Management of Hypertension in Older People

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ABSTRACT

Hypertension affects 30-50% of older people. It is an important reversible risk factor for cardiovascular morbidity and mortality. Multiple large intervention trials have established the efficacy of treating hypertension in people up to the age of 80. However, there is scant and discordant data regarding the benefits of treating hypertension in the very old. Hypertension in the elderly is characterised by specific pathophysiology that must be taken into account when devising a management plan.

Non-pharmacologic therapy can be effective as a first line treatment. Diuretics are still considered first line drug therapy, while β-blockers, calcium channel blockers, and angiotensin converting enzyme (ACE) inhibitors have a role when specific comorbidities are present. ACE inhibitors and angiotensin receptor antagonists are well tolerated, but results of long-term primary prevention trials are awaited. This article reviews literature published within the last decade, providing an approach to managing hypertension in the elderly.

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INTRODUCTION

The world's population is ageing and the fastest growth segment is currently the group aged 75 years and over.[1] Hypertension increases in prevalence with advancing age in Westernised societies, and contributes significantly to cardiovascular disease—often manifest by strokes and myocardial infarction, and death related to these events.[1] There is some recent evidence that hypertension may also be associated with increased cognitive decline and dementia.[2]

Hypertension is a reversible risk factor for these conditions. Treatment is straightforward in most cases, thus optimal management is important.

Prevalence

The third US National Health and Nutrition Examination Survey found a prevalence of hypertension of 35% in white men aged 50-69, and this rose to 50% in white men aged over 69 years.[3] The severity of hypertension also increased, with 25% of the younger group having severe hypertension, rising to 33% in the older group. A study of 300 000 patients (mean age 82.7, range 65–115 years) admitted to aged care facilities in the US found a prevalence of hypertension at admission of 32%. Of the hypertensive patients, 70% were on antihypertensives and concomitant diagnoses included coronary heart disease (CHD) in 26%, congestive cardiac failure (CCF) in 22% and cerebrovascular disease (CVD) in 29%.[4]

A US study of 857 nursing home residents (mean age 84) revealed at least one episode of elevated systolic blood pressure (160 mmHg or more) in 29% of residents. Diastolic hypertension (BP 95 mmHg or more) was seen in only 0.9%.[5]

Definition of Elderly

Lower boundaries were set between 59 and 65 years of age for hypertension studies involving old or elderly patients[6-8] and between 80 and 85 years of age for very elderly or oldest old patients.[1,9]

Diagnosis

Hypertension can be systolic-diastolic, isolated systolic or isolated diastolic. Because blood pressure (BP) is a continuous variable, a line needs to be drawn somewhat arbitrarily in order to maximise the benefits of treatment whilst minimising the risks and expense associated with treating people at lower levels unnecessarily. The most recent US Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure (JNC VI) guidelines and the 1999 World Health Organization–International Society for Hypertension guidelines define hypertension as systolic blood pressure (SBP) of 140 mmHg or more and/or diastolic blood pressure (DBP) of 90 mmHg or more (Table 1).[10,11]

Table 1. Guidelines for the diagnosis of hypertension[10,11]

		SBP (mmHg)	DBP (mmHg)
JNC VI	Optimal	<120	<80
	Normal	<130	<85
	Stage I	140-159	90-99
	Stage II	160-179	100-109
	Stage III	≥180	≥110
WHO–ISH	Optimal	<120	<80
	Normal	<130	<85
	Grade 1 (mild)	140-159	90-99
	Grade 2 (moderate)	160-179	100-109
	Grade 3 (severe)	≥180	≥110
	Isolated systolic hypertension	>140	<90

SBP = systolic blood pressure, DBP = diastolic blood pressure
JNC VI = US Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure
WHO–ISH = World Health Organization–International Society of Hypertension

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Generally a diagnosis should be made on the average of six BP recordings at three separate office visits, when a patient is not acutely unwell, not on antihypertensive drugs, and is relaxed.[10] Alternatively, home BP recording or 24-hour ambulatory BP recordings could be used to diagnose hypertension, although data are somewhat limited and different parameters apply. In a study of 857 nursing home residents (mean age 84), out of 4 BP readings throughout the day, the highest average readings were before breakfast, with the lowest occurring after lunch (SBP 139 ± 24 mmHg v. 132 ± 21 mmHg).[5] They concluded that diagnosis of hypertension in the frail elderly should be based on multiple within day measures, including before and after meals. In an Italian population based sample of four hundred 65–74 year olds, clinic BP was higher than ambulatory BP by approximately 25/10 mmHg, and home-measured BP fell midway between these two methods of measurement.[12] The upper limit of normality for average 24-hour ambulatory BP was 120/76 mmHg, correlating to a clinic BP of 140/90 mmHg.

Home and ambulatory BP monitoring may become more useful in diagnosing hypertension in the elderly, but more data are needed on diagnostic and target BP levels using these methods.[11] In the elderly it is important to record supine and standing BP and heart rate (1 and 3 minutes after standing, or preferably longer) to detect coexistent postural hypotension which is more common in older people due to volume depletion, baroreceptor changes and sympathetic inhibition.

Isolated Systolic Hypertension

In Western societies, SBP tends to rise with age in a linear fashion, whereas DBP rises until the 6th decade and then tends to decline.[1,13] This makes isolated systolic hypertension (ISH) an increasing problem in the elderly.

Prevalence estimates of ISH in all those aged over 65 in the Framingham Heart Study were quoted as 14.4% (male) and 22.8% (female).[14] Of all hypertensives aged 65-89 years, ISH accounted for 57% and 65% respectively. In the Systolic Hypertension in Elderly Persons (SHEP) pilot study, ISH increased from 8% among people in their 60s to 22% by age 80.[15] In these two studies, ISH was defined as a SBP of 160 mmHg or more and a DBP of less than 95 mmHg (Framingham) or 90 mmHg (SHEP).

Systolic hypertension is a stronger risk factor than diastolic hypertension for cardiovascular morbidity and mortality.[16]

Hypertension and Pathophysiologic Changes in Ageing

There are many changes that occur in the ageing body, which impact upon the management of hypertension in older people. Table 2 shows some of the important changes, which can lead to increased postural hypotension on antihypertensive drugs, and increased pharmacological effects of some drugs. ISH is a distinct pathophysiological entity which is mainly related to decreased compliance of the large arteries, which become less able to absorb pressure during systole or recoil in diastole, leading to an altered pulse wave form, increased SBP and pulse pressure (the difference between SBP and DBP).[17,18] This increased pulse pressure has been associated with increased cardiovascular risk.[19]

Table 2. Hypertension and pathophysiologic changes in ageing[1,13]

Increased peripheral vascular resistance
Decreased cardiac output
Decreased heart rate
Decreased myocardial contractility
Left ventricular hypertrophy
Diastolic dysfunction
Decreased renal perfusion
Reduced glomerular filtration rate
Decreased plasma renin activity
Decreased baroreceptor sensitivity
Glucose intolerance
Increased plasma catecholamine levels
Increased central adiposity and dyslipidaemia

Postural (Orthostatic) Hypotension

Postural hypotension is diagnosed by a 20 mmHg fall in SBP on sitting, standing or with head up tilt. It may take 3–5 minutes or even longer for the drop to occur. Associations include falls and syncope.[20] Coexisting autonomic failure may also be present, manifest by a fixed heart rate, inability to sweat, incontinence, constipation, impotence and fatigability.[21] The prevalence of postural hypotension at the beginning of the SHEP study was quoted as 10.4% if measured at 1 minute after standing, and 12% at three minutes.[15] A US study of 9704 ambulatory women aged 65 years and older found postural hypotension in 14%.[20] Treatment includes correcting hypovolaemia, reviewing medications, thigh length elastic stockings, elevating the head of the bed or a trial of fludrocortisone.[21]

Dementia and Cognitive Decline

Data are conflicting regarding the relationship of treatment of hypertension to dementia and cognitive decline.

The SYST-EUR study showed that active treatment of systolic hypertension significantly reduced the incidence of vascular dementia from 7.7 to 3.8 per 1000 person years.[22,23] By treating 1000 hypertensive patients with nitrendipine alone or combined with enalapril and/or hydrochlorothiazide, over 5 years, 19 cases of dementia might be prevented. Dementia was diagnosed in accordance with the DSM-III-R criteria after a screening mini mental state examination (MMSE). The modified ischaemic score was calculated to differentiate between vascular and degenerative dementia.

However, no such reduction was seen in the SHEP study, in which elderly people with systolic hypertension were treated with chlorthalidone.[15] The Framingham study looked at people between the ages of 55 and 88 years, who were not known to have suffered from a stroke, and measured their blood pressure every two years over a ten-year period.[24] They had neuropsychological testing at the beginning of the study and then 12 to 14 years later. Scores of memory and attention were lower in those with higher blood pressure, and in those who had high blood pressure for a longer duration. In the HOPE study (n = 81, mean age 76.1 years), community screened sub-

jects over age 69 with newly diagnosed systolic-diastolic hypertension were treated with captopril or bendrofluazide over 24 weeks.[25] The study sought to evaluate the effect of blood pressure reduction on cognition. The quartile with the greatest DBP drop (19 mmHg or more) had improved psychometric test scores. The study concluded that treatment of hypertension is not hazardous in older people with pre-existing cognitive impairment, and that long-term adequate blood pressure control may even reverse cognitive impairment.

A Swedish study showed that people developing dementia between the ages of 79 and 85 had much higher blood pressure at age 70 (i.e. 10–15 years earlier) than those who were not diagnosed with dementia.[26] In men aged 69–74 years, those who had the lowest diastolic blood pressure when they were 50 showed the best subsequent performance on psychometric testing.[26]

A French study of 1373 hypertensive people aged 59–71 years showed a higher relative risk of cognitive decline (a drop of 4 or more on the MMSE) in those that were not treated (4.3 vs 1.9).[27]

It therefore seems likely that treatment of hypertension may reduce the risk of dementia and cognitive decline.

TREATMENT OF HYPERTENSION

Several large randomised trials of hypertension treatment in older people have been conducted over the last two decades. These studies are summarised in Table 3.

Active treatment with calcium channel blockers (CCBs), diuretics, β-blockers, angiotensin converting enzyme (ACE) inhibitors and/or centrally acting agents was compared with a placebo or control group in these studies. Significant reductions of at least 30% were seen in most studies with respect to cardiovascular mortality and cardiovascular events. In addition, the STOP-HT trial showed a reduction in total mortality of 43%.[29]

Three recent meta-analyses have been performed; two included subjects up to 80 years of age (Holzgreve[8] and Insua et al.[6]) and one included only subjects over 80 years of age (Gueyffier et al.[34]). A significant reduction in stroke, cardiovascular events, cardiovascular mortality, and total mortality was found in the two studies of younger patients (n > 15 000 in each); however, in patients over 80 years of age (n = 1870), stroke, heart failure and cardiovascular events were reduced, but there was no significant reduction in mortality. The outcome of further studies in the oldest old such as the Hypertension in the Very Elderly Trial (HYVET) will help define the risks and benefits of treatment in this age group.[2] Table 4 summarises the three meta-analyses.[6,8,34]

When to Start Treatment

The JNC VI and the WHO-ISH guidelines both suggest treating at Stage I/Grade 1 (see Table 1), initially with lifestyle modification. Time to initiating drug therapy depends on estimated cardiovascular risk for the next 10 years. Risk estimates are based on major risk factors such as smoking, dyslipidaemia, diabetes, age, sex, and family or personal history of cardiovascular disease. If at high or very high risk then drugs should be started immediately, if at medium risk then monitor for 3–6 months rather than 6 months to one year, as is recommended for low risk patients.[10,11]

Goal Blood Pressure

Once diagnosed, treatment should be titrated until an acceptable level of blood pressure is reached. Table 5 shows the most recently published goal blood pressures for different scenarios, according to different guidelines. Separate goals for older people have not been designated for all guidelines.

Table 3. Summary of large hypertension intervention trials in the elderly

Name	Trial design*	Drug	Mean age	n	Type of hypertension	Significant event reductions ($p < 0.05$)†
EWPHE (European Working Party on High Blood Pressure in the Elderly)[28]	R, DB, PC	Diuretic ± methyldopa	72	840	systolic-diastolic	1, 3, 5
STOP-HT (Swedish Trial in Old Patients with Hypertension)[29]	R, DB, PC	Diuretic ± β-blocker	76	1627	systolic-diastolic	5, 6, 8
MRC (Medical Research Council)[30]	R, SB, PC	Diuretic arm (n = 1100) β-blocker arm (n = 1102)	70 70	4396	systolic-diastolic systolic-diastolic	2, 4, 5 Nil
SYST-EUR (Systolic Hypertension in Europe Trial)[22]	R, DB, PC	Calcium channel blocker ± ACE inhibitor, diuretic	70	4695	ISH‡	2, 4, 5, 7
SHEP (Systolic Hypertension in the Elderly Program)[15]	R, DB, PC	Diuretic ± β-blocker, reserpine	72	4736	ISH	2, 4, 5
PPC (Practice in Primary Care)[31]	R, O		69	884	systolic-diastolic	6
STONE (Shanghai Trial of Nifedipine in the Elderly)[32]	R, SB, PC	Calcium channel blocker	66	1632	systolic-diastolic	2
SYST-China (Systolic Hypertension in China Trial)[33]	R, DB, PC	Calcium channel blocker ± ACE inhibitor, diuretic	>60	2394	ISH	1, 5, 6

* R = randomised, DB = double blind, SB = single blind, O = open - control group observational, PC = placebo controlled

† 1= cardiovascular mortality, 2 = cardiovascular events, 3 = fatal myocardial infarction, 4 = coronary events, 5 = stroke, 6 = stroke mortality, 7 = dementia, 8 = total mortality

‡ ISH = isolated systolic hypertension

Table 4. Meta-analyses of intervention trials in hypertension showing reductions in events in the active treatment groups (%)

Author	Age	n	Stroke	Cardiovascular events	Heart failure	Cardiovascular mortality	Total mortality
Gueyffier[34]	≥80	1870	34%*	22%*	39%*	NS	NS 6% excess mortality
Holzgreve[8]	69-76	17 178	40%†	33%†		34%†	20%†
Insua[6]	>59	15 559				Coronary heart disease 25%‡ Stroke 36%‡	12%‡

* All significant, $p < 0.03$, RR 0.66, 0.78, 0.61 respectively; NS = not significant, trend only
† Significant reduction for strokes, only 5/6 studies significant for cardiovascular events
‡ 95% confidence interval did not cross unity, $p < 0.009$

Table 5. Goal blood pressures

Guidelines*	Standard	Diabetic	Older	Home/ABP†
JNC VI[10]	<140/90	or lower		
WHO–ISH[11]	<130/85	or lower	<140/90	
BHS[35]	<140/85	<140/80		<130/75-80
Australia[36]	<130/85	or lower		
New Zealand[37]	<140/80	or lower		

* JNC VI = Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure; WHO–ISH = World Health Organisation–International Society of Hypertension; BHS = British Hypertension Society
† ABP = Ambulatory blood pressure monitoring

Cohort studies have shown a paradoxical increase in survival in elderly with higher systolic blood pressures. This effect disappeared in some studies after adjusting for comorbidities or indicators of poor health, but in others it remained.[1]

One concern was that lowering diastolic BP below 90 mmHg might cause more ischaemic heart disease events. The recent Hypertension Optimal Treatment (HOT) trial of 19 196 hypertensives aged 50–80 years showed that diastolic BP could be reduced below 85–90 mmHg without an increase in ischaemic cardiac events.[38]

NON PHARMACOLOGIC TREATMENT

In the Treatment of Mild Hypertension Study (TOMS), 902 patients (aged 45–69 years) were given lifestyle advice including sodium restriction, weight loss, reduction in alcohol intake, and increased exercise. Despite limited adherence, 240 (27%) remained drug free, and at the end of 4 years average fall in BP was 8.6/8.6 mmHg.[39]

Weight Reduction

Weight loss is advised if more than 10% above ideal body weight or if body mass index [weight in kg/(height in m)^2] is more than 26.[1,40] A loss of 2 kg over 6 months was reported to have reduced BP by a mean 4/5 mmHg in a randomised controlled trial of 56 people (aged 60–85) with mild diastolic hypertension (DBP 85–100 mmHg). However, the intervention involved increased physical activity and sodium restriction as well, so it cannot be concluded that weight reduction alone was responsible for the fall in BP.[41]

Physical Activity

Aerobic activity for 30 to 45 minutes on most days of the week is advised;[1] however, this is unrealistic for many elderly people. Mild aerobic exercise (a one-hour walk three times a week) has been shown to reduce BP by an average of 20/11 mmHg in a small sample of older hypertensives.[42]

Salt Intake

JNC VI advises <6 g of sodium chloride (2.3 g sodium) intake per day.[10]

The DASH-sodium trial split both treatment and control groups into 3 levels of daily sodium intake: high (150 mmol NaCl or 3.5 g sodium), intermediate (100 mmol NaCl or 2.3 g sodium) and low (50 mmol NaCl or 1.2 g sodium).[43] The largest BP reduction noted was between the high sodium phase of the control diet and the low sodium phase of the DASH diet—8.9/4.5 mmHg.

The DASH diet is rich in vegetables, fruits, grain products, low fat and fat free dairy products, fish, legumes, poultry and lean meats.[43] An editorial accompanying this article said that a 2 mmHg drop in DBP equates to a 17% reduction in the prevalence of hypertension, a 6% reduction in the risk of CHD and a 15% reduction in risk of stroke and transient ischaemic attack.[44] As the current US mean salt intake is 9 g a day, there could be a substantial reduction in population risk if all people reduced their intake to 6 g per day.[44]

The TONE study looked at people aged 60–80 on a low sodium diet versus controls.[45] BP was significantly reduced by 4.3/2 mmHg in the low sodium group and primary end points (BP > 150/90, resumption of antihypertensive medications and cardiovascular events) occurred significantly less: 59% v. 73%.

Alcohol Intake

Daily consumption should be limited to no more than two standard drinks. Abrupt withdrawal from heavy alcohol consumption can lead to significant transient hypertension. Moderate alcohol intake has been associated with lower coronary heart disease risk compared to complete abstinence from alcohol.[10]

Smoking

Smoking should be avoided for overall cardiovascular health**.** Smoking was shown to be a risk factor for all cardiovascular events and mortality in the MRC trial, and response to active treatment of hypertension seemed attenuated in smokers with respect to stroke and all cardiovascular events.[30]

Among a cohort of 1893 men and women with angiographic coronary artery disease from the Coronary Artery Surgery Study, continuing smokers had a relative risk of death of at least 1.6 compared to those who quit before enrollment and remained abstinent. This applied to all age groups, including those 65 and older.[46]

There was no association found between smoking and cardiovascular disease developing after age 65 in the Framingham cohort.[16]

Saturated Fats and Cholesterol

Reduced intake is advised for overall cardiovascular health, although effects on BP of cholesterol lowering by diet alone are conflicting.[10]

Caffeine

Caffeine has a pressor effect only in those who abstain for >48 hours—thus regular tea and coffee drinkers may continue.[40]

PHARMACOLOGIC TREATMENT

Generally antihypertensives should be introduced more cautiously in older people because they are more susceptible to postural hypotension as described above. Drugs should be initiated at smaller doses, using smaller dose increments at longer intervals.[1]

In general, adverse drug reactions are two to three times more common in the elderly, often due to polypharmacy, reduced renal function, contracted blood volume and altered drug metabolism.[1]

Which Drug?

All classes of antihypertensive drugs have been shown to be effective in lowering BP in older patients. Diuretics and β-blockers have been shown to reduce cardiovascular morbidity and mortality in large clinical trials,[1] and these two drug classes make up the bulk of the available evidence. However, as mentioned in Table 3, several trials of other drug classes including CCBs, ACE inhibitors and diuretics combined with methyldopa or reserpine have also shown significant cardiovascular event reductions. Only three major trials have been performed solely in ISH.[15,22,33] CCB- and thiazide-based treatment led to a reduction in cardiovascular mortality, stroke and coronary events. Other drug classes have been shown to effectively reduce SBP in ISH, but morbidity and mortality data are awaited.[47,48] The JNC VI guidelines suggest starting with diuretics and β-blockers for uncomplicated hypertension, and using other agents for specific situations.[10]

Diuretics

Thiazide diuretics tend to cause a disproportionate drop in SBP which can be useful in treating ISH. In SHEP, chlorthalidone as initial medication in a stepped treatment plan for ISH reduced the incidence of stroke and major cardiovascular events.[15] Diuretics are the least expensive of the effective monotherapy drugs. Potential adverse effects include hypovolaemia, electrolyte disturbance, hyperglycaemia and exacerbation of gout. Adverse effects can be minimised by prescribing only low doses, and by monitoring electrolytes and renal function before and after commencing diuretics.[1]

In SHEP there were lower mean serum potassium concentrations, and higher mean serum uric acid, glucose and cholesterol concentrations in the active treatment group compared with the placebo group. Mean sodium levels were similar; however, 4.1% in the active group had at least one sodium level below 130 mmol/L, compared to 1.3% in the placebo group.[15] Minor adverse biochemical events were seen in STOP.[29]

In the MRC trial, diuretics were better tolerated than β-blockers—twice as many patients withdrew due to major adverse effects in the β-blocker arm.[30]

β-Blockers

Many large clinical trials have demonstrated the effectiveness of this class of drugs. Most trials used β-blockers in combination with diuretics. β-blockers must be used with caution in peripheral vascular disease, bradycardia and conduction abnormalities, glucose and lipid abnormalities, chronic obstructive airways diseases (COAD), depression, and allergic rhinitis. Slower titration may be necessary in congestive cardiac failure.[1] A baseline electrocardiogram (ECG) is important to exclude heart block or prolonged QT interval before commencing β-blockers.

In the MRC trial, those on β-blockers alone or in combination with a diuretic fared consistently worse than those receiving diuretics alone, with no significant reduction in stroke, coronary events or all cardiovascular events in the β-blocker group.[30]

A recent meta-analysis of 10 randomised trials (16 164 patients aged 60 years or over, mean follow-up 5 years) using diuretics and/or β-blockers, showed that two-thirds of patients on diuretic monotherapy were well controlled, compared with less than one-third on β-blocker monotherapy.[49] Diuretic treatment was superior to β-blockade for all end points; β-blocker therapy reduced the odds for cerebrovascular events, but not for cardiovascular or all cause mortality. The conclusion was that in contrast to diuretics, until proven otherwise, β-blockers should not be considered appropriate first line therapy of uncomplicated hypertension in the elderly.[49]

The effectiveness of β-blockers as first line therapy for ISH has not been assessed in a large randomised controlled trial. A small parallel study in 273 patients (mean age 66.3 years) with ISH showed that atenolol can effectively reduce SBP in ISH—but morbidity and mortality data are awaited in further trials.[47]

Calcium Channel Blockers

A review of CCBs in elderly hypertensives reported that efficacy, safety and tolerability had been clearly demonstrated in the elderly.[50] The authors suggested that they may be a more appropriate choice given that ISH is characterised by reduced arterial compliance, as CCBs tend to induce arterial dilatation. Generally they are a second line choice for when other agents are contraindicated (e.g. due to COAD, gout, renal impairment or cough). They may be a first line choice if there is comorbid ischaemic heart disease, peripheral vascular disease or arrhythmias. Side effects include oedema, constipation, and negative inotropic effects.[1] A baseline ECG is important before commencing CCBs, for the reasons mentioned above for β-blockers.

Trials have shown a reduction in non-fatal cardiovascular events with CCB treatment of systolic-diastolic hypertension (STONE[32]) and ISH (SYST-EUR[22]), and of cardiovascular mortality in ISH (SYST-CHINA[33]).

There has been some controversy over increased adverse events seen in observational studies; however, the WHO–ISH recently concluded that there is insufficient evidence to prove a causal link between CCBs and an increased risk of CHD, cancer or gastrointestinal bleeding.[11]

Most guidelines advise against using short-acting CCBs, as observational studies and meta-analyses have shown higher mortality in the treatment groups.[51,52]

ACE Inhibitors

These are well tolerated in the elderly, but tend to be less effective monotherapy compared with diuretics and β-blockers—this could be because hypertension in the elderly tends to be associated with low renin and salt sensitivity.[1,4] In SYST-EUR and SYST-China, ACE-inhibitors were added to CCBs to optimise BP reduction in patients with ISH resistant to monotherapy.[22,33] In a small Australian study (24 patients, mean age 72.3 years), ACE inhibitors had a greater BP lowering effect compared to diuretics and β-blockers in patients with ISH.[48] The Fosinopril in Old Patients Study was an open label trial in 757 hypertensive patients. It was effective at reducing BP in diastolic hypertension (25/13 mmHg) and ISH (31/6 mmHg).[53] ACE inhibitors have been shown to reduce mortality after myocardial infarction and in patients with heart failure.[54] They are relatively contraindicated in renal artery stenosis, and renal function and serum potassium levels should be monitored during dosage titration, especially if there is a history of renal impairment.[54]

Troublesome cough and renal impairment are common reasons for discontinuation, reported in 5 to 20% of patients.[55]

Further long-term randomised controlled trials in uncomplicated hypertension are needed before these agents can reliably be recommended as first line agents ahead of diuretics and β-blockers; however, they are commonly used, despite the lack of evidence.

Angiotensin Receptor Antagonists

The small parallel study mentioned previously assessed the BP lowering efficacy of atenolol and the angiotensin receptor antagonist losartan in ISH.[47] BP reductions were similar, but losartan appeared better tolerated, with 1.5% withdrawals v. 7.2%.

These drugs are a useful alternative to ACE inhibitors as they are associated with less cough. Again, further long-term studies in the elderly are awaited.

Others

Centrally acting α-adrenoceptor agonists such as methyldopa and clonidine lower blood pressure by decreasing sympathetic outflow. Whilst they are as effective at lowering blood pressure in older people as in younger people, side effects such as dry mouth, fatigue, diarrhoea, sedation, depression and orthostatic hypotension make them generally inappropriate treatment for the elderly.[54]

α-blockers selectively block α adrenoceptors, thereby decreasing peripheral vascular resistance. They can be beneficial in prostatism, but are generally not recommended for hypertension in the elderly as there is a high incidence of orthostatic hypotension. In females they can precipitate urinary stress incontinence. Doxazosin has been reported to improve cholesterol levels.[54]

Nitrates have been used experimentally in the treatment of ISH. A double-blind, randomised crossover trial in 10 elderly people with ISH (mean age 69.4 years) showed that the addition of oral slow release isosorbide mononitrate to standard antihypertensive regimens can partly reverse the exaggerated pulse-wave reflectance and increased augmentation pressure which occur in ISH, thus reducing SBP.[56] Further trials are expected on the use of nitrates in ISH.

Combination Therapy

Generally if monotherapy is failing, it is best to add in a second drug at low dose, rather than increasing to the maximum dose of the first drug. This tends to maximise blood pressure lowering effects whilst minimising unwanted adverse effects.[11] Combination therapy was necessary in 70% of patients in the HOT study.[38] Some of the newer fixed low dose combinations can be useful for this reason, but often need to be titrated individually to start with, especially in the elderly. A single tablet may help with drug compliance. There are limited data on the prognostic benefits of these newer formulations.

Urgent Treatment

Pathophysiological changes of ageing have implications in the sudden lowering of blood pressure in older people. It can be harmful to reduce an elevated BP precipitously, as it is harder for the elderly to counteract such a drop to maintain perfusion of vital organs such as the brain, heart and kidneys, and can lead to delirium, angina, cerebrovascular accident or myocardial infarction. Elderly patients are also more likely to be on antidepressants, psychotropics, levodopa and nitrates which will further compromise their response to a sudden BP drop.[57]

There is no BP level that automatically demands emergent treatment, rather it is the imminent compromise of vital organ function that dictates immediate BP lowering.[58] If there are symptoms and signs of hypertensive crisis (Table 6) then the BP should be lowered gradually by 20–25% over 2–4 hours or to a diastolic pressure of around 100–110 mmHg. This can be achieved using intravenous agents such as nitroprusside, glyceryl trinitrate or hydralazine, or less preferably oral agents. Close monitoring is imperative and antihypertensives should be discontinued if clinical deterioration occurs.[57,58]

The authors have found no evidence to support the use of transdermal glyceryl trinitrate in the emergency treatment of hypertension, although it is commonly used in Australia. Short acting nifedipine should no longer be used, as the inability to control the rate and degree of fall in BP can lead to adverse events.[10] A meta-analyses of short acting nifedipine in people with CHD has shown a dose-related increase in mortality.[52] If there is no evidence of acute target organ compromise, then treat as per the guidelines above, aiming to reduce BP over days to weeks.

Withdrawal of Antihypertensive Therapy

Studies of antihypertensive drug withdrawal have been performed since 1956. Most of these were uncontrolled, and performed in middle-aged patients, but on balance about up to one-third of patients remain normotensive for 1–4 years following drug withdrawal.[59]

Ekbom and colleagues followed 333 subjects, mean age 75.2 years over 5 years after withdrawal of their anti-

Table 6. Symptoms and signs of hypertensive crisis[57]

Cerebrovascular accident/transient ischaemic attack (especially haemorrhagic)
Coma
Headache
Seizures
Altered mental status
Pulmonary oedema
Angina
Acute myocardial infarction
Haematuria
Proteinuria
Azotaemia
Papilloedema
Retinal exudates or haemorrhages
Blurred vision
Haemolysis and thrombocytopenia

hypertensive treatment, in an uncontrolled and non-randomised trial.[60] Criteria for return to treatment included SBP 180–230 mmHg and DBP <90, or isolated high DBP of 105–120 mmHg on three occasions (these BPs are much higher than current recommendations for drug treatment). During the state of no treatment, subjects had a lower total mortality than the general Swedish population, matched for age and sex, and a lower risk of cardiovascular events than those in the treated state. Seventy-four patients (22%) died during follow-up. Thirty-seven per cent returned to treatment because of oedema, CCF, angina, anxiety and headache. It is not surprising that those remaining off treatment had a better outcome, as one assumes these subjects had less severe oedema, CCF and angina than those recommencing treatment, but it is hard to explain the mortality reduction compared to the total population.

The study suggests that with frequent check-ups and gradual dose reduction, withdrawal of antihypertensive therapy in selected elderly can be tried without an increased risk of cardiovascular events and, at 5 years, at least 20% will remain 'normotensive' without drugs. Success was greatest if, prior to withdrawal, the individual was well-controlled on monotherapy, not overweight, and had no ECG evidence of left ventricular hypertrophy. Compliance with lifestyle advice may have also increased success.[60]

CONCLUSION

Multiple randomised controlled trials have shown that treatment of hypertension in older people aged up to 80 years is beneficial in reducing cardiovascular morbidity and mortality. Treatment may also reduce cognitive decline and dementia; however, outcomes of further specific studies are needed to confirm this, and also to clarify the role of treatment in individuals aged 80 years of age or older.

Low-dose diuretics are the ideal first line drug for uncomplicated hypertension. β-blockers may be less ideal than diuretics in older people, but are indicated if there is a history of ischaemic heart disease or CCF. CCBs are indicated for concomitant conditions such as ischaemic heart disease, peripheral vascular disease, and arrhythmias, or where other agents are contraindicated. They may be more effective in ISH. ACE inhibitors and angiotensin receptor antagonists are useful if there is coexisting CCF. Centrally acting agents and α-blockers have only a small role in older people due to their side effect profiles. Nitrate therapy may be a useful adjunct to conventional therapy for the treatment of ISH.

If BP is well controlled on monotherapy or too low, a trial of drug withdrawal could be considered as long as patients are adequately followed up.

Changes in pathophysiology in the older person must be considered when treating hypertension. Postural hypotension and renal impairment must be identified and monitored, and sudden reductions in blood pressure should be avoided.

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