There was a statistically significant difference when comparing EMP levels fasting, at one hour (p= 0.0002) and three hours (p< 0.0001) after the high fat meal. When low fat meal was given, there was not statistical difference when comparing EMP levels fasting and one hour and three hours after low meal.

CONCLUSION: EMP are shed in the circulation and may represent an early marker of endothelial injury. There is a direct correlation between cholesterol and EMP levels in healthy volunteers. A single high fat meal may lead to a detectable elevation of EMP in the circulation even in subjects with normal fasting baseline total cholesterol.

1159-192 The Influence of Simvastatin on the Angiotensin AT1 Receptor Density, Oxidative Stress, and Endothelial Function in Patients With Coronary Disease

Marek Kiliszek, Michal Maczewski, Grzegorz Styczynski, Monika Duda, Andrzej Beresewicz, Grzegorz Opolski, Medical University of Warsaw, Warsaw, Poland, Medical Centre of Postgraduate Education, Warsaw, Poland

Background: On the base of experimental studies we formulated the hypothesis on the development of the endothelial dysfunction: LDL cholesterol -> angiotensin AT_1 receptors (AT_1R) -> oxidative stress -> endothelial dysfunction. We tested this hypothesis in patients (pts) with stable angina. We tested also whether statin: (i) improves endothelial function by reducing oxidative stress and (ii) that this effect is due to the reduction in angiotensin AT_1R density.

Methods: Lipid profile, platelet AT_1 receptor density, serum F_2-isoprostanes (marker of oxidative stress) and nitrate + nitrite concentration, and brachial artery flow mediated dilation (FMD, index of endothelial function) were assessed in 20 pts (LDL cholesterol 75-230 mg%) with proven coronary heart disease, which were not on hypolipemic treatment. These measurements were performed at baseline and after treatment with simvastatin 40mg/24 h for 12 weeks.

Results: At baseline there was a significant linear correlation between (i) LDL cholesterol concentration and AT_1R density (r=0,55; p<0,05) (ii) AT_1R density and F_2-isoprostanes concentration (r=0,62; p<0,05) and (iii) F_2-isoprostanes and FMD (r= –0,65; p<0,05). Simvastatin treatment caused a significant reduction in LDL cholesterol (152±39 vs. 89±27mg/dl; p<0,00001), AT_1R density (14,42±5,42 vs 7,58±2,68 receptors/platelet; p<0,00001), F_2-isoprostanes (39,85±14,03 vs. 27,90±10,65pg/ml, p=0,017), a significant improvement in FMD (8,85±4,80% vs 11,04±3,85%; p=0,031), and significant increase in nitrite + nitrate (17,23±7,53 vs. 20,94±7,93uM; p=0,038). Among these simvastatin-induced effects, only changes in AT_1 receptors and F_2-isoprostane concentrations showed strong linear correlation (r=0,65; p<0,05). **Conclusions:** For the first time we have shown in one study that statin causes, in addition to LDL cholesterol reduction and endothelial function improvement, reduction in AT1R density and oxidative stress. Baseline results suggest relationship between LDL cholesterol, AT_1R density, oxidative stress and endothelial dysfunction. Our results suggest that simvastatin-induced reduction in oxidative stress is due to reduction in AT_1R density.

1159-193 Simvastatin Combined With Ramipril Improved Endothelium-Dependent Vasodilation and Fibrinolysis Potential and Reduced Oxidant Stress and Inflammation Markers in Hypercholesterolemic Patients

Kwang K. Koh, Seung H. Han, Jeong Y. Ahn, Woong C. Kang, Wook-Jin Chung, Tae H. Ahn, Eak K. Shin, Gachon Medical School, Incheon, South Korea

Background: Because the mechanisms of the biological effects of statin and antiotensin converting enzyme inhibitor therapies differ, we studied the vascular responses to these therapies in hypercholesterolemic patients.

Methods: We administered simvastatin 20 mg and placebo or ramipril 10 mg daily during 2 months with washout 2 months to 50 hypercholesterolemic patients. This study was randomized, double-blind, placebo-controlled, crossover in design. *=P<0.05;**=P<0.01;***=P<0.001 vs. Baseline. Data= mean±SEM.

Results: Simvastatin alone did not reduce blood pressure, however, simvastatin combined with ramipril significantly reduced blood pressure after 2 months administration compared with baseline. Compared with each baseline, simvastatin alone or combined with ramipril significantly changed lipoproteins, and improved the percent flow-mediated dilator response to hyperemia by 30±5% and by 53±6%, respectively (both P<0.001) and reduced plasma levels of malondialdehyde (MDA) levels by 4±7% (P=0.026) and by 25±4% (P<0.001), respectively and MCP-1 levels by 3±3% and by 12±2%, respectively (P=0.049 and P=0.001, respectively), and C-reactive protein levels by -4±14% and by 26±5%, respectively (P=0.036 and P<0.001, respectively), and PAI-1 antigen levels by -7±7% and by 17±5%, respectively (P=0.828 and P<0.001, respectively). However, simvastatin combined with ramipril significantly changed more the percent flow-mediated dilator response to hyperemia and plasma levels of MDA, MCP-1, CRP, and PAI-1 antigen than simvastatin alone independent of lowering blood pressure.

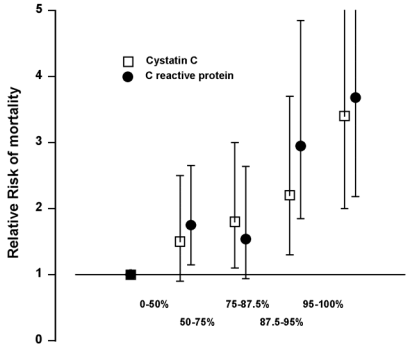
Conclusions; Compared with simvastatin alone, simvastatin combined with ramipril significantly improved endothelium-dependent vasodilation and fibrinolysis potential and reduced plasma levels of oxidant stress and inflammation markers in hypercholesterolemic patients.

	Baseline1	Statin+Placebo	Baseline2	Statin+Ramipril
Apo B (mg/dl)	131±4	89±3***	129±4	92±3***
FMD (%)	4.81±0.24	6.02±0.29***	4.56±0.22	6.58±0.25***
Nitrate (umol/l)	92±7	83±6	89±6	74±5*
MDA (υM)	1.36±0.08	1.17±0.07*	1.45±0.09	1.01±0.07***
MCP-1 (pg/ml)	194±8	178±5*	202±8	174±6***
PAI-1 (pg/ml)	64±4	63±4	68±4	53±3***

1159-194 Cystatin C, a Novel Risk Marker for Mortality in the General Population: Data Obtained From the PREVEND Study

Hans L. Hillege, Jacobien C. Verhave, Stephan J.L. Bakker, Ron T. Gansevoort, Dirk J. van Veldhuisen, Paul E. de Jong, Dick de Zeeuw, University Hospital Groningen, Groningen, The Netherlands

Serum cystatin C (CysC) can generally be recommended as a marker of renal function. We recently showed that CysC was independently of renal function positively associated with a number of cardiovascular risk factors like age, male sex, weight, smoking and C-reactive protein (CRP) levels. We questioned therefore whether CysC, CRP and serum creatinine (SCr), another serum marker of renal function, carry similar prognostic significance for mortality. Data were obtained from the PREVEND study, a longitudinal population based cohort study in the city of Groningen, the Netherlands (n=8,592, age 28-75 yr). Preliminary results of a random sample of 6,135 subjects are presented. Median follow-up time was 5.2 yrs. A total of 180 subjects died. CRP, CysC and SCr were evaluated by dividing the whole range of measurements into 5 for sex stratified groups covering the 0 to 50th, 50 to 75th, 75 to 87.5th, 87.5 to 95th and 95 to 100th percentile. After adjustment for age and sex, CysC , CRP but not SCr contributed independently to an increased risk of death (P< 0.001, P< 0.0001 vs P=0.688, respectively). CysC and CRP remained both statistically significant in the multivariate adjusted model. The figure below gives the age and sex adjusted estimated HR (95% CI) of both CysC and CRP on the risk of death using 0 to 50th percentile as the reference group. In conclusion, CysC is a novel, independent and sensitive prognostic marker, a property that can not be explained by inflammation or renal function. Further mechanistic studies are needed.



1159-195 Spironolactone Improves Coronary Endothelial Function in Patients With Chronic Heart Failure

Keishi Saihara, Shuichi Hamasaki, Takashi Yoshitama, Sanemasa Ishida, Akiko Yoshikawa, Tetsuro Kataoka, Koji Orihara, Naoya Oketani, Tsuyoshi Fukudome, Masakazu Ogawa, Hideki Okui, Takuro Shinsato, Shinichi Minagoe, Chuwa Tei, Kagoshima University, Kagoshima City, Japan

Background: Spironolactone was reported to improve prognosis in patients with chronic heart failure.However, the effect of spironolactone on coronary artery function has not be fully elucidated. Therefore we examined the effect of spironolactone on coronary flow with Doppler flow wire. ***Method:*** Thirty-nine patients treated with chronic heart failure (NYHA class I-II) without significant coronary artery stenosis (% diameter stenosis<30%) underwent Doppler flow study of the left anterior descending coronary artery. Thirteen patients with taking spironolactone served as spironolactone group, and 26 patients without taking spironolactone served as control group. Vascular reactivity was examined by intra-coronary administrating papaverine (12.5 mg / 20 sec), acetylcholine (Ach) (3 and 30 mg / 2 min), and nitroglycerine (200 mg / 20 sec) using a Doppler guidewire. Coronary blood flow (CBF) at control, percent increase in CBF and in coronary artery diameter (CAD) were calculated. The comparisons between groups were analyzed with the Mann-Whitney U test. ***Results:*** There were no significant differences between the two groups in age, gender, coronary risk factor, ejection fraction of left ventricle, circulatory drugs, and CBF at control between two groups. Enddiastolic dimension of left ventricle and left ventricular mass in spironolactone group were significantly higher than those in control group (61±6 vs. 51±9 mm. P<0.01, 515±110 vs. 400±156 g, P<0.02, respectively). The percent increase in CBF and CAD induced by Ach in spironolactone group were significantly greater than those in control group (89±119 vs. 5±105%, P<0.05, -8±21 vs. -41±36%, P<0.03). Whereas, no significant differences were found in reaction induced by papaverin and nitroglycerin between two groups. ***Conclusions:*** These results demonstrate that spironolactone improves coronary endothelial function in patients with chronic heart failure.

1159-196 Does Local Hypertriglyceridemia Impair Resistance Vessel Endothelial Function in Humans?

Nabil E. Choueiri, Philip Roberts-Thomson, Christine A. Sinkey, William G. Haynes, The University of Iowa, Iowa City, IA

Background: Hypertriglyceridemia (HTG) has a modest association with cardiovascular events. Previous studies showed that systemic HTG induces conduit vessel endothelial dysfunction within 60 min. However, the effect of HTG on resistance vessels remains