

TREATMENT OF HIGH BLOOD PRESSURE IN THE ELDERLY

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Epidemiology and pathophysiology in elderly and old patients

Hypertension in the elderly (those over the age of 65 years) is an increasing public health concern [1]. Raised blood pressure, especially systolic pressure, confers a significant cardiovascular risk and should be actively treated in elderly patients, at least up to the age of 80 years. Even in the very old, (those above the age of 80 years) hypertension is a dominant risk factor, although it is yet unclear whether treatment prolongs life, even if it prevents stroke and heart failure. The prevalence of hypertension approaches or even exceeds 50% in people aged 70 and above [2].

Most elderly people with hypertension have isolated systolic hypertension, defined as systolic pressure greater than 140 mm Hg and diastolic pressure less than 90 mm Hg [3, 4]. Systolic hypertension is a more potent risk factor than increases in diastolic pressure.

Sluggish baroreceptor function and reduced cardiovascular sensitivity to catecholamines make the elderly more sensitive to natural or drug-induced falls in blood pressure.

Diagnostic work-up of hypertension in the elderly and target-organ damage

There may be diagnostic problems in the elderly and very old people. 'Pseudohypertension' should be suspected in older patients who, despite high blood pressure measurements, have minimal vascular damage in the retina and who experience inordinate postural dizziness despite cautious therapy. This is a condition in which there is a major discrepancy between intra-arterial and arm-cuff blood pressures, such that cuff pressures are falsely high [5, 6].

Blood pressure readings are far more variable in the elderly, so more readings should be taken initially than for patients in the general population. Blood pressure should be measured in both the sitting and standing positions since there is a high frequency (as much as 30%) of a 20 mm Hg or greater fall in blood pressure in patients with a systolic pressure over 160 mm Hg. In these circumstances standing blood pressure should be used to guide treatment decisions. Side effects like dizziness and light-headedness should alert the investigator of possible over-treatment. Prevalence of clinically significant secondary hypertension is low (probably in the 1–5% range).

Ambulatory and home blood pressure (ABP and HBP)

The last guidelines for the management of hypertension provide detailed suggestions regarding how and when to use ABP monitoring [7]. ABP has been found to be a significant predictor of cardiovascular morbidity, independent of office blood pressure and other risk factors in elderly subjects and those with isolated systolic hypertension [8, 9]. The white coat phenomenon, the difference between office blood pressure and ABP, may be more pronounced in the elderly [10]. The 'reversed white coat phenomenon', when ABP is higher than office blood pressure, has also been revealed in a substantial portion of older hypertensives [11]. However, the reproducibility and therefore the clinical utility of the white coat effect have been questioned [12].

In most people, blood pressure falls at night. The nocturnal dip is less marked with increasing age [12–14] and disappears in centenarians [13].

There is a paucity of data on HBP in elderly subjects. In the Ohasama study, HBP had greater predictive power for mortality and stroke than screening blood pressure [15], suggesting the potential usefulness of HBP measurements. However, physical and intellectual limitations, which are more evident in elderly subjects, may curtail more extensive use of HBP monitoring [7].

Total cardiovascular risk and when to start drug treatment for hypertension in the elderly

The same general rules apply to the whole hypertensive population [16–20]. Calculation of total cardiovascular risk using methods such

as those proposed by the 2003 European Society of Hypertension-European Society of Cardiology Guidelines [21] is recommended. There is limited information on treatment above the age of 80 years, where controversy exists regarding mortality [22]. Treatment of hypertension in very old patients should be restricted to those with concomitant disease and target-organ damage.

Placebo controlled trials

The 2003 European Society of Hypertension-European Society of Cardiology Guidelines [21] for the management of arterial hypertension conclude that randomised controlled trials leave little doubt that elderly patients benefit from antihypertensive treatment in terms of reduced cardiovascular morbidity and mortality, irrespective of whether they have systolic–diastolic or isolated systolic hypertension. Benefits in elderly patients [23–25] have been shown with representative agents from several classes such as diuretics, beta-blockers, calcium antagonists, angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers. Several studies [23, 26–28] have shown major benefits from treating elderly patients with isolated systolic hypertension.

Comparative trials

The first five large comparative trials comprising about 58,000 hypertensive patients showed no difference in the primary cardiovascular endpoint when 'newer' drugs were compared with 'older' drugs. The impression was thus that the most important aspect of management is to lower blood pressure with a combination of well tolerated drugs [29–35].

Several recent comparative trials have included populations with mean ages > 65 years. The LIFE study [35] showed a clear benefit of the angiotensin receptor blocker losartan over the beta-blocker atenolol in patients with left ventricular hypertrophy; thiazide was used similarly as add-on treatment in both arms. The losartan benefits were particularly expressed in two pre-specified subgroups of patients: those with diabetes [36] and those with isolated systolic hypertension [37]. In the SCOPE study [38] the angiotensin receptor blocker candesartan was associated with fewer strokes, but also lower blood pressure [38]. The SHELL Study [39] showed no difference in outcome between calcium antagonists and diuretics in patients with isolated systolic hypertension. In the VALUE trial [40] the angiotensin receptor blocker valsartan and the calcium antagonist amlodipine prevented the primary cardiac endpoint to the same extent, although blood pressure remained higher on valsartan. The VALUE findings [41] strongly suggest that blood pressure should be controlled to a level below 140/90 mm Hg within 3–6 months to prevent new or worsening cardiovascular disease. Finally, in the ASCOT study [42] treatment with the combination of amlodipine plus the ACE inhibitor perindopril was associated with reduced mortality and fewer cardiovascular endpoints than was treatment with atenolol combined with bendroflumethiazide, but the blood pressure was slightly higher in the latter treatment arm.

Target blood pressure and the benefits of acetylsalicylic acid and statin as add-on therapy

The Hypertension Optimal Treatment (HOT) study [43] aimed to study the relationship between three levels of target diastolic blood pressure (≤ 90 , ≤ 85 or ≤ 80 mm Hg) and cardiovascular morbidity and mortality in hypertensive patients, and to examine the effects on cardiovascular morbidity and mortality of a low dose (75 mg daily) of acetylsalicylic acid. Felodipine was given as baseline therapy with the addition of other agents. The HOT study comprised a large group of elderly patients (≥ 65 years) [44]. These subjects ($n = 5987$) averaged 70.6 ± 3.9 years of age, 54% were women and their blood pressures were $175 \pm 15/105 \pm 4$ mm Hg at randomisation. Inten-

sive lowering of blood pressure was associated with a low rate of cardiovascular events. Acetylsalicylic acid significantly reduced major cardiovascular events with the greatest benefit seen in all myocardial infarction. There was no effect on the incidence of stroke or fatal bleeds, but non-fatal major bleeds were twice as common. Likewise, the effect of atorvastatin was at least as strong in the elderly patients as in the younger patients in the lipid-lowering arm of the ASCOT study [45].

Treatment of hypertension in the very old

The HYVET-PILOT study [46] selected and randomised 1283 patients over the age of 80 years with a sustained blood pressure of 160–219/90–109 mm Hg in 10 European countries to one of three treatments: a thiazide based regimen, an ACE inhibitor regime or no treatment. Diltiazem slow-release could be used as add-on therapy. Target blood pressure was < 150/80 mm Hg and mean follow-up was 13 months. In the combined actively treated groups the reduction in stroke events was 53% and the reduction in stroke mortality was 43%. However, the estimate of total mortality suggested excess deaths with active treatment. The preliminary results supported the need for a main HYVET trial, which is ongoing.

Thus there are yet unresolved issues in the diagnosis and treatment of hypertension in very old subjects (those above the age of 80 years). However, while more outcome data from ongoing research is awaited, treatment of uncomplicated hypertension in the very old requires careful clinical judgements, including assessment of the many complicating factors discussed above [47].

Summary

There is little doubt from randomised controlled trials that elderly patients benefit from antihypertensive treatment in terms of reduced cardiovascular morbidity and mortality, whether they have systolic-diastolic or isolated systolic hypertension. Whereas trials in the elderly usually include patients who are at least 60 years old, a recent meta-analysis concluded that fatal and non-fatal cardiovascular events combined were significantly reduced in participants aged 80 years and over in randomised controlled trials of antihypertensive drug treatment, but all-cause mortality was not reduced. The larger randomised controlled trials of antihypertensive treatment versus placebo or no treatment in elderly patients with systolic-diastolic hypertension used a diuretic or a beta-blocker as first line therapy. In trials on isolated systolic hypertension first-line drugs consisted of a diuretic or a dihydropyridine calcium channel blocker. In all these trials active therapy was superior to placebo or no treatment. Other drug classes have only been used in comparative trials. Benefit has been shown in older patients for at least one representative agent of several drug classes, including diuretics, beta-blockers, calcium channel blockers, converting enzyme inhibitors and angiotensin receptor antagonists.

Initiation of antihypertensive treatment in elderly patients should follow the general guidelines. Many patients will have other risk factors, target-organ damage and associated cardiovascular conditions, to which the choice of the first drug should be tailored. Furthermore, many patients will need two or more drugs to control blood pressure, particularly since it is often difficult to lower systolic pressure to below 140 mm Hg.

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