Lower systolic blood pressure goal in non-diabetic patients achieves greater cardioprotection
Triple therapy is more effective than dual therapy in controlling high blood pressure

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Patients with high blood pressure, but without diabetes, who were treated to lower systolic blood pressure levels than currently recommended experienced fewer cardiovascular events than patients receiving usual blood pressure control (Verdecchia P, Staessen JA, Angeli F, et al. Lancet 2009; 374:525-33). A systolic blood pressure target of <140 mm Hg is currently recommended for patients with high blood pressure who do not have diabetes. An Italian study involving 1111 patients with an initial systolic blood pressure >150 mm Hg found that those treated more aggressively to a target of <130 mm Hg had better clinical outcomes than those treated to a target of <140 mm Hg. Over 2 years of follow-up, patients with tighter blood pressure control targets (<130 mm Hg) were 50% less likely to experience a cardiovascular event compared with those receiving usual blood pressure control (<140 mm Hg)(P=0.003). Over the same time period, the likelihood of developing left ventricular hypertrophy was 11.4% in patients receiving tight blood pressure control compared with 17% for those receiving usual control, a risk reduction of 37% (P=0.013). These findings suggest that patients with high blood pressure who do not have diabetes would benefit from lower systolic blood pressure targets than currently recommended by international management guidelines.

Expert commentary

There is an increasing shift away from treating blood pressure according to traditional thresholds and a move towards treating patients according to their absolute risk to avoid major cardiovascular events such as stroke and myocardial infarction. This study provides further evidence that lowering a patient's blood pressure below currently recommended targets can produce further treatment benefits.

The average age of patients was 67 years and 59% were women. At study entry all patients had elevated blood pressure (average SBP 163 mm Hg), were on existing blood pressure treatment and had at least one other cardiovascular risk factor which was not diabetes. Those patients who were assigned more intensive blood pressure treatment achieved an average SBP of 131 mm Hg after 2 years and this was associated with a reduction in risk of left ventricular hypertrophy of just over one-third compared with the less intensively treated group in which the average achieved SBP was only 4 mm Hg higher (135 mm Hg). Whilst the primary outcome in this trial was not stroke or heart attack, ventricular hypertrophy is a strong predictor of cardiovascular outcomes. Furthermore, the results were consistent across subgroups of patients categorized according to age, sex, initial blood pressure, past history of myocardial infarction, smoking status and dyslipidaemia.

Research has comprehensively shown that larger reductions in blood pressure are associated with larger reductions in risk, even among patients who are so-called "normotensive". This study goes one step further and suggests that lowering blood pressure in patients without diabetes should not stop at 140/90 mm Hg but continue down, at least to levels currently recommended for diabetic patients. The nature of the study population suggests these results are likely to be highly generalisable to patients routinely seen in general practice.

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Patients with high blood pressure randomised to triple therapy with amlodipine, valsartan and hydrochlorothiazide were more likely to achieve blood pressure control than patients randomised to dual therapy with the different combinations of these agents (Calhoun DA, Lacourcière Y, Chiang YT, et al. Hypertension 2009; 54:32-39). An 8-week, international study involving 2060 patients with high blood pressure found 71% of patients receiving triple therapy achieved overall blood pressure control (<140/90 mm Hg) compared with 45%-54% of those receiving only dual therapy (Val/HCTZ or Aml/Val or Aml/HCTZ) (P<0.0001). Patients in the study had a BP level (≥ 145/100 mm Hg) on study entry having been on a variable number of antihypertensive agents (0 to 3) all of which were discontinued prior to the 8-week treatment trial. Triple therapy was significantly superior to each dual therapy in reducing sitting systolic and diastolic blood pressure (P<0.0001), and the benefits of triple therapy over dual therapy were observed regardless of baseline systolic blood pressure, age or gender. Triple therapy was also well tolerated.

Expert commentary
This randomised, double-blind trial serves to emphasise that given 3 antihypertensive drugs, each of a different class, the combination of all 3 will be superior in terms of BP lowering than any of the possible 2-drug combinations. Any other result would have been totally surprising, unless there was a significant overlap in the mode of action of the drug classes selected (eg: ACE-inhibitors and ARB's). The study could have provided novel and more useful information by further investigating possible differences in the effects of the various 2-drug combinations. For example, there are several reports that suggest variability in the effects of different two-drug combinations according to patient age and ethnicity. Unfortunately, this was not the aim of the study and these data are not reported.

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