P-250
EFFECT OF PERINDOPRIL AND ATENOLOL ON PLASMA PAI-1 IN HYPERTENSIVE PATIENTS WITH ACUTE ISCHEMIC STROKE
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The aim of this study is to evaluate the effect of perindopril or atenolol addition to standard therapy on plasma PAI-1 in hypertensive patients with acute ischemic stroke.

Sixty-eight acute ischemic stroke patients, aged 56-70 years, with history of hypertension and a DBP > 90 mmHg at admission were enrolled; subjects with obesity and/or diabetes were excluded. The patients were randomized within 24 hours to atenolol 50 mg od (n=34) or to perindopril 4 mg od (n=34) for 12 weeks. Venous blood samples to evaluate PAI-1 antigen levels were drawn before randomization and after 2, 4 and 12 weeks of treatment. The venous samples were collected at the same hour in the morning.

The main results are shown in the table.

During the follow up one patient died in the atenolol group and another in the perindopril group.

In conclusion perindopril has a significant greater impact on PAI-1 improvement than atenolol after an ischemic stroke despite the same antihypertensive effect. This suggests that Renin Angiotensin System may play an important role in the regulation of fibrinolysis in patients during the recovery phase after acute ischemic stroke and that treatment with perindopril may be clinical significant in this type of patients.

<table>
<thead>
<tr>
<th>SBP/DBP (mmHg)</th>
<th>Placebo</th>
<th>Losartan</th>
<th>Placebo</th>
<th>Losartan</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atenolol</td>
<td>171/106</td>
<td>155/93**</td>
<td>149/88*</td>
<td>145/86*</td>
</tr>
<tr>
<td>Perindopril</td>
<td>169/92**</td>
<td>154/92**</td>
<td>148/87*</td>
<td>143/84*</td>
</tr>
<tr>
<td>Plasma PAI-1 (ng/ml)</td>
<td>48±17</td>
<td>36±16</td>
<td>34±15*</td>
<td>39±16</td>
</tr>
<tr>
<td>Atenolol</td>
<td>51±19</td>
<td>29±15*</td>
<td>22±13**</td>
<td>21±13**</td>
</tr>
</tbody>
</table>

* p < 0.05; ** p < 0.01; * p < 0.001 vs baseline; † p < 0.05 vs Atenolol

Key Words: PAI-1, Perindopril, Acute Ischemic Stroke

P-252
CIRCUANNUAL VARIATION IN PLASMA FIBRINOGEN IN DIPPER AND NON-DIPPER HYPERTENSIVE PATIENTS
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Clinical trials and epidemiological observations have indicated that elevated plasma fibrinogen levels are strongly correlated with an increased frequency of vascular events. As such, fibrinogen is recognized as a significant parameter for assessing the potential risk of myocardial infarction and stroke [Wilhelmsen et al. New Eng J Med. 1984;311:501-505]. A seasonal variation has been previously reported in plasma fibrinogen for a small group of patients, with highest values occurring in the coldest months of the year (Stout & Crawford, Lancet. 1991;338:629-630). With the aim to extend and validate these results, we have quantified the yearly variation in plasma fibrinogen in hypertensive patients. We studied 577 mild-moderate hypertensive patients (254 men), 53.8±13.8 (mean±SD) years of age. Blood pressure (BP) was measured every 20 minutes during the day and every 30 minutes at night for 48 consecutive hours. Physical activity was simultaneously evaluated at 1-minute intervals with a wrist actigraph. A complete urine and blood test was performed on the same day before starting BP monitoring.

The circannual variation of plasma fibrinogen was established for all patients as well as for subgroups of dippers (n=287) and non-dippers (n=290); nocturnal BP decline <10% by multiple-component analysis [Fernandez & Hermida. Chronobiol Int. 1998;15:191-204]. For the whole group of patients, plasma fibrinogen is characterized by a highly significant seasonal variation (P<0.001) with a mean value of 324 mg/dl, double circannual amplitude (extent of predictable change along the year) of 75 mg/dl, and orthophase (time of peak value) on the first week of March. This circannual variation can be best represented by a model that includes components with periods of 12 and 6 months. The same model also characterized dippers as well as non-dippers analyzed separately. Non-dippers showed higher plasma fibrinogen throughout the whole year as compared to dippers (P=0.002). Results thus indicate a highly significant seasonal variation in plasma fibrinogen, with highest values in March and lowest values in September. This circannual variation is timely correlated with the reported yearly variation in coronary events [Spencer et al. J Am Coll Cardiol. 1998;31:1226-1233]. Moreover, plasma fibrinogen is significantly elevated in all seasons in non-dipper patients as compared to dippers. These results could support the association between the lack of nocturnal decline in BP with an increase in end-organ-damage and cardiovascular events [Verdecchia et al. Hypertension. 1994;24:793-801].

Key Words: Fibrinogen, Circaannual, Non-Dippers