Differential Regulation of Renal Endothelin ETA and ETB Receptors in Rats With Experimental Heart Failure

Zaid Abussi, Babasa’ N. Francis, Samuel N. Heyman, Tony Karram, Joseph Winaver, Aaron Hoffman. Department of Physiology and Biophysics, Faculty of Medicine, Technion, Haifa, Israel; Department of Vascular Surgery, Rambam Medical Center, Haifa, Israel; Department of Medicine, Hadassah University Hospital, Jerusalem, Israel.

Endothelin-1 (ET-1) exerts its biological actions through two receptor subtypes: ETA and ETB. We demonstrated previously that ET-1 induces systemic and renal cortical vasoconstriction via ETA, whereas ETB mediates medullary vasodilation. Congestive heart failure (CHF) is characterized by increased vascular resistance and impaired renal hemodynamic and excretory function. While the pathophysiological effects of ET-1 in CHF are well established, the status of ETA and ETB receptors in the kidney is poorly characterized. We studied the immunostaining and localization of ETA and ETB in the renal cortex and medulla of rats with experimental CHF induced by aorto-caval shunt. Rats with CHF were further subdivided, based on their daily urinary sodium excretion (UNaV), into rats with compensated (UNaV>1200 µEq/day) and decompensated CHF (UNaV<200 µEq/day). ETA is predominantly localized to the cortex, mainly in the peritubular capillaries, and is upregulated in both rats with compensated and decompensated CHF compared with sham operated controls. In contrast, ETB is preferentially expressed in the CD and vasa recta, decreased in rats with compensated CHF and downregulated in rats with decompensated CHF. Furthermore, ETB is accompanied with enhanced ETA abundance in the vasa recta and remarkable downregulation of this receptor subtype in the CD. The findings suggest that upregulation of ETA may lead to a decrease in cortical blood flow while upregulation of ETB in the vasa recta probably contributed to the preservation of medullary blood flow. Furthermore, downregulation of ETB in the CD, noted only in rats with decompensated CHF, could contribute to sodium retention in that subgroup.

Key Words: Endothelin Receptors, Kidney, Heart Failure

Losartan on Nitric Oxide in Patients with Hypertension

Maria C Armas-Padilla, Rafael Hernandez-Hernandez, Maria J Armas-Hernandez, Beatriz Sosa-Cancache, Beatriz Pacheco, Jaime Guerrero, Atif R Carvajal, Rosalba Cammarata. Clinical Pharmacology Unit, Hypertension Clinic, School of Medicine, Universitrad Centraloccidental Lisandro Alvarado, Barquisimeto, Lara, Venezuela.

With the aim of evaluating the action of losartan on serum and urinary nitric oxide (NO) levels in patients with essential hypertension a group of thirty untreated hypertensive patients (age: 51.34 ± 5.4 years, 15 males 15 females) were included. Determinations of NO (Griess Reagent) in serum and 24-hour urinary excretion were carried out on baseline and after 6 weeks of losartan 50 to 100 mg given once daily. All measurement carried out between 7am and 9am.

Results are shown as follows:

In conclusion, Losartan at a dosage of 50 to 100 mg/daily showed statistically significant clinical antihypertensive action accompanied with increment in serum and urinary NO levels. Renal NO clearance was not modified by treatment. Results indicate that losartan restoring nitric oxide production might improve endothelial function in patients with essential hypertension.

Key Words: Nitric Oxide, Losartan, Heart Failure

Association of Homocysteine Levels with Salt Sensitivity in Non-Diabetic Hypertensives

K. A. Argyrouldis, G. P. Vyssoulis, E. A. Karpanou, A. N. Arapogianni, C. A. Chrysostooou, A. I. Zervoudaki, D. V. Cokkinos, C. I. Stefanadis. 1st Cardiology Department of Athens University, Hippokration Hospital, Athens, Greece; 1st Cardiology Department, Onassis Cardiac Surgery Center, Athens, Greece.

Hyperhomocysteinemia comprises a well-established independent risk factor for cardiovascular atherosclerotic disease. Although it is a common feature in diabetic hypertensives, the incidence of hyperhomocysteinemia and its correlation with salt sensitivity has not been thoroughly investigated in non-diabetic, essential hypertensive patients (pts).

We studied 942 consecutive non-diabetic pts with uncomplicated essential hypertension, after a 2-week wash-out period. Pts with primary hyperhomocysteinemia were excluded. Plasma homocysteine was measured in the same day with 24-hour urine collection for determination of urinary sodium concentration (NaC) and total urine sodium excretion (NaT).

When classified to quartiles according to plasma homocysteine values, a progressive significant increase mainly for NaC (114.0, 122.5, 126.6 and 141.4 mEq/L, F=2.26, p=0.001), but also for NaT (199.7, 224.3, 215.7 and 233.0 mEq/24h, F=3.96, p=0.02) was observed. It is noteworthy that pts of the uppermost quartile had a mean homocysteine value >15 µmol/L, thus considered as suffering from mild hyperhomocysteinemia. Inversely, grouping of pts in NaC quartiles was accompanied by a significant increase in plasma homocysteine levels (11.36, 12.96, 12.40 and 14.57 µmol/L, F=13.65, p<0.00001). Overall, homocysteine levels correlated with NaC (r=0.252, p<0.00001).

In conclusion, increased dietary salt ingestion as expressed by 24-h urine Na measurements, is associated with higher plasma homocysteine levels in non-diabetic hypertensives.

Key Words: Homocysteine, Hyperhomocysteinemia, Salt Sensitivity

Gene Transfer of Human GTP Cyclohydrolase I Restores Superoxide-Induced Arterial Tetrahydrobiopterin Deficiency and Endothelial Dysfunction in DOCA-Salt Hypertensive Rats

Jie-Sheng Zheng, Gregory D Fink, Alex F Chen. Departments of Pharmacology and Neurology and the Neuroscience Program, Michigan State University, East Lansing, MI.

Arterial superoxide (O2•−) is increased in deoxycorticosterone acetate (DOCA)-salt hypertension with elevated endothelin-1 (ET-1) level, resulting in endothelial dysfunction. Tetrahydrobiopterin (BH4), an essential cofactor for eNOS, protects against O2•−-induced endothelial dysfunction. This study tested the hypothesis that a BH4 deficiency caused by ET-1-induced O2•− impairs endothelium-dependent relaxation, and gene transfer of human GTP cyclohydrolase I (GTPCH I), the BH4 rate-limiting enzyme, restores BH4 levels and endothelial function in...