

Hypertension in the elderly: an overview

K. O'Malley, M.D., F.R.C.P.I.,
W. O'Callaghan, M.B.,
M.R.C.P.I.,
and
E. T. O'Brien, M.R.C.P.,
F.R.C.P.I.

*Department of Clinical
Pharmacology, Royal College
of Surgeons of Ireland, and
The Blood Pressure Clinic,
The Charitable Infirmary,
Dublin, Eire*

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Summary

Hypertension in the elderly is associated with a high incidence of cardiovascular disease. There is no convincing data which prove that treatment of mild to moderate hypertension in this age group improves prognosis, but a review of available data suggests that treatment is beneficial. It is suggested that a thiazide diuretic or a beta-adrenoceptor blocking drug should be used as first-line therapy. These drugs may be combined if an inadequate response is seen and other drugs may be used if the blood pressure is not controlled.

Key words: Hypertension — aged — antihypertensive agents

Introduction

Blood pressure is a continuous variable and as the level increases so do the associated risks.²¹ There is no clearly identifiable critical or safe level, so that cut-off points must be arbitrary. The limits set are based on increases in morbidity and mortality. In the present context, the upper limit of normal pressure is taken to be 160/90 mmHg (Korotkoff 5th phase).

It is now recognized that the systolic pressure must also be taken into account as well as the diastolic. Disproportionate systolic hypertension exists when the increase in systolic pressure (SP) is exaggerated compared with the diastolic pressure (DP). It is defined²⁴ as: $SP = (DP - 15) \times 2$.

Isolated systolic hypertension is variously defined as: (i) a systolic pressure greater than 150 mmHg with a diastolic pressure below 90 mmHg²⁴ or (ii) a systolic pressure in excess of 159 mmHg while the diastolic pressure remains below 95 mmHg.¹²

Unless otherwise stated, the term 'elderly' refers to those patients aged 65 years or older.

Prevalence of hypertension

The prevalence of hypertension in the elderly depends on the blood pressure levels which are chosen and on the number and circumstances in which readings

are taken. Using 160/95 mmHg as the lower limit of hypertension, the National Health Survey¹⁷ in the U.S.A. showed there was a prevalence of about 40% in the elderly age group. Estimates of disproportionate systolic hypertension vary and a figure as high as 40% of those attending a high blood pressure clinic has been suggested.²⁵ Isolated systolic hypertension is relatively rare — 2.7% of the population if readings are repeated on separate occasions.⁸

The cardiovascular system, blood pressure and ageing

The ageing process is associated with anatomical, physiological and biochemical changes. Some of these changes may be important in the pathogenesis of hypertension in the elderly while other changes may influence the approach to the management of hypertension in the elderly.

There is an increased rigidity of the aorta and its branches due to loss of elastic fibres in the media, an increase in collagen and calcium content and the presence of atheroma in the intima.¹⁶ The functional consequence is that these vessels are less compliant. In autopsy specimens, Hallock and Benson¹⁵ showed decreased aortic compliance with age. The stiffened large vessels behave more like rigid tubes than distensible vessels.²⁶ Normally, aortic distensibility reduces the work load of the left ventricle as it reduces impedance. In less compliant vessels, the systolic pressure generated in the left ventricle is transmitted with very little buffering to the arterial tree. This results in an increase in systolic pressure, hence the tendency to disproportionate systolic hypertension in old age.

The effects of the ageing process on the precapillary arteriole is not known, but there tends to be an increase in total peripheral resistance with age.⁴

Renin-angiotensin-aldosterone system

The renin-angiotensin-aldosterone system also undergoes changes with age. Low renin essential hypertension is a more common feature in the elderly. Weidmann *et al.*³⁷ have shown that plasma renin concentration, plasma renin activity and aldosterone concentrations are lower in the elderly. Throughout life there tends to be an inverse relationship between plasma renin levels and blood pressure, and some authors²⁹ hold that the decrease in serum renin in the elderly is merely a feedback inhibition induced by their higher arterial pressures.

Neurocirculatory reflexes

Baroreflex function has been shown to be diminished in hypertensives⁶ and with increasing age up to 66 years.¹⁴ One would expect a more pronounced abnormality to be present in aged hypertensives. McGarry *et al.*²⁷ have shown diminished baroreflex response to hypertension induced by nitroprusside infusion in elderly hypertensives compared with young hypertensives.

Risks of hypertension in the elderly

Blood pressure is a risk factor for cardiovascular disease at all ages and particularly in the elderly. It is the major risk factor for stroke, cardiac failure and coronary artery disease in this age group.

Cerebrovascular accident

Strokes account for 11% of all deaths in the U.S.A. and 75% of stroke deaths are in those aged over 65 years. Hypertension is the most potent and most common precursor of atherothrombotic brain infarction.^{19,20} Asymptomatic casual hypertension is associated with a risk of atherothrombotic brain infarction 4 to 30-times greater than that of normotensives. The risk of atherothrombotic brain infarction was as well correlated with systolic blood pressure as with diastolic or mean pressures. The impact of systolic hypertension was not diminished with advancing age, thus supporting the view that systolic hypertension in the elderly is associated with considerable cardiovascular risk. For each 10 mmHg increase in blood pressure the risk of atherothrombotic brain infarction increased about 30%.

Congestive cardiac failure

Systolic blood pressure is a major determinant of left ventricular work and the relationship between systolic blood pressure and congestive cardiac failure is even stronger than that between hypertension and stroke. In the Framingham Study, hypertension was the dominant risk factor at all ages. In the elderly group (age 65 to 74 years), almost 7-times as many hypertensives developed cardiac failure as did normotensives.¹⁹ The occurrence of congestive cardiac failure carried a poor prognosis, as only 50% of those who developed cardiac failure survived 5 years.

Coronary artery disease

High blood pressure is a risk factor for coronary artery disease in the elderly.²³ Prospective studies have demonstrated convincingly a substantial excess rate of development of coronary heart disease in proportion to the degree of elevation of arterial pressure, notably systolic pressure. Risk of coronary heart disease was distinctly and impressively related to antecedent blood pressure at all ages, including the elderly.

Mortality associated with hypertension in the elderly

The Framingham Study¹⁹ has compared mortality in different age groups according to blood pressure status and showed that mortality in hypertensive males (systolic blood pressure 160 mmHg) relative to that in normotensive males (systolic blood pressure 130 mmHg) decreased with age. Between the ages of 45 and 54 years, the relative mortality in the hypertensive group was 277% whereas in the 65 to 74-year group it was 207%. Thus, the relative mortality in elderly hypertensives was still twice that of normotensives, despite a slight decrease in relative mortality with age. Whereas the relative mortality between hypertensives and normotensives is less in the elderly than in middle age, because of the greater number of deaths in the elderly the actual number of hypertension-related deaths is increased. For elderly males, 4.6% of annual deaths were associated with hypertension compared with 1.8% of deaths in the 45 to 54 years age group.

Why treat the elderly hypertensive?

It has been demonstrated that hypertension in the elderly is associated with excess risk of cardiovascular morbidity and mortality but, before one can advocate the treatment of hypertension in all elderly hypertensives, pressure reduction must be seen to be associated with a reduction in morbidity and mortality. Many studies have been undertaken to assess the benefit of antihypertensive therapy in adults, but they have not included sufficient elderly hypertensives to draw definitive conclusions.

Effect of therapy on complications of hypertension

The Veterans Administration Study,^{35,36} unfortunately, had the limitations of including only males and many had complications of hypertension and other illnesses prior to randomization into control and treatment groups.

In the 90 to 114 mmHg group there were 81 patients over 60 years, comprising 21.3% of the entire group. The incidence of major complications of hypertension increased with age, those over 60 years accounting for 48% of total events. In the untreated group, 15.2% of patients under 50 years of age developed morbid events compared to 62.9% of those over 59 years. In the treated group, the incidence of morbid events was 6.9% and 28.9%, respectively.

Hypertension Detection and Follow-up Program (HDFP)

The 5-year findings of the HDFP¹⁸ are particularly interesting. In this community-based randomized controlled trial involving over 10,000 hypertensives, mortality figures are compared between those allocated to a systematic antihypertensive treatment programme (stepped care) and those referred to community medical therapy (referred care). The stepped care group was offered antihypertensive therapy in special centres, free of charge, with a maximum effort to encourage patient compliance with therapy which was increased stepwise to achieve and maintain reduction of blood pressure to or below set goals. The referred care group were referred for treatment to their usual sources of care.

There were 2,376 patients aged 60 to 69 years included in the study. In this age group, there was a 16.4% reduction in mortality in the stepped care group, although the net difference in average diastolic blood pressure between both groups at the end of 5 years was a mere 5.1 mmHg.

Interpretation of the HDFP study results is difficult. Essentially, the study was of differences between two health delivery systems and factors responsible for these differences are more difficult to elucidate than in a treatment versus non-treatment study. As non-cardiovascular deaths were reduced by 14% in the stepped care group it is likely that there was an important contribution from better general medical care.

It is clear that many studies aimed at assessing the benefits of antihypertensive therapy have been directed at the adult population in general with some information on the elderly emerging as a side issue. One multi-centre study, the European Working Party on High Blood Pressure in the Elderly study¹ is currently assessing the role of antihypertensive therapy specifically in elderly hypertensives. While

information on the efficacy and side-effects of therapy have been published,^{2,3,5} mortality and morbidity figures are not yet available.

In summary, benefit has been shown for the treatment of hypertension at all ages but the benefit in the elderly is not as clear-cut as that in younger individuals. In many studies the number of elderly hypertensives included has been too small to make definite conclusions.

Whom to treat

When selecting patients for antihypertensive therapy one is tempered by the knowledge that elderly patients may react differently to drugs than younger subjects. Ageing induces physiological and pathological changes which may influence the pharmacokinetics and response to drugs.^{10,31,34} It is generally agreed that, regardless of age, patients with a sustained diastolic blood pressure of 115 mmHg or more should receive therapy and we treat those with diastolic pressure over 110 mmHg. We carefully consider therapy in elderly patients whose blood pressure is greater than 160/100 mmHg on two occasions. In patients with diastolic blood pressure in the range 100 to 110 mmHg the presence of complications or a simultaneous systolic blood pressure of greater than 180 mmHg would sway one in favour of therapy.³⁰ At present, we do not treat isolated systolic hypertension.

Which drug?

Diuretics. Thiazide diuretics are effective in reducing blood pressure in elderly hypertensives and do not cause major clinical or biochemical disturbances.^{3,28,32} To minimize biochemical disturbances it is best to use a low dose, for example 25 mg hydrochlorothiazide daily.

The elderly are said to be more prone to the potassium-losing effects of thiazide diuretics.²² Potassium supplementation should be given or the thiazide should be combined with a potassium-sparing diuretic such as triamterene. Because many elderly patients find individual potassium preparations unpalatable, the thiazide may be combined with potassium in a single tablet. Potassium supplementation is particularly appropriate if the patient is also on digitalis therapy.

Glucose intolerance is a major risk factor for coronary artery disease. In the EWPHE Study,³ the group treated with a thiazide diuretic showed a significant deterioration in glucose intolerance. Clinical diabetes mellitus is likely to be induced only in those who already have borderline diabetes. We expect that the reduction of blood pressure would more than offset the theoretical risk associated with a small drug-induced increase in blood sugar level.

Serum uric acid levels also increase in patients on thiazide diuretic therapy. In the EWPHE Study,⁵ the group treated with diuretics showed a 25% increase in serum uric acid, but clinical gout was extremely rare.

Beta-adrenoceptor blocking drugs. The role of these agents in the treatment of hypertension in the elderly is not clear because little data are available on their efficacy or limitations in this setting. Many aspects of the pharmacology of

beta-adrenoceptor blocking drugs are different in the elderly than in younger individuals. The pharmacokinetics of propranolol are altered in the elderly and plasma levels are higher in the elderly when compared to younger subjects.⁷ Distribution to tissue is much slower and there is an increase in bioavailability due to diminished first-pass metabolism. The incidence of side-effects due to propranolol is increased in the elderly.¹³

While these changes may increase drug effect, there is evidence for an age-related decrease in sympathetic responsiveness to beta-adrenoceptor agonists and blocking drugs.^{9,11,34} Therefore, it appears that, on the one hand, plasma levels of some beta-blockers are increased in the elderly but, on the other hand, the sympathetic nervous system is less responsive to their action. The degree to which these factors offset each other remains to be elucidated.

The contra-indications and adverse drug reactions associated with beta-adrenoceptor blocking drugs is no different from that observed with younger patients.

Drugs active on the nervous system. Alpha-methyldopa and clonidine act primarily by stimulating α_2 -adrenoceptors in the brain stem vasomotor centres, thereby inhibiting sympathetic outflow and reducing systemic arterial pressure. Though it is generally held that the elderly are more prone to the unwanted central nervous system effects of these drugs, methyldopa seems to be well tolerated in the EWPHE study.² Notwithstanding, we avoid antihypertensive agents such as methyldopa, reserpine and clonidine that may cause central nervous depression. The elderly and particularly those with cerebrovascular disease are susceptible to postural hypotension because they have less 'responsive' baroreflexes. For this reason, adrenergic neurone blocking drugs (guanethidine, bethanidine, debrisoquine) which cause postural hypotension should not be used.

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Discussion

Prof. A. N. Exton-Smith: Have you done any studies on cerebral blood flow specifically in patients with systolic hypertension, before and after treatment? We have been doing cerebral blood flow studies but, as far as I know, there have been no cases of purely systolic hypertension. In the patients with both systolic and diastolic hypertension we have been able to show that when the blood pressure was raised gradually and not too dramatically the autoregulation within the cerebral circulation was maintained. This may not be so, however, in the case of purely systolic hypertension, possibly because of the lack of elasticity and reactivity of the cerebral vessels.

Prof. K. O'Malley: No, we have not investigated cerebral blood flow in elderly patients. I would accept your explanation that the problem in systolic hypertension seems to be one of lack of compliance in the large and medium size blood vessels. This is not fixed however, and clearly they are not as responsive in the elderly as in younger people.

Dr. Bubna-Kasteliz (Bath): In the experience of all of us, I am sure, we have seen elderly patients, who were hypertensive when younger, developing normal blood pressure after a myocardial infarct and no longer requiring antihypertensive treatment. What other mechanisms are there, apart from myocardial infarction, which result in hypertensives becoming normotensives? It is my impression that this happens quite often and many of these patients do not have a history of myocardial infarction.

Prof. K. O'Malley: I agree. One has seen people who, for example, have stopped their medication and 2 or 3 years later they are normotensive. I do not have an explanation for this and I do not know if it occurs more in the elderly than in young people.

Dr. J. P. R. MacFarlane: I, also, am convinced that this happens. One constantly meets people who are normotensive when they come to us in old age but whose case records show them to have been hypertensive some years ago. They become normotensive without having had a myocardial infarction. It is possible that this is due to a weakening of the myocardium which leads to an inability to keep up a high blood pressure.

Dr. J. L. C. Dall: I wonder if we are not just simplifying it too readily into the two aspects of hypertension, the pump and the vessels. Maybe there is a humoral mechanism, or a baroreceptor mechanism, which is capable of readjustment. The hope would be for treatment of hypertension in the elderly that, if you do treat patients and reduce their blood pressure, they are capable of readjusting their baroreceptors to perform at a lower level. If they are capable of doing so, treatment would not necessarily then be life-long. What is interesting in these series that are being reported is not just that patients' blood pressure can be reduced, but that it may well be that some of the patients after they finish the trial — and in a limited experience I have some evidence of this — may not need to continue their antihypertensive treatment: their blood pressure may remain down. Whether it remains down for a month, 2 months, 6 months or even longer, is too early to say, but certainly in some patients who had significant hypertension in the placebo period, after a period of treatment extending beyond 6 months, the blood pressure appears to be reset at a level which is more acceptable. This is a personal observation on some work that has not been published, as yet.

Dr. O. M. P. Jolobe (Birmingham): Granted the fact that there is a tendency for blood pressure to increase with age, is there a threshold, perhaps, at which the complications which are related to blood pressure also increase with age? I think this also has a bearing on the sort of blood pressures we should be aiming for.

Prof. K. O'Malley: It is difficult to say because the mortality rates are much higher in old age and you have blood pressure, age and mortality all interacting. There isn't a threshold as such; all of them are continuous variables, so there is not a cut-off point.

Dr. J. L. C. Dall: Dr. Moore-Smith has recently reviewed the literature very thoroughly. Perhaps he would like to comment.

Dr. B. Moore-Smith (Ipswich): The evidence I produced from reading what few papers there are — and Prof. O'Malley has already commented that there is no hard evidence really for patients over the age of 74 years — is that over this age the systolic pressure at which things start to become dangerous and mortality increases very markedly is 180 mmHg. How far down should this pressure be reduced? Such evidence as there is suggests that there is no gain in terms of decreased mortality or morbidity below 180 mmHg. If there is such a thing as a threshold, therefore, it might be around 180 mmHg systolic. In the case of diastolic pressure, the same sort of thing is seen. If you read the literature, views on what is a dangerous diastolic pressure range from 90 to 110 mmHg. From the point of view of treatment, the evidence suggests that there is no proven benefit from the reduction of diastolic blood pressure below 105 mmHg. In the case, therefore, of the very elderly, i.e. people over the age of 75 years, who have stiff arterial systems and in whom one would expect blood being pushed into a rigid system to produce systolic 'shoot', this 'shoot' only appears to become serious when the pressure is 180 mmHg or over and the diastolic pressure probably does not matter very much once it is below 105 mmHg. This, therefore, should be the sort of level one is aiming at in treatment.

This raises the question, however, of whether one should screen the elderly population and treat all of those with blood pressures of about this level. The difficulty is highlighted in a recent study which showed that, in apparently fit elderly patients, the incidence of hypertension (defined in this instance as 160/90 mmHg or over) was around 17% the first time they saw the clinician. By the third visit, however, the incidence was only 3%, with no treatment.

Prof. K. O'Malley: I am just a little worried by this notion of a cut-off point. As I view it, with continuous variables you really cannot have one. It has to be extremely arbitrary to say *that* is the pressure at which you do or do not treat. The only way you can judge is on the basis of prospective clinical trials where you have a controlled group, and we do not really have that information. Moreover, we do not really have any good information on reducing systolic blood pressure and the effect that has on outcome.

Dr. S. T. McCarthy: We, also, have been looking at cerebral blood flow and autoregulation for some time now and also have looked at patients with hypertension. In fact, it does seem to adjust downwards quite satisfactorily. The only thing that worries me — and we are doing the same thing as everyone else who is running trials — is that we have tried to choose patients who only have the thing we want to look at. One of the exclusion criteria we use is whether or not the patient has postural hypotension anyway, and I suggest that is also true of the European Working Party. Now, if that is true, we may deliberately be selecting out the patients who may be at risk. What happens, therefore, when you come to treat a general population with high blood pressure? I don't know and I don't think the study will tell us.

Prof. K. O'Malley: Curiously enough, we have not come across postural hypotension as being a problem in patients in the European trial. This rather surprises me. I believe that the reason this is not a problem in the patients in the European trial is because of the extremely slow introduction of the drugs.

Dr. S. K. McCarthy: Do you exclude from the trial those patients who have had postural hypotension? ..

Prof. K. O'Malley: Yes, but there are very few of them. I would agree with your general comment, however. When we look at the outcome in the European Study it is pretty clear that we are subconsciously selecting the healthier patients, i.e. those who are ambulant and can come into and out of the clinic, and, in fact, the mortality data in our placebo group is better than would have been expected for that age group with hypertension. So, clearly, we are selecting them even though we do not realize it.