ORIGINAL ARTICLE

Study of low salt diet in hypertensive patients with chronic kidney disease

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ABSTRACT

Introduction: The efficacy of blood pressure (BP) reduction with salt restriction in CKD subjects and its sustainability is not well established.

Methods: We enrolled 75 hypertensive patients with CKD into one-month salt restricting diet. 24-hour urinary sodium and potassium was measured to verify their salt intake followed by 1½ year follow-up.

Results: Their creatinine clearance was 43 ± standard deviation 33ml/min/1.73m^2. Urinary Na excretion (24HUNa) was 173±129mmol/day, reducing to 148±81 by 31±6 day. Mean, systolic and diastolic BP (MBP, SBP, DBP) were reduced from 102±9 to 97±11 (p<0.001), 148±10 to 139±16 (p<0.001), 78±12 to 75±12 mmHg (p=0.012) respectively. Moderate correlations were shown between reductions in 24-hour urinary Na and MBP, SBP, DBP: r=0.366, 0.260, 0.365; p=0.001, 0.025, 0.001; whereas 24-hour urinary Na-K ratio showed mild correlation. Subjects have some tendency to drift back to previous Na intake profile in follow-up and thus repetitive education is necessary.

In subanalysis, 34 subjects with baseline 24HUNa >150 mmol/day, benefited significantly with MBP, SBP, DBP reduction from 102±9 to 95±9 (p=0.001), 146±10 to 135±14 mmHg (p=0.001), 80±11 to 75±11 mmHg (p=0.002) in line with 24HUNa reduction from 253±154 to 163±87mmol/day (p=0.004) and urinary protein-creation ratio reduction from geometric mean of 95 to 65 g/mol. Thirty five subjects with 24HUNa reduction of >20mmol/day have significant reduction in MBP, SBP, DBP: -8 vs -2, -15 vs -4, -5 vs -2 mmHg (p=0.027, 0.006, 0.218) and urinary protein-creatinine ratio: -82 vs 2g/mol (p=0.030) compared to the other forty subjects.

Conclusion: Quantification of 24-hour urinary Na helps in predicting potential antihypertensive effect with dietary salt reduction of CKD subjects. Salt restriction reduces BP especially in patients with estimated daily sodium intake of >150mmol/day. Reduction in sodium intake beyond 20mmol/day reduced both BP and proteinuria.

KEY WORDS:
Low salt diet, hypertension, chronic kidney disease

INTRODUCTION

Hypertension in chronic kidney disease (CKD) has been shown in the elegant studies by Koomans et al. to be salt sensitive.[1,2] Nevertheless salt intakes was not shown to be a determinant of blood pressure status in the CKD subjects from Modification of Diet in Renal Disease study cohort.[3] We aim to verify if salt restriction is an effective tool in reducing in clinical practice for CKD subjects, and whether compliance in dietary salt restriction could be maintained with time.

Hence, we conduct a lifestyle modification prospective study on the effect of salt restriction in hypertensive chronic kidney disease patients. Our primary outcome is reduction in blood pressure and secondary outcome is proteinuria reduction.

METHODS

We enrolled hypertensive subjects with chronic kidney disease (CKD) in routine visit of nephrology clinic of our hospital into 1-month salt reduction period. The inclusion criterias include: 1) All subjects must have no changes of antihypertensive or diuretic medication for at least 1 month prior to enrolment and during 1-month of intensive salt restriction. 2) Systolic Blood Pressure (BP) <180 mmHg and >115 mmHg at enrolment.

Subjects were advised on low salt diet which was defined as 1. no added salt diet, soya sauce or other high sodium food additives to the diet and 2. Avoidance or restriction of preserved or processed food with high salt content. Aim of dietary Na reduction would be measured indirectly with urinary sodium below 100mmol/day.[4-6] Patients were also encouraged to have more vegetable and fruit intake with advice tailored according to their baseline potassium level.

We aim for BP<130/80 mmHg for all subjects in line with the hypertension consensus and past studies on chronic kidney disease.[7-9] We collected 24-hour urinary sodium (Na) and potassium (K) to estimate the salt intake. We reassessed 24-hour urinary Na and K and urine protein-creatinine ratio after one month and 1-1½ year. We define stages in chronic kidney disease according to K/DOQI classification.[10] We utilized the initial normalized 24-hour creatinine clearance to class the staging of CKD. We derived eGFR with MDRD formula.[11]

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This study was approved by Medical Research Ethical Committee http://www.nmrr.gov.my/ (NMRR-09-1078-5007). We obtained informed consents from all patients.

Laboratory Methods
We measured urine sodium with indirect ion-selective electrode,[12] urine creatinine with Jaffe method,[13] and urine protein with dye binding method (Pyrogallol red).[14]

Statistical Methods
The statistical data were analysed using Microsoft excel and SPSS 15.0 (Statistical package for Social Science. SPSS Inc. 233 South Wacker Drive, 11th Floor, Chicago, Illinois 60606-6307).

Kolmogorov Smirnov test was initially used to determine whether the data is in statistical normal distribution. Mean ± standard deviation was shown. If necessary, geometric transformation was performed with natural log in order to achieve the Gaussian distribution. As all data eventually could achieve Gaussian distribution with or without logarithm transformation, paired t-test was performed to verify the changes in clinical parameters with salt restriction advice.

RESULTS

We initially enrolled 77 subjects but two subjects were excluded from the study as one could not come for follow up according to schedule while another one could not collect 24-hour urine. Thus drop up rate is 3%.

Eventually 75 subjects with CKD, i.e., 23 (31%) female and 52 (69%) male have completed the study, as briefly shown in Table I. Forty subjects (53%) have type 2 Diabetes Mellitus. Besides Diabetes Mellitus, other causes of chronic kidney disease included hypertensive nephropathy in 20 subjects (27%); IgA nephropathy (2 subjects); adult polycystic kidney disease (1 subject) and chronic glomerulonephritis (2 subjects).

Their age ranged from 30 to 89 with mean of 61 years. Their creatinine clearance was 43 ± standard deviation 33 ml/min/1.73m2. There were seven, 11, 17, 31 and nine patients in CKD stage I to V respectively. The 24-hour urinary Na excretion (24HUNa) ranged from 38 to 914mmol/day with mean of 173 ± 129mmol/day. This was reduced to 148 ± 81, ranging from 22 to 353 mmol/day by 31 ± 6 day. Overall, subjects with 24-hour urine Na <100mmol/day has increased from 16 (21%) to 25 (33%) after one month.

Mean, systolic and diastolic BP (MBP, SBP, DBP) were reduced with from 102 ± 9 to 97 ± 11 (p<0.001), 148 ± 10 to 139 ± 16 (p<0.001), 78 ± 12 to 75 ± 12 mmHg (p=0.012) respectively.

Figure 1 and 2 showed the changes in SBP and DBP with changes in 24-hour urine Na. Moderate correlations were shown between reductions in 24-hour urinary Na and reductions in MBP, SBP, DBP: r=0.366, 0.260, 0.365; p=0.001, 0.025, 0.001. In contrast, no correlations were observed between changes of 24-hour urinary K and MBP, SBP, DBP: 0.059, 0.018, 0.079 (p=0.616, 0.880, 0.501); whereas mild correlation was observed between changes in 24-hour urinary Na-K ratio and MBP, SBP, DBP: 0.277, 0.197, 0.275 (p=0.016, 0.091, 0.017).

The ratios of urinary Na-K reduced across all the stages (Table II). All except 5th CKD stage have higher number of subjects achieving goal of <100mmol/day urine Na. Nevertheless, the degree of salt reduction was greater for subjects in CKD stage 1 and 2 who have higher baseline urine Na. Among 18 subjects with CKD stage 1-2, 24HUNa have reduced in geometric mean from 204 to 124mmol/day after 1 month (p=0.006) while their urine Na-K ratio has reduced from 3.9 ± 1.3 to 3.4 ± 1.7 (p=0.154). In contrast, among 57 patients with CKD stage 3-5, 24HUNa has minor change with geometric mean from 130 getting to 127mmol/day after 1 month (p=0.846) while their urine Na-K ratio reduced from 4.5 ± 2.8 to 4.0 ± 2.3 (p=0.267).

Overall, creatinine clearance and eGFR has not changed significantly in a month, i.e., from 44 ± 34 to 47 ± 37 ml/min/1.73m^2 and from 36 ± 23 to 35 ± 25 ml/min/1.73m^2 respectively.

For the next one year following the study, the clinicians have modified medication while continue to advise on salt reduction. Only 12 subjects with CKD Stage 1-2 who have geometric mean of 24HUNa 218mmol/day at enrolment and 123mmol/day after a month, have retested 24HUNa at 1-1½ year. Unfortunately, 24HUNa have risen back again to 174mmol/day. On the other hand, only 47 subjects with CKD Stage 3-5 subjects have retested 24HUNa at 1-1½ year. The geometric mean of 24HUNa remained stable around 135mmol/day.

In a subanalysis, 34 patients with baseline 24HUNa >150mmol/day, benefited significantly from salt restriction (Table III) with MBP, SBP, DBP reduction from 102±9 to 95±9 (p=0.001), 146±10 to 135±14mmHg (p=0.001), 80±11 to 75±11 mmHg (p=0.002) in line with 24HUNa reduction from 253±154 to 163±87mmol/day (p=0.004). Their urinary protein-creation ratio reduced from 144±163 to 114±119g/mol. In these patients, moderate correlations were shown between reductions in 24-hour urinary Na and reductions in MBP, SBP, DBP: r=0.574, 0.388, 0.576; p<0.001, 0.023, <0.001. In contrast, others have smaller benefit: 101 to 98, 149 to 142, 77 to 76 mmHg (p=0.089, 0.020, 0.494).

Compared to the rest of subjects, 35 patients with 24HUNa reduction of >20mmol/day have significant reduction in MBP, SBP and DBP: -8 vs -2, -15 vs -4, -5 vs -2 mmHg (p=0.027, 0.006, 0.218) and urinary protein-creatinine ratio: -82 vs 2g/mol (p=0.030) (table IV). The trends in reduction of blood pressures and urinary protein-creatinine ratio persisted even after a year, although the statistical differences between both groups have diminished after adjustment of medication.

DISCUSSION

Essential hypertension is seen primarily in societies in which salt intake is above 100mmol/day (2.3 g sodium)[4] and low salt diet has been shown to reduce blood pressure.[5] It is recommended that patients with hypertension restrict their

Table I: Baseline Characteristics, Blood pressure and 24-hour urine Na trend

		Initial	1 month	p-value
All subjects	(n=75)			
Female:Male		23:52		
DM: No DM		40:35		
Age	year	61 ± 13		
Systolic BP	mmHg	148 ± 10	139 ± 16	<0.001
Diastolic BP	mmHg	78 ± 12	75 ± 12	0.012
Mean BP	mmHg	102 ± 9	97 ± 11	<0.001
24-hour urine Na	mmol/day	173 ± 129	148 ± 81	0.124
24-hour urine K	mmol/day	44 ±27	45±25	0.713
Patients with Urine Na<100 mmol/day	n (%)	16 (21%)	25 (33%)	
Creatinine clearance*	ml/min/1.73m2	44 ± 34	47 ± 37	0.448

*All the parameters were taken from 75 subjects, except creatinine clearance, from 69 subjects, because there were 6 subjects having no creatinine clearance measured in the 1 month sample.
Abbreviation: DM, Diabetes Mellitus; BP, blood pressure.

Table II: Blood pressure and 24-hour urine Na trend in various staging of CKD

		Initial	1 month	p-value
Stage 1	(n=7)			
Systolic BP	mmHg	141 ± 15	120 ± 10	0.028
Diastolic BP	mmHg	86 ± 12	74 ± 8	0.111
24-hour urine Na*	mmol/day	241	107	0.071
24-hour urine Na/K ratio		3.7 ± 1.5	2.8 ± 2.2	0.379
Patients with Urine Na<100 mmol/day	n (%)	1 (14%)	2 (29%)	
Creatinine clearance	ml/min/1.73m^2	118 ± 36	93 ± 43	0.328
eGFR	ml/min/1.73m^2	78 ± 22	75 ± 21	0.416
Stage 2	(n=11)			
Systolic BP	mmHg	145 ± 11	134 ± 12	0.031
Diastolic BP	mmHg	76 ± 15	73 ± 13	0.191
24-hour urine Na*	mmol/day	183	136	0.003
24-hour urine Na/K ratio		4.1 ± 1.2	3.7 ± 1.3	0.207
Patients with Urine Na<100 mmol/day	n (%)	0 (0%)	3 (27%)	
Creatinine clearance	ml/min/1.73m^2	75 ± 9	89 ± 46	0.407
eGFR	ml/min/1.73m^2	61 ± 16	66 ± 26	0.317
Stage 3	(n=17)			
Systolic BP	mmHg	150 ± 11	137 ± 19	0.015
Diastolic BP	mmHg	75 ± 10	74 ± 10	0.507
24-hour urine Na*	mmol/day	171	145	0.275
24-hour urine Na/K ratio		4.8 ± 2.2	4.5 ± 2.9	0.762
Patients with Urine Na<100 mmol/day	n (%)	2 (12%)	6 (35%)	
Creatinine clearance	ml/min/1.73m^2	45 ± 9	50 ± 22	0.332
eGFR	ml/min/1.73m^2	36 ± 10	35 ± 13	0.792
Stage 4	(n=31)			
Systolic BP	mmHg	151 ± 9	144 ± 15	0.021
Diastolic BP	mmHg	81 ± 11	80 ± 12	0.437
24-hour urine Na*	mmol/day	115	125	0.521
24-hour urine Na/K ratio		4.6 ± 3.3	3.9 ± 2.1	0.314
Patients with Urine Na<100 mmol/day	n (%)	10 (32%)	11 (35%)	
Creatinine clearance	ml/min/1.73m^2	24 ± 4	28 ± 12	0.057
eGFR	ml/min/1.73m^2	23 ± 7	22 ± 8	0.056
Stage 5	(n=9)			
Systolic BP	mmHg	143 ± 5	145 ± 17	0.757
Diastolic BP	mmHg	73 ± 7	68 ± 7	0.064
24-hour urine Na*	mmol/day	115	106	0.776
24-hour urine Na/K ratio		3.8 ± 1.1	3.5 ± 1.8	0.679
Patients with Urine Na<100 mmol/day	n (%)	3 (33%)	3 (33%)	
Creatinine clearance	ml/min/1.73m^2	13 ± 2	17 ± 5	0.025
eGFR	ml/min/1.73m^2	15 ± 3	15 ± 3	0.866

Comparison is with paired t-test.
Abbreviation: BP, blood pressure; eGFR, estimated glomerular filtration rate.
*Logarithm transformation was shown and geometric means were compared.

Table III: Blood pressure trend in groups of baseline daily urinary Na

Urine Na <150 mmol/day	(n=41)	Initial	1 month	p-value
Mean BP	mmHg	101 ± 9	98 ± 12	0.089
Systolic BP	mmHg	149 ± 11	142 ± 18	0.020
Diastolic BP	mmHg	77 ± 12	76 ± 12	0.494
UPC*	g/mol	70	68	0.823
Urine Na>=150 mmol/day	(n=34)			
Mean BP	mmHg	102 ± 9	95 ± 9	<0.001
Systolic BP	mmHg	146 ± 10	135 ± 14	<0.001
Diastolic BP	mmHg	80 ± 11	75 ± 11	0.002
UPC*	g/mol	95	65	0.017

Comparison is with paired t-test.
Abbreviation: UPC, Urine protein creatinine ratio; BP, blood pressure.
*Logarithm transformation was performed and geometric means were compared

Table IV: Blood pressure and UPC changes from time of enrolment in groups of urinary Na reduction

		1 month			1 - 1½ year		
Urine Na reduction mmol/day		**<=20 (n=40)**	**>20 (n=35)**	**p-value**	**<=20 (n=37)**	**>20 (n=32)**	**p-value**
Change in daily urine Na from enrolment time	mmol/day	57 ± 63	-118 ± 143	<0.001	30 ± 81	-76 ± 201	0.024
Number of Antihypertensives*		2	2	0.973	3	2	0.454
Number of patients on ACEI or ARB**	n(%)	22 (55%)	23 (66%)	0.345	17 (46%)	16 (50%)	0.737
Mean BP changes	mmHg	-2 ± 10	-8 ± 11	0.027	-6 ± 11	-8 ± 12	0.468
Systolic BP changes	mmHg	-4 ± 16	-15 ± 17	0.006	-10 ± 17	-14 ± 16	0.224
Diastolic BP changes	mmHg	-2 ± 11	-5 ± 10	0.218	-4 ± 10	-4 ± 12	0.817
eGFR changes	ml/min/1.73m2	0 ± 8	-1 ± 6	0.437			
eGFR changes per year	ml/min/1.73m2/year				-8 ± 18	-7 ± 9	0.769
Creatinine clearance changes	ml/min/1.73m2	5 ± 34	1 ± 25	0.551	0 ± 14	-3 ± 21	0.595
UPC changes	g/mol	2 ± 110	-82 ± 181	0.030	36 ± 146	-64 ± 180	0.052

Abbreviation: BP, blood pressure; UPC, eGFR, estimated glomerular filtration rate; Urine protein creatinine ratio.
Student t-test were performed.
*Medians were shown and comparisons were with Mann-Whitney U test.
**2-sided Chi-Square test were performed.

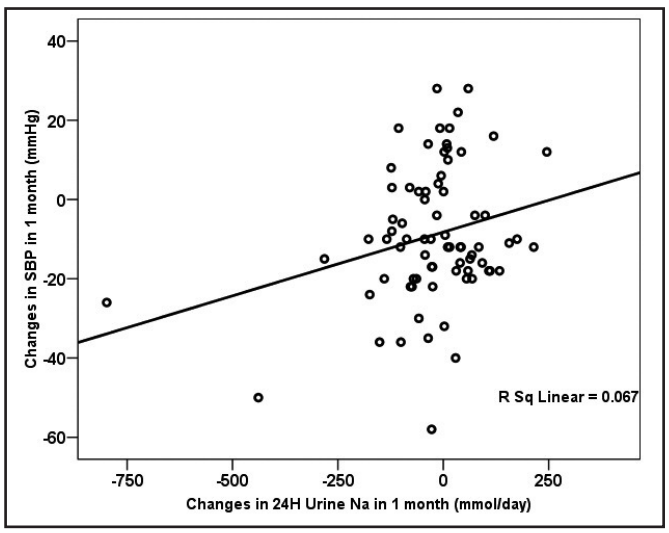

Fig. 1: Changes of SBP and 24-hour urinary Na excretion in 1 month.

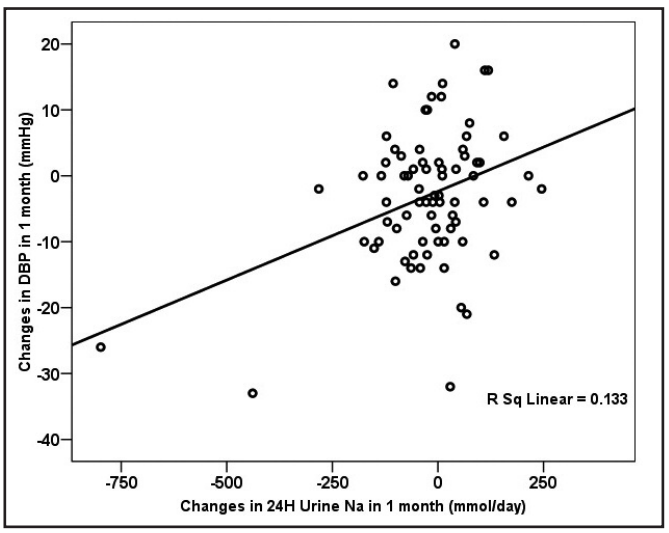

Fig. 2: Changes of DBP and 24-hour urinary Na excretion in 1 month.

salt intake to < 100mmol/day[5,6], and for those with CKD, this has been further brought down to <90 mmol/day in the recent KDIGO clinical practice guideline.[15]

Koomans et al., has shown in the experiments on chronic kidney failure (CKD) subjects that increasing salt intake would result in marked blood pressure increment but this is not so in the healthy control, despite comparable increase in blood volume.[2] Interestingly there is little increase interstitial

fluid volume in contrast to marked increase of interstitial fluid volume in healthy control. This suggested vasoconstriction effect with high salt intake in CKD subjects. Our current study supports the relationship between BP and salt intake, and further affirms the importance of salt restriction in CKD subjects.

In our study, patients with earlier stages of CKD have higher baseline sodium intake and they are able to reduce their sodium intake significantly following advice on dietary sodium restriction and thus achieve significant BP reduction even after a month. In contrast, patients with CKD stage 3-5 in our study already seems to have relatively low sodium intake at baseline and further advice on salt restriction did not have any significant impact on BP reduction. These patients may have been advised repeatedly previously on sodium restriction and they may also have poorer appetite resulting in lower sodium intake at baseline.

The subsequent rise in 24HUNa in the subjects with reasonable subjects in 1½ year time demonstrated to us that in clinical practice, there is always a constant struggle between the salt restriction, patient compliance and thus blood pressure achievement during long-term follow-up. This is because without adequate encouragement and enforcement, patients might fall back to his or her own previous lifestyle. Therefore, timed urinary Na collection perhaps should be repeated on a regular basis in order to monitor as well as encourage patients.

Next, the timed urinary Na collection is a useful tool to estimate patient's sodium intake and predict their response to salt restriction. We observed significant drop in BP and proteinuria within a month for those with initial 24HUNa >150mmol/day. Achieving Na intake of <100mmol/day is difficult and is achieved only in 33% of the patients. However, our result suggests that urinary Na reduction beyond 20mmol/day can result in significant BP and proteinuria reduction.

Potassium supplement has been shown to reduce blood pressure[16] and vegetable and fruit were well known source of dietary potassium.[17] In this study, although we also asked patient to increase vegetable and fruit intake, due to minute potassium intake changes, our study did not show any relationship between potassium intake and changes in blood pressure. Recently there is a study on sodium substitution with potassium resulting in better blood pressure reduction among normal population.[18] This approach would be rather controversial in CKD subjects in view of the risk of hyperkalaemia but it remains a potentially sensible approach for subjects with early CKD.

In view of limited number of subjects, this study has insufficient power to detect whether dietary sodium restriction might actually improve the renal outcome. The authors are currently enlarging the study pool while continuing to follow-up these patients and study their clinical outcome.

Recent study by Kirsten Bibbins-Domingo et al has projected the potential benefit of sodium restriction by reducing cardiovascular events and medical costs.[19] Meanwhile, Redelinghuys M et al., further demonstrated that the central pulse pressure was increased with high salt intake affecting the cardiovascular risk.[20] Kagiyama S et al., also showed that the cardiac function could potentially be adversely affected with higher Na intake especially in diabetic population.[21]

Anyway, our study has shown that even among CKD subjects who are most likely to benefit from it, dietary salt restriction remained a difficult target to achieve especially over long term as patients have high tendency to drift back to their old dietary habit. The subsequent rise in 24HUNa after one year demonstrated to us that in clinical practice, it is difficult to have sustained clinical response with salt restriction. Without adequate encouragement and enforcement, most patients will fall back to his or her own previous life style and dietary habits. Future study should probably tackle the issues of dietary and behavioural modification with the hope that lower salt intake would become a norm. This of course should include strategy in modifying the food pattern of the general population.[22] On the other hand, short-term hospitalization has been advocated by Yamaji K et al., to achieve effective Na restriction in CKD subjects.[23] It remains a question whether the dietary behaviour that was acquired by this approach will be sustainable in longer duration. Therefore, 24HUNa should be repeated on a regular basis in order to monitor as well as encourage patients.

Recently most clinicians stress the importance of sodium restriction[24] but again it is remarkably hard to achieve the target of sodium restriction. Only 11.2% of the patients in the study by Ohta Y et al., was able to achieve dietary sodium intake <6g/day (i.e., about 103mmol/day of NaCl).[25]

Overall, our study showed that time urinary sodium collection helps in predicting potential antihypertensive effect with dietary salt reduction. This is most effective in those with Na intake >150mmol/day and those in early stages of CKD. In these patients, a period of salt restriction may be tried to lower their BP. In contrast, those with low Na intake or more advanced stages of CKD may not have significant effect with dietary salt restriction and early adjustment of antihypertensive medications is warranted. While it is difficult to achieve Na intake <100mmol/day, our study suggested that sodium reduction beyond 20mmol/day from baseline can reduce both BP and proteinuria in CKD subjects.

REFERENCES

1. Koomans HA, Roos JC, Boer P, Geyskes GG, Mees EJ. Salt sensitivity of blood pressure in chronic renal failure. Evidence for renal control of body fluid distribution in man. Hypertension 1982; 4(2): 190-7.
2. Koomans HA, Roos JC, Dorhout Mees EJ, Delawi IM. Sodium balance in renal failure. A comparison of patients with normal subjects under extremes of sodium intake. Hypertension 1985; 7(5): 714-21.
3. Buckalew VM Jr, Berg RL, Wang SR, Porush JG, Rauch S, Schulman G. Prevalence of hypertension in 1,795 subjects with chronic renal disease: the modification of diet in renal disease study baseline cohort. Modification of Diet in Renal Disease Study Group. Am J Kidney Dis 1996; 28(6): 811-21.
4. Elliott P, Stamler J, Nichols R, Dyer AR, Stamler R, Kesteloot H, et al. Intersalt revisited: Further analyses of 24 hour sodium excretion and blood pressure within and across populations. BMJ 1996; 312: 1249-53.
5. Law MR, Frost CD, Wald NJ. By how much does dietary salt reduction lower blood pressure? I-An analysis of observational data among populations; III-Analysis of data from trials of salt reduction. BMJ 1991; 302: 811-5.

6. Beard TC, Stowasser M. Cochrane and the salt debate. Lancet 2003; 362(9381): 403.
7. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr et al. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: The JNC 7 Report. JAMA 2003; 289: 2560-72.
8. Hansson, L, Zanchetti, A, Carruthers, SG, Dahlöf B, Elmfeldt D, Julius S et al. Effects of intensive blood- pressure lowering and low-dose aspirin in patients with hypertension: Principal results of the Hypertension Optimal Treatment (HOT) randomised trial. Lancet 1998; 351: 1755-62.
9. Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 38. UK Prospective Diabetes Study Group. BMJ 1998; 317(7160): 703-13.
10. National Kidney Foundation. Definition and Classification of Stages of Chronic Kidney Disease. Am J Kid Dis 2002; 39(2): S46-75.
11. Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D. A more accurate method to estimate glomerular filtration rate from serum creatinine: A new prediction equation. Modification of Diet in Renal Disease Study Group. Ann Intern Med 1999; 130: 461-70.
12. Guagnellini E, Spagliardi G, Bernardi G, Stella P. Reliability of IL Monarch ion-selective electrode module for sodium, potassium, and chloride measurements. Clin Chem 1988; 34(4): 746-8.
13. Junge W, Wilke B, Halabi A, Klein G. Determination of reference intervals for serum creatinine, creatinine excretion and creatinine clearance with an enzymatic and a modified Jaffé method. Clin Chim Acta 2004; 344(1-2): 137-48.
14. Lefèvre G, Bloch S, Le Bricon T, Billier S, Arien S, Capeau J. Influence of protein composition on total urinary protein determined by pyrocatechol-violet (UPRO vitros) and pyrogallol red dye binding methods. J Clin Lab Anal 2001; 15(1): 40-2.
15. Kidney Disease: Improving Global Outcomes (KDIGO) Blood Pressure Work Group. KDIGO Clinical Practice Guideline for the Management of Blood Pressure in Chronic Kidney Disease. Kidney Int Suppl 2012; 2(5): 337-414.
16. Whelton PK, He J, Cutler JA, Brancati FL, Appel LJ, Follmann D, et al. Effects of oral potassium on blood pressure, meta-analysis of randomised controlled clinical trials. JAMA 1997; 277: 1624-32
17. He FJ, Markandu ND, Coltart R, Barron J, MacGregor GA. Effect of short-term supplementation of potassium chloride and potassium citrate on blood pressure in hypertensives. Hypertension 2005; 45(4): 571-4.
18. China Salt Substitute Study Collaborative Group. Salt substitution: a low-cost strategy for blood pressure control among rural Chinese. A randomized, controlled trial. J Hypertens 2007; 25(10): 2011-8.
19. Bibbins-Domingo K, Chertow GM, Coxson PG, Moran A, Lightwood JM, Pletcher M et al. Projected effect of dietary salt reductions on future cardiovascular disease. N Engl J Med 2010; 362(7): 590-9.
20. Redelinghuys M, Norton GR, Scott L, Maseko MJ, Brooksbank R, Majane OH, et al. Relationship between urinary salt excretion and pulse pressure and central aortic hemodynamics independent of steady state pressure in the general population. Hypertension 2010; 56(4): 584-90.
21. Kagiyama S, Koga T, Kaseda S, Ishihara S, Kawazoe N, Sadoshima S, et al. Correlation between increased urinary sodium excretion and decreased left ventricular diastolic function in patients with type 2 diabetes mellitus. Clin Cardiol 2009; 32(10): 569-74.
22. Charlton K, Yeatman H, Houweling F, Guenon S. Urinary sodium excretion, dietary sources of sodium intake and knowledge and practices around salt use in a group of healthy Australian women. Aust N Z J Public Health 2010; 34(4): 356-63.
23. Yamaji K, Kurusu A, Okamoto M, Sekiguchi Y, Horikoshi S, Tomino Y. Effect of educational hospitalization on chronic kidney disease (CKD) patients. Clin Nephrol 2007; 68(6): 401-4.
24. Soi V, Yee J. Sodium Homeostasis in Chronic Kidney Disease. Adv Chronic Kidney Dis 2017; 24(5): 325-31.
25. Ohta Y, Kimura Y, Kitaoka C, Sakata T, Abe I, Kawano Y. Blood pressure control status and relationship between salt intake and lifestyle including diet in hypertensive outpatients treated at a general hospital. Clin Exp Hypertens 2017; 39(1): 29-33.