Cardio DIGEST
The easy way to stay up to date with developments in cardiovascular care

Editorial

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Blood pressure treatment – where to now?

Given the prevalence of macrovascular disease in diabetes and the frequency of its prominent risk factor, hypertension, antihypertensive treatment is close to the heart of the clinical diabetologist. Evidence is now available that demonstrates the benefits of antihypertensive treatment in diabetes, emanating from trials such as the Hypertension Optimal Treatment (HOT) trial (Hansson et al, 1998), the Captopril Prevention Project (CAPPP) trial (Hansson et al, 1999) and the United Kingdom Prospective Diabetes Studies (UKPDS, 1998).

However, debate continues regarding the optimal first-line antihypertensive agent. Previous meta-analysis of the trials for treatment of hypertension suggested that ACE inhibitors and calcium-channel blockers are likely to reduce cardiovascular morbidity and mortality by the same order of magnitude as older agents such as β-blockers and thiazide diuretics. In relation to diabetes, the debate has continued as to whether the newer agents such as ACE inhibitors have superior effects to the older treatments based on thiazide diuretics. The potential benefits of ACE inhibitors were avidly debated as a result of the HOPE study (HOPE, 2000).

Various studies have compared treatment with ACE inhibitors with conventional treatments, including the Second Swedish Trial in Old Patients with Hypertension (Hansson, 2000), CAPPP and the UKPDS studies. Further information was eagerly anticipated from the recently published ALLHAT trial (2002) and the Second Australia National Blood Pressure Study Group Trial in Elderly Patients (ANBP2, Wing et al, 2003).

The ALLHAT trial investigated 12 063 people aged over 55 years, who had diabetes, mild to moderate hypertension and one additional cardiovascular risk factor. The trial compared four antihypertensive treatments based on initial treatment with: the diuretic chlortalidone (12.5–25 mg daily); the ACE inhibitor lisinopril (10–40 mg daily); the calcium-channel blocker amlodipine (2.5–10 mg daily); and the α-blocker doxazosin (1–8 mg daily). Treatment with doxazosin was discontinued prematurely after a reported excess of cardiovascular events, especially heart failure, compared with chlortalidone. In the remaining three groups there were no significant differences in the cardiovascular primary endpoints, although the lisinopril group demonstrated less well controlled blood pressure by 2–4 mmHg (which may have a significant epidemiological impact on cardiovascular outcomes). Secondary endpoints were in favour of chlortalidone. However, as anticipated, 63% of patients required two or more drugs to control blood pressure, making it difficult to differentiate between groups of agents.

The ANBP2 trial studied 6083 patients (aged 65–84 years) for 4.1 years. Total cardiovascular events/deaths from any cause, and the likelihood of a first cardiovascular event/death, were reduced considerably in patients randomised to the ACE inhibitor enalapril, compared with treatment based on hydrochlorothiazide as a diuretic (risk reduction 11%). The effect was more pronounced in male subjects. It is important to note that in this study 66% of patients received the appropriate monotherapy as their antihypertensive agent.

Where do these data leave the practising clinician in terms of treating individual patients? A few important messages emanate from these studies. The first is the need to actually complete the process of blood pressure measurement. Secondly, it is quite clear that treatment of blood pressure is the key. Given that two or more drugs are often needed in order to achieve appropriate targets, it seems that ACE inhibitors should be used with thiazide diuretics (with the obvious caveat of evaluation of metabolic control), either separately or in combination. The data also suggest that the use of agents from other classes as first-line agents is acceptable, particularly in the presence of other conditions such as angina. The ALLHAT study dismissed concerns about the safety and efficacy of calcium-channel blockers, which may therefore be a useful adjunctive treatment, perhaps in combination with aspirin. The overwhelming primary message is to lower elevated blood pressure.

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