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ENHANCED ENDOTHELIUM-DEPENDENT VASODILATION AFTER CHRONIC IRBESARTAN TREATMENT
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Essential hypertension is associated with abnormal endothelial function, characterized by an imbalance between vasodilators and vasoconstrictors. The effect of antihypertensive treatment on this endothelial function is poorly known. The aim of the study was to evaluate the effect of antihypertensive treatment with the angiotensin receptor blocker irbesartan on endothelial function, assessed by strain-gauge plethysmography, in a group of essential hypertensive patients.

Fourteen essential hypertensive patients, without evidence of target organ damage were studied. Endothelial function was evaluated by strain-gauge plethysmography. Measurements of baseline forearm blood flow (FBF), the effect of increasing doses of acetylcholine (endothelium dependent vasodilation: EDV) and sodium nitroprusside (endothelium independent vasodilation: EIV) on FBF, as well as the effect of L-NMMA, a NO synthase inhibitor, on this FBF were performed at baseline and at the end of a 6 month treatment period with irbesartan (150-300 mg/day).

Irbesartan significantly decreased BP, both systolic and diastolic. Baseline forearm blood flow did not significantly change at the end of treatment. On the contrary, irbesartan promoted an increased (p=0.055) vasodilating response to acetylcholine and a non-significant increase in sodium nitroprusside-induced vasodilation. According to this enhancement in endothelium-dependent vasodilation, the effect of L-NMMA on baseline forearm blood flow was more increased (p=0.089) after irbesartan treatment. In conclusion, chronic treatment with irbesartan tends to increase both endothelium-dependent and independent responses. The effect of L-NMMA on baseline FBF suggests anamelioration of NO bioavailability.

Key Words: Nitric oxide, Endothelium, Angiotensin receptor blockers

P-104
EFFECT OF AGE ON ENDOTHELIN-1 RECEPTORS IN RAT CARDIAC MEMBRANES
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Aging is associated with different changes in the cardiovascular system that lead to an increase in pathological processes. Since endothelin (ET)-1 may have a role in the pathogenesis of cardiovascular disease, we wished to establish whether ET-1 receptors exhibit age-dependent changes in density, affinity and subtype distribution. Cardiac membranes were obtained from right atrium (RA) and left ventricle (LV) of 1, 3, 12, 24 months-old male Sprague-Dawley rats. Affinity (Kd, nM), density (Bmax, fmol/mg protein) and subtype distribution of binding sites were derived from competition and displacement experiments (125-I-ET-1: 10 nM). The ET binding parameters (mean±SEM) are reported in the following table:

<table>
<thead>
<tr>
<th>Age months</th>
<th>RA Bmax (fmol/mg protein)</th>
<th>LV Bmax (fmol/mg protein)</th>
<th>RA LV</th>
<th>RA LV</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>600 ± 30</td>
<td>800 ± 60</td>
<td>84.16</td>
<td>86.14</td>
</tr>
<tr>
<td>3</td>
<td>1664 ± 541</td>
<td>1560 ± 411</td>
<td>73.27</td>
<td>83.17</td>
</tr>
<tr>
<td>12</td>
<td>15360 ± 411</td>
<td>15360 ± 411</td>
<td>73.27</td>
<td>85.15</td>
</tr>
<tr>
<td>24</td>
<td>929 ± 334</td>
<td>648 ± 325</td>
<td>48.52</td>
<td>61.39</td>
</tr>
</tbody>
</table>

*1 month vs 24 months p<0.001, § 3 month vs 24 months p=0.02, * 12 months vs 24 months p=0.01.

No significant differences in density of ET-1 binding sites in atrial and ventricular membranes were observed as a function of the age, although a tendency to increase can be observed. Moreover our results show that ET-A% decreases significantly with increasing age, with no change in affinity (Kd range: 0.3-0.6 nM). ET-B receptors have been reported mainly mediate the in vivo clearance of ET, thus the up-regulation of ET-B subclass in the 24 months-old rats could be in accordance with the age-related increase of ET-1 levels, enhancing the removal of ET-1 from circulation.

Key Words: endothelin, receptors, aging

P-105
EFFECTS OF ACE INHIBITION ON ENDOTHELIAL FUNCTION AND INSULIN RESISTANCE IN ESSENTIAL HYPERTENSION
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Endothelial dysfunction has been suggested to provide a link between hypertension and insulin resistance. ACE inhibition has shown to im-