Hypertension in 377 genetically homogeneous essential hypertensives. We have investigated the role of HSD11B2 in sensitivity to hypertension. The non-selective mineralocorticoid (MR) receptor from occupation by enzyme inactivates 11-hydroxy steroids in the kidney, thereby protecting the non-selective mineralocorticoid (MR) receptor from occupation by enzyme inactivates 11-hydroxy steroids in the kidney, thereby protecting.

Key Words: Angiotensin Receptor Blocker Therapy, Chronic Kidney Disease, Hypertension

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**ROLE OF HSD11B2 POLYMORPHISMS IN ESSENTIAL HYPERTENSION AND THE DIURETIC RESPONSE TO THIAZIDES**

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The renal 11-beta-hydroxysteroid dehydrogenase type 2 (11beta HSD2) enzyme inactivates 11-hydroxy steroids in the kidney, thereby protecting the non-selective mineralocorticoid (MR) receptor from occupation by glucocorticoids. Loss-of-function mutations in the gene encoding 11beta HSD2 (HSD11B2), result in overstimulation of the MR and cause salt-sensitive hypertension. We have investigated the role of HSD11B2 in hypertension in 377 genetically homogeneous essential hypertensives from North Sardinia. Thirty of these patients displayed increased urinary cortisol metabolite ratios (greater than or equal to 2) (tetrahydrocortisol [THF]+alloetiohydrocortisol [aTHF]/tetrahydrocortisone [THE]) reflecting a mild reduction in 11beta HSD2 activity. No mutations in HSD11B2 were detected in these patients. All 377 patients were genotyped for a CA repeat microsatellite in intron 1 of HSD11B2 and a G534A polymorphism in exon 3 of HSD11B2. CA repeat length was associated with the (THF+aTHF)/THE ratio which in turn was significantly related to PRA levels. No associations were found between the G534A polymorphism and the other parameters. There were no differences in blood pressure (BP) levels between HSD11B2 genotypes but, in a subgroup of 91 patients that underwent diuretic therapy, CA repeat length was strongly associated with the BP response to hydrochlorothiazide. This study highlights the role of this HSD11B2 polymorphism in sodium handling and is consistent with a role in the BP response to thiazide diuretics.

Key Words: 11Betahydroxysteroid Dehydrogenase Type 2, Genetic Polymorphisms, Pharmacogenomics

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**EFFECTS OF BENAZEPRIL ON EXPRESSION OF AQUAPROTEIN-2 IN SHR AND WKY KIDNEY**

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To explore the effect of benazepril on the expression of water channel-2 (aquaporin 2, AQP2) in spontaneously hypertensive rat (SHR) kidneys, 16 male SHR, aged 12 wks, weighed 200-300 g, were randomly divided into 2 groups: benazepril (SHRl) and saline control (SHRc). After 8 weeks’ medication, the rats were decollated, and plasma concentration of vasopressin (AVP) was measured with radioimmunoassay. The expression levels of AQ2 mRNA and AQ2 protein were determined with RT-PCR and immunohistochemistry. All data were expressed as mean±SD. There was no difference of initial blood pressure of SHR before treatment. After 8 weeks’ administration of benazepril, the blood pressure of SHRL was significantly lower than that of SHRc. The expression levels of AQ2 mRNA (0.48±0.11 vs 0.72±0.17, P<0.05) and AQ2 protein (0.47±0.09 vs 0.62±0.12, P<0.05) and concentrations of AVP (6.17±9.19 vs 87.16±8.2 pg/mL, P<0.05) was significantly decreased as compared with SHRc. It is concluded that Benazepril may inhibit the high expression of AQ2 in SHR kidney.

Key Words: Aquaporin 2, Benazepril, Spontaneously Hypertensive Rats

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**EFFECTS OF LOSARTAN AND AMLODIPINE ON MACROALBUMINURIA AND 24-H BLOOD PRESSURE IN HYPERTENSIVE TYPE 2 DIABETIC PATIENTS WITH OVERT NEPHROPATHY**

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In hypertensive type 2 diabetic patients with overt nephropathy, a loss of nocturnal blood pressure (BP) reduction due to impaired diurnal autonomic nervous rhythm is associated with albuminuria. However, few studies have assessed whether 24-h BP control achieved by antihypertensive agents improves macroalbuminuria. We evaluated the effects of losartan and amlodipine on 24-h BP and autonomic nervous activity in hypertensive type 2 diabetic patients with overt nephropathy. The study was designed as an open-label, parallel-prospective, randomized study for 24 weeks, comparing the effects of losartan (n=44) and amlodipine (n=43). BP and urinary albumin excretion for 24 h were measured before and after treatment. Simultaneously, power spectral analysis of the heart rate was performed to calculate the low frequency (LF) components, high frequency (HF) components and LF/HF ratios as an index of the sympathovagal balance. Losartan significantly (P<0.01) decreased BP (systolic/diastolic) from 162±15/91±10 to 150±15/82±10 mmHg during waking and from 146±16/82±10 to 137±15/74±10 mmHg during sleeping. In the amlodipine group, BP also decreased (P<0.01) from 159±13/90±2 to 147±14/82±8 mmHg during waking and (P<0.01) from 143±15/81±12 to 131±15/72±11 mmHg during sleeping. After both treatments, LF and HF components did not change, with no alteration in the sleep/waking ratio for the LF and HF components. Consequently the sleep/waking ratio for the LF/HF ratio also did not differ after treatment in both groups, showing no change in the diurnal autonomic nervous rhythm. In the losartan group, the 24-h urinary albumin excretion was 1.0±0.6 g/day before treatment and significantly decreased (P<0.01) to 0.7±0.5 g/day after treatment. In the amlodipine group showed no difference (P>0.05) in 24-h urinary albumin excretion before and after treatment (1.2±0.6 vs. 1.0±0.8). Our results suggest that in type 2 diabetes with overt nephropathy, 24-h BP regulation alone is not