More Hype Than HOPE

To the Editor:

In the recently published Heart Outcomes Prevention Evaluation (HOPE study), treatment with the ACE inhibitor ramipril was reported to reduce cardiovascular morbidity and mortality independent of blood pressure (BP) reduction. High-risk “normotensive” (BP=140/80 mm Hg) patients (n=9541) were randomized to receive either 10 mg of ramipril or placebo in addition to their current medical regimen. They were followed for 4.5 years. The group receiving ramipril had an approximately 35% reduction in cardiovascular events despite no significant reduction in blood pressure. The reported blood pressure reduction was 3 mm Hg systolic and 2 mm Hg diastolic, which was dismissed as insignificant.

The conclusions of this study were that ACE inhibition is beneficial, independent of its antihypertensive effects, and should be initiated in all high-risk patients despite their baseline blood pressure.

In a recently published HOPE substudy, published in the journal Hypertension, December 2001, the details of the HOPE study protocol are revealed with some surprising revelations. Ramipril was actually dosed in the evening and outpatient blood pressure was measured the following day, on average 10 to 14 hours after dosing. The reported change in blood pressure in the HOPE study (3/2 mm Hg) was a snapshot reading reflecting the trough level and nadir effect of the medication. When the investigators actually looked at the average overnight blood pressure on ambulatory blood pressure monitoring, there was a whopping 17/8 mm Hg reduction in blood pressure during the evening hours. For the entire 24-hour ambulatory blood pressure recording, the average reduction in blood pressure was 10 mm Hg systolic and 4 mm Hg diastolic when the pronounced nighttime reduction was included.

Certainly, the average ambulatory blood pressure is a much more accurate and meaningful reflection of the effect ramipril had on blood pressure rather than the one-time measurement that occurred 10 to 14 hours after dosing as was initially recorded in the HOPE trial. A reduction of 10 mm Hg systolic and 4 mm Hg diastolic is most significant because all the major hypertension trials (SHEP, MRFIT, HOT, etc) showed similar reductions in cardiovascular morbidity and mortality with the same degree of blood pressure reduction. The HOPE authors themselves acknowledged that blood pressure reduction may have played a much larger role than originally ascribed.

The HOPE trial, I believe, is simply another hypertension trial, supporting the already strong JNC VI recommendation that high-risk patients should be treated to a blood pressure of less than or equal to 130/80 mm Hg. Although there may very well be excellent rationale and data to support the use of ACE inhibitors in normotensive patients, the HOPE study by no means proves or even strongly supports this. It would be very premature, based on this trial, to advocate the addition of an ACE inhibitor to truly normotensive patients simply in the “hope” of reducing future cardiovascular events.

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Hypertension. 2003;41:e4; originally published online March 3, 2003;
doi: 10.1161/01.HYP.0000060824.84130.4F
Hypertension is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0194-911X. Online ISSN: 1524-4563

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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