

## Are Conventional and Newer Antihypertensives Comparably Effective?

Hansson L, Lindholm LH, Ekbom T, Dahlof B, Lanke J, Schersten B, et al. Randomised trial of old and new antihypertensive drugs in elderly patients: cardiovascular mortality and morbidity in the Swedish Trial in Old Patients with Hypertension-2 study. *Lancet* 1999;354:1751-6.

### Study Overview

**Objective.** To compare the effects of conventional (diuretics,  $\beta$  blockers) and newer antihypertensive drugs (angiotensin-converting enzyme [ACE] inhibitors, calcium antagonists) on cardiovascular mortality and morbidity in elderly patients.

**Design.** Prospective, randomized, open-label trial.

**Setting and participants.** 6614 patients aged 70 to 84 years with hypertension, defined as having blood pressure  $\geq 180$  mm Hg systolic,  $\geq 105$  mm Hg diastolic, or both. Patients were enrolled from 312 health centers throughout Sweden between September 1992 and December 1994 and were followed through December 1998.

**Methods.** Patients were randomly assigned to 1 of 3 treatment groups: (1) conventional antihypertensive drugs (atenolol 50 mg, metoprolol 100 mg, pindolol 5 mg, or hydrochlorothiazide 25 mg plus amiloride 2.5 mg daily), (2) ACE inhibitors (enalapril 10 mg or lisinopril 10 mg daily), or (3) calcium antagonists (felodipine 2 to 5 mg or isradipine 2.5 mg daily).

**Main outcome measures.** Fatal stroke, fatal myocardial infarction, and other fatal cardiovascular disease. Analysis was done on an intention-to-treat basis, with only the first event measured.

**Main results.** Blood pressure reductions were similar in all treatment groups. Among survivors at 24 months, the decrease from baseline to the last visit was 34.8/16.6 mm Hg (systolic/diastolic) in the conventional drug group, 34.5/16.2 mm Hg in the ACE inhibitor group, and 34.5/17.5 mm Hg in the calcium antagonist group. At the last visit, 46% of all patients were receiving more than 1 antihypertensive drug. In the conventional drug group, 62.3% of patients were still taking their randomized treatment at the

last visit, compared with 61.3% in the ACE inhibitor group and 66.2% in the calcium antagonist group.

On an intention-to-treat basis, the primary combined endpoint of fatal stroke, fatal myocardial infarction, and other fatal cardiovascular disease occurred with equal frequency in the 3 groups: 19.8 events per 1000 patient-years in the conventional drug group, 20.5 events per 1000 patient-years in the ACE inhibitor group, and 19.2 events per 1000 patient-years in the calcium antagonist group. There was no difference in relative risk (RR) between the conventional group and the new groups overall (RR, 0.99; 95% confidence interval [CI], 0.84 to 1.16;  $P = 0.89$ ). The combined endpoint of fatal and nonfatal stroke, fatal and nonfatal myocardial infarction, and other cardiovascular mortality occurred in 20.8% of patients taking conventional drugs and in 20.2% taking newer drugs (RR, 0.96; 95% CI, 0.86 to 1.08;  $P = 0.49$ ).

### Conclusion

Conventional and new antihypertensive drugs produced similar effects in decreasing blood pressure and preventing cardiovascular mortality or major events.

### Commentary

Treating hypertension effectively in older persons has repeatedly been shown to reduce cardiovascular morbidity and mortality [1,2]. With the development of new antihypertensive therapies have come questions about how their effectiveness, safety, tolerability, and effect on outcomes compare with older therapies. The current study (STOP-Hypertension-2) attempts to address some of these questions, but design problems (eg, use of intention-to-treat analysis, analysis of only the first outcome event, and the choice of drugs selected for comparison) weaken the validity of its findings. First, physicians in this trial prescribed multiple therapies for their patients nearly half of the time. Pure intention-to-treat analysis cannot account for the complexity of actual therapeutic regimens or the reasons for modification

of the original regimens. Second, the omission of any cardiovascular events after the first endpoint may hide real and possibly different outcomes between the comparators. Finally, some leading drugs were omitted from the therapeutic classes studied. It should be noted that angiotensin-II blockers were not studied because they were unavailable at the time of patient enrollment.

### **Applications for Clinical Practice**

Given the design flaws of this study, it is premature to describe the effects of all newer antihypertensive drugs as similar to those of the older therapies. Future studies must be

designed in a way that allows a more comprehensive assessment of the clinical outcomes of these drugs.

### **References**

1. Prevention of stroke by antihypertensive drug treatment in older persons with isolated systolic hypertension. Final results of the Systolic Hypertension in the Elderly Program (SHEP). SHEP Cooperative Research Group. *JAMA* 1991; 265:3255-64.
2. Medical Research Council trial of treatment of hypertension in older adults: principal results. MRC Working Party. *BMJ* 1992;304:405-12.

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