10,11]

Lp-PLA2, also called platelet-activating factor acetylhydrolase (PAF-AH), is an enzyme which can catalyze the hydrolysis of lipoprotein and glyceryl phosphatide second acyl ester bond in the cell membrane, producing non-esterified fatty acid and lysophospholipase. In blood circulation, Lp-PLA2 is mainly produced and secreted by mature macrophage and lymphocyte, in which platelet activating factor can promote the secretion.[12]

In the blood circulation, Lp-PLA2 is combined with lipoprotein particle, among which 80% was combined with LDL, 15%~20% with HDL and the rest with very low density lipoprotein (VLDL).[13] PAF can promote the gather of platelet, the chemotaxis of neutrophils and monocyte, the release of inflammatory mediator like leukotrienes, the formation of thrombus and inflammatory response. A latest research found that Lp-PLA2 can hydrolyze the proinflammatory cytokines PAF into the inactive lyso-PAF, which can reduce the occurrence of inflammation and thrombus, anti-inflammatory and antiatherosclerotic.[14] On the other hand, Lp-PLA2 also can hydrolyze oxydic lecithin of the blood vessel intima, producing Lysophosphatidylcholine (lyso-PC) and oxidized free fatty acids (ox-FFA), and these two products are proinflammatory mediator which can stimulate and produce adhesion molecule and cytokines, and further the gathering movement of monocyte from lumen to intima. Macrophage is derived from the gather of monocyte in intima and then turns into foam cell by phagocytosing oxidised low density lipoprotein (ox-LDL) and finally gather to form AS plaque which can release cytokines and protease, degradate smooth muscle cell and collagen matrix of fibrous cap, leading to the fragility and rupture of plaque, further resulting in the formation of thrombus and occurrence of cardiovascular events.[15,16] The role that LP-PLA2 plays in the process of AS is still controversial, but more and more evidence indicates that LP-PLA2 can facilitate AS.

This study found that after the adjustment for age, gender, the concentration of plasma Lp-PLA2 in the subgroups of CHD varied greatly from the control group as well as from each other: great difference appeared between SAP group and either UAP group or AMI group; so did between AMI group and UAP group. With the comparison, it can be found that Lp-PLA2 may play a stimulative role in AS, related to the occurrence and development of CHD and its clinical type, which was valuable for the judgment of CHD. The concentration of plasma Lp-PLA2 in AMI group was higher than that in UAP group, which may result from that for patients with AMI, the rupture of AS plaque and formation of thrombus led to angiemphraxis and the formation of atheromatous plaque caused by inflammatory response was stronger in AMI group than in UAP group.

The study showed the increasement of hs-CRP was associated with the instability (severity) of atherosclerotic plaque, but there was no statistically significant; while the concentration of Lp-PLA2 rose with the increase of the instability (severity) of atherosclerotic plaque, and there was statistically significant. Meanwhile, in the analysis on the correlation between Lp-PLA2 and the inflammation marker of hs-CRP, it was found that the concentration of Lp-PLA2 was slightly related to the level of hs-CRP. It meant that Lp-PLA2 may, associate with hs-CRP inflammatory factor, take part in the inflammatory response of AS. The reason may be that Lp-PLA2 shared different physiopathologic mechanism with hs-CRP in the process of AS, or

it may be the cause that these two markers play different roles in AS: hs-CRP maybe is a product in the acute nonspecific inflammatory response while Lp-PLA2 may play a more specific role in cardiovascular inflammation.

Lp-PLA2 had no correlation with other laboratory index, which can be learned from their correlation analysis. This result was different from some other domestic research, which may be accounted for the difference of ares, group characteristics and the number of cases involved in this study.

In conclusion, this research investigated the changes of concentration of Lp-PLA2 in different group of CHD patients and its correlation with blood lipid and hs-CRP. Though there is no recognized theory about the role which Lp-PLA2 plays in the process of AS, this study confirmed that Lp-PLA2 can promote AS and had close correlation with CHD. Moreover, it may predict the occurrence of CHD events. It remains to be confirmed by further studies on the exact impact and mechanism of Lp-PLA2, which shows importantly clinical significance for the prevention and treatment of AS events. It presents more predictive value for the fact that traditional risk factors cannot be identified on those people at risk. Therefore, Lp-PLA2 may be a potential target for CHD diagnosis.

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