obesity, dyslipidemia and left ventricular hypertrophy are more often microalbuminurics.

Key Words: Microalbuminuria, Non-diabetics patients, Essential hypertension

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DIFFERENT RENAL EFFECTS OF L-ARGININE.HCL AND L-ARGININE.CITRIC ACID IN HEALTHY (C) AND HYPERTENSIVE SUBJECTS (HTN): EVIDENCE FOR AN ABNORMAL TUBULOGLomerULAR FEEDBACK (TGF) IN ESSENTIAL HYPERTENSION

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In order to investigate whether buffering anion plays a role in the renal effects of L-arginine (ARG) infusion in C and HTN humans, two 3-hours' infusion studies of .012 mmol.Kg.min-1 ARG- the first with 1.5 M HCl, the second with 1.5 M citric acid (CITR) as the buffer anion for ARG- were performed in 10 C and 10 untreated HTN on a 240 mM Na diet. Mean arterial pressure (MAP), GFR and RBF (inulin and PAH), fractional excretion of Na (FENa), Cl (FECl) and exogenous lithium (FELi) (p=ns) were measured for one hour at baseline and at each hour of infusion. Changes in cation excretion in C were opposite between HCl and CITR, with marked increase in FELi (+40%), FECl (+51%) and FENa (+95%) (.001 for all) under HCl and with decrease in FECl and FENa (-11% and -33%, .001 for both) and no change in FELi under CITR. Such changes were the same in HTN (p=ns). MAP decreased in C by 3% with CITR (.001) and did not change with HCl, while in HTN it fell with both HCl and CITR (-3% and -7%, .001 for both). GFR increased with CITR in C and HTN (+9.7 and +5.4%, .001 for both), while with HCl it did not change in C and declined in HTN (-4.6%, .05). RBF increased equally with CITR in C and HTN (+34, +33%, .001 for both) with no difference between the response curves (p=ns). With HCl, RBF also increased in C and HTN (+22 and +13%, respectively, .001 for both), although at a lesser extent than with CITR (.001 for both C and HTN). RBF response to HCl was significantly smaller in HTN than in C (by 41%, .001) and the difference in RBF response curve between CITR and HCl was greater in C than in HTN (.05). The present data show that the degree of renal hemodynamic response to ARG is different according to the accompanying anion, with much greater vasodilation with CITR than with HCl. Because ARG.HCl and not ARG.CITR inhibits tubular reabsorption, with consequent marked increase in NaCl distal delivery, these findings suggest that activation of TGF mediates the blunted hemodynamic response to ARG.HCl in comparison with ARG.CITR. Renal vasodilation is not impaired in HTN during ARG.CITR but it is with ARG.HCl which presumably activates TGF. This is consistent with the hypothesis that impaired nitric oxide- dependent, ARG-induced renal vasodilation observed by us and Others in HTN undergoing ARG.HCl infusion is explained by an abnormality in TGF-mediated glomerular hemodynamic regulation in HTN kidney.

Key Words: L-Arginine, Kidney, Hypertension

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NATURAL HISTORY OF RENAL DAMAGE ASSOCIATED WITH UNTREATED ESSENTIAL HYPERTENSION

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Target-organ damage associated with hypertension is used as a surrogate end-point in drug trials, and a risk factor in decision-making of individual treatment. The evolutivity of “benign” renal damage is not well understood.

Renal function (urinary albumin excretion, UAE, effective renal plasma flow, ERPF, glomerular filtration rate GFR estimated by the continuous infusion technique and urine collections, using 131I-hippuran and 99mTc-DTPA respectively) and echocardiography (left ventricular mass index, LVMI) were assessed in 57 patients (40 female, 17 male, aged 38±2 years) with essential hypertension at baseline, then after 68±3 months without treatment. Within this time period, there was an increase in blood pressure (from 150±2/91±2 to 160±3/94±2 mmHg), body mass index (BMI, by 0.7±0.2 kg/m²), LVMI (by 13±3 g/m²), and UAE (by 25±8 mg/24h), in contrast with a decrease in GFR (from 104±3 to 97±2 ml/min/1.73m² [all p<0.05]. The increase in SBP was directly correlated with age at baseline, with the increase in BMI, UAE, and LV relative wall thickness, as well as the decrease in ERPF and the increase in filtration fraction (FF). The decline in GFR was directly correlated with basal values of SBP, LVMI, UAE, ERPF, GFR, and FF.

These observations suggest that mild to moderate, untreated, essential hypertension is associated with progressive renal damage (reduction in glomerular filtration and increase in urinary albumin excretion), especially in patients with left ventricular hypertrophy and/or microalbuminuria at baseline.

Key Words: albuminuria, renal function, nephrosclerosis

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GENE POLYMORPHISMS OF THE RENIN-ANGIOTENSIN SYSTEM AND URINARY ALBUMIN EXCRETION IN ESSENTIAL HYPERTENSION

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Microalbuminuria (30-300 mg/24h) is observed in 15 to 25% of patients with essential hypertension (EH), and systolic arterial pressure (SAP) is the strongest correlate with the log of urinary albumin excretion (UAE). Studies were conducted in 173 patients with never-treated EH in whom diabetes or impaired glucose tolerance were excluded. UAE was determined in 24-hr urine collections. We tested whether variants of genotypes of the renin-angiotensin system may influence the relationship between SAP and log(UAE). Genotyping was performed for different variants of the angiotensin I-converting enzyme (ACE) genes [I/D and 4656(C/T)/2/3], angiotensinoing (AGT) gene [M235T], and type 1 angiotensin II receptor (AT1R) gene [A1166C]. The distribution of AT1R A1166C genotype was 59% for AA, 32% for AC, and 9% for CC. The slope of the correlation SAP vs UAE was much steeper in CC (0.0036±0.0074) vs 0.0094±0.0025 for AA and 0.0077±0.0029 for AC genotypes. Tendency to a steeper slope was observed in TT vs MM and MT AGT genotypes. In contrast, no influence of ACE I/D and 4656 was detected.

Analysis of UAE with respect to SAP allowed to demonstrate that the existence of homozygous mutation of 1166 A->C on the AT1R locus enhances the impact of SAP on UAE in essential hypertension. Investigation of the effect of AT1R antagonists on UAE according to AT1R genotypes may be of interest.

Key Words: albuminuria, gene polymorphism, essential hypertension

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NA/K-ATPase ISOFORM SPECIFICITY OF ENDOGENOUS BUFADIENOLIDE SODIUM PUMP INHIBITOR FROM HYPERTENSIVE DAHL RATS

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The Dahl-deWardener concept of natriuretic hormone implicates abnormal regulation of the renal Na,K-ATPase (NKA) by digitalis-like factors in salt-sensitive hypertension. A putative natriuretic hormone is expected to potently inhibit renal NKA and to contribute to blood pressure (BP)