Prescribing for uncomplicated hypertension in the elderly

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Abstract

The treatment of older people with high blood pressure (BP) is a challenge as under- and over-treatment can lead to poorer outcomes. There is strong evidence from epidemiological and trial data to show that older people with high BP should be treated at the same threshold and to the same target BP (BP <140/90 mmHg) as younger patients, with the exception of the very elderly (those over the age of 80 years), in whom a less aggressive treatment target is recommended (BP <150/90 mmHg). With anti-hypertensive therapy, older people can experience orthostatic hypotension, drug–drug interactions and adverse drug reactions; older people often have complex co-morbidities and may have barriers to adherence to therapy. Drug therapy should be tailored to achieve a satisfactory BP reduction with minimal adverse effects. Other risk factors for cardiovascular disease in older people should be identified and addressed. Particular consideration should be given to the use of statins.

Key words: Older people; Blood pressure; Drug therapy; Elderly

The management of blood pressure (BP) in the elderly is complex, and there is a J-shaped relationship between BP and cardiovascular (CV) outcomes (Gorelick et al, 1999; Lewington et al, 2002). Morbidity and mortality are increased by both under-and over-treating BP. Treatment to achieve a low BP target may have adverse outcomes, as aggressive over-treatment leads to hypoperfusion of vital organs, orthostatic hypotension and an increased risk of falls. However, under-treatment of BP will increase the risk of CV events, such as stroke and myocardial infarction, and may lead to the development of renal dysfunction.

Evidence supporting the treatment of older adults (over 65–80 years old) with high BP is clear. Data accrued since the landmark Systolic Hypertension in the Elderly Program (SHEP, 1991) trial have demonstrated that lowering BP in those aged 60 years and over with isolated systolic hypertension reduced the incidence of total stroke by 36%, with 5-year absolute benefit of 30 stroke events avoided per 1000 treated, and 55 CV events avoided per 1000 treated. A meta-analysis by the Blood Pressure Lowering Trialists' Collaboration demonstrated similar benefits in terms of the reduction of CV events related to BP lowering for those aged under 65 years compared with those aged over 65 years (Blood Pressure Lowering Treatment Trialists' Collaboration, 2008).

A recent meta-analysis sought to assess the impact of antihypertensive therapies on activities of daily living (ADLs) and found that very few trials included this as an end-point; however, in the small number that did, ACLs were less likely to be impaired in patients on anti-hypertensive therapy (Cananvan et al, 2015), hence BP treatment reduces CV events and maintains the ability to carry out ADLs. Current guidance from the National Institute for Health and Care Excellence (NICE, 2011) supports BP reduction in all people under the age of 80 years old to achieve a treatment target of <140/90 mmHg.

The very elderly

Despite the high prevalence of hypertension in the very elderly (>80 years), the evidence-base informing the most appropriate management strategy is weak. Traditionally, older people have been excluded from clinical trials, and hence many guidelines for the treatment of older people have been based on the extrapolation of data from cohorts of younger patients and on the clinical consensus of best practice among experts. Epidemiological evidence and, more recently, trial evidence indicates that the treatment of the very elderly does need to be approached differently from cohorts of younger patients, particularly in terms of BP treatment targets.

Epidemiological data

Observational studies have suggested that BP and risk of death are inversely related in older people; hence, older people with lower BPs are at greater risk of death. This has been demonstrated in a number of studies:

- A low systolic BP was associated with an increased risk of death (Rastas et al 2006)
- In men age 85 years and older, a higher systolic BP

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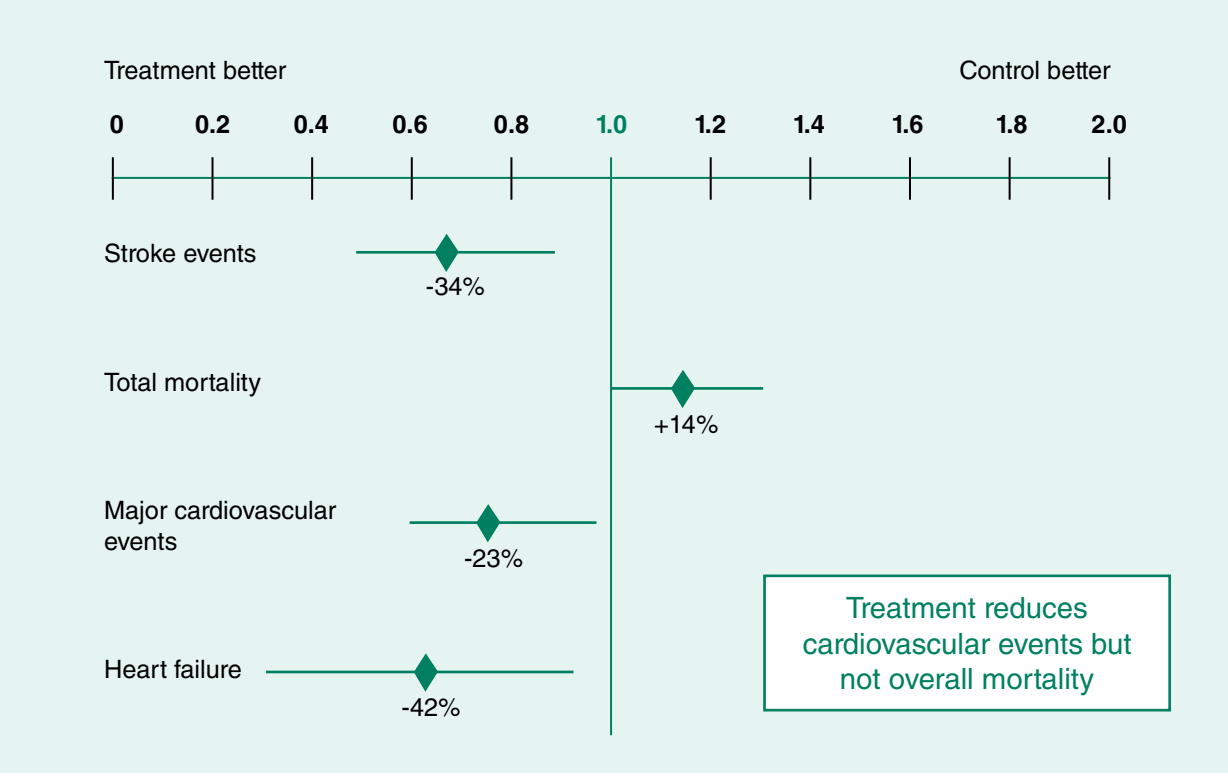

Figure 2. Results of a meta-analysis of antihypertensive drugs in very old people (Gueyffier et al, 1999)

was associated with better survival (Satish et al, 2001)

- A fall in diastolic pressure of 5 mmHg was associated with poor survival in men after the age of 75 years. This risk was strongest in men who took antihypertensive medication (Langer et al 1993).

One study (Oates et al, 2007) specifically sought to determine the relationship between BP and all-cause mortality in subjects aged 80 years and older with hypertension. The retrospective cohort study of 4 371 ambulatory patients with 5 years' follow-up looked at the likelihood of survival during follow-up. Results showed a lower 5-year survival in patients achieving a systolic BP <140 mmHg compared with those with systolic BP >140 mmHg. These trial data suggest that clinicians should have caution in their approach to BP lowering in this age group.

Randomized controlled trials

Until recently, randomized controlled trial data in this setting has been sparse as a result of the exclusion of older people from trials or because older people were recruited to studies in number so low that no meaningful analysis of the subgroup could be carried out.

Gueyffier et al (1999; *Figure 1*) published a meta-analysis on antihypertensive drugs in very old people; data on 1670 patients over 80 years of age from all randomized trails of antihypertensive treatment were included. The authors reported that 57 strokes (6.5%) and 34 deaths (3.9%) occurred in 874 patients being treated, while 77 strokes (9.6%) and 28 deaths (3.5%) occurred in the 796 controls. The authors concluded that anti-hypertensive treatment conferred a 34% reduction in strokes, but was associated with a non-significant excess in all-cause mortality (6%). The study findings were non-conclusive and highlighted the need for a large scale specific trial in this patient group. At this time, the position was that (Gueyffier et al, 1999):

- Elderly patients with high BP were at a high risk of events
- Epidemiological data showed a possible inverse link between BP and mortality
- Few randomized controlled trials had been undertaken in very elderly patients specifically, and they were under-represented in other trials on BP
- The meta-analysis was inconclusive regarding the safety and efficacy regarding the BP treatment.

The European Society of Hypertension (ESH) and the European Society of Cardiology (ESC) stated, in 2007, that 'in subjects of 80 years or over, evidence for benefits of anti-hypertensive treatment is as yet inconclusive' (Mancia et al, 2007).

The HYVET study

The HYpertension in the Very Elderly Trial (HYVET) was designed to address the outstanding questions regarding the safety and efficacy of antihypertensive therapy in older people (Beckett et al, 2008). In this international, multi-centre, randomized, double-blind, placebo-controlled trial, participants with recruitment BP >160 mmHg were randomized to receive either active BP treatment to achieve a BP target of 150/80 mmHg or placebo. Active treatment consisted of indapamide 2.5 mg MR daily,

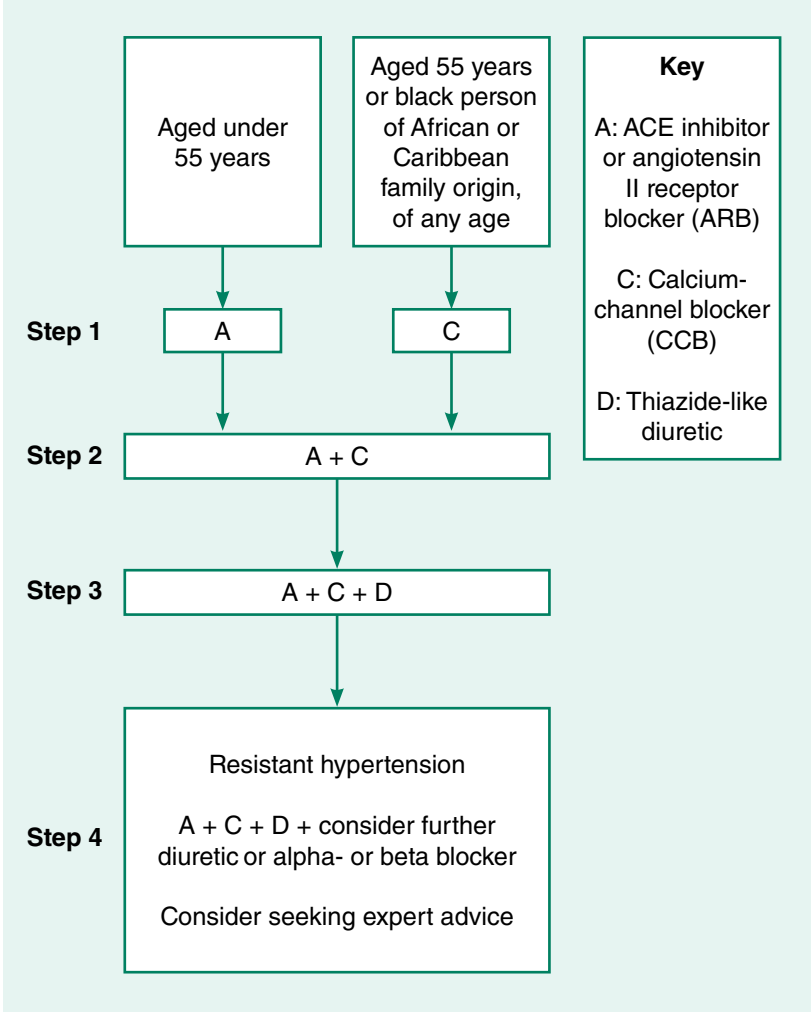

Figure 2. The AC(D) algorithm for initiating antihypertensive medication (National Institute for Health and Care Excellence, 2011).

with the addition of perindopril 2 mg daily, which was increased to 4 mg daily if it was required to achieve the BP target. The primary objective was to investigate the effect of BP lowering on stroke rate (fatal plus nonfatal), and the secondary end-points were the impact of antihypertensive therapy on total mortality, CV mortality, cardiac mortality, stroke mortality, and skeletal fracture rate.

Intention-to-treat analysis demonstrated that patients in the active treatment group achieved a lower BP—on average a 15 mmHg lower systolic BP and a 6 mmHg lower diastolic BP over the 1.8 years of the study. This translated into a non-significant 30% reduction in the primary end-point of all stroke (P=0.055), but a significant 39% reduction in fatal stroke (P=0.046), a 21% reduction in total mortality (P=0.019) and a 64% reduction in the incidence of heart failure (P<0.0001). A pre-specified analysis of patients who remained on double-blind treatment for the course of the study demonstrated significant reductions in the primary end-point and all secondary end-points. From HYVET, it was concluded that treatment of the very elderly with anti-hypertensive therapy with a BP target of 150/80 mmHg was beneficial and that the treatment regimen used was safe and effective (Becket et al, 2008). However, when interpreting these results for clinical practice, it is important to note that the participants in HYVET were generally healthier that those in the general population of the same age.

Treatment guidelines

Data from HYVET had a significant influence of NICE's (2011) guidelines on the clinical management of hypertension in adults (CG127). A new BP treatment target of 150/90 mmHg was set for this older cohort of people in view of the evidence of benefit (NICE, 2011). However, there remains no evidence to support a more aggressive treatment target in the older group of patients.

Similarly, the 2011 American College of Cardiology Foundation (ACCF) Task Force and 2013 ESH/ESC guidelines recommend a systolic BP goal of 140–150 mmHg in patients older than 80 years (Aronow et al, 2011; Mancia et al, 2013). In patients younger than 80 years, a systolic BP less than 140 mmHg can be considered. In the fragile elderly population, systolic BP goals should be adapted to individual tolerability as aggressive treatment can have adverse outcomes (Mancia et al, 2013).

Practical issues in controlling blood pressure in the elderly

There are a number of challenges in the treatment of hypertension in the elderly:

- The risk of orthostatic hypotension
- Drug–drug interactions
- Adverse drug reactions
- Co-existing morbidities
- Barriers to adherence (such as decreased cognitive function, memory loss and inability to take medication from medication containers).

With increased age, various pathophysiological changes result in an increase in BP. Atherosclerotic and arterial rigidity (arterial ageing) result in arteries becoming unable to expand and contract efficiently—this leads to sustained increased BP, equating to an increase in CV risk. This arterial ageing leads to the development of isolated systolic hypertension (ISH), diastolic heart failure, and small vessel disease in the brain and other organs. ISH is defined as systolic BP greater than or equal to 140 mmHg with diastolic BP less than 90 mmHg, as seen in 87% of hypertension cases in older adults (Franklin et al, 2001a). This elevated systolic BP is more strongly associated with CV risk than diastolic BP in the elderly, and increases the risk of stroke, heart failure and end-organ damage (Franklin et al, 2001b).

Increased large artery stiffness involving the carotid arteries results in decreased baroreceptor sensitivity and eventually increased BP variability—a newly recognized CV risk factor that tracks with increased pulse pressure

in elderly patients with ISH (Rothwell, 2010). CV risk is a result of both increased systolic BP (a marker of cardiac afterload) and concordant decreased diastolic BP, resulting in increased pulse pressure—a marker of CV stiffness and a predictor of diastolic dysfunction (Kass et al, 2004).

Lifestyle modifications should be recommended to all patients with hypertension, irrespective of age. Smoking cessation, exercise, healthy eating, decreasing alcohol consumption and lowering salt intake will have positive benefits to lowering blood pressure. Before the initiation of antihypertensive therapy, elderly patients should be offered ambulatory BP monitoring (ABPM), owing to the increased incidence of the 'white coat' effect in the elderly (NICE, 2011). Where ABPM is unsuitable or refused, home BP monitoring is an alternative and is better than office BP monitoring as it has a better predictor of CV morbidity and mortality (NICE, 2011). BP should be checked in supine, seated, and standing positions to assess for orthostatic changes.

The British Hypertension Society (BHS) and NICE (2011) recommend using the AC(D) algorithm to initiate antihypertensive medication (*Figure 2*). In patients over 55 years of age, a calcium channel blocker (CCB) should be offered and diuretics (thiazides) should be an alternative if patients are unable to tolerate CCBs or if there is evidence of dependent oedema, which is more common in the elderly. If add-on therapy is required to control BP, an angiotensin-converting enzyme (ACE) inhibitor or angiotensin II type-1 receptor blocker (ARB) should be added. NICE (2011) advises that patients aged 80 years and over should be offered the same antihypertensive drug treatment as people aged 55–80 years and comorbidities should be taken into account.

Elderly patients are more sensitive to the adverse effects of drug therapy and prescribers should tailor the medication regimen to suit the individual and take their preferences and lifestyle choices into account. While there are many studies demonstrating the efficacy of the differing drug classes in hypertension, achieving a satisfactory BP reduction is more important than focusing on the rationale for the use of one specific agent over another to accomplish the BP reduction (Wang and Staessen, 2003). Hence, all the drug classes, from thiazide and calcium channel blockers, to ACEI, ARB and even fourth-line drugs, such as spironolactone, doxazocin and beta-blockers, are needed to develop individualized drug regimens to manage BP with minimal side-effects. It is generally advised that no more than two antihypertensives should be prescribed in the elderly, owing to the risk of polypharmacy, increased side-effects and adverse events (Mallery et al, 2014).

A study by Gribben et al (2010) showed that in the elderly, the prescribing of thiazides was associated with an increased risk of falling and that this risk was highest in the 3 weeks following the first prescription. Many elderly patients are poorly compliant with diuretics owing to the inconvenience of a constant need to go to the toilet and are fearful of 'accidents'. There are also concerns that rushing to the toilet may increase the risk of falling. However, it should be remembered that older people are more likely to experience oedema and may benefit from the fluid off-loading provided by diuretic therapy.

Many drugs have an effect on BP, including non-steroidal anti-inflammatory drugs (NSAIDs), steroids and cold and flu medication. NSAIDs and steroids inhibit the removal of sodium and water in the kidney in a dose–related manner and inhibit vasodilatory prostaglandins; these effects will increase BP. Where possible, the use of NSAIDs should be avoided in people with hypertension, and simple paracetamol-containing products should be used instead. Elderly patients should also be made aware that over-the-counter medication for colds and flu may contain sympathomimetic agents, such as pseudoephedrine, which can raise BP.

Top tips for prescribing antihypertensives in the elderly

- When initiating antihypertensives, start low and go slow, as elderly patients are more prone to adverse effects, which may lead to non-adherence
- Prescribe the dose of antihypertensive to be taken at night so that if the patient feels dizzy or light headed (hypotensive episode), the patient is safer in bed. If the patient is on more than two antihypertensives do not prescribe them all at the same time—space the medication into twice-daily regimes
- Do not prescribe more than two antihypertensive agents unless the patient has resistant hypertension
- For the very elderly (>80 years), treat to achieve a BP <150/90 mmHg. Do not treat to strict targets of SBP <140 mmHg as the incidence of adverse effects increases
- Regularly perform a clinical review of the patient's medication for indication, appropriateness, and safety. This is a good opportunity to assess adherence to therapy and address the patient's concerns
- Monitor urea and electrolytes, and liver and renal function regularly and respond to any changes in a timely fashion

Managing adverse effects

Each class of antihypertensives has characteristic class-related adverse effects.

Calcium-channel blockers

CCBs, particulary amlodipine, can cause the ankles to swell. In most cases, ankle swelling is minimal and is well-tolerated; however, occasionally CCB-induced swelling is significant and may affect the calf in addition to the ankle. Where this is the case, the swell can be managed by changing to a later generation CCB, such as lercanidipine, which is less likely to cause ankle swelling, or an alternative antihypertensive drug class can be used.

ACE inhibitors

ACE inhibitors (ACEIs) cause a characteristic dry cough in around 20% of patients. The dry cough is irritating and can affect normal speech. These symptoms can be severe enough for patients to stop adhering to the regimen. In these cases, the ACEI can be switched to an ARB, which does not cause a dry cough. Both ACEIs and ARBs are associated with an increased risk of acute kidney injury, hypotension and hyperkalaemia (Schoolwerth et al, 2001; Elgeny et al, 2014).

Diuretics

Diuretics, such as indapamide MR, increase micturition (urination), this remove sodium and water, resulting in lower BP. A heightened urge to urinate can affect a patient's quality of life and social activities. Elderly patients tend to avoid taking their diuretics if they are going out of the home in the mornings as they are fearful of urgency and 'having an accident' in public. These factors can increase the risk of the patient having a fall.

Elderly patients should have quarterly or biannual routine tests to check renal function, liver function and urea and electrolytes. Elderly patients are at a higher risk of acute kidney injury (from urinary tract infections or dehydration), which can have profound consequences, such as increased confusion from hyponatremia (leading to an increased risk of falls). Hypokalaemia or hyperkalaemia have adverse cardiac effects especially if the patient is on cardiac medications, for example, digoxin. Diuretics increase the risk of dehydration especially if the daily fluid intake is decreased, and this is compounded by urinary tract infections or cystitis in female patients.

Morning vs evening dosing of antihypertensives

A Cochrane review (Zhao et al, 2011) found that evening dosing with antihypertensive drugs gave slightly better control of BP than the morning dosing regimen, but its effects on death and adverse CV outcomes are not known.

Managing other risk factors

Use of statins in the elderly and the very elderly

The decision to initiate a statin in the elderly should come after an informed discussion between the clinician and the patient about the risks and benefits of statin treatment, which takes into account additional factors, such as potential benefits from lifestyle modifications, informed patient preference, comorbidities, polypharmacy, general frailty and life expectancy. The QRISK2 risk assessment tool should be used to assess the risk of cardiovascular disease (CVD) for the primary prevention of CVD in people aged 84 years or younger. For 85 years or older, NICE (2014) recommends that atorvastatin 20 mg daily should be considered, as statins may be of benefit in reducing the risk of non fatal myocardial infarction in the older patient cohort.

Use of aspirin in the elderly

Aspirin is no longer routinely used for the primary prevention of CVD as the benefits in this setting are finely balanced against the risks of bleeding. Aspirin may be used on an individual patient basis where there is a very high CV risk, which is deemed to outweigh the risk of bleeding. The evidence to support aspirin for secondary prevention of CVD is robust and therefore all elderly patients with established CVD should be prescribed aspirin 75 mg daily with gastrointestinal protection with a proton pump inhibitor, such as omeprazole.

Conclusions

BP is an important risk factor that should be identified and addressed in older people to reduce their risk of a cardiovascular event. Prescribers should be aware of the risk of both over- and under-treatment of high BP. Management decisions should take into account the specific challenges, particularly in the very elderly when less aggressive treatment thresholds apply. Lifestyle advice should be offered to all patients and the NICE (2011) treatment algorithm used to guide drug choice. Patients must be appropriately monitored throughout therapy to reduce the risks of adverse outcomes; special care should be taken to avoid precipitating orthostatic hypotension, identify and manage drug interactions, and address adverse drug reactions should they occur during therapy.

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