The Impact of Systolic Blood Pressure Control in Angiotensin II Antagonist Blockade

Hansson L

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The Impact of Systolic Blood Pressure Control in Angiotensin II Antagonist Blockade

L. Hansson

Elevated systolic blood pressure is nowadays recognized as an even stronger predictor than elevated diastolic blood pressure of cardiovascular morbidity and mortality. Even borderline isolated systolic hypertension is associated with significant increases in cardiovascular risks. Moreover, large prospective intervention trials on the treatment of patients with isolated systolic hypertension have shown significant reductions in the risks of stroke and coronary heart disease. In this perspective it is of interest to note that the new angiotensin II receptor antagonist, the AT₁ receptor selective agent eprosartan, has been shown to effectively reduce systolic blood pressure, both in patients with severe hypertension as well as in other patient groups. J Clin Basic Cardiol 2001; 4: 131–134.

Key words: systolic hypertension, cardiovascular morbidity, angiotensin II receptor blockade, eprosartan
Isolated systolic hypertension

Hypertension Detection and Australian National Study 3,427 1980 95 6
Australian National Study 3,943 1979 100 5
Wolff and Lindeman 87 1966 110 2
Hamilton et al. 64 1964 110 (phase IV) 1

A stronger risk indicator than the diastolic blood pressure in a regression equation would yield higher correlation coefficients than simultaneously obtained diastolic pressure in a regression equation would yield higher correlation coefficients than the diastolic, any application of values of systolic blood pressure encompasses a wider range of values than the diastolic, as alluded to above, and since the blood pressure can be measured with a smaller error of measurement than the diastolic, any application of values of systolic blood pressure will appear particularly attractive in the antihypertensive armamentarium.

However, the recent emphasis of systolic blood pressure as a stronger risk indicator than the diastolic blood pressure is not based just on a technicality. Solid evidence from the Framingham Heart Study shows that the systolic blood pressure is at least as strong a risk indicator as the diastolic blood pressure [11]. Moreover, intervention trials based on the level of systolic blood pressure such as SHEP [12], Syst-Eur [13] and Syst-China [14] have shown at least as good benefits of antihypertensive therapy on "hard endpoints" as studies based on diastolic blood pressure entry criteria.

In particular the impressive results shown in the intervention trials comprising patients with isolated systolic hypertension [12–14] have had a great impact on the present view on the importance of systolic blood pressure. It is also worth noting that the 1993 guidelines from WHO/ISH, for the first time listed systolic blood pressure criteria for the definition of hypertension [15]. This view is augmented in the most recent guidelines from WHO/ISH, issued in 1999, which also include definitions of isolated systolic hypertension and borderline isolated systolic hypertension (Table 2) [16]. That even borderline systolic hypertension leads to increased risks for stroke, coronary heart disease, congestive heart failure and other fatal or non-fatal cardiovascular events was clearly shown in a long-term follow-up from the Framingham Heart Study (Table 3) [17].

In a recent issue of "Blood Pressure", another important aspect of systolic blood pressure was presented. Howes and coworkers showed that the prevalence of isolated systolic blood pressure in patients attending general practice in Australia is 8%, a percentage that can be expected to increase considerably with ageing [18]. Since most Westernized populations show that the proportion of elderly individuals increases it is to be expected that the management and treatment of systolic hypertension will assume greater importance in the future.

The significant impact of isolated systolic hypertension as a risk factor for cardiovascular morbidity and mortality was recently reviewed [19]. It was emphasised that the benefit of treating isolated systolic hypertension has been proven beyond doubt and that most likely also borderline isolated systolic hypertension, although not yet demonstrated in an appropriate prospective intervention trial, would benefit from treatment [19]. There may be many spin-offs from this. One could be that antihypertensive drugs that have been shown to be especially effective in lowering the systolic blood pressure will appear particularly attractive in the antihypertensive armamentarium.

Table 1. Improvement of prognosis by antihypertensive therapy in non-malignant hypertension

<table>
<thead>
<tr>
<th>Authors</th>
<th>Number of patients</th>
<th>Year</th>
<th>Benefits shown at diastolic blood pressure &gt; (mm Hg)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hamilton et al.</td>
<td>64</td>
<td>1964</td>
<td>110 (phase IV)</td>
<td>1</td>
</tr>
<tr>
<td>Veterans Administration</td>
<td>87</td>
<td>1966</td>
<td>110</td>
<td>2</td>
</tr>
<tr>
<td>Australian National Study</td>
<td>3,943</td>
<td>1979</td>
<td>100</td>
<td>5</td>
</tr>
<tr>
<td>Australian National Study</td>
<td>3,427</td>
<td>1980</td>
<td>95</td>
<td>6</td>
</tr>
</tbody>
</table>

Table 2. Definitions and classification of blood pressure levels in the 1999 guidelines from the World Health Organization and the International Society of Hypertension

<table>
<thead>
<tr>
<th>Category</th>
<th>Systolic (mmHg)</th>
<th>Diastolic (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Optimal</td>
<td>&lt; 120</td>
<td>&lt; 80</td>
</tr>
<tr>
<td>Normal</td>
<td>&lt; 130</td>
<td>&lt; 85</td>
</tr>
<tr>
<td>High-normal</td>
<td>130–139</td>
<td>85–89</td>
</tr>
<tr>
<td>Hypertension</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 1 (mild)</td>
<td>140–149</td>
<td>90–99</td>
</tr>
<tr>
<td>Subgroup Borderline</td>
<td>140–149</td>
<td>90–94</td>
</tr>
<tr>
<td>Grade 2 (moderate)</td>
<td>160–179</td>
<td>100–109</td>
</tr>
<tr>
<td>Grade 3 (severe)</td>
<td>≥ 180</td>
<td>≥ 110</td>
</tr>
<tr>
<td>Isolated systolic hypertension</td>
<td>≥ 140</td>
<td>&lt; 90</td>
</tr>
<tr>
<td>Subgroup Borderline</td>
<td>140–149</td>
<td>&lt; 90</td>
</tr>
</tbody>
</table>

Based on [16]

Table 3. Long-term cardiovascular morbidity and mortality in subjects who were free of cardiovascular disease at baseline in the Framingham Heart Study

<table>
<thead>
<tr>
<th>Events</th>
<th>Number of events</th>
<th>Normal Blood Pressure (n = 2416)</th>
<th>Borderline Isolated Systolic Hypertension (n = 351)</th>
<th>Hazard Ratio 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>All CV disease</td>
<td>821</td>
<td>189</td>
<td>55</td>
<td>1.47 (1.24–1.74)</td>
</tr>
<tr>
<td>CHD</td>
<td>557</td>
<td>125</td>
<td>55</td>
<td>1.44 (1.18–1.77)</td>
</tr>
<tr>
<td>Stroke or TIA</td>
<td>208</td>
<td>55</td>
<td>55</td>
<td>1.42 (1.03–1.94)</td>
</tr>
<tr>
<td>CHF</td>
<td>173</td>
<td>55</td>
<td>55</td>
<td>1.60 (1.15–2.22)</td>
</tr>
<tr>
<td>Fatal CV disease</td>
<td>316</td>
<td>102</td>
<td>102</td>
<td>1.57 (1.24–2.00)</td>
</tr>
<tr>
<td>All cause mortality</td>
<td>926</td>
<td>206</td>
<td>206</td>
<td>1.14 (0.97–1.34)</td>
</tr>
</tbody>
</table>

CV = cardiovascular, CHD = coronary heart disease, TIA = transient ischaemic attacks, CHF = congestive heart failure. From Sagie et al. 1993 [17].

In recent years the systolic blood pressure has been presented as a stronger risk indicator than the diastolic blood pressure, not the least based on data from the Framingham Heart Study [11]. It could be argued that since the systolic blood pressure can be measured with a smaller error of measurement than the diastolic, as alluded to above, and since the systolic blood pressure encompasses a wider range of values than the diastolic, any application of values of systolic blood pressure in a regression equation would yield higher correlation coefficients than simultaneously obtained diastolic blood pressure values.

However, the recent emphasis of systolic blood pressure as a stronger risk indicator than the diastolic blood pressure is
Systolic Blood Pressure Control with Angiotensin II Receptor Blockade

Angiotensin II receptor antagonists of the AT₁ subtype have been in clinical use since the mid-1990s. The new, highly selective AT₁ receptor antagonist eprosartan is of special interest in this context since it also induces sympathetic suppression by inhibiting angiotensin II-stimulated presynaptic noradrenaline release [20]. In animal studies eprosartan has been shown to inhibit sympathetic outflow in contrast to several other AT₁ receptor antagonists [21].

In an 8-week placebo-controlled dose-ranging study in 351 hypertensive patients, eprosartan at doses of 400, 600, 800 and 1200 mg daily was found to lower systolic blood pressure significantly at all doses [22]. Of particular importance is that eprosartan was found to be significantly more effective than enalapril in reducing systolic blood pressure in patients with severe hypertension (Figure 2) [23]. Eprosartan was also numerically, although not statistically significant, more effective in lowering the diastolic blood pressure [23]. African-American patients, a group of patients often considered to be relatively unresponsive to antihypertensive therapy based on the blockade of the renin-angiotensin-aldosterone system, have been found to respond especially well to eprosartan, the systolic blood pressure being reduced more in that patient group than in all other patients (Figure 3) [23]. Data of this kind indicate that angiotensin II receptor blockade with the AT₁ receptor blocker eprosartan is very effective in lowering systolic blood pressure. This is of relevance in view of the established importance of systolic blood pressure as a risk indicator of cardiovascular morbidity and mortality.

References
3. Veterans Administration Cooperative Study Group on Antihypertensive Agents. Effects of treatment on morbidity in hypertension. Results in patients with diastolic blood pressure averaging 113 through 129 mm Hg. JAMA 1967; 202: 1028-34.
4. Veterans Administration Cooperative Study Group on Antihypertensive Agents. Effects of treatment on morbidity in hypertension. II. Results in patients with diastolic blood pressure averaging 90 through 114 mm Hg. JAMA 1970; 213: 1143-52.
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