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EDITORIAL

CKD and Hypertension: Pogo and Pragmatism

In this inaugural issue of *Advances in Chronic Kidney Disease*, 2011, the Guest Editors, Drs. Raymond Townsend and Domenic Sica, have undertaken the task of compactly compiling and synthesizing the evidence regarding hypertension in individuals with CKD. Their team of experts addresses a diverse set of topics that must be considered by practitioners who care for patients with CKD, those who require no form of renal replacement therapy, and those who do. Several themes within the theme of this issue have emerged. First and foremost, hypertension as a concomitant, global cardiovascular and renal risk factor remains the overarching principle on which all therapy must be based. This is followed closely by exposition of how high blood pressure (BP) issues progression of CKD. In addition, the "tools of the trade" or the antihypertensive agents are reviewed, so as to prevent pitfalls of pharmacotherapy. Similarly, treatment of hypertension in populations with special interest to the nephrologist, such as kidney allograft recipients, individuals with diabetes, and those undergoing renal replacement therapy by hemodialysis or peritoneal dialysis, has also been included. Finally, one article has been devoted to newly available BP-lowering devices that may augment antihypertensive therapy in those individuals who truly have resistant hypertension.

Recently released statistics regarding the prevalence, awareness, and control of high BP reveal improvement in the latter 2 of these metrics, as evaluated by the 5 National Health and Nutrition Examination Surveys spanning the period between 1988 and 2008.[1] However, the prevalence of hypertension in the adult population has continually increased during the 20-year span of observation. Even more sobering is the thought that eight-tenths of the one-quarter of a billion persons with diabetes worldwide have high BP.

However, awareness and control of hypertension remain suboptimal from the standpoint of a population, despite many advances in medical therapy of hypertension. The inability to attain target BPs has tremendous healthcare consequences, and for nephrologists, possibly the most. Patients with CKD are nearly inextricably linked to hypertension. Almost 80% of patients with CKD have hypertension, and the proportion successfully treated to the American Heart Association and National Kidney Foundation guideline of $<130/<80$ mm Hg is relatively low. Within the confines of a clinical trial, only about one-half of African American hypertensive patients with CKD can attain such BP control.[2] Whether the CKD induced hypertension or so-called benign hypertension provoked CKD is often indiscernible at patient presentation. In addition, whether *MYH9*, a gene encoding a myosin heavy chain isotype and expressed in the glomeruli, is causative, or whether the more recently described gene *APOL1* should be implicated in the pathogenesis of hypertension-related kidney disease, that is, hypertensive nephrosclerosis, will probably be delineated in the near future.[3] However, what must be done in the meanwhile is self-evident; the elevated BPs of patients with CKD must be better treated and brought to a lower range than it had been formerly.

Why does this not occur? The reasons given are diverse and aplenty. High patient-driven sodium intake, nonadherence to the medical regimen, which may include various forms of cultural resistance, adverse medication events, and the expense of the medications themselves may foil even the most favorably formulated antihypertensive regimen. However, another culprit, often ignored, is ourselves. In the words of Walt Kelly: "We have met the enemy; and he is us."[4] Simply, we often do not achieve the BP goals that we espouse.

With regard to our own treatment of patients with CKD and hypertension, control rates of BP are highly variable, and this is dependent on the goal BP of the treating party. Upper systolic blood pressure limits of <130 or <140 mm Hg have been promulgated, and the

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target is modified, by some, in the presence of diabetes.[5] Moreover, data are insufficient at present to definitively state the best upper limit of systolic blood pressure in nondialysis-dependent patients with CKD. Hopefully, the ongoing National Institutes of Health-sponsored, randomized, multicenter Systolic Blood Pressure Intervention Trial (SPRINT) will provide a more evidence-based answer to this conundrum in patients with CKD and eGFRs of >25 mL/min/1.73 m^2 by studying 2 different levels of BP control: <140 mm Hg (standard group) versus <120 mm Hg (treatment group).[6] In addition, the SPRINT-Senior component of this 9-year comparative effectiveness research study will determine best BP management practices in persons of age >75 years. By comparison, careful observations by Agarwal and colleagues demonstrate that the ideal BP in patients with ESRD on maintenance hemodialysis may be 20 to 30 mm Hg less than previously conceived.[7] Moreover, in this circumstance, ambulatory BP monitoring and interdialytic BP measurement are the benchmarks. Still, these procedures have not even been typified in patients without CKD, much less in those with CKD.

Although the primacy of volume in patients with CKD was established decades ago, the "dry weight" of patients is not reached in many instances. Insufficient estimation of ultrafiltration volume, high sodium concentration dialysate/modeling, and high levels of sodium intake by the patient conspire to maintain high BPs in such individuals, and upward ratcheting of existing medications and/or addition of more antihypertensive agents often proves to be futile. The same lesson applies to nondialysis-dependent patients with CKD; diuretics and optimization of the "dry weight" inexplicably eschewed. Notably, the skin as a reservoir for osmotically inactive sodium and the magnitude of host lymphatic networks may play important roles in the pathogenesis of hypertension in such individuals.[8]

Thus, together we must pledge as our New Year's resolution to treat our patients' BPs more optimally and successfully. Certainly, the tools, agents, and knowledge to treat high BP are available, but only metrics count, and one of them is the proportion of patients who attain the target BP. Others would include the number of pills that a patient takes out of his/her daily allotment, that is, patient adherence; sodium restriction with attendant volume contraction and its demonstration by the amount of sodium in a 24-hour urine collection; the percentage of proteinuria reduction; and others. Overcoming one's own therapeutic inertia must be a mantra this year and in those to come. Successful treatment of hypertension rarely occurs solely because of a highly motivated patient or a highly motivated healthcare provider; it takes 2 to tango. Consequently, antihypertensive therapy may require more practice-based "soft" skills, such as greater patient engagement, than theoretical ones. This, however, does not imply mitigation of the "hard" skills: medication reconciliation, correction of suboptimal doses of drugs, deletion of inappropriate medications, and use of cost-saving strategies such as combination therapies (eg, benazepril/amlodipine), and generic drug substitution. Frequent BP evaluations and the utilization of ambulatory BP monitoring may be required. The turn-of-the century American philosophy of *Pragmatism* is succinctly summarized by the statement: "if 'it' worked, whatever 'it' was is probably true." Paraphrased, all of the methods that we have concocted to lower BP will be meaningless and "false" if we cannot effectively apply them to the hypertensive population. As a corollary to the fundamental statement of *Pragmatism*, when reality (BP targets) changes, the truth, which is never absolute, will change too. We still have plenty of work to do before that issue requires resolution, while we await informative trials regarding optimal methodologies for the treatment of hypertension in CKD, including the Aliskiren Trial in Type 2 Diabetes Using Cardio-Renal Endpoints (ALTITUDE)[9] and the Veterans Administration NEPHROpathy iN Diabetes (VA NEPHRON-D) Study.[10]

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