New Recommendations for Treating Hypertension in Black Patients
Evidence and/or Consensus?

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Hypertension is the major cause of morbidity, mortality, and disability in black populations in the United States and increasingly worldwide. Its greater severity, resistance to treatment, and more frequent financial challenges to achieve control in this population make it critical that population-specific recommendations for hypertension management be based on the very best evidence. In 2003, the International Society of Hypertension in Blacks (ISHIB) published its first consensus statement. The 2003 Statement has been widely promoted as the authoritative guideline for managing hypertension in black patients. The consensus statement in this issue of Hypertension updates the 2003 statement, and, although the authors are careful not to call it a guideline, it may become viewed similarly. Thus, it could dramatically impact the management of hypertension in this population.

The ISHIB statement has a number of commendable features. Written by a very impressive group of experts, it is a well-organized, comprehensive document providing an excellent update on the epidemiology, significance, and pathophysiology of hypertension in the black population, as well as substantial practical advice on its management. A particularly worthwhile feature is the discussion of psychosocial factors influencing blood pressure (BP) control in this population, including those related to patient-provider interaction. However, it makes several sweeping recommendations that are both unsupported by randomized clinical trial evidence and, moreover, are inconsistent with the most recent results of large randomized clinical outcome trials in black hypertensive patients.

While acknowledging that less than one third of black hypertensive patients are controlled to \( <140/90 \) mm Hg, the ISHIB statement recommends substantially lower BP goals in patients already \( <140/90 \) mm Hg. In uncomplicated hypertensive patients without target organ damage, preclinical cardiovascular disease (CVD), or history of CVD, it recommends lowering the target BP from \( <140/90 \) to \( <135/85 \) mm Hg. The selection of this new BP target appears both arbitrary and unfounded. To support the new lower goal, the authors cite evidence from observational studies and the results from 3 clinical trials: the Treatment of Mild Hypertension Study (TOMHS) (n=902 with 177 blacks); CardioSis, a European trial (n=1111, no blacks identified); and the Trial of Preventing Hypertension (TROPHY) (n=772, 79 blacks). Only the TOMHS and CardioSis reported clinical outcomes; more than half of the outcomes in the TOMHS were based on a screening questionnaire for angina (the Rose questionnaire). In CardioSis, the primary outcome was ECG evidence of left ventricular hypertrophy.

The ISHIB statement also references end-of-study, achieved BP data from the Antihypertensive and Lipid Lowering Heart Attack Prevention Trial (ALLHAT) to support the \( <135/85 \) mm Hg target in uncomplicated hypertensive patients. However, the ALLHAT BP goal was \( <140/90 \) mm Hg, and trial participants were, by trial design, extremely high risk patients: mean age was 67 years, more than half had CVD, >25% had coronary heart disease, 35% had diabetes mellitus, and \( \approx 60\% \) met criteria for the metabolic syndrome. Entry into CardioSis also required \( \geq 1 \) additional risk factor. Thus, both CardioSis and the ALLHAT studied populations substantially different from the low-risk patients for which the lower BP target is recommended.

Even more problematic is the recommendation for a BP goal of \( <130/80 \) mm Hg in those with diabetes mellitus, prediabetes, high Framingham risk, left ventricular hypertrophy, metabolic syndrome, or glomerular filtration rate <60. This recommendation would mean that the majority of black hypertensive patients would have a goal BP of \( <130/80 \) mm Hg. Data from clinical outcome trials designed to compare BP goals of \( <130/80 \) mm Hg with those \( <140/90 \) mm Hg in hypertensive patients with left ventricular hypertrophy, high Framingham risk, or metabolic syndrome are not available. However, we now do have such data in black patients with chronic kidney disease or diabetes mellitus.
The African American Study of Kidney Disease and Hypertension (AASK) trial studied black hypertensive patients with hypertensive renal disease. It was as large (n=1094) as any of the 3 trials that were used to justify the lower BP goals, and the number of black participants in AASK far exceed the cumulative number in all 3 of the trials. Although it was a trial of kidney disease progression and not powered to assess CVD outcomes, it still had more than twice the number of CVD events of those other studies, and it was a direct test of a BP goal approximating 140/90 mm Hg versus a lower goal in a black hypertensive population. Despite maintaining a 13/7-mm Hg BP difference (141/85 versus 128/78 mm Hg) over 3 years of mean follow-up, no benefit on renal (or CVD) outcomes was seen in those randomized to the lower goal either overall or in the subgroup of patients with baseline urine protein/urine creatinine <0.22 (equivalent to ~300 mg/d). Long-term (~10 years) post-trial follow-up suggests potential benefit of the lower BP goal on chronic kidney disease progression but not CVD events in the subgroup of patients with baseline urine protein/urine creatinine >0.22; however, there was no apparent benefit overall or in participants with urine protein/urine creatinine ≤0.22.

The National Heart, Lung, and Blood Institute–funded Action to Control Cardiovascular Risk in Diabetes Trial results were published recently comparing systolic BP goals of <140 mm Hg versus <120 mm Hg in diabetic hypertensive patients. Overall, in this trial of ~5000 participants, 24% black (n=1142) and mean follow-up of 4.7 years, there was no difference in the primary composite outcome consisting of nonfatal myocardial infarction, stroke, or CVD death, although a significant benefit of the lower BP goal was observed for stroke, one of the components of the primary outcome and a prespecified secondary outcome. The Action to Control Cardiovascular Risk in Diabetes Trial retinopathy BP results also reported no benefit of this lower BP goal on diabetic retinopathy progression. Importantly, although the stroke subgroup data have not yet been reported, the subgroup data by race for the primary composite CVD outcome shows that nonwhite participants (61% black) in the trial were not more likely to benefit from the lower BP goal (hazard ratio: 0.97 [95% CI: 0.71 to 1.33]; P=0.87). Thus, it is very difficult to make the case that black hypertensives with diabetes mellitus would benefit from a lower BP goal. The authors of the ISHIB statement appear to accept the results on CVD outcomes and retinopathy of the much smaller Appropriate Blood Pressure Control in Diabetes normotensive trial with only 480 participants as rebuttal to the Action to Control Cardiovascular Risk in Diabetes trial results, although the similarly small Appropriate Blood Pressure Control in Diabetes hypertensive trial (n=470) reported no benefit for renal, retinopathy, or CVD outcomes. The National Institutes of Health–funded Systolic Blood Pressure Intervention Trial will provide a definitive test of this question in high-risk nondiabetic patients.

Rather than setting new lower BP goals, we suggest a greater focus on increasing the number of patients controlled to the conventional goal of <140/90 mm Hg. At present, less than half of treated black hypertensive patients are controlled to even this level. There are several reasons to resist recommending lower BP goals not demonstrated to confer major benefits in randomized clinical outcome trials. Adherence to a more complex regimen and other proven effective therapies may be compromised. Furthermore, far more resources will be expended to reach lower goals, for example, more medications, more monitoring, more frequent clinic visits, and, consequently, higher costs.

The recommended approach to treatment is also a strength of the document, with one exception. The recommendation for the initiation of multiple drugs in those >15 mm Hg above their target systolic BP and/or >10 mm Hg above their target DBP (an innovation first proposed in the first ISHIB guideline) has been retained. The recommendation for this population of a renin-angiotensin-aldosterone system inhibitor as initial therapy in those without a compelling indication, a weakness of the 2003 document, has been deleted in this update. However, the recommendation in this update of a renin-angiotensin-aldosterone system inhibitor/calcium channel blocker combination over other possible 2-drug regimens in those receiving combination therapy has few data to support it. It currently recommends including diuretics for initial combination therapy only in those with edema or fluid overload.

This recommendation is based on the results of a single trial, the Avoiding Cardiovascular Events Through Combination Therapy in Patients Living With Systolic Hypertension (ACCOMPLISH) trial, with results in blacks thus far only referenced by a personal communication. There are several other inconsistencies in this recommendation. The ACCOMPLISH trial compared an angiotensin-converting enzyme inhibitor (ACEI)/calcium channel blocker with only 1 other 2-drug regimen, ACEI/hydrochlorothiazide (HCTZ), but the latter used a dose of HCTZ substantially lower than that used in other clinical trials demonstrating CVD outcome benefits with HCTZ. It also provides no evidence comparing it with other 2-drug regimens. Furthermore, this recommendation treats all thiazide-type diuretics as one class, although in other places, it recommends a preference for chlorthalidone over HCTZ and a higher dose of HCTZ than was used in ACCOMPLISH. In recommending the renin-angiotensin-aldosterone system inhibitor/calcium channel blocker combination, it treats ACEIs, angiotensin receptor blockers, and direct renin inhibitors as a group, yet ACCOMPLISH only provided data comparing an ACEI/calcium channel blocker versus an ACEI plus a very low-dose diuretic. Finally, the recommendation ignores the vast clinical outcome trial literature from the first Veterans Administration Cooperative Trials to ALLHAT demonstrating the benefit of thiazide-type diuretics in preventing major clinical outcomes in black hypertensive patients in favor of the results of a single study.

In summary, the new ISHIB consensus document presents useful, practical information to guide practitioners in the diagnosis, prevention, and treatment of hypertension in black patients. However, there is insufficient evidence to support the recommendations for the lower BP goals and the preferential use of 1 combination drug therapy.
Disclosures

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