Strategies for BP Control in Developing Countries and Effects on Kidney Function

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CKD is a major public health threat worldwide. The prevalence of CKD among adults has been estimated to be 10%–15% globally (1–3), with evidence showing a continually increasing trend made worse by the rising rates of diabetes and hypertension, the primary causes of CKD as well as the most commonly observed comorbid conditions in this high-risk group. This trend is particularly concerning in developing countries, where heightened resource constraints and underdeveloped health care infrastructure limit access to appropriate care. It is well established that management of patients with kidney disease, particularly those related to ESRD, is associated with enormous financial cost. For example, in the United States, approximately 26 million people suffer from CKD (4), with >660,000 people requiring some form of RRT (5), incurring a cost of $30.9 billion to Medicare in 2013 (6). The exorbitant costs associated with ESRD therapy make certain life-saving treatments, such as dialysis, simply unaffordable in many developing countries, highlighting the particular importance of preventive measures in these settings.

Of the strategies aimed at controlling established modifiable renal and cardiovascular risk factors among patients with CKD, control of BP has been considered the “single most effective intervention” (7). High BP is observed in the majority of patients with CKD, in whom a log-linear relationship (8,9) between elevated BP and an increased risk of ESRD has been reported. Accordingly, observational and trial data (10–14) have sufficiently established that reducing BP delays renal progression of CKD to ESRD. BP control is, thus, a cornerstone of management to both prevent the onset and delay the progression of CKD, and current clinical guidelines (15) widely advocate BP reduction strategies, including both pharmacologic and lifestyle interventions. Given the increasing prevalence of CKD in developing countries and the excessive costs associated with CKD management, there is a strong need for efficient, cost-effective prevention strategies aimed at adequate BP control to delay or prevent CKD progression in countries with developing health care systems.

In this issue of the Clinical Journal of the American Society of Nephrology, Jafar et al. (16) assessed the effectiveness of interventions involving (1) a home-based communication strategy highlighting the importance of lifestyle changes and adherence to antihypertensive medication (referred to as home health education [HHE]) and/or (2) general practitioner (GP) education involving a single-day training session discussing standard BP management strategies on the basis of clinical guidelines (17,18) on kidney function and long-term renal and survival outcomes among patients with hypertension on the basis of an extended follow-up study of the previously completed Control of Blood Pressure and Risk Attenuation (COBRA) Trial. The COBRA Trial was a 2×2 cluster, randomized, controlled trial, which randomized 12 low- to middle-income communities in Karachi, Pakistan to HHE, GP training, both interventions, or usual care to assess their effects on BP levels among adults (age ≥40 years old) with hypertension (19). This post–trial observational study included 7 years of follow-up (2 years in trial and 5 years post-trial; eGFR measurements were recorded at baseline and the 7-year follow-up visit). The primary outcome assessed was change in eGFR from baseline to the 7-year post–trial follow-up visit across the original four treatment groups, whereas secondary outcomes included a >20% decline in eGFR from baseline to the 7-year follow-up, death caused by kidney failure, and composite outcomes involving a combination of the individual secondary outcomes. Of the original 1341 participants of the COBRA Trial, 1271 (94.8%) were included in this observational study, with relatively similar numbers of patients across the four treatment groups of the original trial. The majority of patients had relatively well preserved kidney function (89% with eGFR ≥60 ml/min per 1.73 m²) at baseline. After adjustment for certain differences in baseline characteristics across the treatment groups (literacy and comorbid conditions, including history of stroke or heart disease), mean eGFR among patients who were randomized to both interventions remained unchanged (88 versus 89.3 ml/min per 1.73 m² at baseline and the 7-year follow-up, respectively), whereas a significant decline in eGFR of ~3.6 ml/min per 1.73 m² (87.5 versus 84.9 ml/min per 1.73 m²) was observed among patients in the usual care group. Compared with usual care, the combined HHE and GP training group was associated with a lower risk of experiencing a >20% decline in baseline eGFR (adjusted risk ratio, 0.53; 95% confidence interval, 0.29 to 0.96) as well as a lower risk of the composite outcome of death from kidney failure or >20% decline in baseline eGFR (adjusted risk ratio, 0.47; 95% confidence interval, 0.29 to 0.72).
interval, 0.25 to 0.89). The combined HHE and GP training group was not associated with a lower risk in the composite outcome of all-cause death or >20% decline in baseline eGFR.

Comparable associations of benefit with similar interventions related to education and behavioral change have been reported among patients with early CKD in other developing countries (20,21). A pilot cluster, randomized, controlled trial (20) conducted in Mexico involving two primary health care units providing care to patients with type 2 diabetes and early CKD (mean eGFR = 81.2–85.7 ml/min per 1.73 m²) assessed the effects of a 6-month GP education-based intervention (including training sessions on the role of BP in CKD progression and clinical guideline recommendations for the management of CKD among others). The study showed that GPs who received the education-based intervention attained improved clinical competence compared with the control group and achieved significantly better BP control and preservation of kidney function in their patients. Similar levels of benefit have been reported in studies that have assessed education-based hypertension management strategies in broader patient groups in developing countries (22,23), many of whom are at high risk of developing CKD. For example, in the COBRA Trial (19), the study from which the study by Jafar et al. (16) derives its cohort, a reduction in BP of almost 11 mmHg at the end of the trial in the group that received the HHE and GP training intervention was reported. Importantly, subsequent cost-effectiveness analyses showed that the combined intervention of HHE and GP training was significantly more cost effective than usual care or the individual components of the combined strategy (24).

Do the results reported by Jafar et al. (16) then warrant the implementation of such interventions in public health programs of health systems in developing countries? Their results along with other early reports are promising and suggest that, among patients at high risk of developing CKD or those with early-stage CKD in low- and middle-income countries, behavioral change-based interventions are associated with significant improvements in short-term outcomes, including BP, and other quality of care indicators associated with long-term outcomes, such as antihypertensive medication adherence. However, although these results are encouraging, health services interventions with the objective of assessing the effect of CKD management strategies in developing countries are scarce overall, and studies to date have been relatively small and did not assess long-term clinical outcomes, such as ESRD and death. There are also limitations to the study by Jafar et al. (16) that should be noted. Only 14% (n = 182) of the study cohort had CKD defined as eGFR<60 ml/min per 1.73 m², and therefore, whether such strategies would be associated with similar evidence of renal benefit among patients with further progressed CKD is unknown. Although baseline eGFR was available in all 1271 patients, 7-year follow-up eGFR was missing in >50% (n = 641) of the study cohort, and their values were imputed on the basis of statistical models (also of note is that change in eGFR was on the basis of only two measurements, which were 7 years apart). In addition, the proportion of patients with missing eGFR at the 7-year visit varied, ranging from 39% to 60% across the four treatment groups, increasing the potential for attrition bias.

Despite these limitations, given that adequate BP control among high-risk patient groups, such as those with CKD, is as low as 13.2% (25) and that awareness of CKD is significantly lower in developing countries compared with in developed countries (26), it follows that simple interventions on the basis of education and communication of the importance of established prevention strategies, including BP management, may have a significant effect at the population level. This, therefore, warrants further consideration, including the assessment of the cost-effectiveness and sustainability of prevention strategies specific to CKD management in developing countries.

Disclosures
None.

References


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