Letter by Ben-Dov and Bursztyn Regarding Article, “Role of Diuretics in the Prevention of Heart Failure: The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial”

To the Editor:

In their article, Davis et al1 for the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT) Collaborative Research Group characterize the differences in heart failure incidence according to treatment assignment in patients enrolled to ALLHAT. On the basis of time-dependent analyses and comparison with previous trials, they conclude that blood pressure (BP) differences alone cannot account for the superior prevention of heart failure afforded by chlorthalidone compared with lisinopril and amlodipine (and also doxazosin2). We suggest that ambulatory BP differences may bridge the gap between the achieved clinic BP and the ensuing outcome. In both treated and untreated hypertensive subjects, ambulatory BP has been shown to predict mortality beyond clinic BP. Furthermore, nonclassic BP parameters, such as the sleep-related dip and the white-coat phenomenon, have emerged as prognosticators.

For example, in our cohort of subjects referred for 24-hour ambulatory monitoring, adjustment for baseline covariates disclosed higher ambulatory pressures during sleep in subjects treated with α-blockers, whereas their manual BP tended to be lower.3 Assuming the same is true in ALLHAT subjects, this may partly explain the superiority of chlorthalidone despite the metabolic advantages of doxazosin.

In addition, it has been shown that volume-overload states such as salt-sensitive hypertension, diabetic nephropathy, and congestive heart failure are characterized by a nondipping BP pattern.4 Diuretics have been convincingly shown to reverse nondippers to dippers in such conditions.5 Conversely, we and others have shown that α-blockers, which cause volume overload, are associated with decreased dipping.3 In our cohort, the covariates’ adjusted odds ratio for nondipping among α-blocker treated subjects was 1.7 (95% confidence interval, 1.1 to 2.8), whereas β-blockers, calcium blockers, and renin-angiotensin antagonists were not associated with dipping. Diuretics conveyed a reduced odds ratio for nondipping, at 0.65 (95% confidence interval, 0.45 to 0.94).3

Because clinic BP was used to screen and guide the treatment of ALLHAT subjects, it is possible that in patients achieving similar clinic BP, ambulatory BP may have differed according to the treatment assigned. This, in turn, could lead to dissimilar outcomes, including differences in heart failure incidence. Perhaps a future large-scale hypertension trial should also involve ambulatory BP monitoring, at least in a subset of patients.

Disclosures

None.

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(Circulation. 2007;115:e18.)
© 2007 American Heart Association, Inc.
Circulation is available at http://www.circulationaha.org
DOI: 10.1161/CIRCULATIONAHA.106.639617

e18
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_Circulation_. 2007;115:e18
doi: 10.1161/CIRCULATIONAHA.106.639617

_Circulation_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/115/2/e18

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