1201-83 **eta-Adrenergic Inhibition of Leptin Production is Attenuated in Obese Individuals**

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Background: Leptin regulates body weight and may affect cardiovascular function. Leptin expression from adipocytes is suppressed by beta-receptor stimulation. Obese subjects have high leptin levels and are at increased risk for cardiovascular disease. We tested the hypothesis that suppression of leptin production from adipocytes following beta-receptor stimulation is attenuated in obese subjects.
Methods: We studied 8 obese (age 35 ± 3 yrs, BMI 35 ± 2 kg/m2) and 8 age and gender matched lean controls (age 35 ± 3 yrs, BMI 24 ± 1 kg/m2). All subjects were normotensive, free of disease and were not taking any medications. In a randomized fashion, subjects received either a 4 hour infusion of normal saline or isoproterenol (to increase resting heart rate by 25%) on two separate days. Blood samples for plasma leptin were drawn at baseline and at 30 minute intervals during both infusions.
Results: Leptin levels decreased by 7.8 ± 1.5% at the end of isoproterenol and increased by 3.1 ± 4.8% during normal saline in obese subjects ($p < 0.05$). In controls, leptin decreased by 16.8 ± 3.4% and 9.0 ± 4.8% with isoproterenol and normal saline, respectively ($p < 0.05$). During isoproterenol, the maximum percent decrease from baseline in leptin was 10.3 ± 3.3% in obese subjects and 19.2 ± 2.1% in lean controls ($p < 0.02$). The area under the curve (AUC) for percent change in leptin levels with isoproterenol was significantly less in obese subjects compared to lean controls (1799 ± 287 versus 2818 ± 203, $p < 0.05$). The infusion rate of isoproterenol in obese subjects was 0.47 ± 0.1 mcg/min and 0.36 ± 0.06 mcg/min in controls ($p = 0.05$).
Conclusion: Isoproterenol significantly decreased plasma leptin levels in both obese and lean subjects compared to normal saline. Beta-adrenergic stimulation that induced comparable increases in heart rate in both lean and obese subjects resulted in a lower level of leptin suppression in obese subjects. This blunted suppression of leptin production is even evident during higher doses of isoproterenol in obese subjects. Thus, there appears to be an attenuated beta-adrenergic suppression of leptin production in obese individuals.

1201-84 **Difference of High-Sensitive C-Reactive Protein Levels in Patients Treated With Statins, Aspirin, and Angiotensin II Modulators**

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Objectives The anti-inflammatory effects of statins, aspirin, and angiotensin II modulators (A II-M), such as angiotensin-converting enzyme inhibitors and angiotensin II type I receptor blockades, were examined by measuring serum high-sensitive C-reactive protein (hs-CRP) levels in patients with and without ischemic heart disease (IHD). **Background** Statins, aspirin and A II-M may have a clinical anti-inflammatory action. Although statins have been shown to reduce CRP levels, the relationship between the effects of statins, aspirin and A II-M on CRP levels remains to be determined. **Methods** We examined serum hs-CRP levels in consecutive patients who were scheduled for coronary angiography with (n=979, 65± 1 years, male/female 731/248) and without (n=200, 64±1 years, male/female 102/98) IHD. The blood was withdrawn on the day of catheterization. Hyperlipidemia (HL) was defined as total cholesterol >220 and/or triglycerides >150 mg/dl. **Results** In IHD patients, hs-CRP levels were significantly higher than in non-IHD patients (0.34±0.02 vs 0.26±0.03 mg/dl, p<0.05), although no difference in hs-CRP levels was observed between patients with and without HL in each group. The low levels of hs-CRP in the non-IHD patients were not reduced by the treatment with statins, but the high levels of hs-CRP in the IHD patients were significantly reduced by the treatment with statins (0.27±0.02 mg/dl, p<0.05). In all patients included, neither aspirin nor A II-M had any effect on hs-CRP levels in both groups. Interestingly, however, in the patients not treated with statins, A II-M, but not aspirin, significantly reduced hs-CRP levels only in IHD patients (A II-M, 0.41±0.04 vs 0.32±0.03 mg/dl, p<0.05; aspirin, 0.34±0.03 vs 0.38±0.03 mg/dl, ns). **Conclusions** Statins have an anti-inflammatory action assessed by measurement of CRP levels in IHD, but not in non-IHD, patients. A II-M also have an anti-inflammatory action only in IHD patients, but the effect is smaller than that of statins in terms of CRP levels.

POSTER SESSION

1202 Risk Assessment: Emerging and Traditional Risk Factors

Tuesday, March 19, 2002, 3:00 p.m.-5:00 p.m.
Georgia World Congress Center, Hall G
Presentation Hour: 3:00 p.m.-4:00 p.m.

1202-85 **Folic Acid Supplementation Substantially Reduces Hyperhomocysteinemia Induced by Fenofibrate**

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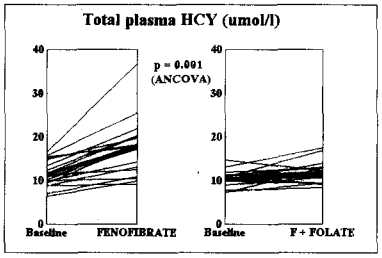
BACKGROUND: Plasma homocysteine (Hcy) is an independent risk factor of atherosclerosis. An increase of Hcy levels during treatment with fibrates has been reported. This phenomenon may explain lower efficacy of fibrates on mortality. The effect of Folic acid (FA) on fibrate-induced Hcy elevation has never been studied.
METHODS: 37 subjects (15 wo, 50±10y) with hyperlipidemia were randomized to 8 weeks of treatment with micronised fenofibrate (F) 200mg/day or F 200 mg/day + Folic acid 5 mg/day (F+FA). Subjects with vitamin B use or deficiency, diabetes, renal or thyroid disease were excluded. Blood lipids, creatinine (Creat), plasma FA, cysteine (Cys) and Hcy (by HPLC) were determined before and after treatments. The between-group differences were tested by ANCOVA.
RESULTS: Serum Hcy increased after F by 52.5% (from 11.5 ± 3.0 to 17 ± 6.5 µmol/l), after F+FA only by 12.5% (from 10.4 ± 1.9 to 11.7± 2.5 µmol/l), ($p = 0.001$). Cys increased after F by 14% (from 321 ± 32 to 366 ± 53 µmol/l) and after F+FA by 16.6% (from 292 ± 34 to 340 ± 30 µmol/l), (NS). Creat increased after F by 20% (from 90 ± 12 to 108 ± 14 µmol/l), after F+FA by 9% (from 90 ± 10 to 98 ± 10 µmol/l), ($p = 0.015$). Plasma folate was unchanged after F, after F+FA increased by 152% (from 5.7 ± 1.7 to 14.4 ± 3.9 mg/l). Groups did not differ in lipid levels.
CONCLUSIONS: Fenofibrate-induced Hcy elevation can be effectively reduced by Folic acid co-administration. Folic acid can enhance therapeutic efficacy of fibrates.



1202-86 **Secretory Phospholipase Is Related to Other Coronary Heart Disease Risk Factors**

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Background: Secretory Phospholipase ($sPLA_2$) remodels LDL and HDL particles, and may contribute to vascular inflammatory. This cross-sectional analysis evaluated the relations between $sPLA_2$ and certain CHD risk factors.
Methods: Plasma lipoprotein subclasses and particle sizes were measured by nuclear magnetic resonance (NMR) spectroscopy (LipoMed, Raleigh, NC). Enzyme immunoassays were used to determine $sPLA_2$ (Cayman Chemical, Ann Arbor, MI) and high-sensitivity C-reactive protein or hs-CRP (Wampole, Cranbury, NJ). Pearson correlations were done between log-transformed $sPLA_2$ levels and hs-CRP, lipoproteins, age, gender, race, BMI (body mass index), hypertension, diabetes, and use of tobacco or hormones. Patients were divided into two groups: high $sPLA_2$ levels (Kugiyama et al., Circulation 1999;100:1280) and low $sPLA_2$ levels. Mann Whitney U tests and multiple logistic regression analyses was performed between the two groups.
Results: Ninety-six subjects (40 female, 56 male) with average age of 49 years. The means ± SD (medians) of biochemical variables include TG, 254 ± 363 (162) mg/dL; TC, 229 ± 58 mg/dL; HDL-C, 40±14 mg/dL; LDL-C, 150 ± 53 mg/dL; sPLA2, 176.6 ± 200 (125.8) pg/mL; hs-CRP, 3.85 ± 6.72 (1.61) mg/dL. Log-transformed sPLA2 levels were correlated with hs-CRP (r=.50, p<0.00005), HDL size (r=.22, p=0.044), age (r=.26, p=0.012) and BMI (r=.23, p=0.033). Significantly higher hs-CRP (p=0.00005), larger HDL particles, greater BMI (p=0.003), more diabetes, but lower TG (p=0.02) were found in subjects with higher sPLA2 (≥ 246pg/mL) levels as compared to those with lower levels.
Conclusion: $sPLA_2$ levels is a novel inflammatory marker that is elevated in diabetics and associated with certain other CHD risk factors characteristic of the metabolic syndrome.

1202-87 **Predictors of 13-Year Changes in the Total Cholesterol to High-Density Lipoprotein Cholesterol Ratio**

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Background: Many clinical and lifestyle factors modify the total cholesterol to HDL (TC/HDL) ratio, yet few studies have determined what predicts changes in this ratio over time. We examined the predictors of the 13-year change in TC/HDL ratio among 4,543 men free of coronary artery disease from the Physicians' Health Study who provided baseline and follow-up blood samples.
Methods: Baseline coronary risk factors were included in multivariate linear regression models to determine significant predictors of a change in the TC/HDL ratio. The final model had an r^2 of .38.
Results: These men had a mean age of 48.7 ± 7 years with a mean total and HDL cholesterol in 1982 of 214 ± 36 mg/dL and 42 ±15 mg/dL, respectively. After a mean follow up of 13 years, average total cholesterol decreased by 8 mg/dL, HDL increased by 1 mg/dL and the ratio decreased by 0.38. The parameter estimates and P values for the change in TC/HDL ratio are as follows: baseline TC/HDL ratio (-0.49, p<0.0001), age in years (-0.03, p<0.0001), systolic blood pressure per mmHg (+0.01, p<0.002), alcohol consumption of 1-6 drinks/week (-0.16, p=0.02), alcohol consumption of ≥ 1 drinks/day (-0.25, p=0.004), body mass index > 25 kg/m^2 (+0.27, p<0.0001), hypertension treatment (-0.34, p=0 .0002), and hyperlipidemia treatment (-0.65, p<0. 0001). Smoking history, exercise, and diabetes were not significant but were included in the model. The exclusion of 92 individuals with an MI during the study period did not appreciably change the parameter estimates.
Conclusions: These data suggest that the greatest reductions in the TC/HDL ratio were among men receiving pharmacological treatment for hypertension or hyperlipidemia. 13-