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**ALDOSTERONE AND REFRACTORY HYPERTENSION**

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Resistant hypertension (blood pressure ≥140/90 mmHg on 3+ antihypertensive agents) is a common problem in clinical practice. Several factors induce treatment resistance, especially unrecognized secondary hypertension. Aldosterone/renin ratio (ARR) is an index for inappropriate aldosterone activity and it could be helpful to predict the response to antihypertensive agents. Aim of our study was evaluate inappropriate aldosterone activity in causing resistance to antihypertensive therapy. Among the patients from the Hypertension Outpatient Clinic that were consecutively evaluated for the first time between 1995 and 2001, we selected all the patients (n=157) with aldosterone-associated hypertension (AAH, ARR (ng dL⁻¹ /ng mL⁻¹ h⁻¹) ≥25, plasma aldosterone ≥12 ng/dL). 58 were diagnosed as idiopathic hyperaldosteronism (IHA, aldosterone after captopril suppression test >15) and 91 as “high aldosterone hypertension” (HAAH, aldosterone after captopril <15). Patients with Conn adenoma (n=8) were excluded from the study. As a control group, we randomly chose 160 patients with essential hypertension and plasma aldosterone <12 (EH). Antihypertensive treatment was given in accordance to WHO Guidelines (1999). The study end-point was blood pressure <140/90 mmHg. At baseline, there was no significant difference between the AAH and EH group with respect to age, BMI, systolic blood pressure, serum potassium, and creatinine. On the contrary, those with AAH had higher diastolic blood pressure (104±2 vs 98±1 mmHg, p<0.001), serum sodium (142±0.2 vs 141.4±0.2 mEq/L, p<0.05), and lower serum uric acid (4.09±0.03 vs 4.11±0.03 mg/dl, p<0.01) in comparison with EH group. During the follow-up (22±2 months), 59 (40%) patients with AAH and 72 (54%) patients in EH group reached the end point. According to survival analysis the patients with AAH reached the end-point in a smaller fraction and in a longer time compared with EH group, with no difference between IHA and HAAH. At the end of follow-up, diastolic blood pressure was higher in AAH group compared with EH group. In IHA, spironolactone-based therapy was associated with a lower blood pressure at the end of follow-up in comparison with those without spironolactone. Inappropriate aldosterone activity in HAAH is a risk factor for resistance to antihypertensive agents and the benefits of spironolactone is worth testing.

Key Words: Aldosterone, Resistant Hypertension, Secondary Hypertension

**P-630**

**GLYCEMIC CONTROL AND THE STATE OF RESPONSIVENESS OF THE RENIN SYSTEM IN TYPE 1 DIABETES MELLITUS**

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In diabetes mellitus, hyperglycemia, risk factor for nephropathy, increases renin secretion. We investigated whether short term glycemic perturbations, measured in hours, or long term ones, measured by hemoglobin A1c (HbA1c), influence the reactive renin response to captopril.

55 type 1 diabetic subjects were enrolled. Angiotensin blockade was discontinued 2 weeks prior to study. Subjects were in high salt balance. After an all night fast and in the supine position, they received insulin IV. starting at a rate of 0.015 U/kg/hour, and a glucose IV to keep serum glucose between 100 and 150 mg/dL (target). When target was reached, captopril 25mg PO was given. Time needed to reach target from start of IVs varied from 0’ in the controlled, and up to 3 hours in the uncontrolled subjects. Serum glucose drawn before insulin infusion had a median of 143 mg/dl, defining two groups (table). Plasma renin assay (PRA) and finger stick glucose (FSG) were drawn serially every 45 minutes for 225 minutes. Peak drug effect occurred 90 minutes (90’) after administration, defining peak PRA response.

Before captopril, both groups had similar age (p = 0.3), gender distribution (p = 0.9), duration of diabetes (p = 0.08), urine albumin/creatinine (p = 0.7), urine sodium (p = 0.7), and PRA levels. Glucose level at start of IV insulin did not correlate with baseline PRA, but correlated with peak PRA level (F = 12.6; r = 0.6; p = 0.002), hence, with peak PRA response. HbA1c correlated neither with PRA level at captopril administration (r = 0.08; p = 0.6), nor with peak PRA response (r = 0.07; p = 0.8).

In type 1 diabetes mellitus, short term hyperglycemia, but not long term glycemic control, amplified the renin response to captopril.

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**EVIDENCE FOR ABNORMAL LEFT VENTRICULAR STRUCTURE AND FUNCTION IN NORMOTENSIVE INDIVIDUALS WITH FAMILIAL HYPERALDOSTERONISM TYPE 1**

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**Objectives:** Experimental and clinical evidence suggests that aldosterone excess may induce adverse cardiovascular effects independently of effects on blood pressure (BP). We sought to determine whether disturbances in cardiovascular structure or function could be detected in normotensive individuals with primary aldosteronism.

**Methods:** Seven normotensive subjects with genetically proven familial hyperaldosteronism type 1 (FH-I, glucocorticoid-remediable aldosteronism) were compared with 21 age- and sex-matched normotensive controls in terms of 24-h ambulatory BP, biochemical parameters, carotid-radial and carotid-femoral pulse wave velocity (PWV) and echocardiographic characteristics, including left ventricular (LV) wall thicknesses, and parameters of LV diastolic filling, systolic function (LV ejection fraction, long axis strain rate (SR), peak systolic strain and cyclic variation (CV) of integrated backscatter (IBI)), and structure (posterior wall calibrated IB).

**Results:** Subjects with FH-I demonstrated higher serum aldosterone levels (mean 21.0±16.2 SD vs 11.1±8.4 ng/dL; P<0.05) and aldosterone/renin ratios (89.7±121.8 vs 6.5±5.0; P<0.01) than controls, as expected. Despite having similar 24 h ambulatory BPs (SBP 121.4±9.5 vs 117.8±10.4 mmHg, NS; DBP 71.7±11.8 vs 69.7±5.4 mmHg, NS), subjects with FH-I demonstrated greater septal (9.6±1.1 vs 7.9±0.9 mm; P<0.001) and posterior wall (9.3±1.8 vs 7.9±1.0 mm; P<0.05) thicknesses, and lower LV end-diastolic volumes (69.5±10.5 vs 90.1±21.7 ml; P<0.05), mitral early peak velocities (0.73±0.10 vs 0.89±0.16 m/s; P<0.05) and ratios of early to late peak diastolic transmitral flow velocity (1.54±0.25 vs 1.99±0.36; P<0.01), and a tendency towards lower early myocardial peak velocities (8.0±1.8 vs 10.1±2.7 cm/s; P=0.06). There were no significant differences in serum type III procollagen propeptide

**Key Words:** Diabetes Mellitus, Glycemic Control, Renin Response