0.25 m/sec) (p=NS).
Conclusion: Long-term combined HRT has no favorable effects on large artery compliance in hypertensive postmenopausal women. In the same population, abnormal circadian BP variability does not attenuate the estrogen-induced alterations in arterial elasticity.

1160-169 Short Term Estrogen Replacement Therapy Improves Cardiovascular Autonomic Response in Postmenopausal Women: A Double-Blind Randomized Placebo Controlled Trial

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BACKGROUND: Estrogen deficit may lead to cardiac autonomic function imbalance in the postmenopausal women that may potentially increase cardiovascular risk. The physiological mechanism by which estrogen replacement therapy (ERT) regulates the autonomic nervous system in postmenopausal women remains unclear.
METHODS: Thirty nine patients aged 45-65 years with a previous total hysterectomy and amenorrhea for 1 year prior to the surgery were enrolled in this prospective, randomized double-blind, placebo-controlled trial. Women with obesity, cardiovascular, neurological or metabolic disease were excluded. Conjugated estrogens were administered at a dose of 0.625 mg daily during 12 weeks in 19 patients (52.6± 7.1 years), and matched placebo in 20 women (53.8± 5.4 years). Cardiopulmonary and arterial baroreceptor response was determined after 3 months of treatment in both groups. Arterial baroreflex sensitivity (BRS) was determined after the intravenous bolus administration of vasoactive substances (phenylephrine 150 mcg, sodium nitroprussiate,100 mcg). Cardiopulmonary baroreflex response(CBR) was calculated using venous occlusion plethysmography by determining forearm blood flow changes (FBF) and peripheral vascular resistance (PVR) to –10mmHg lower-body negative pressure (LBNP). All measurements were performed between 8am-12m. All signals were analyzed with the winCPRS software (Absolutely Aliens, Finland).
RESULTS: A significant increase in BRS was found after 3 months of ERT compared with placebo; Phenylephrin; 9.28 ±3.72 vs 15.93±10.22, p=0.09 and Nitroprussiate; 6.7±2.73 vs. 12.68±8.40, p<0.01. During LBNP a higher FBF (1.10±0.39 vs. 0.81±0.15,p<0.05) was associated with lower PVR (97.7±32.5 vs. 129.4±43.5, p<0.05) in the group receiving ERT compared to the placebo group.
CONCLUSIONS: Short term ERT (3 months) may modulate cardiovascular autonomic responses leading to reduced sympathetic activity (PVR) and improving cardiovagal response by increasing arterial baroreflex sensitivity in postmenopausal women. (Colciencias Grant: 6566-04-11788)

1160-170 Irbesartan Significantly Reduces C-Reactive Protein After One Month of Therapy in Unstable Angina

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Background: A growing body of evidence supports the patophysiological role of renin-angiotensin-system (RAS) in the athero-trombotic process, in cardiac remodelling and in apoptosis. Angiotensin II (AgII) blockade seems to be able to reduce the progression of atherosclerotic lesion, through an anti-inflammatory mechanism. A reduction of coronary events has also been observed in trials with these classes of drugs. Therefore we evaluated whether Irbersartan (a selective AgII blocking agent) may modulate the inflammatory response in unstable angina (UA). **Methods:** We studied 25 UA (Braunwald's class IIIB) patients (pts) without hypertension, diabetes, heart failure. Patients were treated with full conventional anti-ischemic therapy (i.v. nitrates, aspirin, clopidogrel, β -blockade, statins, low molecular weight-heparin) except Angiotensin Converting Enzyme-inhibitors and/or AgII inhibitors. Pts were divided into two groups of treatment: group 1 receiving Irbesartan (300 mg/die) on the top of conventional treatment and group 2 receiving conventional treatment and placebo. Patients were discharged with aspirin, clopidigrel, β -blocking agents plus Irbesartan (group 1) or placebo (group 2). In all patients we measured High Sensitivity-CRP levels (Dade-Behring) at Coronary Care Unit entry and after 1 and 3 months of follow up. **Results:** At entry, CRP levels (median and range) were similar in group 1 and group 2 (3.1; 0.7-17.7 and 2.5; 1.1-21.9 mg/L). In group 1, CRP significantly decreased after 1 and 3 months of follow up, being respectively 1.2 mg/L; 0.16-10.07 and 0.86; 0.58-4.17 mg/L (P=0.038 versus entry), whereas no changes were observed in group 2 (2.25; 0.99-4.09 and 1.57;0.22-5.75 mg/L at 1 and 3 months respectively). **Conclusions:** Our data demonstrate that Irbesartan has an in vivo antinflammatory effects as shown by reduction of CRP levels in patients receiving full medical therapy, including statins,and after only one month of treatment. Our data suggest a role for AgII inhibitors in plaque stabilization and may help to explain the reduction of coronary events in patients treated with AgII Inhibitors.

1160-197 Decreased Serum Ghrelin and Insulin-Like Growth Factor-I Levels Associated With Insulin Resistance in Patients With Acute Heart Failure: Analysis by Steady-State Plasma Glucose Method

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Background: Ghrelin, a novel and key peptide of energy homeostasis, is associated with the growth hormone – insulin-like growth factor (IGF)-I axis. Previous studies demonstrated that IGF-I plays a role in pathogenesis of heart failure (HF), in which metabolic abnormalities such as insulin resistance may be induced. Thus, the present study was designed to investigate the role of insulin resistance and its relation with ghrelin and/or IGF-I in patients with HF.
Methods: We studied 14 patients; seven healthy control subjects (M/F=4/3, age: 62±4 [mean±SD] years), and seven patients with acute HF (NYHA class IV), without diabetes mellitus or obesity (M/F=5/2, age: 63±11 years). Insulin sensitivity was assessed at 1 week and 3-6 months following acute HF by the steady-state plasma glucose (SSPG) method using a somatostatin derivative, octreotide acetate. Blood samples were collected to measure the levels of ghrelin and IGF-I. Serum ghrelin level was measured by newly developed enzyme immunoassay system.
Results: In comparison with the control (76±8 mg/dl), the SSPG level in HF patients was significantly increased at 1 week (118±30 mg/dl, *P*<0.01), indicating insulin resistance. However, at 3-6 months following acute HF, the SSPG level was restored to the control level (80±21 mg/dl) with the significant increase in serum ghrelin (from 12±6 to 29±28 fmol/mL, *P*<0.05) and IGF-I levels (from 106±17 to 122±18 ng/mL, *P*<0.05). In patients with HF, ghrelin level correlated inversely with insulin resistance (R=-0.625, *P*<0.01) and positively with IGF-I level (R=0.675, *P*<0.01).
Conclusions: In patients with acute HF, insulin resistance is induced in association with decreased ghrelin and IGF-I levels. The present findings suggest a potential interaction between the ghrelin-IGF-I system and glucose metabolism by insulin, which may contribute to pathophysiology of HF.

POSTER SESSION

1161

Genes, Molecules, and Hypertension

Tuesday, March 09, 2004, 3:00 p.m.-5:00 p.m.
Morial Convention Center, Hall G
Presentation Hour: 3:00 p.m.-4:00 p.m.

1161-171 Blood Pressure Response to Strength Training Is Influenced by AGT (-20) Genotype in the Elderly

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Background: Several linkage and association studies support the role of the Angiotensinogen (AGT) gene in the development of essential hypertension. The C/A polymorphism at -20 position has been shown to modify the expression of AGT, which can elevate BP by raising blood levels of AGT. The purpose of the investigation was to study the relationship of AGT (-20) genotype with resting BP response to Strength Training (ST) in middle-aged to older adults.
Methods: Fifty-five sedentary, healthy men and women who were homozygous for adenine allele (A/A, n=37, 21 men & 16 women) or heterozygous (A/C, n=18, 11 men & 7 women) at AGT gene locus were enrolled in the study. All subjects went through three to six months of ST done 3 days per week using Keiser air-powered variable resistance exercise machines, each session lasting for approximately 45 minutes. One-repetition maximum (1RM) strength, Body Fat (%) and Fat Free Mass were measured before and after the ST program. Resting Systolic and Diastolic BP were measured on six separate occasions before and after ST for each subject. AGT genotyping was performed from each subject's genomic DNA.
Results: Significant training induced reductions were noticed in systolic BPs of female subjects, which dropped from 123.4 ± 11.3 mm Hg to 120.1 ± 11.4 mm Hg (P<0.05). The male subjects dropped their diastolic BPs from 77.2 ± 7.9 mm Hg to 75.0 ± 7.1mm Hg (P<0.05). When analyzed using ANCOVA, accounting for the genotype and the differences in pre-systolic BP between the two genotypes, the change in systolic BP was significantly greater in AA genotype than AC/CC genotype. Systolic BP in AA genotype dropped from 128.2 ± 2.0 mm Hg to 123.8 ± 1.6 mm Hg (P<0.05), while AC/CC genotype dropped their systolic BP from 121.0 ± 2.5 mm Hg to 119.8 ± 3.2 mm Hg (P<0.05). When controlled for the differences in pre-diastolic BP between the two genotypes, the change in diastolic BP was not significantly different between the two genotypes.
Conclusion: AGT (-20) genotype influences resting blood pressure response to strength training such that training reduces systolic BP in homozygotes to a more degree than that in heterozygotes.

1161-172 Upregulation of Akt and Endothelial Nitric Oxide Synthase Induces Vascular Smooth Muscle Cell Differentiation in Hypertension In Vivo

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Background Recent studies have shown that angiotensin II type 1 (AT1) receptor-mediated Akt activation induced vascular smooth muscle cell (VSMC) dedifferentiation *in vitro*. However, the critical signal transductions affecting the VSMC phenotype remain unclear *in vivo*. We examined which signal transduction acting through the AT1 receptor could regulate the VSMC phenotype in SHRSP *in vivo*. ***Methods and Results***- Male stroke-prone hypertensive rats (SHRSP) were randomized and treated for 6 weeks with a vehicle (n=20), an AT1 receptor antagonist (E4177; 30 mg/kg/day, n=20), or an angiotensin-converting enzyme (ACE) inhibitor (cilazapril; 10 mg/kg/day, n=20). Protein expressions were analyzed by immunoblots, and NAD(P)H oxidase activity measured by luminescence assay. Both drugs showed equipotent effects on blood pressure, aortic morphology, collagen deposition, p38 mitogen-activated protein kinase and p42/44 extracellular signal-regulated kinase expression in the aorta (*P*<0.05 vs. the vehicle group, respec-