ORIGINAL INVESTIGATIONS

Pathogenesis and Treatment of Kidney Disease and Hypertension

Quality of Life in the African American Study of Kidney Disease and Hypertension: Effects of Blood Pressure Management

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● ***Background:*** **The African American Study of Kidney Disease and Hypertension was a multicenter trial comparing the effects of 2 levels of blood pressure control (usual or low goal) and initial therapy with metoprolol, ramipril, or amlodipine. We examined effects of treatment-group assignment on health-related quality of life (HRQOL) measures and reported symptoms during 4 years of follow-up.** ***Methods:*** **HRQOL was assessed at baseline and annually by using the Medical Outcomes Study 36-Item Short Form (SF-36) and a symptom checklist. Using a 2-slope model, treatment effects were evaluated for change from baseline to year 1 and for average change during the first 4 years of follow-up.** ***Results:*** **A total of 1,094 participants were randomly assigned. Average age was 55 years, 61% were men, and the mean of the first glomerular filtration rate in the study was 46 mL/min/1.73 m^2 (0.76 mL/s). No significant differences in HRQOL were seen between the low- and usual-blood-pressure groups. Reported side effects also were similar between blood-pressure groups. Mean Physical Health Component (PHC) and Mental Health Component (MHC) scores had a significantly smaller decrease in the ramipril than metoprolol group in both the initial period from baseline to year 1 (PHC, 2.08 ± 0.56; MHC, 1.89 ± 0.62) and during the first 4 years of follow-up (PHC, 1.60 ± 0.44; MHC, 1.48 ± 0.48). The MHC also had a slightly smaller decrease during the first 4 years in the ramipril group than amlodipine group (1.20 ± 0.61).** ***Conclusion:*** **Aggressive blood pressure control is well tolerated in African Americans with hypertensive kidney disease, measured by using the SF-36 and reported symptoms. The clinical significance of smaller decreases in PHC and MHC scores in the ramipril compared with metoprolol group is not clear.** ***Am J Kidney Dis*** **47:956-964.**

INDEX WORDS: Health-related quality of life (HRQOL); hypertension; African Americans; chronic kidney disease (CKD).

ALTHOUGH HEALTH-RELATED quality of life (HRQOL) has been studied extensively in patients with end-stage renal disease (ESRD),[1-4] much less is known about patients with chronic kidney disease (CKD). Better understanding of HRQOL for this population is important because it is dramatically increasing in size. It is estimated that 5.6 million Americans older than 17 years have elevated serum creatinine levels (≥1.6 mg/dL [≥141 μmol/L] in men and ≥1.4 mg/dL [≥124 μmol/L] in women).[5] Furthermore, the impact of antihypertensive therapy on HRQOL is particularly important because blood pressure control is the cornerstone of therapy for patients with CKD.[6]

The African American Study of Kidney Disease and Hypertension (AASK) was a multi-

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center randomized controlled clinical trial using a 2 × 3 factorial design to evaluate effects of 2 levels of blood pressure control and 3 antihypertensive drug regimens on progression of CKD caused by hypertension (hypertensive nephrosclerosis).[7] Participants were randomly assigned to 1 of 2 mean arterial blood pressure goals, 102 to 107 mm Hg (usual-blood-pressure group) or 92 mm Hg or less (low-blood-pressure group) and to initial therapy with either a β-blocker (metoprolol), angiotensin-converting enzyme inhibitor (ramipril), or dihydropyridine calcium channel blocker (amlodipine).

Compared with metoprolol or amlodipine, the ramipril-based drug regimen significantly decreased the rate of a composite end point (which included confirmed decrease in glomerular filtration rate [GFR] by 50% or by 25 mL/min/1.73 m^2 [0.42 mL/s] from the mean of 2 baseline measurements, kidney failure, or death), but did not slow the decrease in renal function.[7] The low blood pressure goal did not decrease the rate of the composite end point or the rate of decrease in renal function compared with the usual blood pressure goal.

This report compares HRQOL measured by using the Medical Outcomes Study 36-Item Short Form (SF-36)[8] among 2 blood-pressure-treatment groups and 3 antihypertensive drug regimens during the course of follow-up. This is the first analysis examining longitudinal changes in HRQOL measures in a large population of patients with mild to moderate CKD.

METHODS

Study Design

The design, recruitment experience, and major findings of the AASK Study were described previously.[7,9,10] Administration of the 3 classes of study drugs (metoprolol, ramipril, or amlodipine) was double blind. If blood pressure was not controlled, the following open-label medications were added sequentially: furosemide, doxazosin, clonidine, and hydralazine or minoxidil. Achieved mean blood pressures were 141/85 ± 12/7 mm Hg in the usual-blood-pressure group and 128/78 ± 12/8 mm Hg in the low-blood-pressure group. Number of antihypertensive agents used in the usual-goal group was 2.42 ± 1.14 compared with 3.07 ± 1.11 in the low-goal group.[7]

Progression of renal disease was measured as rate of decrease in GFR determined by using renal clearance of iodine 125 iothalamate. Subjects were eligible for the trial if they self-reported as being African American, were between 18 and 70 years of age, and had a diastolic blood pressure of 95 mm Hg or greater and GFR of 20 to 65 mL/min/1.73 m^2 (0.33 to 1.08 mL/s). Potential subjects were excluded if they had a history of malignant or accelerated hypertension, known secondary causes of hypertension, known history of diabetes mellitus, ratio of urinary protein to creatinine exceeding 2.5 in a 24-hour urine sample, and clinical or renal biopsy evidence of renal disease other than hypertensive nephrosclerosis. Institutional review boards at all participating institutions approved the protocol, and written informed consent was obtained from all participants.

HRQOL Measures

The AASK Study adopted a global conceptualization of HRQOL, including physical, mental, and social well-being, in addition to reported symptoms. HRQOL data were obtained for AASK participants at baseline and annual visits by administration of the SF-36 and a symptoms questionnaire.[8] Median follow-up was 4.0 years.

Physical and mental composite scores from the SF-36 were used as summary measures for the 8 SF-36 subscales. Initially, the analysis plan called for use of the Ware Physical (PCS) and Mental Composite Scores (MCS). However, initial analyses showed that results for the Ware MHC score provided an incongruent representation of treatment effects on the 8 SF-36 subscales, apparently resulting from the constraint of the Ware composites to be orthogonal to one another in a reference population.[11] Similar results were reported previously.[12] Hence, analyses presented in this report are based on the Rand Physical Health Composite (PHC) and Mental Health Composite (MHC) scores.[13]

A symptom checklist was administered to participants at follow-up study visits. This list was based on known side effects of the primary- and secondary-level drugs used in the study and also was derived from a review of the Modification of Diet in Renal Disease Study database for symptoms commonly reported in that study.[14]

Clinical and Demographic Variables

Methods used for blood pressure measurement and determination of GFR were described elsewhere.[7,9] Coexisting medical conditions were self-reported by study participants in response to a questionnaire listing major illnesses. Demographic variables were obtained by self-report.

Data Analysis

HRQOL measures were examined by using a 2-slope mixed-effects model that incorporated HRQOL measurements through the 5-year follow-up visit. The 2-slope model incorporated 1 slope to represent mean change in HRQOL measure from baseline to 1 year and a second slope from 1 year through the remainder of follow-up. To account for attrition caused by renal failure or death, a mixture informative censoring[15-17] approach was used in which mean slopes in HRQOL measures first were estimated conditionally given censoring variables related to patient duration of follow-up and reason for dropout. Results of the conditional analysis were averaged over distributions of censoring variables within each treatment group.

Estimated mean slopes under the 2-slope model were used to obtain treatment effects on initial change (initial Δ) in HRQOL