B029

THE EFFECTS OF ANGIOTENSIN II ANTAGONIST LOSARTAN ON URINARY ALBUMIN EXCRETION IN NON INSULIN-DEPENDENT DIABETES MELLITUS

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Microalbuminuria is associated with higher cardiovascular risk in non insulin-dependent (type 2) Diabetes Mellitus.

Thirty-four type 2 diabetic patients with persistent microalbuminuria (60-299 ug/min) were randomized to receive Losartan (100 mg) or placebo. The mean age of the patients was 74.8 ± 6.6 years (range: 63-85 years). Mean plasma creatinine levels were 69.6 ± 17.4 umol/l (range: 47-128 umol/l). The intervention period lasted for 12 months.

The mean values of urinary albumin excretion (UAER) were 119 ± 51 ug/min (range: 30-299) at baseline and 112 ± 37 ug/min (range: 10-299) in the control group. In the Losartan treated group, the mean values were 125 ± 47 ug/min (range: 30-299) at baseline and 101 ± 28 ug/min (range: 10-253) after 12 months of treatment. The difference between the two groups was statistically significant (p<0.02).

Key Words: Losartan, type 2 Diabetes Mellitus.

B030

THE EFFECTS OF CLAMPING ANGIOTENSIN II LEVELS DURING ACE-INHIBITION IN HEALTHY VOLUNTEERS ON A HIGH AND LOW SALT DIET


This study investigated the effects of sodium intake on the hemodynamic and hormonal sequelae of ACE-inhibition (CEI) during clamping of plasma Angiotensin II (AngII). To this end, we measured both during low and high sodium diet the effects of CEI alone (placebo experiment) and those of CEI with concurrent AngII infusion (clamping plasma AngII levels). Seven volunteers were studied both on a low (55 mmol) and a high (220 mmol) sodium diet. Each diet included two experiments (separated by 2 weeks of washout) during which simultaneous infusions of enalapril (E) or placebo (P) were performed. E either alone or with 0.5 ng/kg/min AngII was given. The AngII was given concurrently with E during the first 30 min. After 30 min of combined infusion, the AngII/P infusion was stopped, whereas E was continued for another 4 h. Mean arterial pressure (MAP), effective renal plasma flow (ERPF), renin (APRC), AngI and aldosterone (Aldo) were assessed at baseline, after 30 min of combined infusion and 30 and 60 min after cessation of the AngII/P. When only E was infused, the fall in MAP and APRC (both p<0.003) were significantly more pronounced during the low than during the high salt diet. When E was combined with AngII, levels of AngII remained unchanged. Despite the same plasma AngII, the MAP fell significantly whereas APRC remained unchanged.

Key Words: Sodium-angiotensin II-ACE-inhibition-kidney.

B031

COMPARISON OF THE ACUTE RENAL EFFECT OF LOSARTAN AND CAPTOPRIL IN AHERATOMOUS RENAL DISEASE

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Administration of angiotensin converting enzyme inhibitors may be complicated by deterioration of renal function in patients with renal artery stenosis (RAS) mainly when bilateral or in a single functioning kidney. The advent of losartan (L), an angiotensin AT1 receptor antagonist, prompted us to compare the renal effects of both drugs in patients with atheromatous renovascular disease, with angiotensin converting enzyme inhibitor captopril (C, 50 mg) in 17 patients (age 63 ± 2 y) with atheromatous RAS and mild to moderate alteration in renal function (serum creatinine 88-336 umol/l). Effective renal plasma flow (ERPF) and glomerular filtration rate (GFR) were estimated by clearances of 131I-hippuran and 99m TC-DTPA respectively. Within 2h after L administration, the pressor effect of a test dose of AII was blunted by 95%. Basal values were similar for all parameters, including MAP (127 ± 5 vs 126 ± 6 mmHg), GFR (59 ± 5 vs 57 ± 3 ml/min/1.73 m²) and PRA. Transient anuria occurred after both agents in one patient with bilateral RAS. Results (expressed as % change from basal value) are given for the remaining 16 patients (* and $ indicate p<0.05 for baseline vs blockade, and L vs C respectively).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>MAP</th>
<th>ERPF</th>
<th>GFR</th>
<th>FF</th>
<th>UNaV</th>
<th>PAl</th>
<th>L</th>
<th>C</th>
</tr>
</thead>
<tbody>
<tr>
<td>L:50mg vs P0mg</td>
<td>-4%</td>
<td>-2%</td>
<td>-1%</td>
<td>-1%</td>
<td>11%</td>
<td>12%</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>C:25 mg vs 50mg</td>
<td>2%</td>
<td>5%</td>
<td>5%</td>
<td>1%</td>
<td>-1%</td>
<td>-4%</td>
<td>$</td>
<td>$</td>
</tr>
</tbody>
</table>

Of note, the decrease in FF, but not GFR was directly correlated with the change in MAP induced by L and C. In the presence of an almost complete blockade of AII, similar baseline PRA and a similar fall in PAC induced by L, the decrease in arterial pressure was attenuated in L when compared to C. In atheromatous renovascular disease, the deleterious renal effect of losartan and captopril is similar.

Key Words: renovascular disease; renin system.

B032

ANGIOTENSIN II STIMULATES LEFT VENTRICULAR HYPERTROPHY IN HYPERTENSIVE PATIENTS INDEPENDENT OF BLOOD PRESSURE

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Objective: Angiotensin II (AII) is known to be a growth stimulating factor for myocardial cells. We examined whether an exaggerated responsiveness of AII might aggravate left ventricular (LV) hypertrophy in human essential hypertension.

Methods: To determine the physiologic response to AII changes in mean arterial pressure (MAP) (SpaceLabs 92020), renal blood flow (RBF) and glomerular filtration rate (GFR) (steady state clearance technique with PAH and insulin, respectively) and aldosterone secretion (radioimmunoassay) to AII infusion (0.5 and 3.0 ng/kg/min.) were examined in 71 male normotensive and 48 hypertensive subjects (age 26 ± 3 years; 24 hour ambulatory blood pressure: 121 ± 5/71 ± 4 mmHg and 138 ± 7/82 ± 7 mmHg, respectively).

Results: Changes to AII were similar between the normotensive and hypertensive group, with exception of an exaggerated MAP increase (18 ± 7 vs. 17 ± 8 ng/kg/min, p<0.022) and RBF decrease (-203 ± 123 vs. -270 ± 137, p<0.007) in hypertensives at 3.0 AII. Most important, the change in GFR to AII was correlated with LV mass (2-D-guided M-mode echocardiography) in the hypertensive group (AII 0.5: r = 0.41, p<0.006, AII 3.0: r = 0.52 p<0.03). After taking baseline MAP and body mass index into account, the increase in GFR to the subhypertensive dose of AII still correlated with LV mass (partial r = 0.37, p<0.01).

Conclusion: Since the increase in GFR is a marker of the responsiveness to AII (mainly vasodilatation at the postglomerular site), a major target of AII, our data suggest that sensitivity of AII modulates LV-hypertrophy in early essential hypertension independent of the level of blood pressure.

Key Words: Angiotensin II, LVH, hypertension.