P-211
ADMINISTRATION TIME-DEPENDENT EFFECTS OF VALSARTAN ON AMBULATORY BLOOD PRESSURE IN NONDIPPER PATIENTS WITH GRADE 1–2 ESSENTIAL HYPERTENSION
Ramón C. Hernández, Carlos Calvo, Diana E. Ayala, María J Domínguez, Manuel Covelo, Artemio Mejón, Jose R Fernández, Jose L Lopez, Bioengineering and Chronobiology Labs., University of Vigo, Vigo, Spain; Hypertension and Vascular Risk Unit, Hospital Clínico Universitario, Santiago de Compostela, Spain.

Previous results on the potential differing effects of valsartan as a function of its time of administration indicated that this ARB efficiently reduces blood pressure (BP) throughout the 24 hours independently of treatment time [Hypertension. 2003;42:283–290]. However, valsartan administration at bedtime as opposed to upon waking resulted in a significant reduction in the number of nondippers (patients with <10% decline in the nocturnal relative to the diurnal BP mean). Accordingly, we investigated the administration time-dependent antihypertensive efficacy of valsartan in nondipper patients. We studied 120 nondipper patients with grade 1–2 essential hypertension (45 men), 53.1±12.7 years of age, randomly assigned to receive single daily valsartan monotherapy (160 mg/day) either on awakening or before bedtime. BP was measured by ambulatory monitoring at 20-min intervals from 07:00 to 23:00 hours and at 30-min intervals at night for 48 consecutive hours before and after 3 months of therapeutic intervention. Physical activity was simultaneously monitored every minute by wrist actigraphy, and the information used to determine diurnal and nocturnal BP means for each patient according to individual resting time. The highly significant BP reduction after 3 months of treatment with valsartan (P<0.001) was similar for both treatment times (13.9 and 8.9 mm Hg reduction in the 24-hour mean of systolic and diastolic BP after valsartan on awakening; 14.9 and 10.4 mm Hg when valsartan was administered before bedtime). The day/night ratio measured as the nocturnal decline of BP relative to the diurnal mean was unchanged after valsartan on awakening (0.2 and 1.3 for systolic and diastolic BP; P>0.173). This ratio was significantly increased (7.7 and 8.0 for systolic and diastolic BP, P<0.001) when valsartan was administered before bedtime, which resulted in 74% of the patients reverted to dippers. Results indicate that, independently of the time of administration, a single daily dose of 160 mg/day of valsartan effectively reduces BP for the whole 24 hours of the day. In hypertensive patients who are nondippers at baseline, dosing time with valsartan should be chosen at bedtime, for improved efficacy during the nocturnal resting hours, and the potential associated reduction in cardiovascular risk.

Key Words: Valsartan, Chronopharmacology, Nondippers

At baseline the degree of carotid atherosclerosis was equal in the two treatment groups and related to high LV mass index (r=0.27, P=0.01) independently of high systolic blood pressure (r=0.26, P<0.05) (adj. R²=0.15, P<0.001). Systolic and diastolic blood pressures were reduced equally in the two groups. The degree of atherosclerosis progressed only in patients treated with atenolol. The relative degree of atherosclerosis was significantly lower in losartan-treated patients already after one year of treatment (Table 1).

Table 1

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>1 year</th>
<th>2 year</th>
<th>3 year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atherosclerosis (losartan)</td>
<td>0.83</td>
<td>0.81</td>
<td>0.84</td>
<td>0.92</td>
</tr>
<tr>
<td>Atherosclerosis (atenolol)</td>
<td>0.71</td>
<td>0.80</td>
<td>0.84**</td>
<td>0.92**</td>
</tr>
<tr>
<td>Atherosclerosis index</td>
<td>1.01 vs. 1.43*</td>
<td>1.04 vs. 1.63**</td>
<td>1.19 vs. 2.06**</td>
<td></td>
</tr>
</tbody>
</table>

The degree of carotid atherosclerosis was related to LV hypertrophy independently of systolic blood pressure. Progression of carotid atherosclerosis was arrested only in patients treated with losartan despite equal blood pressure reductions.

Key Words: Hypertension, Arteriosclerosis, Angiotensin II

P-212
THE EFFECT OF LOSARTAN VERSUS ATENOLOL ON CAROTID ATHEROSCLEROSIS IN THE COMMON CAROTID ARTERIES IN HYPERTENSION. ICARUS, A LIFE SUBSTUDY
Aud Holeggen, Eigil Fossun, Michael H. Olsen, Kristian Wachell, Elsa Hjerkinn, Richard B. Devreese, Hans Ibsen, Sverre E. Kjeldsen. Department of Nephrology, Ullevaal University Hospital, Oslo, Norway.

We have previously demonstrated that losartan, but not atenolol, reduces carotid artery wall thickness. Therefore, we investigated whether losartan also reduces carotid atherosclerosis.

In 95 LIFE patients with hypertension and electrocardiographic left ventricular (LV) hypertrophy, we measured LV mass index by echocardiography and carotid atherosclerosis by ultrasound at baseline and after one, two and three years of anti-hypertensive treatment with either an atenolol or a losartan-based regimen. The semi-quantitatively (0=none, 0.5=very light, 1=light, 1.5=moderate 2=severe) assessments of the amount and density of the atherosclerotic lesions were added together.

At baseline the degree of carotid atherosclerosis was equal in the two treatment groups and related to high LV mass index (r=0.27, P=0.01) independently of high systolic blood pressure (r=0.26, P<0.05) (adj. R²=0.15, P<0.001). Systolic and diastolic blood pressures were reduced equally in the two groups. The degree of atherosclerosis progressed only in patients treated with atenolol. The relative degree of atherosclerosis was significantly lower in losartan-treated patients already after one year of treatment (Table 1).

At baseline the degree of carotid atherosclerosis was equal in the two treatment groups and related to high LV mass index (r=0.27, P=0.01) independently of high systolic blood pressure (r=0.26, P<0.05) (adj. R²=0.15, P<0.001). Systolic and diastolic blood pressures were reduced equally in the two groups. The degree of atherosclerosis progressed only in patients treated with atenolol. The relative degree of atherosclerosis was significantly lower in losartan-treated patients already after one year of treatment (Table 1).

Table 1

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>1 year</th>
<th>2 year</th>
<th>3 year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atherosclerosis (losartan)</td>
<td>0.83</td>
<td>0.81</td>
<td>0.84</td>
<td>0.92</td>
</tr>
<tr>
<td>Atherosclerosis (atenolol)</td>
<td>0.71</td>
<td>0.80</td>
<td>0.84**</td>
<td>0.92**</td>
</tr>
<tr>
<td>Atherosclerosis index</td>
<td>1.01 vs. 1.43*</td>
<td>1.04 vs. 1.63**</td>
<td>1.19 vs. 2.06**</td>
<td></td>
</tr>
</tbody>
</table>

The degree of carotid atherosclerosis was related to LV hypertrophy independently of systolic blood pressure. Progression of carotid atherosclerosis was arrested only in patients treated with losartan despite equal blood pressure reductions.

Key Words: Hypertension, Arteriosclerosis, Angiotensin II

P-213
COMPARISON OF BLOOD PRESSURE REDUCTION OF CILINDIPINE VS. AMLODIPINE ON AMBULATORY BLOOD PRESSURE
Satoshi Hoshide, Kazuomi Kario, Kazuo Eguchi, Kazuyuki Shimada. Department of Cardiology, Jichi Medical School, Tochigi-ken, Japan.

Cilnidipine is a novel and unique 1, 4-dihydropyridine derivative calcium antagonist that has potent inhibitory actions not only on L-type but also on N-type voltage-dependent calcium channels. Amlodipine has a long half-life and reduce blood pressure (BP) levels throughout the day and night in hypertensive patients. We performed 24-hr ambulatory BP monitoring before and after once-daily use of cilnidipine (C: n=28) and amlodipine (A: n=23) in 51 hypertensive patients. At baseline, the office, 24hr, daytime and nighttime systolic BP (SBP) were similar in cilnidipine and amlodipine groups. After treatment, the office (C: 169±13 vs. 140±13mmHg; p<0.001, A: 172±16 vs. 148±19mmHg, p<0.001), 24hr (C: 148±12 vs. 139±12mmHg; p<0.001, A: 146±15 vs. 132±13mmHg, p<0.001), daytime SBP (C: 154±21 vs. 143±13mmHg, p<0.001, A: 151±13 vs. 137±12mmHg, p<0.001), and nighttime SBP (C:135±14 vs. 129±16mmHg, P=0.006, A: 136±23 vs. 124±17mmHg, p<0.001) was significantly reduced both groups. There were significant difference in morning SBP (the average of SBP after waking) between before and after treatment on both groups (C: 153±11 vs. 142±13mmHg; p=0.006, A: 152±22 vs. 139±16mmHg; p=0.005). Cilnidipine is effective as a once-daily antihypertensive agent as amlodipine. Calcium antagonist has the effects of morning blood pressure reduction.

Key Words: Blood Pressure Monitoring, Calcium Antagonist

P-214
EFFICACY AND SAFETY OF COMBINATION OF VALSARATN WITH HYDROCORTROTHIZIDE IN THE MANAGEMENT OF PATIENTS WITH ESSENTIAL HYPERTENSION
Qi Huang, Dongbao Li. Department of Cardiology, Beijing Xuanwu Hospital, Beijing, China.

To observe the antihypertensive efficacy and safety of Valsartan combined with Hydrochlorothiazide.

151 hypertensive patients were divided into three groups: Valsartan group, Valsartan and Hydrochlorothiazide group, Hydrochlorothiazide