Retrospective Analysis: Consensus Statement of the Hypertension in African Americans Working Group of the International Society on Hypertension in Blacks (ISHIB)

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The goal of this analysis is to reflect on the landmark consensus statement on the management of hypertension in African Americans as published in the *Archives of Internal Medicine* on March 10, 2003. Increasingly, primary care providers (including physicians, nurse practitioners, and physician assistants) rely on evidence-based guidelines to effectively treat a wide range of conditions including hypertension. The Hypertension in African Americans Working Group was a panel of leading clinical experts from ISHIB who were able to synthesize in a concise manner, clinically relevant scientific knowledge in evaluating and treating hypertension in Blacks. This group of ISHIB experts made several recommendations, which preceded and were eventually expanded upon by the seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7).

Evaluation of Cardiovascular Risk in African-American Adults

One of the more prominent components of the consensus statement was outlining elements of the initial cardiovascular risk assessment in African-American adults. Clinicians and researchers in cardiovascular disease should not isolate an individual risk factor, but rather recognize the importance of risk clustering in the development of cardiovascular disease. The conventional major risk factors noted in the ISHIB guidelines included cigarette smoking, elevated blood pressure (whether treated or untreated), elevated lipids, diabetes, and advancing age. In addition, other components of the history were included that may affect a patient's ability to sustain lifestyle modification and adherence to pharmacotherapy, including a history of psychiatric disease, the environmental assessment, socioeconomic factors, and recognition of the importance of over-the-counter medications, including supplements and herbal products. In terms of laboratory studies, the importance of microalbuminuria as a marker of cardiovascular risk was noted by the ISHIB panel.

Similarly, the JNC 7 report subsequently included not only the conventional major risk factors as noted, but also highlighted microalbuminuria, an estimated glomerular filtration rate less than 60 mL/min as major risk factors. Prior to the ISHIB report, microalbuminuria had been noted to be an independent risk factor for cardiovascular and renal disease in epidemiological report but had not been prominently placed in major guidelines as a screening tool for risk assessment. An additional highlight of the ISHIB report was recognizing the importance of the metabolic syndrome as an important aspect of increasing cardiovascular risk. The guidelines from the Working Group specifically suggested that the provider not only assess blood pressure appropriately, but also include multiple other laboratory tests as needed, confirming the interaction of risk factors, more common in African Americans and a potential source of their increased cardiovascular morbidity and mortality.

Setting Blood Pressure Goals

Over the last several years, lowering blood pressure as close to optimal levels has been confirmed as a primary approach for reducing risk of CV events. Epidemiological studies have demonstrated that blood pressure above 115/75 mm Hg is an increasing risk for cardiovascular events and stroke. A significant component of evaluating the benefit of treating hypertension is recognizing that renal function and cardiovascular health are deleteriously affected with elevated blood pressure, even prior to the conventionally defined hypertensive level (140/90 mm Hg or above). Since the ultimate goal of public health is the reduction of cardiovascular and renal morbidity and mortality, the Working Group appropriately identified the need to treat high-risk patients prior to the previously defined as hypertensive cutoff. The classification of blood pressure stages listed in the ISHIB report did not include the subsequent JNC classifications of "prehypertension" with systolic blood pressure 120–139 mm Hg or diastolic blood pressure 80–89 mm Hg. Nevertheless, the optimal blood pressure listed in the ISHIB report of less than 120/80 mm Hg mirrors to normal blood pressure category finally determined by the JNC 7 committee.

Therapeutic Life Changes

A large portion of the ISHIB report addressed the importance of therapeutic life changes in affecting the public health and the control of high blood pressure. Indeed, the Working Group specifically recognized the Dietary Approaches to Stop Hypertension (DASH) dietary plan. The DASH diet has potential benefit particularly to African Americans. The ability of

the expert panel from ISHIB to propose that the DASH diet as part of the Heart Healthy program from which all Americans can benefit, and the suggestion that the DASH diet be specifically recommended to all African Americans with or without high blood pressure, demonstrates the commitment to not only medical treatment but also early identification and prevention of high blood pressure in this high-risk population. Table 5 of the ISHIB guidelines, Therapeutic Lifestyle Changes, is prescient to a large extent, when compared to Table 3 of the JNC 7 report, Lifestyle Modifications to Manage Hypertension. Both guidelines include recognition of the importance of weight reduction, adoption of the DASH eating plan, dietary sodium reduction, increase in physical activity, and moderation of alcohol consumption. Furthermore the ISHIB guidelines recognized the importance of the National Cholesterol Education Program classification of lipids. Recent studies have confirmed that hypertensive patients with average lipid levels appear to benefit from intervention not only treating blood pressure but also by lipid lowering.

ANTIHYPERTENSIVE MEDICATIONS

The ISHIB guidelines appropriately recognize the importance of two recent landmark studies, the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT) and the African-American Study of Kidney Disease and Hypertension (AASK). These trials confirm the benefit of blood pressure reduction for hypertension using a wide range of agents including diuretics, long-acting calcium channel blockers, and angiotensin converting enzymes (ACE) inhibitors. In order to help clinicians understand and utilize these large, important blood pressure trials, the ISHIB guidelines included a table which described ALLHAT and AASK at a glance (Table 10). While noting that chlorthalidone, lisinopril, and amlodipine did not differ in preventing major cardiovascular events, the panelists did note that the thiazide-type diuretic was superior to lisinopril in reducing strokes and heart failure and superior to amlodipine in reducing heart failure in ALLHAT. Nevertheless, because some clinicians may unfortunately consider ACE inhibitors as less efficacious for reducing outcomes in African Americans, the ISHIB committee specifically highlighted the results of AASK, a randomized double-blind controlled trial with 1,094 non-diabetic African Americans with hypertensive renal disease. Ramipril reduced clinical events by 46% compared with amlodipine and reduced decline in kidney function to a significantly greater extent than amlodipine or metoprolol in Blacks. Nevertheless, without renal disease, a calcium channel blocker along with a thiazide diuretic remains effective for blood pressure reduction and cardiovascular protection.

RENIN ANGIOTENSIN SYSTEM-BLOCKING (RAS) AGENTS

As noted, there remains controversy regarding RAS-blocking agents in African Americans. Several studies have indicated less blood pressure lowering effects with ACE inhibitors, angiotensin blocking agents (ARBs), and Beta blockers as monotherapy in African Americans. The use of a diuretic at appropriate doses removes any racial or ethnic differences in response. In terms of ACE inhibitors specifically, the ISHIB committee confirms that African Americans who are at increased risk for hypertensive nephropathy would clearly benefit based on the strong evidence with ACE inhibitors in AASK specifically, in reducing the decline in renal function in patients with proteinuria.

The recent International Verapamil/Trandolapril Study (INVEST) demonstrated the benefit of a calcium channel blocker strategy with additional long-acting ACE inhibitors in hypertensive patients, including Blacks, with coexisting atherosclerosis and diabetes. Outcome studies demonstrating the benefit of ARBs in African Americans become more problematic. In the Losartan Intervention for End-Point Reduction in Hypertension (LIFE) study, the 533 Blacks randomized to the ARB losartan vs the Beta blocker atenolol in the setting of hypertension with left ventricular hypertrophy, actually demonstrated less effective reduction in cardiovascular morbidity including stroke than in the small group of Blacks on losartan-based therapy. One benefit of ACE inhibitors and ARBs in high-risk hypertensive patients may be protection against new onset diabetes and glucose intolerance. The recent Valsartan Antihypertensive Long-term Use Evaluation (VALUE) trial confirmed that amlodipine-based therapy had lower blood pressures especially earlier in the study vs valsartan-based therapy. Despite the trend toward less hospitalization for heart failure with valsartan, the composite cardiac events, stroke, and all-cause mortality were not superior to amlodipine with the ARB. The benefits of ARBs in African Americans will probably be realized in the ability to protect against new onset diabetes and diabetic nephropathy, but needs the addition of diuretics or calcium channel blockers to control blood pressure as effectively in this population. If RAS-blocking for heart failure is needed and an ACE inhibitor is not tolerated, the ISHIB panel notes that ARBs are alternative agents based on the benefit with valsartan and heart failure.

ISHIB GUIDELINES AS PRE-CURSOR TO JNC 7

Several aspects of the JNC 7 guidelines were earlier highlighted by the Working Group from ISHIB. Both guidelines confirm the robust current data demonstrating the benefits of lowering blood pressure and intensive treatment of hyperten-

sion. Moreover, both panels note that systolic blood pressure is as important a component of risk and target for control in almost all patients and that blood pressure itself is an independent cardiovascular risk requiring early and aggressive treatment. Especially for patients older than 50 years of age, systolic blood pressure is a more important goal of treatment and harder to control than diastolic blood pressure. Both guidelines developed an algorithm confirming the benefit of initiating therapy with two agents at higher levels of blood pressure (20/10 over goal as the point of initiating therapy in the JNC 7 report and 15/10 or more above target as the basis for combination therapy in the ISHIB repot). Both groups recognize the importance of thiazide diuretics as first line therapy or a part of a multi-drug treatment regimen and include a recommendation of two or more medications to aggressively control higher-risk patients. Specifically, the goal of less than 130/80 mm Hg was noted in the ISHIB consensus guidelines for patients with diabetes or non-diabetic renal disease and was suggested for these patients in the JNC 7. Both panels also recognize the clinical efficacy of calcium channel blockers for African Americans. However the ISHIB report highlights the need for not overlooking renal protection with ACE inhibitor in African Americans with renal disease. Since the ISHIB and JNC 7 reports, the VALUE trial and others confirmed protection against new onset-diabetes with ARBs but the recent trials do not necessarily indicate superiority over the calcium channel blockers or diuretics in blood pressure reduction and cardiovascular risk reduction.

Additional research will hopefully clarify the potential benefit of RAS-blockade in Blacks, independent of blood pressure reduction. However, at this time, reducing blood pressure itself is the primary need of curtailing excessive cardiovascular and renal risk in African Americans.

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