Sodium nitroprusside (SNP) was used as endothelium-independent NO (control vasodilator).

Valsartan and amlodipine each lowered the clinic blood pressure to the same extent (Table). The vasodilatory response to ACh was significantly increased with valsartan but remained unchanged with amlodipine. The response to SNP was not different between treatments suggesting that the endothelium-independent pathway was unaffected. Valsartan and amlodipine similarly increased the vasoconstrictive response to L-NMMA (Table).

Valsartan, an AT1 receptor antagonist, increased both stimulated and basal endothelial nitric oxide release whereas for the same degree of blood pressure control, amlodipine had no effect on stimulated NO release. Thus, AT1 receptor blockade may offer superior vascular protection in hypertension.

Table legend:

SBP/DBP: systolic and diastolic blood pressure (SD); FBF = Forearm Blood Flow (SEM).

* p<0.05 versus baseline; ** p<0.001 versus baseline. [Table]

Key Words: amlodipine, nitric oxide, valsartan

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MYOCARDIAL AND VASCULAR REMODELING AND BIOCHEMICAL MARKERS OF VASCULAR DYSFUNCTION IN REFRACTORY HYPERTENSIVES

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In this study, left ventricular mass index (LVM1), ejection fraction (EF), carotid thickness (based on ultrasound) and plasma nitric oxide (NO2/NO3), cGMP, and thromboxane B2 levels were evaluated in refractory hypertensives (RH, n=11) and healthy volunteers (Control, n=11). The LVM1 was higher in the RH group (138.3 ± 19.8 vs 108.3 ± 17.3), but there was no significant difference in EF between the two groups. Carotid thickness was significantly higher in RH patients (1.6±0.2 vs 1.0±0.1; p<0.001), whereas the plasma NO2/NO3, cGMP and thromboxane B2 concentrations were similar (Table; mean±SEM).

These results show that there was no correlation between the biochemical markers assessed and myocardial/vascular remodeling in refractory hypertensive patients.

Key Words: endothelium, refractory hypertension, remodeling

P-113

VITAMIN C REVERSES ENDOTHELIAL DYSFUNCTION IN THE BRACHIAL ARTERY OF CHRONIC UREMIC PATIENTS ON HEMODIALYSIS

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Endothelium (END)-dependent vasodilation (VD) is reduced in the brachial artery of dialyzed uremic patients on hemodialysis (HD). In 30 patients with advanced uremia on conservative treatment (CT, 53±11 years, 140±21/83±11 mmHg, serum creatinine 5.3±5.8 mg/dl), 20 HD patients (55±12 years, 130±20/75±11 mmHg, serum creatinine 11.2±2.0 mg/dl) and 30 healthy subjects (54±9 years, 119±10/78±9 mmHg, serum creatinine 1.1±0.2 mg/dl), we evaluated END-dependent VD (flow mediated dilation, FMD) to forearm reactive hyperemia induced by ischemia (cuff inflated at 300 mmHg for 5 minutes) and END-independent VD induced by sublingual nitroglycerine (GTN, 25 µg) on end-diastolic longitudinal scans of brachial artery obtained by high resolution ultrasounds (Esaote AU5 Armonic). Diameter was measured by an automatic edge detection system from end-diastolic frames acquired every second on personal computer. Baseline FMD and GTN response were calculated as the maximum percent increase in diameter above baseline (measurements obtained 1 minute prior ischemia). As indexes of oxidative status, we measured plasma antioxidant capability (ferric reducing ability of plasma, FRAP), lipoperoxide (LOOH) and malondialdehyde (MDA) by colorimetric method. FMD, response to GTN and oxidative status were measured at baseline and 2 hours after oral vitamin C (2 g) administration.

CT patients showed a reduced FMD as compared to controls (5.7±2.9% vs 7.1±2.7%; p<0.01). In HD patients FMD was further reduced (3.7±2.1%; p<0.01 vs CT). Response to GTN was similar in patients and controls and was not changed after vitamin C. In CT patients, vitamin C significantly (p<0.001) increased FRAP (from 483±172 to 682±204 µmol/l), decreased LOOH (from 5.6±3.6 to 3.8±1.9 µmol/l) and MDA (from 8.8±4.5 to 7.6±4.0 µmol/l), without changing FMD (5.5±2.7%). In HD patients, vitamin C significantly (p<0.001) increased FRAP (from 401±81 to 550±101 µmol/l), decreased LOOH (from 5.8±3.8 to 4.0±2.0 µmol/l) and MDA (from 11.5±4.7 to 9.8±3.9 µmol/l) and enhanced FMD (4.8±2.4%). In conclusion, uremic patients showed a reduced END-dependent VD in the brachial artery. This alteration is more marked in HD than in CT patients, as a consequence of a greater HD-associated oxidative stress.

Key Words: flow mediated dilation, oxidative stress, uremia

P-114

RELATIONSHIP BETWEEN THE HEMODYNAMIC AND PLATELET CYCLIC GMP CHANGES INDUCED BY NITRATES IN ESSENTIAL HYPERTENSIVES

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Nitric oxide (NO) induces vasorelaxation and inhibits platelet aggregation via an increase of the second messenger cGMP, synthesized by soluble guanylyl cyclase in vascular smooth muscle cells and platelets, respectively. To test whether the acute hemodynamic effects of an NO-donor are associated with changes of platelet cGMP, in 15 essential hypertensives grade I-II (age 46±3 yrs) isosorbide dinitrate (ISDN) was infused at 1 microgr/kg/min for 30 min. Platelet (PLT) and plasma cGMP, systolic and diastolic arterial pressure (SAP, DAP, sphygmom), heart rate (HR), stroke volume index (SVI, impedance cardiography) were measured and total peripheral resistance index (TPRI) calculated at baseline and after ISDN. TABLE shows means±SEM. * p<0.05

The decrease of arterial pressure was secondary to SVI decrements, as both HR and TPRI were unchanged. PLT-cGMP changes were inversely related to SAP decrements (r=-0.69, p<0.01). No relationship was present between PLT and plasma cGMP, which tended to decrease after ISDN (from 8.6±1.0 to 7.8±0.9 nmol/l).

These data indicate that in EH patients the acute venodilating effect of an NO-donor is directly related to its stimulating effect of cGMP in platelets.

Key Words: cyclic GMP, Nitric oxide, Platelets