

## Treatment of Hypertension in the Elderly

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### Abstract

Diastolic blood pressure is considered an important risk factor for the development of cerebrovascular disease, congestive heart failure and coronary heart disease. However, it is now clear that isolated systolic hypertension and elevated pulse pressure play an important role in the development of these diseases, which are the major causes of cardiovascular morbidity and mortality among subjects aged 65 years and older. The benefit of antihypertensive therapy in reducing the incidence of cardiovascular and cerebrovascular complications has been shown for systolic and systolo-diastolic hypertension in all age groups. Because of the higher risk of cardiovascular disease in the elderly, the effect of antihypertensive treatment appears greater in patients over 60 or 65 years when expressed as an absolute risk reduction.

### Definition

Essential (i.e. primary) hypertension is the main cause of hypertension in the elderly population. However, secondary, especially renovascular hypertension is more common in older than in younger adults. The incidence of hypertension in the elderly is high. In an ambulatory population aged 65–74, the overall prevalence is 49.6 % for stage 1 hypertension (140–159/90–99 mmHg), 18.2% for stage 2 (160–179/100–109 mmHg), and 6.5% for stage 3 (>180/110mmHg).<sup>1,2,3</sup> The prevalence of Isolated Systolic Hypertension (ISH) in the global population is approximately 7, 11, 18 and 25% in the age classes 60–69, 70–79, 80–89 and over 90, respectively.<sup>3</sup>

Misdiagnosis due to inappropriate length of the cuff, as a result of either obesity or very low weight, and fluctuations in blood pressure (BP) due to postural hypotension and/or anxiety (white coat effect) should encourage the development of ambulatory BP measurement in elderly persons.

### Risk of Hypertension

Hypertension stands out as the major risk factor for cardiovascular disease and mortality in elderly persons.<sup>4</sup> Both systolic (SBP) and diastolic blood pressure

(DBP) are involved but, with advancing age, SBP has been identified as a better predictor of cardiovascular risk than is DBP, in both men and women.<sup>5</sup> At any given level of SBP, mortality was found to increase as DBP decreased, suggesting that pulse pressure (difference between SBP and DBP) must also be considered as a risk factor.<sup>6</sup>

Systolic, diastolic and combined (i.e. systolo-diastolic) hypertension increases the risk of stroke. Data from the Framingham study have shown that, apart from this risk, elevated SBP is a major risk factor for all cardiovascular diseases, including left ventricular hypertrophy, congestive heart failure, ischemic cardiomyopathy and peripheral artery disease.

High mid-life BP has also been shown to be a strong independent predictor of later cognitive impairment. However, some authors who studied very old patients reported a J curve profile, with higher cognitive impairment in subjects with low BP. This may result from a decrease in BP secondary to certain pathological processes that also affect cognitive functioning, or alternatively, it may be a consequence of dementia. In addition, hypertension appears to be the strongest risk factor for vascular demen-

tia and possibly Alzheimer disease.<sup>7</sup>

Research has also demonstrated a correlation between mortality and high BP, mainly associated with SBP.<sup>5</sup> However, in people over the age of 80, some authors reported either no association between BP and mortality or an inverse association, which disappears after adjustment for indicators of poor health.<sup>8</sup>

### The Benefits of Treatment in the Elderly

Several randomized, double-blind, placebo-controlled intervention studies have provided strong evidence in favour of treating hypertension in elderly patients. Reports of the first outcome trials published in 1985 and 1991, which focused attention on systolo-diastolic hypertension, showed a reduction in cardiovascular and cerebrovascular morbidity and mortality in patients over 65 years old.<sup>9,10,11</sup>

More recent trials specifically addressed the problem of ISH in the elderly. A meta-analysis by Staessen *et al.*<sup>6</sup> showed that, in 15,693 patients over the age of 60 with ISH who were included in eight trials, antihypertensive treatment reduced stroke by 30%. Total mortality also decreased by 13%, cardiovascular mortality by 18%, all cardiovascular complications by 26% and coronary events by 23%. Treatment prevented strokes more effectively than it prevented coronary events.

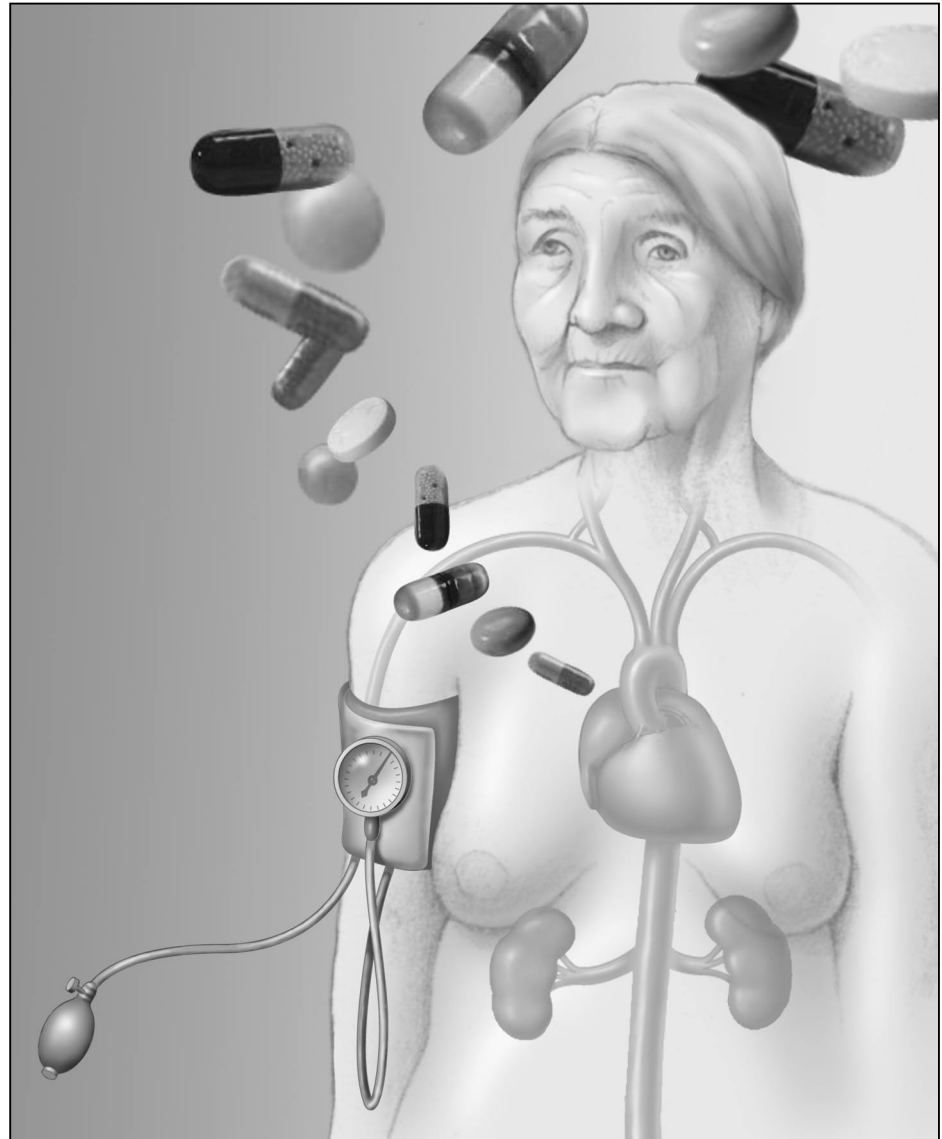
An important finding in the investigation of Systolic Hypertension in Europe (Syst-Eur,<sup>12</sup>) was that in older people with ISH, antihypertensive treatment which started with the calcium-channel blocker nitrendipine significantly reduced the incidence of dementia by half, from 7.7 to 3.8 per 1,000 person-years. After treatment, the incidence of Alzheimer disease actually dropped further than did that of either vascular or mixed dementia. By contrast, in the Systolic Hypertension in the Elderly Program (SHEP),<sup>13</sup> active treatment based on diuretics and beta-blockers failed to

reduce the incidence of dementia significantly. These negative results argue against conferring pivotal protection simply by lowering BP. It is possible that the calcium-channel blockers exert a neuroprotective effect, reducing the incidence of dementia. Further research is needed to confirm the results of this trial.

The value of antihypertensive treatment is well established for patients aged 60 years and over. However, the results are more discordant for the oldest age group of 80 years and over. In a meta-analysis of data from 1,870 participants over 80, Gueyffier *et al.*<sup>14</sup> suggested that treatment significantly reduced the rates of stroke, major cardiovascular events and heart failure by 30%. On the other hand, there was no reduction in mortality due to cardiovascular disease or in total mortality. The results of this meta-analysis, which were favourable for morbidity, argue against the existence of a threshold age, beyond which hypertension should not be treated. Results of ongoing randomized trials of treatment in the oldest old will be welcome in clarifying this controversial issue.

### Pharmacological and Non-Pharmacological Interventions

Most trials have been conducted with diuretics and beta-blockers as first line drugs. Over the past 20 years, the efficacy and safety of these two classes of drug have been demonstrated in elderly subjects.<sup>9,10,11,13</sup> However, in a meta-analysis including 10 trials with a total of 16,164 elderly patients, Messerli *et al.*<sup>15</sup> showed that two-thirds of the patients assigned to diuretics were well controlled on monotherapy, whereas less than a third of the patients treated with beta-blockers were well controlled on monotherapy. The benefit of calcium-channel blockers<sup>16,17</sup> and angiotensin-converting-enzyme inhibitors<sup>18</sup> was recently shown for the prevention of cardiovascular and cerebrovascular complications in older patients. Thus, there is still considerable uncertainty as to whether lowering BP is the major beneficial intervention or whether the use of specific drug classes



(e.g., diuretics, calcium-channel blockers) is important.

Because age- and disease-associated factors affect the metabolism and distribution of pharmacologic agents, antihypertensive therapy should be given at low doses and gradually increased. However, despite alterations in metabolism, most elderly patients tolerate medication without a significant increase in adverse events compared to younger patients or control groups.

First-line treatment of hypertension should consist of diuretics or beta-blockers.<sup>2</sup> In ISH, diuretics and calcium-channel blockers are recommended.<sup>13,16</sup> However, concomitant diseases may influence the choice of therapy. In patients with coronary artery disease,

beta-blockers may be useful, but peripheral artery disease, heart failure or obstructive lung disease may limit their use in elderly persons. In older patients with coronary artery disease, calcium-channel blockers may be considered. In cardiac dysfunction and congestive heart failure, diuretics, angiotensin-converting-enzyme inhibitors or co-prescription of both are appropriate initial choices.

In elderly subjects, fixed-dose combination therapy might have the advantage of increasing compliance, reducing the cost of antihypertensive therapy and achieving a higher response rate.

Older hypertensive patients can also benefit from non-pharmacologic interventions designed to lower BP<sup>2</sup> including weight control, reducing excessive

alcohol consumption, cessation of smoking and increased exercise training.

## Treatment Targets

As an intermediate goal BP, most studies recommended either reducing SBP to under 160 mmHg and DBP to under 90 mmHg, or reducing the initial SBP and DBP by 20 mmHg. Blacher *et al.*<sup>19</sup> have highlighted the role of pulse pressure as a major cardiovascular risk and they have emphasized the need for randomized trials with antihypertensive drugs acting differently on the pulsatile component of blood pressure.

Despite evidence that treatment is beneficial in terms of reducing morbidity and mortality, hypertension is still poorly controlled in elderly persons. Achieving the goal is relatively easy for DBP, but much harder for SBP. Moreover, the new indication of pulse pressure as the most powerful risk factor must now lead doctors to consider SBP rather than DBP when determining treatment goals. Consequently, drugs that more effectively lower SBP should be developed.<sup>6</sup> Different questions remain unanswered such as the benefit of treating elderly patients with stage I systolic hypertension and the determination of the most appropriate agents for managing hypertension in the elderly. Ongoing trials should also determine the benefit of antihypertensive drugs in the very elderly patients. ♦

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