

The influence of common simple investigations on treatment and outcome in hypertensive patients

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Cardiovascular hazards of hypertension

Hypertension is a highly prevalent, major, independent contributor to atherosclerotic cardiovascular disease. Hypertension imparts a two-to-threefold increased risk of cardiovascular events.¹

The prevalence of hypertension is high (at least one in four adults), and it increases with age. In addition, hypertension has a rather large risk ratio, and these two factors contribute to the fact that approximately 35% of atherosclerotic cardiovascular events may be attributable to hypertension.¹

The relative risk of adverse events associated with hypertension is continuous and graded, and the absolute risk of adverse events depends on the degree of blood pressure elevation, and the presence of other cardiovascular risk factors.

From the Framingham data, the biennial age-adjusted rate per 1 000, for coronary disease due to hypertension, is 22.7 for normotensives, and 45.4 for hypertension: a risk ratio of 2 for hypertension.² Risk ratios are larger for stroke and heart failure, but coronary disease is much more common. Hypertension is only one of many risk factors causing atherosclerosis, and at least 80% of hypertensives have other risk factors. This compelling argument mandates that all hypertensives be tested for cholesterol (lipogram) and blood glucose, and also that a history of smoking be noted. Elevated cholesterol in hypertensives needs to receive a statin to reduce the number of myocardial infarctions, as shown in the Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT), where there was a relative risk reduction of myocardial infarction of 36%.³

Smoking cessation is also important as hypertension, hypercholesterolemia and smoking, account for around 85% of the cardiovascular risk for cardiovascular disease that can be modified.⁴

Compelling indications for specific drugs in this regard are post-myocardial infarction [angiotensin-converting enzyme (ACE) inhibitors, angiotensin-specific receptor blockers

(ARBs), beta blockers], angina (beta blockers, calcium-channel blockers), heart failure (ACE inhibitors, ARBs, beta blockers, diuretics, aldosterone antagonists).⁵

Left ventricular hypertrophy, measured on an electrocardiogram, chest X-ray, or echocardiography due to pressure overload, as well as multiple cardiovascular risk factors, may identify individuals who are more exposed to the adverse effects of high blood pressure. Regression of left ventricular hypertrophy with therapy significantly decreases cardiovascular risk.⁶

The measured level of systolic blood pressure is of critical significance, as increased systolic blood pressure is independently associated with an adverse, or increased, cardiovascular risk. The goal should be a systolic blood pressure of below 140 mmHg in everyone, including the elderly.⁷ It is also true that a reduction of systolic blood pressure of 20 mmHg can potentially halve cardiovascular risk. In people, usually the elderly, with isolated systolic hypertension (systolic blood pressure \geq 140 mmHg, and diastolic blood pressure $<$ 90 mmHg), those with a diastolic blood pressure of \leq 70 mmHg or lower represent a category that has a higher risk, and is either untreatable or difficult to treat. This is because it is possible to lower the already low diastolic blood pressure even further, to possible dangerous levels.⁸

What about age? The Blood Pressure Lowering Treatment Trialists Collaboration (BPLTTC) published a meta-analysis of 31 trials, of more than 190 000 randomised patients. They demonstrated that a reduction in blood pressure, using various antihypertensive drugs, was independent of the patient's age.⁹ They also strongly advocated early and aggressive management of hypertension, irrespective of age. This analysis did not exclude the possibility that ACE inhibitors, and other renin system inhibitors, given as first-line treatment in older people, might be less efficacious than diuretics, or calcium-channel blockers.⁴ Age should not exclude patients from treatment.

When diabetes mellitus occurs together with hypertension, the BPLTTC has shown similar benefit of treating

hypertension for hypertensives, with, or without, diabetes mellitus, using the major drug classes.¹⁰ Compelling indications for ACE inhibitors, ARBs, and other drugs, are made for hypertensive diabetics. In general, the goal of blood pressure reduction in diabetics should be < 130/80 mmHg.

Patients with renal disease with an estimated creatinine clearance of < 60 ml/minute have significantly higher adjusted risk ratios for cardiovascular mortality and all-cause mortality: risk ratio 1.80 (95% CI 1.33-2.44).⁶ Microalbuminuria, a marker of impaired renal function, and also of a more generally endothelial dysfunction, is an established risk factor for cardiovascular morbidity and mortality, and for the development of end-stage renal disease in individuals with a high cardiovascular risk profile.⁶ A compelling indication for ACE-inhibitors or ARBs is made, although other drugs have also been shown to reduce albuminuria, such as aldosterone antagonists, dihydropyridine, calcium-channel blockers, and carvediol.⁵

General principles in hypertension treatment¹¹

First-line treatment

Blood pressure lowering is the major driver of benefit of treatment, and the response to different classes of drugs is similar when compared head to head in heterogeneous populations. However, individual responses to different classes can be significantly different. No antihypertensive drug has been found to be more effective than others in reducing all-cause mortality, or cardiovascular mortality. In broad terms, there is no difference between diuretics, calcium-channel blockers and inhibitors of the renin system, as optimal first-step treatment.

Beta blockers may not be an optimal first-line agent. In general, people above the age of 55 years old, or those of black ethnic origin at any age, will generally have a greater blood pressure response with thiazide-type diuretics, or calcium-channel blockers. In young people, who have a more active renin-angiotensin system, inhibitors of the renin-angiotensin system will have a greater effect. Inhibitors of the renin-angiotensin system are also associated with a lower risk of the development of diabetes mellitus, a risk that can have a considerable impact in young people.

Initial combination treatment

Traditionally, combination treatment is used when monotherapy fails. However, for patients whose blood pressure is 20 mmHg or more above their systolic blood pressure goal (< 140 mmHg or < 130), the recommendation is to initiate combination therapy. The best combination is currently under debate, but an inhibitor of the renin-angiotensin system, and a calcium-channel blocker, seems to be the preferred combination.

Combination therapy should also be initiated in high-risk hypertensives as early risk reduction is possible. This group of patients should also receive a statin, and very high-risk patients with well-controlled hypertension, aspirin, as well. These high-risk individuals should be diagnosed (risk stratified) using global risk estimation, making use of risk charts such as Systematic Coronary Risk Evaluation (SCORE), or Framingham Risk Score.

Initial combination therapy is likely to become common practice. Would initial combination therapy not also solve the question of which drug to start with?

Resistant hypertension

Refractory hypertension is defined as blood pressure that is higher than target: 140/90 mmHg for most individuals, and 130/80 mmHg for those with diabetes or renal disease, despite the use of three different classes of antihypertensives that include a diuretic. Poor compliance should be excluded before embarking on expensive tests to search for a secondary cause of hypertension. Obstructive sleep apnoea is becoming an important co-morbidity that causes resistant hypertension. Primary hyperaldosteronism is another cause of resistant hypertension.

Lifestyle changes

Lifestyle modifications are effective in lowering blood pressure, and should be recommended to all patients with hypertension, even those on pharmacological drugs. Exercise, a higher intake of fruit and vegetables, a reduction in animal fat, moderation in alcoholic intake, and a reduction in salt intake, should be initiated in all patients.³

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