POSTER SESSION

1054 Vascular Biology and Inflammation

Sunday, March 30, 2003, 3:00 p.m.-5:00 p.m.
McCormick Place, Hall A
Presentation Hour: 4:00 p.m.-5:00 p.m.

1054-134 Oral Rapamycin Attenuates Progression of Atherosclerotic Plaque in ApoE Knockout Mice

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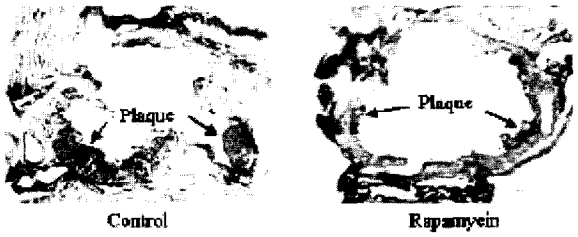
Background: Rapamycin, a macrorlide antibiotic has been shown to inhibit in stent restenosis when delivered locally by drug eluting stents. In order to determine the effectiveness of oral rapamycin on proliferative vascular diseases, we tested the effect of oral rapamycin on atherosclerotic plaque progression.
Methods: Eight week old ApoE knock-out (ApoE) mice were either fed with normal mouse diet containing 0.25% cholesterol (ConD) or with ConD containing 100 µg/kg rapamycin (RapaD). Eight weeks after starting on the diet animals were weighed, blood samples were drawn, euthenized and the hearts were dissected out, fixed in neutral-buffered formalin, embedded in croyomatrix, sectioned and stained with Oil-Red-O and counterstained with Harris modified hematoxylin. Rapamycin levels in the blood were determined and lesion area of 5 sections from each mouse was measured.
Results: Mice fed with RapaD weighed less then the ones fed with ConD (18.5 ± 1.5g vs. 20.6 ± 0.9g, p = 0.01). 117 ± 7 pg/ml of rapamycin was detected in the blood of mice fed with RapaD whereas, none could be detected in the blood of mice fed with ConD. Plaque area of the mice fed with RapaD is 47% less then the plaque area of the mice fed with ConD (0.185 ± 0.07 mm vs. 0.35 ± 0.076 mm , p = 0.001).



Conclusion: Oral administration of rapamycin is effective in attenuating the progression of atherosclerosis plaque in the mice, and may have a role when given sytemically in halting the progression of atherosclerosis in addition to its effect of restenosis prevention.

1054-135 Does *Helicobacter pylori* Infection Relate to the Prevalence of Coronary Artery Disease?

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Helicobacter pylori(*HP*) is one of the most widespread infectious agents which can cause serious diseases. Some epidemiological studies showed that *Helicobacter pylori* might be involved in the pathogenesis of atherosclerosis and there are also negative findings. The present research was to elucidate the possible relationship between *Helicobacter pylori* infection and coronary artery disease (CAD) in a large cohort obtained both *in vivo* and *in vitro* bases. Blood samples from 672 patients underwent coronary angiography were tested for serum C-reactive protein (CRP) and specific IgG and IgM antibodies against *Helicobacter pylori* by ELISA. Among which, 488 cases were diagnosed as coronary artery disease (CAD) and the other 184 cases were grouped as non-CAD controls. Of the 488 CAD patients, 317(64.9%) had HP-specific IgG antibodies; while in the control group, 100 (54.5%) had HP-specific IgG antibodies. HP-specific IgM were not found at all serum samples examined. CAD prevalence was 76.02% in HP-specific IgG-seropositive and 67.06% in HP-specific IgG-seronegative patients. The data showed no significant relationship between *Helicobacter pylori* and CAD after adjustment for traditional atherosclerosis risk factors. PCR aimed to detect *Helicobacter pylori*-specific gene showed that there was no *Helicobacter pylori* present in the atherosclerotic lesions of coronary artery samples obtained from CABG operations. CRP level, an inflammatory marker, was significantly higher in atherosclerosis patients than that of non-atherosclerosis (59.122±37.945 vs 28.708±17.612, *P*=0.0001), but *Helicobacter pylori* seropositivity is not a predictor of risk for elevated CRP levels. In addition, *Helicobacter pylori* could not change expression of MCP-1 and RANTES of human umbilical vein endothelial cell (HUVEC) ECV-304. Though inflammation was associated with atherosclerosis, but this study revealed no relationship between *Helicobacter pylori* and CAD.

1054-136 C-Reactive Protein, Clinical Presentation, and Ischemic Activity in Patients With Chest Pain and Normal Coronary Angiograms

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Background. High sensitive C-reactive protein (hs-CRP), a marker of inflammation, has been related to atherogenesis, endothelial dysfunction and coronary events. Endothelial activation and microvascular dysfunction leading to myocardial ischemia has been shown to occur in patients with typical chest pain and normal coronary arteriograms (CPNCA). However, the relationship between hs-CRP and clinical features of CPNCA patients has not been previously investigated. We sought to investigate the relationship among hs-CRP, clinical characteristics, exercise stress test responses and daily life ST segment changes in patients with CPNCA. **Methods.** We studied 137 consecutive CPNCA patients (mean age 57±9, 33 men). All patients completed standardised angina questionnaires, underwent exercise stress testing (EET) and 24-hour ambulatory ECG monitoring as well hs-CRP measurements, which were carried out at study entry. **Results.** Eighty-six patients had chest pain and > 1 mm ST segment depression during stress testing and 61 had ischemic ST segment shift during ambulatory ECG monitoring. hs-CRP levels were significantly higher in patients with frequent (≥ 5 episodes/week) and prolonged chest pain episodes, in patients with a positive ETT (2.6± 2.8 mg/L vs 1.1 ± 1.1 mg/L) and in those with at least one episode of ST segment depression during Holter monitoring (3.4± 3.1 vs 0.9 ± 0.7 mg/L) compared to those with negative tests and occasional chest pain during daily life. Moreover, we found a direct correlation between hs-CRP concentration and number of ischemic episodes during the ambulatory monitoring (r = 0.65, p<0.001), as well as with the magnitude of ST segment depression on exercise testing (r=-0.43, p<0.001). Multivariate logistic regression analysis showed that hs-CRP concentration was the only independent variable capable to predict positive findings on Holter (OR:3.35, CI:2.16-5.19) and exercise test results (OR:1.83, CI:1.31-2.56). **Conclusion.** hs-CRP correlates with symptoms and markers of ischemic activity in CPNCA patients.Whether hs-CRP is related to the physiopathology of chest pain in CPNCA patients desires futher investigation.

1054-137 Mechanical Disruption of Atherosclerotic Plaques During Percutaneous Coronary Intervention Results in Acute Plasma Increases in Oxidized Low-Density Lipoprotein and Lp(a): Implications for Understanding Vulnerable Plaques

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Background: The role of oxidized LDL (OxLDL) in plaque rupture is not established. This study was performed to establish whether OxLDL is released from atherosclerotic plaques during mechanical plaque disruption. Methods: 143 patients with stable angina undergoing successful balloon angioplasty or stenting (PCI) had 9 serial blood samples drawn over 6 months. Plasma measurements were made of OxLDL, using antibody E06, which detects minimally oxidized phospholipids (OxLDL-E06). We also measured IgG and IgM autoantibodies (ABs) to malondialdehyde(MDA)-LDL, a model oxidation-specific epitope. Results: OxLDL-E06 and Lp(a) increased 35±45% and 80±117% (P<0.001 for both, Figure) immediately post procedure, then returned to baseline by 24 hours. A strong correlation was noted between OxLDL-E06 and Lp(a) (r=0.87, p<0.0001). Both IgG (-8.2±25.5%, P<0.001) and IgM (-6.6±15.9%, P<0.001) ABs actually decreased post-procedure, suggesting acute consumption (removal as immune complexes) of pre-existing circulating OxLDL ABs due to acute release of OxLDL antigens. Conclusion: Mechanical disruption of atherosclerotic plaques in stable patients results in acute increases of OxLDL-E06 and Lp(a), suggesting acute release from disrupted plaques or acute generation and/or synthesis of these atherogenic lipoproteins. This observation has important implications in understanding spontaneous plaque disruption and suggests novel diagnostic and therapeutic modalities targeting OxLDL in the vessel wall.