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Increased Sodium Intake Correlates With Greater Use of Antihypertensive Agents by Subjects With Chronic Kidney Disease

Neil Boudville, Sharon Ward, Mark Benaroia, and Andrew A. House

Background: Hypertension is a common disease in patients with chronic kidney disease (CKD) and predisposes to heart disease, stroke, and progression of renal failure. In the general population, sodium restriction has been shown to improve blood pressure (BP) control, but this is not widely recommended in CKD patients. The aim of this study was to assess the sodium balance in a CKD clinic and its effect on BP management.

Methods: We retrospectively reviewed charts from June 1998 through to June 2003 and included all patients with an estimated glomerular filtration rate (GFR) of <30 mL/min who completed a 24-h urine collection for sodium. Patients were divided into tertiles based upon their 24-h sodium excretion and analyzed by ANOVA.

Results: We included 141 CKD patients who had a mean (± SE) sodium excretion of 145.7 ± 4.7 mmol/day. There were a significantly greater number of antihypertensive agents used with increasing sodium excretion (2.00 ± 0.16, 2.61 ± 0.20, and 2.77 ± 0.19 medications, respectively for each tertile; $P = .01$). This difference was even more prominent when only those patients with a GFR ≤15 mL/min ($n = 77$) were examined (1.69 ± 0.19, 2.52 ± 0.27, and 3.08 ± 0.26 medications, respectively; $P = .001$). Control of BP was equivalent in all groups. Multivariable analysis revealed sodium excretion ($P = .00005$) and age ($P = .007$) to be significantly associated with use of antihypertensive medication.

Conclusions: We have demonstrated that increased sodium intake is associated with an increased number of antihypertensive medications to achieve comparable BP control in a population with CKD. Am J Hypertens 2004;18: 1300–1305 © 2004 American Journal of Hypertension, Ltd.

Key Words: Antihypertensive agents, chronic kidney failure, hypertension, sodium balance, dietary sodium.

High blood pressure (BP) occurs with increasing frequency as renal function deteriorates, with up to 85% to 100% of patients having hypertension by the time they reach end-stage renal failure (ESRF).[1,2] Improved control of high BP may lead to a reduction in the rate of progression of renal failure in persons with chronic kidney disease (CKD).[3–5] High sodium intake has been shown to exacerbate hypertension and to reduce the efficacy of antihypertensive medications in the general population.[6,7] In addition, irrespective of the effect of sodium on BP, there is mounting evidence that high sodium intake may have a more direct effect on the progression of renal failure.[8,9] However, many nephrologists do not prescribe specific sodium restrictions to patients with CKD.[1,10] Even in ESRF, the practice of sodium restriction is not widely accepted.[11,12] The American Dietetic Association guidelines allow patients with CKD and ESRF to consume up to 175 mmol/day of sodium.[13]

The Modification of Diet in Renal Disease (MDRD) Study reported that "salt intake was not a determinant of BP status"[1] and Fine et al concluded that ". . . 200mEq of sodium per day, i.e., a normal sodium intake, is easily tolerated in stable . . . dialysis patients, and the recommended sodium intake . . . is too restrictive."[12] Sodium restriction, although it may increase aldosterone and improve potassium excretion,[14] may also aggravate volume contraction and worsen renal function. Hence, the question of whether sodium restriction is a safe and efficacious adjunct to the management of hypertension in CKD patients can only be answered through prospective clinical

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From the Department of Medicine (NB, MB, AAH), University of Western Ontario, London, Ontario, Canada; Division of Nephrology (NB, SW, MB, AAH), London Health Sciences Centre, London, Ontario, Canada; School of Medicine and Pharmacology (NB), University of Western Australia, Perth, Western Australia, Australia; and Lawson Health Research Institute (AAH), London, Ontario, Canada.

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Address correspondence and reprint requests to Dr. Neil Boudville, University of Western Australia, School of Medicine and Pharmacology, Hackett Drive, Nedlands WA, Australia 6009; e-mail: nboudville@aol.com

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Table 1. Demographic data of study subjects

	GFR <30 mL/min	GFR <15 mL/min
N	141	77
Age (y)	65.0 ± 1.2	66.9 ± 1.8
Male:Female	93:48	50:27
Etiology of renal failure		
Diabetes mellitus	44 (31.2%)	23 (29.9%)
Hypertension	45 (31.9%)	29 (37.7%)
Glomerulonephritis	14 (9.9%)	8 (10.4%)
Polycystic kidney disease	6 (4.3%)	4 (5.2%)
Unknown	19 (13.5%)	5 (6.5%)
Reflux	4 (2.8%)	2 (2.6%)
Other	9 (6.4%)	6 (7.8%)
Glomerular filtration rate (mL/min)	16.4 ± 0.67	10.6 ± 0.32
Normalized protein catabolic rate (g/kg/day)	0.85 ± 0.02	0.77 ± 0.02
24-hour urine sodium (mmol)	145.7 ± 4.7	124.7 ± 5.4
Systolic blood pressure (mm Hg)	141.7 ± 1.1	142.8 ± 2.7
Diastolic blood pressure (mm Hg)	75.1 ± 1.0	74.4 ± 1.4
Number of patients using diuretics	88 (69%)	51 (74%)

GFR = glomerular filtration rate.
Values are mean ± standard error

trials. In the absence of such prospective trials, and with a paucity of observational evidence from studies in CKD patients, we designed a study to investigate the effect of sodium balance on the BP control of patients who did not yet require dialysis or transplantation and who were attending a multidisciplinary CKD clinic.

Subjects and Methods

Study Population

We reviewed the records of patients attending the CKD clinic at University Campus of the London Health Sciences Center (London, ON, Canada). The CKD clinic is a quaternary referral clinic, with all patients referred by nephrologists working within University Campus for multidisciplinary care, intensive education, and preparation for dialysis or transplantation. Patients attending this clinic typically have CKD stage 4 or 5 according to the criteria of the National Kidney Foundation's Dialysis Outcomes Quality Initiative (NKF-DOQI), corresponding to an estimated glomerular filtration rate (GFR) of <30 mL/min.

Between June 1998 and June 2003, patients attending the CKD clinic regularly collected 24-h urine specimens with blood testing as part of a prospective cohort study examining assessments of renal function and nutritional parameters in CKD patients. Potentially eligible subjects for this study were all patients with 24-h urine samples that included urinary sodium excretion and who were not on dialysis. We assumed a steady state with respect to sodium balance; thus, the 24-h urine sodium excretion was considered a marker of daily sodium intake. We then limited the analysis to patients with an estimated GFR of <30 mL/min, corresponding to CKD stage 4 (15 to 29 mL/min) and stage 5 (≤15 mL/min or on dialysis).[15] All patients were >18 years of age, and only the first collection was included for each patient. This study was approved by the University of Western Ontario Research Ethics Board.

Outcome Measures

At each clinic visit, patients had their BP checked in the sitting position by a trained registered nurse or medical doctor using a mercury sphygmomanometer. In addition, a list of all medications currently taken was recorded. Patients were given requisitions for blood tests and a 24-h urine collection to be performed immediately after the clinic and analyzed at the patient's local laboratory. Glomerular filtration rate was estimated by the average of the creatinine clearance and urea clearance, a method with acceptable precision in subjects with significant CKD.[16]

Because of the retrospective nature of this study, BP measurements were not performed under a rigorous study protocol but BP management in the CKD clinic did follow the contemporary guidelines of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC-6).[17] The choice and number of antihypertensive agents used was left to the discretion of the nephrologist, but a systolic BP (SBP) of <130 mm Hg and a diastolic BP (DBP) of <85 mm Hg was targeted for all patients. Therefore, the number of antihypertensive medications, rather than the actual BP measurements, was preferentially used as a marker of BP control.

Statistical Analysis

Values are expressed as mean ± SE unless otherwise specified. Patients were divided into tertiles based on their 24-h urine sodium excretion. Analysis of variance was then used to compare between-group differences. Pear-