Exercise Training Increases the Number of Endothelial Progenitor Cells in Patients With Coronary Heart Disease and Cardiovascular Risk Factors

Sabine Stainer, Alexander Niessen, Bernhard Richter, Sophie Zieger, Martina Penka, Erich Minar, Christoph William Kopp, University of Vienna, Vienna, Austria, Austria

Background – Endothelial Progenitor Cells (EPCs) circulating in peripheral blood differentiate into new vascular cells and tissue. Anti-oxidant CD34+, KDR+ and CD133+ CD34+CD133+ positive peripheral blood mononuclear cells (BMCD34+CD133+) represent a more mature fraction of EPCs. CD34+/KDR+/CD133+ positive peripheral blood mononuclear cells (BMCD34+/KDR+/CD133+) were shown to contribute to neovascularization and rejuvenate arterioles. Vascular function and cardiovascular risk factors were inversely correlated with the number of EPCs. As regular physical exercise improves endothelial dysfunction and promotes cardiovascular health we studied the effect of exercise in patients with coronary heart disease and cardiovascular risk factors.

Methods – 15 patients with documented coronary heart disease and/or cardiovascular risk factors joined a 12-week supervised exercise training. The number of circulating EPCs was determined before and after the exercise period by whole blood flow cytometry.

Results – A significant increase in exercise frequency (pre 1.5±1 versus post 3.7±1.7 weekly training episodes; P<0.001) and duration (pre 74±88min versus post 186±87min weekly training time; P<0.0001) was observed in the study group (mean age±sd: 59±10.1). The proportion of EPCs defined as CD34+/KDR+/CD133+ positive peripheral blood mononuclear cells (BMCD34+/KDR+/CD133+) pre: 0.7±0.8%; versus post: 2.7±2.2%; P<0.006) as well as CD34+KDR+ positive cells (BMCD34+/KDR+; pre: 3.1±1.1% versus post: 3.8±2.6%; P=0.02) and CD34+CD133+ positive (BMCD34+CD133+; pre: 45.5±14.8% versus post: 51.8±11.9%) did not increase significantly with exercise. In contrast, the total number of CD34+ positive cells (BMCD34+) did not increase in response to exercise training (pre 0.09±0.05% versus post: 0.09±0.05%; P=0.95).

Conclusions – Endurance training increases the number of EPCs in patients with CHD and cardiovascular risk factors which may contribute to the antathero-protective effect attributed to regular physical activity.

The Effect of Losartan Versus Atenolol on Circulating Adhesion Molecules in Essential Hypertension: A LIFE Substudy

Michael H. Olsen, Peter Clausen, Kristian Wachtell, Ulrik Andersen, Keld Neland, Hans Ibsen, Harriet Dige-Pedersen, Glostrup University Hospital, Copenhagen, Denmark, Rigshospitalet, Copenhagen, Denmark

Background: Hypertension and diabetes are associated with disturbances in circulating adhesion molecules. We wanted to investigate a) the relation of adhesion molecules to blood pressure and metabolic disturbances and b) the effect of a losartan vs. an atenolol based antihypertensive regimen on adhesion molecules.

Methods: In 43 LIFE patients with stage II-III hypertension and electrocardiographic left ventricular hypertrophy we measured insulin sensitivity (M/I) by a three-hour isoglycemic hyperinsulinemic clamp, ambulatory 24-hour blood pressures (BP), plasma levels of VCAM, ICAM, E-selectin, ICAM, E-selectin was not elevated in the patients as compared to the controls. In patients, VCAM (n=0.39+ and n=0.24), ICAM (n=0.45+ and n=0.34) and E-selectin (n=0.41+ and n=0.39) were lower than serum insulin and M/I, but not to ambulatory or office BP serums. In patients receiving losartan (48±127 mg/ml vs. 484±97 mg/ml) and ICAM (39±24 mg/ml vs. 217±44 mg/ml) were significantly reduced without any difference between the two groups. E-selectin decreased insignificantly in patients receiving losartan (64.5±34 mg/ml vs. 50.7±19 mg/ml) and the relative change was closely related to the relative change in 24-hour systolic BP (R=0.88**) and in serum insulin (R=0.61*) in patients receiving losartan. Although M/I and serum insulin and BP showed a significant relationship in the data collected with losartan (R=0.76, P<0.002), we were not able to demonstrate any significant relationship between changes in insulin sensitivity and concentrations of adhesion molecules. P<0.09, ***,P<0.01, **P<0.001.

Conclusion: Circulating VCAM and ICAM decreased during anti-hypertensive treatment with losartan as well as atenolol based regimens. The decrements were independent of concomitant changes in insulin resistance, although the levels of these circulating adhesion molecules were related to insulin resistance rather than high BP at baseline.

Oral Folic Acid Does Not Reduce Plasma Concentrations of the Endogenous Nitric Oxide Synthase Inhibitor Asymmetric Dimethylarginine in Hypercholesterolemic Subjects

Markus C. Staehling, Bernhard Paulweber, Jan Schimmofer, Otmar Pachinger, Olaf Stanger, University Clinic for Innsbruck, Innsbruck, Austria, Landeskrankenhaus Salzburg, Salzburg, Austria

Endothelial function, as assessed in hypercholesterolemic subjects, however, the mechanism for endothelial dysfunction in hypercholesterolemia remains unclear. We could previously show that homocysteine (Hcy) inhibits NO production by accumulating asymmetric dimethylarginine (ADMA), an inhibitor of NO synthase (NOS), in endothelial cells. We also found that hypercholesterolemia after oral methionine leads to elevations of ADMA in humans. In order to better understand the relationship between PAI-1 and these associated factors, we investigated a more diverse population of subjects. In the present study, 54 subjects were studied, (33% Male, 37% African-American, 56% hypertensive, 82% overweight or obese, mean age 49 ± 10). Hepatic, weight, blood-pressure and serum risk factors, plasma activity and PAI-1 were measured. The mean blood pressure of our population was 135/88 ± 15/12 mmHg, BMI 30 ± 5 kg/m2, PRA 0.85 ± 0.65 ng/ml/mg, plasma aldosterone 6.0 ± 3.4 pg/ml, plasma PAI-1 18 ± 17 ng/ml. While BMI correlated with plasma PAI-1, clearly this relationship is influenced and confounded by gender and the relative active state of the renin-angiotensin-aldosterone system.

Aldosterone and Plasma Renin Activity Influence Plasma Plasminogen Activator Inhibitor-1 Levels in Overweight Subjects

James A. S. Middendorf, Blanca, Roberts, Joseph W. Covington, John A. Schoenherr, Nancy J. Brown, Douglas E. Vaughan, Vanderbilt University Medical Center, Nashville, TN

Plasminogen activator inhibitor-1 (PAI-1) is an important predictor of mortality in myocardial infarction, and serves as a key regulator of the fibrinolytic system. We have previously shown that plasma PAI-1 correlates with body mass index (BMI), plasma renin activity (PRA), and aldosterone levels. In order to better understand the relationship between PAI-1 and these associated factors, we investigated a more diverse population of subjects. In the present study, 54 subjects were studied, (33% Male, 37% African-American, 56% hypertensive, 82% overweight or obese, mean age 49 ± 10). Plasma renin activity, plasma aldosterone, and plasma PAI-1 were measured. The mean blood pressure of our population was 135/88 ± 15/12 mmHg, BMI 30 ± 5 kg/m2, PRA 0.85 ± 0.65 ng/ml/mg, plasma aldosterone 6.0 ± 3.4 pg/ml, plasma PAI-1 18 ± 17 ng/ml. While BMI correlated with plasma PAI-1 in the composite group, BMI is a particularly strong predictor of plasma PAI-1 levels in low renin subjects (R = 0.676, P = 0.002). This correlation did not hold true in subjects with a PRA > 0.5. In addition, in overweight and obese subjects (BMI > 25), there is a correlation between plasma aldosterone and PAI-1 levels (R = 0.376, P = 0.012), but not in lean subjects. This relationship was gender-specific, with a strong correlation between aldosterone and PAI-1 levels in men (R = 0.602, P = 0.008), but not women (R = 0.001, P = 0.993). We conclude that BMI predicts PAI-1 in low renin individuals. Plasma aldosterone levels also correlate with PAI-1 levels in men and overweight individuals. BMI is widely recognized as a strong predictor of plasma PAI-1, clearly this relationship is influenced and confounded by gender and the relative active state of the renin-angiotensin-aldosterone system.