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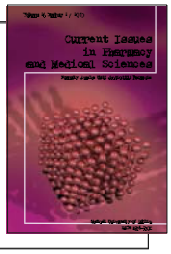

Concentration of lipoprotein- associated phospholipase A2 in chronic dental diseases and stable coronary artery disease

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ABSTRACT

Lipoprotein-associated phospholipase A2 (Lp-PLA2) is an enzyme that has been shown to be a risk factor of cardiovascular disease (CVD) and that is involved in the degradation of the phospholipid mediator platelet-activating factor (PAF), a potent mediator of inflammation. The aim of the present study was to investigate concentration of Lp-PLA2 in control group and patients with chronic dental diseases and stable coronary artery disease (CAD). We studied 10 patients with chronic dental diseases, 10 patients with stable coronary artery disease and 10 healthy individuals as controls. Our patients with stable coronary artery disease were using anti-hypertension medicaments, acetylsalicylic acid and statins although patients with chronic dental diseases were not. A plasma Lp-PLA2 assay kit (ELISA, Human, Life Inc., Wuhan, China) was used. Our results showed that both groups of patients with chronic dental diseases and stable coronary artery disease had significantly increased Lp-PLA2 mass as compared to controls. However, Lp-PLA2 mass in patients with chronic dental diseases and stable coronary artery disease was non-significant statistically. We concluded that patients with chronic dental diseases have increased the serum lipoprotein-associated phospholipase A2, which is believed to be an independent cardiovascular risk factor, although future studies are required.

Keywords: Lipoprotein-associated phospholipase A2, chronic dental diseases, stable coronary artery disease

INTRODUCTION

Phospholipase A2 is known as lipoprotein-associated phospholipase (Lp-PLA_2) and platelet-activating factor acetylhydrolase (PAF-AH), is calcium-independent glycoprotein that belongs to the phospholipase A2 superfamily [1-3]. Lp-PLA2 is secreted into the plasma by hematopoietic cells such as monocytes/macrophages, lymphocytes, mast cells, megacariocytes and platelets and is then transported mainly by low-density lipoprotein (LDL) (80-85%), and in lesser amounts by high-density lipoproteins (HDL-20%) and lipoprotein (a) [4]. LDL associated PLA2 then hydrolyzed the oxidized phospholipids to release lysophosphatidylocholine. Increased plasma levels of the Lp-PLA2 have been shown to be a good predictor of cardiovascular disease and have a strong association with atherosclerosis [5]. It was reported that cardiovascular diseases (CVD) were associated with dental infections [6]. Periodontal diseases are infection/inflammatory diseases, mechanisms mediated by oral microorganisms and the inflammation triggered by them have been proposed to their involvement in atherogenesis. Bacteria associated with periodontal diseases can colonize the atheromatous plaques and could cause their damage by inducing local inflammation, resulting in propagation of the inflammatory events that lead to atheroma formation, development and eventual rupture. Alternatively, a low grade systemic inflammation could result from bacteremias, or as a consequence of proinflammatory cytokines generated at the site of the periodontal lesion gaining access to the blood stream [7]. However, clinical utility of lipoprotein-associated phospholipase A2 (Lp-PLA2) in cardiovascular disease and chronic dental diseases are still unexplored.

The aim of present study was to investigate concentration of Lp-PLA2 in control group and patients with chronic dental diseases and stable coronary artery disease (CAD).

MATERIAL AND METHODS

We studied 10 patients with dental diseases at the age between 25-61 and 10 patients with stable coronary artery disease at the age 42-68 and the control group constituted of 10 healthy individuals as controls. The study was con-

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ducted in accordance with the guidelines of the Ethics Committee, Medical University of Lublin.

The patients with chronic dental diseases did not have heart disease, acute inflammatory disease, renal disease, diabetes mellitus, liver disease, malignancy obesity and did not have any treatment. The patients with stable coronary artery disease did not have acute coronary syndroms (ACS), acute inflammatory disease, renal disease, diabetes mellitus, liver disease, malignancy, obesity, although they were using anti-hypertension medicaments, acetylsalicylic acid and statins.

Venous blood was drawn after a 14-hour overnight fasting, and plasma was obtained by centrifugation at 3000 rpm at 4°C immediately after blood collection. Sample were stored frozen at -60°C.

Detection of LpPLA2 mass.

A plasma Lp-PLA2 assay kit (ELISA, Human, Life Inc., Wuhan, China) was used. The microtiter plate in this kit has pre-coated with an antibody specific to Lp-PLA2. Standards or samples are then added to the appropriate microtiter plate wells with a biotin-conjugated antibody preparation specific for Lp-PLA2. Next, Avidin conjugated to Horse radish Peroxidase (HRP) is added to each microplate well and incubated. After TMB substrate solution is added, only those wells that contain Lp-PLA2, biotin-conjugated antibody and enzyme-conjugated Avidin will exhibit a change in color. The enzyme-substrate reaction is terminated by the addition of sulphuric acid solution and the color change is measured spectrophotometrically at a wavelength of 450 nm ± 10 nm. The concentration of Lp-PLA2 in the sample is then determined by comparing the O.D. of the samples to the standards curve.

Statistical Analysis

The data were expressed as median (minimum-maximun), median (quartile rang), and mean ± SD. Kruskal--Wallis test was used to compare group of patients and controls. The statistical significance of all variables was established at P 0.05, and statistical analysis was performed using the Statistica programme (StatSoft, Krakow, Poland).

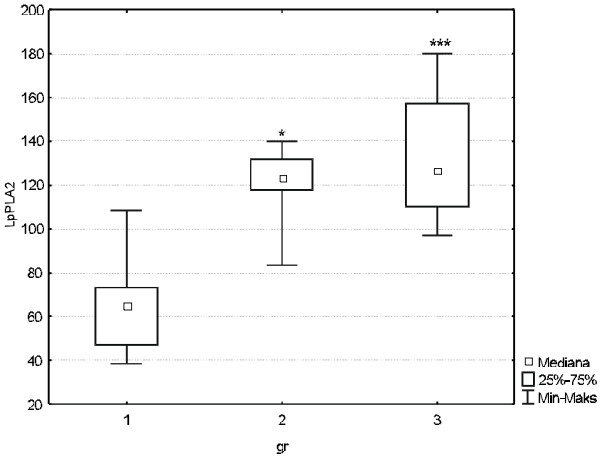
RESULTS

Table 1 presents the results of concentration of plasma Lp-PLA2 in controls and patients with chronic dental diseases and stable coronary artery disease. The results showed that both groups of patients with chronic dental diseases and stable coronary artery disease had significantly increased Lp-PLA2 mass as compared to controls. However, Lp-PLA2 mass in patients with dental disease and stable coronary artery disease was non-significant statistically (Table 1, Fig 1).

Table 1. Lipoprotein associated phospholipase A_2 ($LpPLA_2$) concentration of control group, patients with chronic dental diseases and stable coronary artery disease

	Control group n=10	Patients with chronic dental diseases n=10	Patients with stable coronary artery disease n=10
mean ± SD	65.20 ± 21.77	119.37 ± 21.69	131.99 ± 29.4
median (min-max)	64.79 (38.51-108.39)	123.11 (83.63-140.17)*	126.48 (96.84-180.06)***
median (quartiles)	64.79 (46.91-73.25)	123.11 (118-131.91)*	126.48 (110.18-157.22)***

*vs. control group; ** p<0.05; *** p<0.001



*vs. control group; ** p<0.05; *** p<0.001

Fig. 1. Lipoprotein associated phospholipase A_2 ($LpPLA_2$) concentration in control group (1), patients with chronic dental diseases (2) and stable coronary artery disease (3) (median(min-max)). Kruskal-Wallis test was used to compare group of patients and controls.

DISCUSSION

Lp-PLA2 has been suggested to have dual role in atherosclerosis. Because it degrades and inactivates PAF and PAF-like pro-inflammatory phospholipid mediators, it is suggested to play an anti-atherogenic/anti-inflammatory role [3]. However, LDL bound PLA2 also has a crucial role in the formation of atherosclerotic plaques [1]. When LDL is trapped in the subendothelial space at the site of new plaque formation (as result of the interaction between its basic apolipoprotein B100 and negatively-charged subendothelial proteoglycans), the associated lipids are subjected to oxidative modifications [8]. LDL associated phospholipase A2 then hydrolyzed the oxidized phospholipids to release lysophosphatidylcholine and oxidized non-estrified fatty acid, both of which are pro-inflammatory, and ultimately lead to foam cell formation. The balance between the pro- and anti- inflammatory roles of phospholipase A2 may depend on the concentration of the available substrates [8]. Increased plasma levels of Lp-PLA2 enzyme have been shown to be a good predictor of cardiovascular disease (CVD) and have a strong association with atherosclerosis. Lp-PLA2 mass and activity are cor-

related with age, male gender, smoking and LDL cholesterol levels and are reduced significantly by statins [8].

Our results showed that both patients with chronic dental diseases and stable coronary artery disease (CAD) had significantly increased Lp-PLA2 as compared to controls. Patients with stable coronary artery disease received stain therapy but patients with chronic dental diseases did not. Lp-PLA2 activity and mass predicted the risk of CVD and vascular death [8, 9]. Both mass and activity were predictors of ischemic stroke, vascular mortality and non--vascular mortality. These associations were also observed in people with and without known vascular disease. The magnitude of risk was comparable to that of non-HDL cholesterol or systolic blood pressure [8, 9]. The effect of Lp-PLA2 on chronic heart disease (CHD) risk remains significant after adjustment for CRP [9, 10]. Our preliminary studies indicated that chronic dental diseases lead to an increase in serum Lp-PLA2, which is comparable to this with stable artery disease. These results suggest that chronic dental diseases, systolic blood pressure can accelerate atherosclerosis and cardiovascular disease in these patients. Therefore, patients with chronic dental diseases must be controlled for cardiovascular risk factors. Our results were confirmed with other authors. Löscher et al. [11] show that moderate periodontitis is also associated with an enhanced activity of Lp-PLA2. They demonstrated that clinical measure of periodontitis such as bleeding on probing, pocket depth or attachment loss, was positively correlated with the serum activity of Lp-PLA2 and that local periodontal treatment resulted in a significant decrease in the enzyme activity by about 10%. In case-control studies in which Lp-PLA2 was proved to be an independent risk factor for CVD, the differences in the plasma levels of the enzyme between cases and controls were found to be about 5%. Therefore, the 10% difference between the post- and pre-treatment activities of lipoprotein-associated PLA2 that are observed is in the significant range for CVD risk reduction. They concluded that periodontal therapy has an effect on those markers of systemic inflammation, which are risk factors and contribute to the development of CVD [11]. Fentoglu et al. [12] reported that periodontal disease is associated with an increased severity of hyperlipidemia, and serum Lp-PLA2 and CRP, which are lipoprotein-associated inflammatory markers associated with a worsening periodontal and hyperlipidemic state. Recently the authors have shown that elevated level of Lp-PLA2 is associated with periodontal inflammation, indicating that periodontal treatment could reduce the risk of cardiovascular disease in periodontitis subjects with hyperlipidaemia [13]. However, future studies are required including patients with chronic dental diseases, severe periodontitis and CVD to clarify the role of serum Lp-PLA2 and CRP levels and hyperlipemia and hyperlipoproteinemia, and developing therapeutic approaches that will be useful for treating dental disease.

CONCLUSION

The results indicate that patients with chronic dental diseases have increased the serum lipoprotein-associated phospholipase A2, which is believed to be an independent cardiovascular risk factor, although future studies are required.

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