Dietary Sodium Reduction Reduces Albuminuria: A Cluster Randomized Trial

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Objectives: The objective of the study was to assess the impact of sustained dietary salt reduction on albuminuria in nearly 2000 community-dwelling adults.

Design and Methods: The present study is a prespecified secondary analysis of the China Rural Health Initiative Salt Reduction Study cluster randomized trial undertaken in 120 villages in rural China. Villages were randomized to a sodium reduction program of education and access to reduced-sodium salt substitute or control. Urinary albumin-to-creatinine ratio (uACR) and albuminuria (uACR >22.1 or 31.0 mg/g for men and women, respectively) were assessed at 18 months in a stratified random sample of predominantly older individuals living in participating rural villages.

Results: A total of 2,566 participants from 119 villages provided 1,903 eligible urine samples. The sodium reduction program reduced sodium intake by an equivalent of 0.82g of salt/day (0.06-1.68 g) (322 [24-661] mg sodium/day). The mean uACR was 8.85 (8.05-9.82) mg/g (1.00 [0.91-1.11] mg/mmol) in intervention participants compared with 10.53 (9.73-11.33) mg/g (1.19 [1.10-1.28] mg/mmol) in control participants (p=0.008). The corresponding odds ratio for albuminuria was 0.67 (0.46-0.99).

Conclusions: Dietary sodium reduction was associated with significantly lower uACR and less albuminuria after 18 months. Whether CKD progression can be slowed by dietary sodium reduction should be a global research priority.

This article has an online CPE activity available at www.kidney.org/professionals/CRN/ceuMain.cfm

Introduction

CHRONIC KIDNEY DISEASE (CKD) and its sequelae are a leading cause of disease burden in both developing and developed countries, compromising the quality and quantity of life for millions and encumbering health systems and national budgets. Although substantial advances in the treatment and prevention of CKD have been made with pharmaceutical interventions, there remains
an unmet need for large scale, affordable and sustainable, nondrug approaches to management of this disease.

Dietary sodium intake is an established cause of elevated blood pressure, and this observation provides a strong rationale for evaluating the effects of sodium-reduction strategies on measures of kidney function. Several studies have suggested beneficial effects for sodium reduction on albuminuria, although these have been conducted in small, selected populations and are of short duration.1-5

The China Rural Health Initiative Salt Reduction Study (CRHI-SRS) was a large-scale cluster randomized trial performed in 5 provinces in Northern China which was designed to determine the efficacy of a multifaceted salt-reduction strategy including a community-based health education program and the availability of reduced-sodium added-potassium salt substitute in village shops, on dietary sodium intake. In rural China, the majority of dietary sodium intake comes from salt added in cooking and condiments at home.6 The study was conducted over an 18-month period and involved 120 rural villages.7 The CRHI-SRS showed clear effects of the intervention on its primary outcome of dietary salt intake which was assessed through the urinary sodium excretion.7

In this prespecified renal substudy of the CRHI-SRS, we assessed the effects of the community-based salt-reduction strategy on albuminuria in individual participants.

Methods

The CRHI-SRS is a large-scale cluster randomized study designed with the primary objective of determining the effects of a practical and sustainable salt-reduction strategy on dietary sodium intake as determined from measures of 24-hour urinary sodium excretion. The study was performed between May 2011 and November 2012 and was registered with clinicaltrial.gov (NCT01259700).

Institutional Review Board Approval and Consent

Approval for the study was provided by the Ethics Committee of the Peking University Health Science Center in Beijing, China, and the Duke University Health System in Durham, USA. Consent was obtained at both the cluster level and the individual level. Cluster-level consent was obtained through a consultative process involving provincial, country, and township levels of government local community leaders. Individuals provided written consent after reviewing a participant information sheet and before participating in the outcome survey. The trial design has been described previously in detail.5

Villages and Participants

The CRHI-SRS was conducted in villages drawn from five Northern Chinese provinces (Hebei, Liaoning, Ningxia, Shanxi, and Shaanxi) where the incidence of high blood pressure and vascular disease is high. Two counties were selected from each province on the basis of interest in participating, proximity to local research infrastructures, and being broadly representative of the socioeconomic development of counties in that province. Within each county, 12 villages were selected on the basis of available support from local authorities and geographic distance from other participating villages.

Randomization

Villages were randomized in a 1:1 ratio to either the salt-reduction program or continued usual practices. The random number sequence was computer generated centrally and stratified by county. Intervention villages were then further randomized in the same way to price parity for the reduced-sodium, added-potassium salt substitute, or not. All villages agreed to participate before random assignment.

Intervention and Control

Intervention villages all underwent a community-based salt-reduction program, which was a multifaceted strategy comprising of general community health education and a food supply measure.4 The health education component included broad-based community education and specific interactive sessions targeted toward people at high risk of vascular diseases. The food supply measure involved making available in the community a reduced-sodium, added-potassium salt substitute for sale at village shops. Half the intervention villages, selected at random, received a price subsidy for the salt substitute so that it was available in store at the same price as conventional salt (price parity). The salt substitute replaces one-fifth to one-third of the sodium chloride in normal salt with potassium chloride (local manufacturing specifications: NaCl: 70.00% ± 10.00%, KCl: 20.00%-35.00%).

Outcome Assessment

Outcomes were assessed at the end of the intervention period among an age- and sex-stratified random sample of 20 or more consenting adults drawn from each village.5 Participants filled a short interviewer-administered questionnaire and had their height and weight measured. Participants were asked about the number of years they had spent in formal education. Blood pressure was recorded with the participant seated after 5 minutes of rest in duplicate measures taken at least 2 minutes apart using an automated electronic sphygmomanometer (Omron Intellisense HEM 7301 IT). Participants were given materials and instructions for the collection of a 24-hour urine sample. After volume measurement, an aliquot of urine was extracted and analyzed at a central laboratory for sodium, potassium, creatinine, and albumin. Urine samples were excluded if participants reported missing the first morning void or missing more than one void, the collection period was less than 22 hours or longer than 26 hours, more than 10% of the total volume was believed to have been split, or the sample was contaminated with feces. Collections
that had a measured volume of less than 500 mL or greater than 6000 mL or an outlying 24-hour creatinine excretion (less than 4 mmol or greater than 25 mmol in women and less than 6 mmol or greater than 30 mmol in men) were likewise excluded. Laboratory personnel performing the evaluation of sodium, potassium, creatinine, and albumin were blinded to the randomized allocation.

Outcomes

The main outcome for the renal analyses of the CRHI-SRS study was urinary albumin-to-creatinine ratio (uACR). Secondary outcomes were any albuminuria, microalbuminuria (uACR of 22.1 – 220.35 mg/g for men and 31.0 – 308.85 mg/g for women), and macroalbuminuria (uACR of ≥220.35 mg/g for men and ≥309.73 mg/g for women). Other relevant outcomes are the mean values of 24-hour urinary Na (mmol/day), 24-hour urinary K (mmol/day), urinary Na/K ratio, systolic blood pressure (SBP), diastolic blood pressure (DBP), height (cm), weight (kg), and body mass index (BMI).

Statistical Power

The CRHI-SRS was designed to have 90% power \((P = .05)\) to detect a difference in the mean 24-hour excretion of sodium of 11 mmol/day (0.65 g/day salt or 256 mg/day sodium) or more between participants in the 60 intervention villages and in the 60 control villages. This estimate assumed that the outcome evaluation would include data on 24-hour urinary Na for 2400 individuals drawn in approximately equal numbers from the 120 clusters. For the renal substudy analyses, the 1,903 eligible 24-hour urine samples obtained from the 2,566 participants selected for inclusion in the follow-up surveys were powered to detect a difference in the log-transformed uACR of 0.11 between groups, which is equivalent to a 10% reduction in mean uACR in intervention group compared with that in the control group, in 120 villages with 1900 participants. This is based on 80% power (type-I error rate = 5%), a standard deviation of 0.90, and an interclass correlation of 0.05 for the log-transformed uACR.

Statistical Analyses

The distribution of uACR is skewed and so between-group comparisons were made for the geometric mean values after natural log-transformation. Analyses were by intention to treat with no imputation of missing data. Differences in the mean values of uACR, urinary sodium excretion, urinary sodium potassium, urinary sodium-to-potassium ratio, blood pressure levels, weight, height, and BMI and differences in the frequencies of antihypertensive agent use were calculated by means of a linear regression model (for mean value) and logistic regression model (for frequency) with a generalized estimating equation to account for interclass correlation of clusters of villages, using the procedure “GENMOD” in SAS, as appropriate. The differences in the frequencies of albuminuria were tested using a logistic regression model with a generalized estimating equation by means of a cumulative logistic model with a multinomial distribution to account for clustering. Sensitivity testing was performed by recalculating the effects on albuminuria using all 2,079 urine specimens obtained (not just the 1,903 complete 24-hour specimens) and by including adjustment for participant characteristics. Statistical analyses were performed using SAS (version 9.4, SAS Institute Inc., Cary, NC). A p-value of less than 0.05 was considered significant.

Results

Contribution Villages and Participant Recruitment

Sixty villages were randomized to the salt-reduction intervention and 60 to control (Appendix Figure 1). Among the 60 intervention villages, 30 were further randomized to receive price-subsidized salt substitute with the remaining 30 villages provided with access to salt substitute but without price subsidy. Follow-up was achieved in 60 intervention and 59 control villages (one control village was urbanized, and the residents were relocated). From these 119 villages, there were 2,566 individuals selected for the follow-up survey. A total of 2,079 urine samples were obtained, which yielded 1,903 eligible collections that passed the quality checks imposed to ensure that primary analyses were performed on complete and uncontaminated 24-hour urine collections (Appendix Figure 1).

Participant Characteristics

Participants in the follow-up survey were on average 55 years old (Table 1), and around half were women. Nearly one-third of the participants were current smokers, and a little over half had received less than 6 years of formal education. These demographic characteristics were similar for individuals sampled from villages randomized to salt reduction and control and also for the subset randomized to salt reduction with a price subsidy for salt substitute and the subset randomized to salt reduction without a price subsidy for salt substitute (Table 1).

Impact of Dietary Sodium Reduction on Mean uACR and Albuminuria

Dietary sodium intake, as reflected by 24-hour urine samples, was lower by a mean 14 mmol/day (95% confidence interval [CI]: −27 to −1; 322 [−1.6 to −0.7] mg sodium) in participants from the intervention group than that in participants from control villages. Dietary potassium levels were higher by a mean 7 mmol/day (95% CI: 4 to 10) (Table 2).

Mean uACR was lower in the intervention group villages (8.85 [8.05-9.82] mg/g) than that in control group villages (10.53 [9.73-11.33] mg/g) corresponding to a 15% difference in log-transformed uACR (95% CI: 4.3 to 25.2; \(P = .008\)) (Fig. 1). The risk of any albuminuria was also significantly reduced with an odds ratio of 0.67.
Impact of Dietary Sodium Reduction on Blood Pressure Parameters and BMI

Participants randomized to the salt-reduction program and the control program had similar SBPs and DBPs (Table 2). The proportion taking blood pressure–lowering agents was 24.0% (95% CI: 21.0 to 27.3) of control participants and 20.3% (95% CI: 17.9 to 22.9) of salt-reduction–program participants giving an odds ratio of 0.80 for antihypertensive utilization in the salt-reduction program (95% CI: 0.64 to 1.02, P = .07) (Table 3). Weight, height, and BMI were similar (Table 2).

Impact of the Secondary Randomization to Salt Substitute-Price Subsidy Within Intervention Villages

Among participants randomized to the salt-reduction program, those further randomized to salt substitute–price parity recorded numerically, but not statistically significant, lower urinary sodium and higher urinary potassium than those not randomized to salt substitute–price parity (Table 2).

Although participants randomized to the salt-reduction program overall had a lower uACR, than control participants, there was no clear difference between those further randomized to salt substitute–price parity and those who were not (Fig. 1). However, among participants randomized to the salt-reduction program, those further randomized to salt substitute–price parity had significantly lower odds of meeting the threshold for “albuminuria” than controls (0.59, 0.37 to 0.96), which was not the case for those randomized to no price parity (0.77, 0.44 to 1.33) (Table 3).

Height, weight, BMI, SBP, and DBP were similar among all groups (Table 2). BMI was numerically but nonstatistically lower among participants randomized to the salt-reduction program with salt substitute–price parity (P = .06) which was driven numerically by lower weight and similar height (Table 2). Within the salt-reduction program, the proportion taking blood pressure–lowering agents was 21.1% (95% CI: 18.2 to 24.4) among those randomized to no salt substitute–price parity and 19.2% (95% CI: 15.7 to 23.3) among those randomized to price parity giving an odds ratio for antihypertensive utilization of 0.86 (95% CI: 0.66 to 1.11, P = .24) and 0.76 (0.57 to 1.03, P = .08), respectively (Table 3).

Sensitivity Analyses

The findings for urinary albumin measures were essentially unchanged by adjustment for demographic characteristics or blood pressure and were likewise the same when the analysis was repeated using all 2,079 collected urine samples regardless of whether they met the urine sample quality criteria.

Discussion

The CRHI-SRS salt-reduction program produced a difference in 24-hour urinary sodium excretion between intervention and control villages which was equivalent to about three-quarters of a gram of salt consumed per person per day over a sustained period of 18 months. Associated with this were clear differences in renal albumin excretion, with a 15% lower level of urinary albumin to creatinine ratio (95% CI: 0.46 to 0.99) (Fig. 2; Table 3) in intervention villages compared with that in control villages. Similar, but nonsignificant, effects were observed for macroalbuminuria (0.48; 95% CI: 0.18 to 1.32) and microalbuminuria (0.70; 95% CI: 0.47 to 1.06) (Fig. 2).
### Impact of the Salt-Reduction Program on End-of-Study Differences (95% CIs) in Urinary Parameters, Blood Pressure Levels, and Albuminuria of Participants, Overall and According to the Presence of Price Parity for Salt Substitute

#### Control and All Sodium-Reduction Program Villages

<table>
<thead>
<tr>
<th>Participant Biological Characteristics</th>
<th>Control (59 Villages, 975 Participants)</th>
<th>Sodium-Reduction Program (60 Villages, 975 Participants)</th>
<th>Absolute Difference</th>
<th>Percentage Difference</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urinary Na (mmol/day)</td>
<td>250 (241 to 259)</td>
<td>236 (227 to 245)</td>
<td>14 (227 to 259)</td>
<td>6 (11 to 0.4)</td>
<td>.03</td>
</tr>
<tr>
<td>Urinary K (mmol/day)</td>
<td>45 (44 to 47)</td>
<td>53 (50 to 55)</td>
<td>7 (4 to 10)</td>
<td>16 (9 to 22)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Urinary Na/K ratio</td>
<td>6.1 (5.8 to 6.3)</td>
<td>5.2 (4.9 to 5.5)</td>
<td>-0.9 (1.2 to 0.5)</td>
<td>-15 (20 to -9)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>BMI</td>
<td>24.8 (24.5 to 25.1)</td>
<td>24.5 (24.2 to 24.7)</td>
<td>-0.3 (0.7 to 0.1)</td>
<td>-1.2 (2.8 to 0.4)</td>
<td>.2</td>
</tr>
<tr>
<td>Height (inches)</td>
<td>63.3 (63.1 to 63.5)</td>
<td>63.3 (63.1 to 63.6)</td>
<td>0.04 (0.3 to 0.4)</td>
<td>0.1 (0.5 to 0.6)</td>
<td>.8</td>
</tr>
<tr>
<td>Weight (lb)</td>
<td>141.5 (138.6 to 143.7)</td>
<td>140.0 (138.2 to 142.0)</td>
<td>-1.5 (4.2 to 1.3)</td>
<td>-1.1 (3.0 to 0.9)</td>
<td>.3</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>141 (140 to 143)</td>
<td>140 (139 to 142)</td>
<td>-1.0 (3.4 to 1.4)</td>
<td>-0.7 (2.4 to 1.0)</td>
<td>.4</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>86 (85 to 87)</td>
<td>86 (85 to 87)</td>
<td>0.04 (2.3 to 0.9)</td>
<td>0.08 (2.7 to 1.0)</td>
<td>.4</td>
</tr>
</tbody>
</table>

### Control Villages and Intervention Program Villages With and Without Price Parity for Salt Substitute

<table>
<thead>
<tr>
<th>Participant Biological Characteristics</th>
<th>Control Villages and Intervention Program Villages With and Without Price Parity for Salt Substitute</th>
<th>Sodium-Reduction Program Villages With Price Parity</th>
<th>Sodium-Reduction Program Villages Without Price Parity</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urinary Na (mmol/day)</td>
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<td>236 (227 to 245)</td>
<td>14 (227 to 259)</td>
<td>6 (11 to 0.4)</td>
</tr>
<tr>
<td>Urinary K (mmol/day)</td>
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<td>53 (50 to 55)</td>
<td>7 (4 to 10)</td>
<td>16 (9 to 22)</td>
</tr>
<tr>
<td>Urinary Na/K ratio</td>
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<td>5.2 (4.9 to 5.5)</td>
<td>-0.9 (1.2 to 0.5)</td>
<td>-15 (20 to -9)</td>
</tr>
<tr>
<td>BMI</td>
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<td>24.5 (24.2 to 24.7)</td>
<td>-0.3 (0.7 to 0.1)</td>
<td>-1.2 (2.8 to 0.4)</td>
</tr>
<tr>
<td>Height (inches)</td>
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</tr>
<tr>
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</tr>
<tr>
<td>DBP (mmHg)</td>
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<td>0.04 (2.3 to 0.9)</td>
<td>0.08 (2.7 to 1.0)</td>
</tr>
</tbody>
</table>

BMI, body mass index; CI, confidence interval; DBP, diastolic blood pressure; SBP, systolic blood pressure; uACR, urinary albumin-to-creatinine ratio. Data are presented as the mean value (95% confidence interval) and percentage (95% confidence interval) as appropriate. All confidence intervals account for the effects of clustering. To convert mmol sodium to mg sodium, multiply by 23.

*Difference is presented as percentage change (95% confidence interval) for the log-transformed value of uACR and as the absolute difference (95% confidence interval) for all other variables.

†Absolute difference between the groups presented as a percentage of the mean value of the control group.

‡Price parity meant that salt substitute was accessible at the same price as conventional salt. The absence of price parity meant that salt substitute was available at a higher price than conventional salt. Salt substitute was not available in control villages.

§P-value for the comparison with participants from control villages.
Multipronged intervention

Sodium plays a complex role in intrarenal physiology, and a one-third reduction in rates of any microalbuminuria or macroalbuminuria. Although the achieved blood pressure was not significantly affected, there was lower usage of antihypertensive agents among those randomized to the salt-reduction program and salt substitute–price parity. In this medium- to long-term randomized study testing the feasibility of salt-reduction programs, a significant drop in the dietary sodium intake was achieved in association with a benefit for salt reduction and RAAS blockade. Three short-term cross-over studies of differing dietary salt intake have jointly examined the impact of salt reduction and RAAS blockade which appears independent of its role in systemic blood pressure. High-salt diets exacerbate the disease in rodent models of renal injury, with hyperfiltration which can be attenuated by a low-salt diet. In the nephropathy models of early diabetes and renal injury associated with salt-sensitive hypertension, hyperfiltration states stimulating Sodium glucose cotransporter 2 (SGLT2) activity are thought to induce changes in tubuloglomerular feedback and connecting tubuloglomerular feedback. In these models, albuminuria and hyperfiltration precede the loss of glomerular function. High sodium intakes are associated with a correlation between increasing glomerular filtration rate and increasing BMI. Although the intrarenal impact of high-sodium states is the subject of ongoing research, it is possible to postulate both blood pressure–dependent and blood pressure–independent effects of salt reduction on renal pathology.

Our results may also be due in part to benefits on albuminuria consequent upon the increased potassium provided by the salt substitute. Urinary potassium excretion was about 7 mmol/day higher in intervention villages than in control villages, which is a substantial difference. Salt substitutes, when used to replace a substantial proportion of dietary salt intake, are known to produce significant reductions in blood pressure, although potassium supplementation alone has only moderate effects. Salt substitution might also provide renoprotection through direct intrarenal effects of potassium on the kidney tubule, with a prior single small study of potassium chloride supplementation reporting a significant reduction in albuminuria.

Reductions in albuminuria of the magnitude reported, while lesser than those typically achieved with pharmacological agents that blockade the renin angiotensin aldosterone system (RAAS), might nonetheless be anticipated to drive important reductions in clinical kidney endpoints. In the Action in Diabetes and Vascular disease: preterAx and diamicron-MR Controlled Evaluation (ADVANCE) trial, for example, angiotensin-converting enzyme inhibitor–based therapy reduced the risk of new-onset microalbuminuria by 21% and resulted in a reduction of new or worsening nephropathy (doubling serum creatinine requirement for renal replacement therapy, renal death, or new macroalbuminuria) of 18%. In the Reduction of Endpoints in NIDDM with the Angiotensin II Antagonist Losartan (RENAAL) trial, angiotensin receptor blockade that reduced albuminuria by 35% led to a reduction in end-stage kidney disease of 28%. Finally, cohort analyses of the ADVANCE trial demonstrated that increases in albumin-to-creatinine ratio, even within the “normal” reference range, are associated with increased risk for clinical renal and cardiovascular events.

Furthermore, the benefit for salt reduction appears to be synergistic with that of RAAS blockade.
reporting effects on albuminuria that were additional to those gained with blockade of the renin angiotensin system.\(^1,2,5\) In this same vein, a post hoc subgroup analysis of some 1200 patients with diabetic kidney disease included in the RENAAL and Irbesartan Diabetic Nephropathy Trial (IDNT) studies showed that the renal benefits derived from RAAS blockade were present at all levels of baseline sodium intake.\(^3,5\)

Although the effect in the CRHI-SRS is highly significant, the magnitude of the reduction in uACR is less than 20% to 50% observed in smaller randomized cross-over trials performed in a range of patient populations with diabetes and clinical manifestations of CKD.\(^1,5\) This may well be because the reduction in salt intake we achieved in the long-term CRHI-SRS project was substantially less than the salt reduction of around 5 g/day that was achieved in some of these studies. The lesser efficacy seen in our study may be due to one of two factors. First, our study was conducted over a sustained period of 18 months compared with these cross-over studies that were of much shorter duration of 2 to 6 weeks. Second, our intervention was education-based, with salt substitute accessible at the same or higher price than regular salt in the intervention villages. By contrast, access to a comprehensive dietary intervention was provided to participants of the smaller studies.

The CRHI-SRS benefits from its large size and randomized design, which provided good power to detect plausible effects on urinary markers of renal function. In the real-world setting in which the CRHI-SRS was carried out, the pragmatic nature of the intervention and the limited uptake of the interventions meant that the contrast in exposure to sodium between groups was only small. Although the findings give a realistic interpretation of what might be achieved in a community setting, it is likely that more intensive interventions, perhaps in clinical settings, would achieve much greater effects than those observed in this study. The study is substantially longer than previous randomized trials studying the impact of dietary sodium reduction on renal measures. However, at 18 months duration and without baseline measures, the study is still too short to assess the impact on CKD progression. The centralized gold standard measurement methods used for urinary albumin and the use of 24-hour urine collections to estimate the consumption of sodium and potassium were other important strengths of the study. The trial was, however, an open rather

Table 3. Impact of the Salt-Reduction Program on the Likelihood of Having Albuminuria or Requirement for Antihypertensive Agents Overall and According to the Presence of a Price Parity for Salt Substitute

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>N of events/ participants</th>
<th>Favors sodium reduction</th>
<th>Favors control</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium reduction</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>(59 Villages, 928</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Participants)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All Program</td>
<td>(60 Villages, 975</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Participants)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No Price Parity</td>
<td>(30 Villages, 447</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Participants)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Price Parity</td>
<td>(30 Villages, 528</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Participants)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any albuminuria*</td>
<td>69/ 975</td>
<td>94/ 928</td>
<td></td>
<td>0.67 (0.46 to 0.99)</td>
</tr>
<tr>
<td>Microalbuminuria†</td>
<td>64/ 969</td>
<td>84/ 916</td>
<td></td>
<td>0.70 (0.47 to 1.06)</td>
</tr>
<tr>
<td>Macroalbuminuria‡</td>
<td>5/ 975</td>
<td>10/ 928</td>
<td></td>
<td>0.48 (0.18 to 1.32)</td>
</tr>
</tbody>
</table>

*Price parity meant that salt substitute was accessible at the same price as conventional salt. The absence of price parity meant that salt substitute was available at a higher price than conventional salt. Salt substitute was not available in control villages.

†P value for the comparison with participants from control villages.

‡Albuminuria defined as urinary albumin-to-creatinine ratio of ≥22.1 mg/g for men and ≥31.0 mg/g for women.
Practical Applicability

To avoid bias in outcome ascertainment, considerable efforts were made to ensure that the population surveys were performed identically in intervention and control villages. The analyses of urinary albumin, creatinine, and electrolytes were performed by technicians masked to the randomized allocation of participants. The lack of baseline measures limits the sophistication of the analyses possible such as the ability to adjust for baseline albuminuria, but the large size of the study in conjunction with the randomization process should have ensured balance in the main prognostic variables across groups.

Summary

The importance of albuminuria as an independent predictor of clinical renal events, cardiovascular disease, hospitalizations, and mortality is well understood. Reductions in albuminuria correlate well with benefits for renal and other outcomes in randomized trials of RAAS blockade. Whether the impact of dietary sodium reduction on albuminuria will translate into similar clinical benefits as those achieved through pharmaceutical measures remains unknown. The potential for both blood pressure–dependent and blood pressure–independent protection against adverse kidney outcomes suggests that salt reduction and salt substitute could produce large benefits, making a strong case for further trials examining effects on clinical renal outcomes. The widespread availability and low cost of dietary salt interventions mean that a positive result from such trials would have far-reaching implications for the global burden of kidney disease.

Practical Applicability

A multipronged intervention for dietary salt reduction, including education and the use of a potassium-supplemented salt substitute significantly reduced dietary sodium intake and increased dietary potassium intake in rural Chinese participants. The intervention significantly lowered albuminuria, an established marker of cardiovascular and renal risk. After 18 months, intervention participants did not have significantly lower blood pressure but were taking few blood pressure medications, suggesting the possibility that benefit is not solely reliant on blood pressure reduction. Large randomized studies are needed to see whether the benefit seen for albuminuria translates into a benefit for cardiovascular outcomes and a reduction in CKD progression.

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Authors' contributions

The China Rural Health Initiative Salt Reduction Study was designed and administered by a scientific committee including B.N., Y.W., and L.L.Y. N.L. was the senior research fellow responsible for daily oversight of the study. The renal substudy was conceived by M.J.J.; designed by M.J.J., N.L., H.L.H., V.P., and B.N.; and overseen by M.J.J., N.L., X.F., J.Z., J.S., Y.Z., R.Z., VP., Y.W., L.L.Y., and B.N. Statistical analyses were performed by T.N. and N.L., and T.N. had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. M.J.J. wrote the first draft, and all authors have reviewed and approved the draft. Each author contributed important intellectual content during manuscript drafting or revision and accepts accountability for the overall work by ensuring that questions pertaining to the accuracy or integrity of any portion of the work are appropriately investigated and resolved.

Supplementary data

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