

In Hypertension and Coronary Artery Heart Disease
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EOB

Drug treatment of hypertension in the elderly

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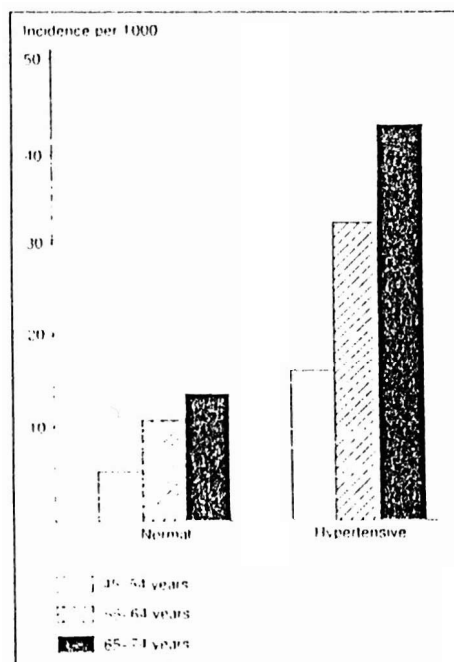
Complications of hypertension in the elderly

Blood pressure is a risk factor for cardiovascular disease at all ages but particularly in the elderly (1,2). Hypertension is the major risk factor for stroke, cardiac failure, coronary artery disease and myocardial infarction in this age group.

Cerebrovascular accident

Strokes account for 11% of all deaths in the United States 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 (3,4).

Asymptomatic casual hypertension is associated with a risk of atherothrombotic brain infarction four to thirty times greater than that of normotensives. The risk of atherothrombotic brain infarction is as well correlated with systolic blood pressure as with diastolic or mean pressures. The impact of systolic hypertension is not diminished with advancing age thus supporting the view that systolic hypertension in the elderly is associated with considerable cardiovascular risk (2) (see figure 1). For each 10 mmHg



rise in blood pressure, the risk of atherothrombotic brain infarction increases about 30% (1).

In a 10 year longitudinal study of 191 elderly females aged up to 100 years (average 80), it was shown that the incidence of cerebrovascular events was significantly correlated to systolic blood pressure (5). Twenty percent of the hypertensive and 10% of the normotensive patients suffered from a cerebrovascular event during the study.

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 extremely strong. In the Framingham Study (6), hypertension was the dominant risk factor for all ages. In the elderly group (age 65-74 years) almost seven times as many hypertensives developed cardiac failure as did normotensives. The occurrence of congestive cardiac failure carried a poor prognosis as only 50% of those who developed cardiac failure survived five years.

Coronary artery disease

High blood pressure is a risk factor for coronary artery disease in the elderly (7). Prospective studies have convincingly demonstrated 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 is distinctly and impressively related to antecedent blood pressure at all ages, including the elderly.

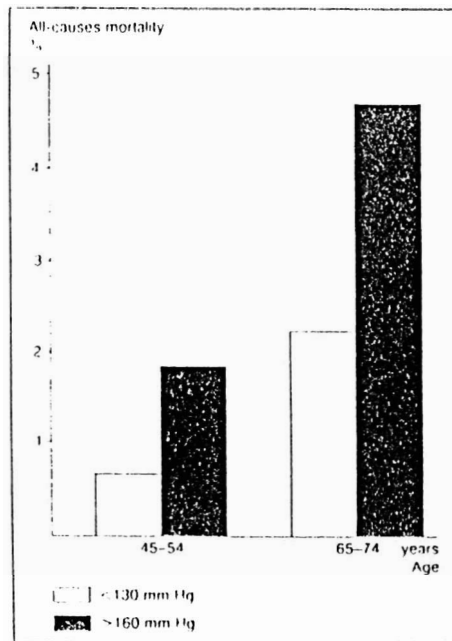
Myocardial infarction

In a 10 year study, Forette et al. (5) have reported that the incidence of myocardial infarction was significantly and independently correlated to diastolic blood pressure in female patients over 60 years of age.

Twenty seven of the 94 hypertensive patients (28%) and 4 of the 51 normotensives (7.8%) had myocardial infarction during the follow-up. Thus, the incidence of myocardial infarction was more than three times higher in the hypertensive patients than in the normotensive.

Mortality associated with hypertension in the elderly

The Framingham Study (7) has compared mortality in different age groups according to blood pressure status and showed that mortality in hypertensive males with systolic blood pressure above 160 mmHg is much greater than in normotensive males. Mortality in elderly hypertensives is 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 45-54 year age group (see figure 2). Thus, in the elderly, high blood pressure remains an important risk factor for cardiovascular disease.



Changes in the cardiovascular system with raised 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.

There is 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. The functional consequence is that these vessels are less compliant (8). The stiffened large vessels behave more like rigid tubes than distensible vessels. Normally, aortic distensibility reduces the workload 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 a rise in systolic pressure, hence the tendency to disproportionate systolic hypertension in old age (9, 10).

The renin-angiotensin-aldosterone system also undergoes changes with age. Low-renin essential hypertension is a more common feature in the elderly. Plasma renin concentration, plasma renin activity and aldosterone concentration are all lower in the elderly. Some hold that the decrease in plasma renin in the elderly is merely a feedback inhibition induced by their higher arterial pressure.

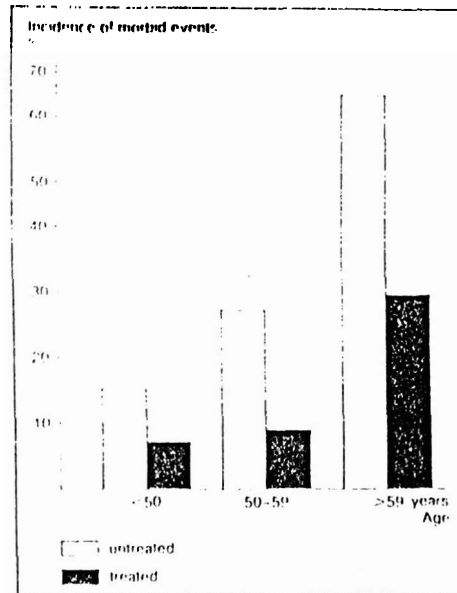
Why treat the elderly hypertensive

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 (11).

Treatment and complications

The Veterans Administration Study (12) unfortunately had the limitations of including only males and many had the complications of hypertension and other illnesses prior to randomisation into control and treatment groups.

In those with diastolic pressure between 90 and 114 mmHg there were 81 patients over 60 years and they comprised one fifth of the entire study group. The incidence of major complications of hypertension increased with age, and this one fifth accounted for almost half of total events. In the untreated group 15.2% of patients under 50 years of age developed morbid events compared with 62.9% of those over 59 years. In the treated group the incidence of morbid events was 6.9% and 28.9%, respectively (see figure 3).



Treatment and reduction of mortality

The five-year findings of the Hypertension Detection and Follow-up Program Co-operative Study (13) are particularly pertinent. In this community-based randomised 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 care (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. A 17% reduction in 5 year total mortality was reported in the specially treated group. There were 2,367 patients, aged 60-69, included in the study. In this age group there was a 16.4% reduction in mortality in the stepped care group although the difference in diastolic blood pressure between the two groups compared at the end of 5 years was a mere 5.1 mmHg.

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It is not clear if this reduction in mortality was caused by reduction of diastolic blood

pressure by 5 mmHg or if better general medical care contributed to the successful result in the stepped care, especially as also non-cardiovascular deaths were reduced by 14%. 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. The multicentre study by the European Working Party on High Blood Pressure in the Elderly (14, 15, 16, 17) is currently assessing the role of antihypertensive therapy specifically in elderly hypertensives. The antihypertensive therapy has been shown to be efficacious and relatively well tolerated in the long term. However, the results of the effects of the treatment on mortality and morbidity 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 in younger individuals.

What is hypertension in the elderly?

Blood pressure is a continuous variable and as the level rises, so do the associated risks (1). As in young people there is no clearly identifiable critical or safe level, so cut-off points must be arbitrary. The limits set are based on increase in morbidity and mortality. In the present context we take 160/90 mmHg (5th phase) as the upper limit of normal pressure.

It is now recognised that we must take systolic pressure into account as well as the diastolic. Disproportionate systolic hypertension exists when the rise in systolic pressure is exaggerated compared with the diastolic pressure. It is defined as systolic pressure = (diastolic pressure - 15) x 2.

Isolated systolic hypertension is variously defined as a systolic pressure greater than 150 mmHg (18) or a systolic pressure in excess of 159 mmHg (19), while the diastolic pressure remains below 90 mmHg. A third definition, and perhaps the most appropriate, is a systolic pressure of 160 or greater with a diastolic pressure of 95 mmHg (20). Disproportionate systolic hypertension and isolated systolic hypertension are presently under investigation and a plan of management is not known.

How common is hypertension in the elderly?

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. In the United States the National Health Survey (21), using 160/95 mmHg as the lower limit of hypertension, found 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 (11). Using 159/90 as the systolic and diastolic limits, isolated systolic hypertension is relatively rare: 2.7% of the population if readings are repeated on a separate occasion (19). Clearly, if 95 mmHg is used as the cut-off level for diastolic pressure, a higher prevalence will pertain.

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 (22).

Ageing induces physiological and pathological changes which may influence the pharmacokinetics and response to drugs (23, 24).

There are varying opinions concerning the level of blood pressure at which to start

treatment in the elderly patients. It is generally agreed that, regardless of age patients with a sustained diastolic blood pressure of 115 mmHg or more should receive treatment. In fact, most doctors treat those with diastolic pressure over 110 mmHg. We should carefully consider therapy in elderly patients whose blood pressure is higher than 160/100 mmHg on two occasions. In patients with diastolic blood pressure in the range 100-110 mmHg the presence of complications or a simultaneous systolic blood pressure of greater than 180 mmHg would sway the balance in favour of therapy. At present most European physicians do not treat isolated systolic hypertension (25). However, when a group of North American physicians were 'polled' at a recent meeting of Chest Physicians, it was clear that the vast majority of those present treated isolated systolic hypertension. This reflects their more aggressive approach to treatment of hypertension in general, but also indicates that the Americans are prepared to anticipate the results of studies of the efficacy of blood pressure reduction on mortality and morbidity in the elderly.

Investigations

Investigations are mainly aimed at assessing the effects rather than the cause of hypertension and should be kept to a minimum: electrocardiogram, dipstick urinalysis, serum creatinine, serum electrolytes and urate.

Clinically significant left ventricular hypertrophy is detectable on the conventional electrocardiogram. The dipstick urinalysis is usually sensitive enough to detect abnormalities and only if the findings are positive is it worthwhile progressing to a mid-stream urinalysis with culture and sensitivity testing. Serum creatinine is not a sensitive measure of renal function and will be raised only if approximately 70% of kidney tissue is not functioning. Therefore, if an accurate assessment is deemed, necessary creatinine clearance should be measured. Changes in serum electrolytes and serum urate are unlikely prior to drug treatment and the main reason for doing them is to assess the possible deleterious effect of diuretic treatment.

Even if secondary hypertension is suspected extensive investigations must be carried out unless surgical intervention is feasible and desirable.

Choice of drug

In choosing a particular drug the physician must attempt to combine efficacy with a minimum of unwanted effects.

In general, it is best to avoid antihypertensive agents such as methyldopa, reserpine, and clonidine that cause depression of the central nervous system. Though good data are lacking, it is generally held that the elderly are more prone to the unwanted central-nervous-system effects of these drugs. This generalisation must be tempered by an interim report of an ongoing study by the European Working Party on High Blood Pressure in the Elderly (EWPHE) (15), in which complications with methyldopa do not appear to be a problem. In this study, however, methyldopa is used in low doses. The elderly and particularly those with cerebrovascular disease are susceptible to postural hypotension because they have less responsive baroreflexes (26, 27). For this reason, adrenergic-neuron blocking drugs (guanethidine, bethanidine and debrisoquine) that cause postural hypertension should not be used. Vasodilators hold promise for the future, particularly in systolic hypertension, but at present data are insufficient to make an informed decision (8).

the brainstem vasomotor centre thereby inhibiting sympathetic outflow and reducing systemic arterial pressure. Both these agents may produce several side-effects like drowsiness and depression and should therefore be used restrictively. Adrenergic-neuron blocking drugs (guanethidine, bethanidine and debrisoquine) cause postural hypotension and should not be used in the present context.

Diuretics

Thiazide diuretics are effective in reducing blood pressure in elderly hypertensives and do not cause major clinical or biochemical disturbances but to minimise biochemical disturbances it is best to use a low dose of for example hydrochlorothiazide (25 mg daily). The elderly are said to be more prone to the potassium-losing effects of thiazide diuretics. Hypokalaemia may induce ventricular ectopic activity (33) and the risk of arrhythmias is more marked when a hypokalaemic patient performs exercise (34). Patients with abnormal potassium levels may also have a poorer prognosis in case of myocardial infarction with higher risk of arrhythmias (35). Therefore, potassium supplementation should be given or the thiazide should be combined with a potassium-sparing diuretic such as triamterene. As many elderly patients find individual potassium preparations unpalatable one may combine the thiazide with potassium in one tablet. Potassium supplementation is particularly appropriate if the patient is also on digitalis therapy. Glucose intolerance is one of the major risk factors for coronary artery disease. In the EWPHE study the group treated with thiazide diuretics showed a significant deterioration in glucose tolerance (17, 36). 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 rise in blood sugar level.

Serum uric acid levels also rise in patients on thiazide diuretic therapy. In the EWPHE study the group treated with diuretics showed a 25% increase in serum uric acid but clinical gout was extremely rare. The same indications and contraindications apply as in younger patients.

Summary

High blood pressure in the elderly is associated with a high incidence of cardiovascular disease but there are no definite data which prove that treatment of mild to moderate hypertension in this age group improves prognosis. However, a review of available literature suggests that treatment is beneficial. We adopt a policy as outlined above. We suggest a thiazide diuretic or a beta-adrenoceptor blocking drug 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.

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Discussion

Verhoeven:

Why do you avoid the use of alpha-methyldopa?

O'Malley:

Mainly because it has a CNS depression effect.