

Abstract

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Acute and chronic effects of vitamin C on endothelial fibrinolytic capacity in overweight and obese adult humans.

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OBJECTIVE AND METHODS: We determined the effects of acute intra-arterial vitamin C administration and chronic oral vitamin C supplementation on the capacity of the endothelium to release t-PA in overweight and obese adults. Net endothelial t-PA release was determined in vivo in response to intra-brachial infusions of bradykinin and sodium nitroprusside in thirty-three sedentary adults: 10 normal weight (BMI: 23.4 +/- 0.5 kg m⁻²; 7M/3F); and 23 overweight/obese (BMI: 31.2 +/- 0.8 kg m⁻²; 15M/8F). In 10 normal weight and 8 overweight/obese adults the dose-response curves to bradykinin and sodium nitroprusside were repeated with a coinfusion of the antioxidant vitamin C (24 mg min⁻¹). Seventeen of the 23 overweight/obese adults completed a 3-month chronic oral vitamin C (500 mg day⁻¹) supplementation intervention.

RESULTS: Intra-arterial administration of vitamin C significantly potentiated t-PA release in overweight/obese adults. Net release of t-PA was ~95% higher ($P < 0.01$) after (from -0.9 +/- 1.1 to 94.6 +/- 16.2 ng (100 mL tissue⁻¹) min⁻¹) compared with before (from -0.8 +/- 0.8 to 49.9 +/- 7.7 ng (100 mL tissue⁻¹) min⁻¹) vitamin C administration. Daily vitamin C supplementation significantly increased t-PA release in overweight/obese adults (from 0.2 +/- 0.9 to 48.2 +/- 6.5 ng (100 mL tissue⁻¹) min⁻¹) before supplementation vs. 0.3 +/- 0.5 to 66.3 +/- 8.7 ng (100 mL tissue⁻¹) min⁻¹) after supplementation).

CONCLUSION: These results indicate that the antioxidant vitamin C favorably affects the capacity of the endothelium to release t-PA in overweight/obese adults. Daily vitamin C supplementation represents an effective lifestyle intervention strategy for improving endothelial fibrinolytic regulation in this at-risk population.

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Abstract

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Vitamin C consumption is associated with less progression in carotid intima media thickness in elderly men: A 3-year intervention study.

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BACKGROUND AND AIM: Plant foods may lower the risk of cardiovascular disease.

METHODS: We assessed changes in the intima media thickness (IMT) of the carotid artery and diet in elderly men. Men (n=563) aged 70+/-5 years were randomly assigned to 1 of 4 groups (dietary intervention, omega-3 supplementation, both or neither) using a 2x2 factorial design. B-mode ultrasound of the carotid arteries and calculation of dietary intake were performed at baseline and after 3 years. We previously showed that omega-3 supplementation did not influence the IMT, thus the dietary intervention (n=233) and no dietary intervention (n=231) groups were pooled.

RESULTS: The dietary intervention group had less progression in the carotid IMT compared with the controls (0.044+/-0.091mm versus 0.062+/-0.105mm; P=0.047). This group increased their daily vitamin C intake (P=0.005) and intake of fruit, berries and vegetables (P<=0.001). Increased intake of vitamin C and of fruit and berries was inversely associated with IMT progression (r=-0.181; P=0.006 and r=-0.125; P=0.056, respectively). Multivariate linear regression analysis showed that increased intakes of vitamin C and of fruit and berries were associated with less IMT progression in the intervention group and in the total study population, after adjustment for consumption of dietary cholesterol, cheese, saturated fat and group assignment.

CONCLUSION: Vitamin C containing foods may protect against the progression of carotid atherosclerosis in elderly men.

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Abstract

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Effect of vitamin C supplementation on lipid peroxidation, muscle damage and inflammation after 30-min exercise at 75% v.o(2max).

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AIM: Hypothetically, supplementation with the antioxidant vitamins C could alleviate exercise-induced lipid peroxidation. The purpose of this study was to evaluate the effect of vitamin C supplementation on exercise-induced lipid peroxidation, muscle damage and inflammation.

METHODS: Sixteen healthy untrained male volunteers participated in a 30-min exercise at 75% Vo2max. Subjects were randomly assigned to one of two groups: 1) placebo and 2) vitamin C (VC: 1 000 mg vitamin C). Blood samples were obtained prior to supplementation (baseline), 2 h after supplementation (immediately pre-exercise), post-exercise, 2 and 24 h after exercise. Plasma levels of VC, total antioxidant capacity (TAC), creatine kinase (CK), malondealdehyde (MDA), total leukocytes, neutrophils, lymphocytes, interleukin-6 (IL-6) and cortisol were measured.

RESULTS: Plasma vitamin C concentrations increased significantly in the VC in response to supplementation and exercise ($P < 0.05$). TAC decreased significantly in Placebo group 24 h after exercise compared to pre-exercise ($P < 0.05$). Although MDA levels were similar between groups at baseline, it increased significantly 2 h after exercise only in the Placebo group ($P < 0.05$). CK increased immediately and 2 h after exercise in both groups and 24 h after exercise only in placebo group compared to pre-exercise ($P < 0.05$). Markers of inflammation (total leukocyte counts, neutrophil counts and IL-6) were increased significantly in response to the exercise ($P < 0.05$). In VC group, there was significant increase in lymphocyte counts immediately after exercise compared with pre-exercise ($P < 0.05$). Serum cortisol concentrations significantly declined after supplementation compared with baseline ($P < 0.05$) as well as declined 2 and 24 h after exercise compared with immediately after exercise in VC group ($P < 0.05$).

CONCLUSION: VC supplementation prevented endurance exercise-induced lipid peroxidation and muscle damage but had no effect on inflammatory markers.

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Abstract

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Relationship of ascorbic acid to blood lead levels.

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CONTEXT: Some animal studies suggest that orally administered ascorbic acid may chelate lead and decrease the risk of the toxic effects of lead. However, results from several small studies in humans have yielded inconclusive evidence of a beneficial effect of ascorbic acid on lead toxicity.

OBJECTIVE: To examine the relationship between serum ascorbic acid levels and prevalence of elevated blood lead levels.

DESIGN, SETTING, AND PARTICIPANTS: Cross-sectional analysis of a probability sample of the US population enrolled in the Third National Health and Nutrition Examination Survey, 1988-1994 (4213 youths aged 6-16 years and 15365 adults aged > or =17 years) without a history of lead poisoning.

MAIN OUTCOME MEASURES: Elevated and log blood lead levels by serum ascorbic acid level.

RESULTS: A total of 22 youths (0.5%) and 57 adults (0.4%) had elevated blood lead levels (defined as > or =0.72 micromol/L [15 microg/dL] and > or =0.97 micromol/L [20 microg/dL], respectively). After controlling for the effects of age, race, sex, income level, and dietary energy, fat, calcium, iron, and zinc intake, youths in the highest serum ascorbic acid tertile had an 89% decreased prevalence of elevated blood lead levels compared with youths in the lowest serum ascorbic acid tertile (odds ratio, 0.11; 95% confidence interval, 0.04-0.35; P for trend = .002). Adults in the highest 2 serum ascorbic acid tertiles had a 65% to 68% decreased prevalence of elevated blood lead levels compared with adults in the lowest serum ascorbic acid tertile (P for trend = .03). As a continuous predictor, serum ascorbic acid level was independently associated with decreased log blood lead levels among adults (P<.001), but not among youths (P=.14).

CONCLUSIONS: Our data suggest that high serum levels of ascorbic acid are independently associated with a decreased prevalence of elevated blood lead levels. If these associations are related causally, ascorbic acid intake may have public health implications for control of lead toxicity.

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Abstract

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Distribution and correlates of lipoprotein-associated phospholipase A2 in an elderly cohort: the Cardiovascular Health Study.

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OBJECTIVES: To determine whether high levels of lipoprotein-associated phospholipase A(2) (Lp-PLA(2)) are associated with prevalent cardiovascular disease (CVD) and to evaluate factors most influencing Lp-PLA(2) levels in a community-based cohort of older adults.

DESIGN: Cross-sectional.

SETTING: The Cardiovascular Health Study (CHS), a population-based cohort study of men and women aged 65 and older.

PARTICIPANTS: Five thousand five hundred thirty-one CHS participants.

MEASUREMENTS: Levels of Lp-PLA(2) activity were determined using stored blood samples from the baseline examination.

RESULTS: Mean Lp-PLA(2) was higher in participants with electrocardiographically determined ventricular conduction defect and major Q-wave abnormality and was positively correlated with left ventricular (LV) mass. It was high in those with echocardiographically determined abnormal LV ejection fraction, which persisted after adjustment. Mean Lp-PLA(2) was also higher in participants with mild renal insufficiency and kidney disease. After multivariable adjustment, there was a modest but significant 27% greater risk of prevalent CHF per standard deviation increment of Lp-PLA(2) and a modest but significant 12% greater risk of prevalent myocardial infarction. Lp-PLA(2) was weakly but mainly most strongly correlated with cholesterol and lipoproteins, but those correlations were not especially strong. Lp-PLA(2) was weakly positively correlated with soluble intercellular adhesion molecule-1 but not interleukin-6. In total, all factors considered could explain only 29% of Lp-PLA(2) activity.

CONCLUSION: Novel findings in the study are the associations, in those aged 65 and older, between Lp-PLA(2) activity and LV dysfunction, CHF, and renal disease. CVD risk factors only minimally explain levels of Lp-PLA(2).

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Abstract

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Cardiovascular events with increased lipoprotein-associated phospholipase A(2) and low high-density lipoprotein-cholesterol: the Veterans Affairs HDL Intervention Trial.

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OBJECTIVE: Lipoprotein-associated phospholipase A(2) (Lp-PLA(2)), a proinflammatory enzyme that predominantly circulates with low-density lipoprotein (LDL), has been shown in general populations to predict cardiovascular (CV) events. We sought to determine whether increased Lp-PLA(2) would also predict CV events in the absence of high LDL-cholesterol (LDL-C), in a population with low high-density lipoprotein-cholesterol (HDL-C).

METHODS AND RESULTS: Plasma Lp-PLA(2) activity was measured at baseline and after 6 months on-trial in 1451 men with low HDL-C (mean, 32 mg/dL) and low LDL-C (mean 110 mg/dL), randomized to either placebo or gemfibrozil therapy in the Veterans Affairs HDL Intervention Trial (VA-HIT). Over a quartile range of increasing Lp-PLA(2) there was a significant increase in LDL-C and decrease in HDL-C ($P < 0.0001$), and an increased percentage of myocardial infarction (MI), stroke, or CHD death ($P=0.03$ for trend). In Cox models, adjusted for major CV risk factors, a 1-SD increase in Lp-PLA(2) was associated with a significant increase in CV events (hazard ratio [HR] 1.17 95% CI 1.04 to 1.32). Although gemfibrozil reduced Lp-PLA(2) only modestly (6.6%), at higher levels of Lp-PLA(2) gemfibrozil produced a significant reduction in CV events.

CONCLUSIONS: In VA-HIT, a population with low HDL-C and LDL-C, high Lp-PLA(2) independently predicted CV events that were reduced by gemfibrozil.

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Abstract

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Enhanced expression of Lp-PLA2 and lysophosphatidylcholine in symptomatic carotid atherosclerotic plaques.

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BACKGROUND AND PURPOSE: Circulating lipoprotein-associated phospholipase A(2) (Lp-PLA(2)) has emerged as a novel biomarker for cardiovascular diseases. However, the correlation between the plaque expression of Lp-PLA(2) and plaque oxidative stress, inflammation, and stability as well as the clinical presentation remains poorly defined, especially for cerebrovascular disease. Therefore, this study was performed to test the hypothesis that Lp-PLA(2) expression is higher in symptomatic than in asymptomatic carotid plaques of patients undergoing carotid endarterectomy.

METHODS: The expression of Lp-PLA(2) in 167 carotid artery plaques was determined by immunoblotting and immunostaining. Plaque oxidative stress, inflammation, and stability were quantified by NAD(P)H oxidase p67phox and MMP-2 immunoblotting, oxidized LDL (oxLDL) immunoreactivity, macrophage and Sirius red collagen staining. Lysophosphatidylcholine 16:0 (lysoPC) concentration was measured in 55 plaques using liquid chromatography tandem mass spectrometry.

RESULTS: Lp-PLA(2) expression was significantly higher in plaques of symptomatic patients than asymptomatic patients (1.66±0.19 versus 1.14±0.10, P<0.05) and localized mainly to shoulder and necrotic lipid core areas in colocalization with oxLDL and macrophage content. Similarly, Lp-PLA(2) expression was related to collagen content, which was lower in plaques from symptomatic patients than in plaques from asymptomatic patients (9.1±2.2 versus 18.5±1.7% of staining/field, P<0.001). LysoPC plaque concentration was significantly higher in plaques of symptomatic than asymptomatic patients (437.0±57.91 versus 228.84±37.00 mmol/L, P<0.05).

CONCLUSIONS: Symptomatic carotid artery plaques are characterized by increased levels of Lp-PLA(2) and its product lysoPC in correlation with markers of tissue oxidative stress, inflammation, and instability. These findings strongly support a role for Lp-PLA2 in the pathophysiology and clinical presentation of cerebrovascular disease.

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Abstract

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Lipoprotein-associated phospholipase A2 as an independent predictor of coronary heart disease. West of Scotland Coronary Prevention Study Group.

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BACKGROUND: Chronic inflammation is believed to increase the risk of coronary events by making atherosclerotic plaques in coronary vessels prone to rupture. We examined blood constituents potentially affected by inflammation as predictors of risk in men with hypercholesterolemia who were enrolled in the West of Scotland Coronary Prevention Study, a trial that evaluated the value of pravastatin in the prevention of coronary events.

METHODS: A total of 580 men who had had a coronary event (nonfatal myocardial infarction, death from coronary heart disease, or a revascularization procedure) were each matched for age and smoking status with 2 control subjects (total, 1160) from the same cohort who had not had a coronary event. Lipoprotein-associated phospholipase A2, C-reactive protein, and fibrinogen levels, and the white-cell count were measured at base line, along with other traditional risk factors. The association of these variables with the risk of coronary events was tested in regression models and by dividing the range of values according to quintiles.

RESULTS: Levels of C-reactive protein, the white-cell count, and fibrinogen levels were strong predictors of the risk of coronary events; the risk in the highest quintile of the study cohort for each variable was approximately twice that in the lowest quintile. However, the association of these variables with risk was markedly attenuated when age, systolic blood pressure, and lipoprotein levels were included in multivariate models. Levels of lipoprotein-associated phospholipase A2 (platelet-activating factor acetylhydrolase), the expression of which is regulated by mediators of inflammation, had a strong, positive association with risk that was not confounded by other factors. It was associated with almost a doubling of the risk in the highest quintile as compared with the lowest quintile.

CONCLUSIONS: Inflammatory markers are predictors of the risk of coronary events, but their predictive ability is attenuated by associations with other coronary risk factors. Elevated levels of lipoprotein-associated phospholipase A2 appear to be a strong risk factor for coronary heart disease, a finding that has implications for atherogenesis and the assessment of risk.

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