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

Juan C. Guzman, Ronald G. Garcia, Juan P. Casas, Luis A. Diaz, Patricia Lopez-Jaramillo, Carlos A. Morillo, Karina Montes, Fundacion Cardiovascular de Colombia, Bogota, Colombia; Universidad Autonoma de Bucaramanga, Bucaramanga, Colombia.

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 women 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 nitroprusside,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 ~10 mmHg lower-body negative pressure (LBNP).

RESULTS: 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 to placebo; Phenylephrine: 9.28 ± 3.72 vs. 15.93±10.22, p=0.09 and Nitroprusside; 6.7±2.73 vs. 12.4±7.40, p=0.01. During a LBNP a higher FBF (1.15±0.39 vs. 0.81±0.15, p=0.05) was associated with lower PVR (87.7±32.5 vs. 129.4±43.5, p<0.05) in the group receiving ERT as compared to the placebo group.

CONCLUSIONS: Short term ERT (3 months) may modulate cardiovascular autonomic responses leading to reduced sympathetic activity (PVR) and improving cardiovascular response by increasing arterial baroreflex sensitivity in postmenopausal women. (Co-"ciated Grant: 6556-04-11788)

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

Mariaelena Lombardi, Luigi M. Bianco, Maddalena Piro, Giovanna Di Giannuario, Giulia Aguzzi, Sonia Iacovella, Giovanna Liuzzo, Filippo Crea, Institution of Cardiology. Catholic University, Rome, Italy.

Background: A growing body of evidence supports the pathophysiological 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 RAS in the athero-trombotic process, in cardiac remodelling and in apoptosis. Aguzzi, Sonia Iacovella, Giovanna Liuzzo, Filippo Crea, Institution of Cardiology. Catholic University, Rome, Italy

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

Anish Meerasahib, Ben Hurley, G. Martel, Steve Roth, University of Maryland, College Park, College Park, MD.

Background: Several linkage and association studies support the role of the Angiotensinogen (AGT) gene in the development of essential hypertension. The CIA 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 and older adults.

Methods: Fifty-five sedentary, healthy men and women who were homozygous for ad- nine 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 Kaiser 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 BP 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 BP from 77.2 ± 7.6 mm Hg to 70.5 ± 7.1 mm Hg (P<0.05). When analyzed using ANCOVA, accounting for the genotype and the differences in pre-diastolic 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). During ST, AA 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.

Conclusions: 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.

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

Shrii Kawahara, Seiji Uemoto, Masakazu Tanaka, Kyoko Umeji, Ryo Hashimoto, Susumu Matsuda, Masunori Matsuzaki, Yamaguchi University Graduate School of Medicine, Ube,Yamaguchi, Japan.

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 transactions affecting the VSMC phenotype remain unclear in vivo. In the present study, 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 (olazapril, 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 equivalent effects on blood pressure, aortic morphol- ogy, 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, respect-