Editorial Commentary

Diuretic Treatment of Systolic Hypertension in the Elderly

Robert W. Schrier

The publication, in 1991, of the results of the Systolic Hypertension in the Elderly Program (SHEP) constituted a major therapeutic advance for treating isolated systolic hypertension—systolic blood pressure 160 to 219 mm Hg and diastolic blood pressure <90 mm Hg in patients >60 years of age. The results demonstrated not only a decrease in strokes but also coronary heart disease. In earlier studies, the ability to demonstrate a beneficial effect of treating combined systolic diastolic hypertension on the incidence of coronary heart disease was difficult to demonstrate: one possibility that was entertained to explain the difficulty was related to the dose of diuretic used. The relatively high doses of thiazide diuretics (50 to 100 mg/d) used in previous hypertension studies may have increased ventricular arrhythmias and sudden deaths and worsened glucose and lipid profiles, secondary to the occurrence of hypokalemia. These effects could have obscured any beneficial effects that lowering blood pressure has on the occurrence of coronary heart disease. In the SHEP study, a lower dose of chlorthalidone was used, generally starting with 12.5 mg/d and only increasing to a maximum of 25 mg/d. If the goal of lowering systolic blood pressure to <160 mm Hg or by ≥20 mm Hg was not achieved, the β-blocker atenolol or reserpine was added.

As noted in this issue of Hypertension, in spite of the lower doses of chlorthalidone, a thiazide diuretic, 7% of the active treatment group versus 1% of the placebo group had a serum potassium concentration <3.5 mEq/L in the SHEP study. What was remarkable was that this hypokalemic group of patients (n=151) did not demonstrate any significant reduction in the rate of cardiovascular events, coronary heart disease, or stroke as compared with the placebo group of patients (n=203) in contrast to the active treatment patients (n=1951) who had serum potassium concentrations greater than 3.5 mEq/L. This observation persisted when adjusted for a number of cardiovascular risk factors.

Although these results are from a subgroup analysis of the SHEP study, their implications cannot be ignored. A larger percentage of hypokalemic than normokalemic patients in the active treatment group received the higher dose (25 mg) of chlorthalidone (53% versus 33.5%, P<0.001) more frequently. However, the stratification for dose and restriction of the analysis to those participants with a >80% study drug compliance did not alter the conclusions.

With the increased recognition of primary hyperaldosteronism as a cause of hypertension, this diagnosis should certainly be considered in hypertensive patients who develop hypokalemia (<3.5 mEq/L) when receiving only 12.5 to 25.0 mg/d of a thiazide diuretic including potassium supplements. Some of these patients may also respond better to potassium-sparing diuretics than potassium supplements.

One disturbing aspect of the present report is the increase in all-cause mortality rates in normokalemic versus hypokalemic patients in the active treatment group (24.5 versus 13.5 per 1000 person years with a hazard ratio of 1.33), even though this difference did not reach statistical significance. Because cardiovascular events are the major cause of death in the elderly and because hypokalemic patients in the active treatment population had a significant increase in any cardiovascular event, coronary heart disease, and stroke than the normokalemic patients (all P<0.05), it would have been expected that all-cause mortality would be greater, not less, in the hypokalemic patients. Even so, maintaining serum potassium concentrations >3.5 mEq/L during the treatment of elderly patients with systolic hypertension seems indicated on the basis of the results of the paper by Franse et al.

References


Key Words: diuretics • hypokalemia • elderly
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Hypertension. 2000;35:1031
doi: 10.1161/01.HYP.35.5.1031

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