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ARTICLE

Effect of simplified dietary advice on nutritional status and uremic toxins in chronic kidney disease participants

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Background: Traditional chronic kidney disease (CKD) dietary advice is challenging with many restrictions, consequently adherence to the CKD diet is low. Recent literature has proposed less restrictive dietary guidelines in CKD to improve dietary adherence and outcomes; however, limited evidence of its implementation exists.
Objectives: This study (trial number: PACTR202002892187265) investigated the effect of simplified dietary advice on nutritional outcomes and adherence after four weeks of dietary advice.
Design: A before-and-after study was conducted.
Outcome measures: Sociodemographic, clinical and biochemical information was collected and anthropometric measurements performed on Stage 3–5 CKD participants attending a pre-dialysis clinic. Uremic toxins were quantified by UPLC/fluorescence detection. Dietary intake was assessed using a quantified food frequency questionnaire (QFFQ). Participants were educated by the study dietitian on simplified dietary advice using an infographic. A diet-adherence score sheet monitored adherence. All outcomes were measured at baseline and four weeks after the diet was advised. IBM SPSS® version 27 was used for statistical analysis.
Results: Fifty-nine participants, mean age 41.0 ± 11.6 years, completed the study. After four weeks, significant improvements were found in body mass index ($p < 0.006$), waist circumference ($p < 0.001$), mid-upper arm circumference ($P < 0.001$), serum total cholesterol ($p < 0.045$), serum triglycerides ($p < 0.017$), energy ($p < 0.001$), protein ($p< 0.001$) and most dietary intake variables. Overweight and obesity prevalence was high at 68%. Uremic toxin concentrations remained stable. Dietary adherence was 88.6%.
Conclusion: The simplified dietary advice suggests improved nutritional outcomes in CKD patients who were predominantly overweight and obese, without compromising kidney function. This study highlights the importance and feasibility of simplified nutrition education in CKD.

Keywords: dietary adherence in CKD, infographic, nutrition education in CKD, simplified CKD advice, uremic toxins

Background

Chronic kidney disease (CKD) is highly prevalent globally and in sub-Saharan Africa.[1–3] Globally, there has been an increase in CKD morbidity, mortality and disability-adjusted years of life, with an increased burden of CKD in sub-Saharan Africa.[3] There are many complications related to CKD including anemia, malnutrition, anorexia, mineral and bone disease, electrolyte disturbances, cardiovascular disease and progression to end-stage kidney disease (ESKD).[4] In addition, patients with CKD may have several co-morbidities including obesity, hypertension and diabetes.[5] Traditional CKD nutritional advice has been challenging to convey to patients owing to the complexity of the diet. Patients had been advised to restrict fruits, vegetables, legumes, wholegrains, dairy and nuts owing to their phosphate and potassium content.[6] In addition, protein restrictions are needed to mitigate deterioration of kidney function; these factors and disease-related symptoms such as nausea, vomiting and anorexia result in low adherence to dietary advice.[7] To ensure sound nutritional advice and to improve adherence, these and additional factors including side effects of medications, financial constraints and dietary acceptance should be considered by healthcare professionals.

Dietary practice guidelines that formulated the traditional CKD advice originated from the Kidney Disease Quality Initiative (KDOQI) as well as the Kidney Disease Improving Global Outcomes (KDIGO).[8,9] These guidelines were partly evidence-based and partly based on expert opinion, or extrapolated from research on individuals without CKD.[10] Limited clinical trials investigating nutritional interventions were reported. Nutritional recommendations were mainly driven by the clinical judgement of physicians and dietitians rather than graded scientific evidence; the trials that were included had small sample sizes and primarily focused on one or two aspects of the diet.[10] The CKD nutrition guidelines have recently been updated and include more robust evidence for nutritional recommendations, including advice on dietary patterns, with less emphasis on specific nutrients.[11]

Recent studies have suggested that CKD dietary advice should be simplified to improve adherence.[6,12] Dietary pattern studies have shown that Western diets high in fat, sugar and energy are associated with increased mortality in CKD, whereas dietary patterns that reflect a healthier diet show improved outcomes in CKD.[13,14] The KDOQI 2020 updated dietary guidelines suggest that there is sufficient evidence that diets rich in fruits, vegetables, lean meats, low-fat dairy and low salt improves clinical outcomes, notably mortality.[11]

The current focus of CKD nutritional management should therefore be on natural, healthy foods with the exclusion of processed and 'fast' foods and foods high in salt and sugar

content. This will allow for the dietary goals for CKD to be met, while still permitting the consumption of a greater variety of foods.

Uremic toxins are retained in CKD, which enhances cardiovascular morbidity and mortality and the progression to ESKD.[15] Several of these uremic toxins are intestinally generated by the gut microbiota and are increased when there is gut dysbiosis.[15] Low-fibre diets and prolonged colonic transit time can contribute to this dysbiosis by reducing saccharolytic bacteria and favouring proteolytic bacteria.[16] The uremic toxins *p*-cresyl sulfate (*p*CS), *p*-cresyl glucuronide (*p*CG), indoxyl sulfate (IxS) and indole-acetic acid (IAA) have been shown to interact negatively with biological functions and to affect CKD progression, with levels being much higher in CKD patients than in healthy individuals. Prebiotic and probiotic supplementation has shown a reduction in uremic toxin levels and improved kidney function in CKD.[17–20] While these studies focus on prebiotics, probiotics or synbiotics, there are no studies of which we are aware, investigating CKD diet interventions only on uremic toxins in adults with CKD.

A previously developed simplified CKD dietary infographic based on a review of the scientific evidence was used to educate participants.[21] In this sub-study we aimed to investigate the effect of simplified dietary advice on nutritional outcomes and dietary adherence. Adherence to the diet would allow dietary changes to be made during the run-in period before the main trial commenced. This was investigated by educating participants on the dietary advice, and thereafter measuring outcomes such as anthropometry, kidney function, dietary intake and adherence, clinical factors, biochemical values and uremic toxin levels at baseline and after four weeks.

Subject and methods

Ethics and informed consent

The study was conducted in accordance with the Declaration of Helsinki. Ethics approval was obtained from the Human Research Ethics Committee at Stellenbosch University (reference number: S18/03/064) and participants were enrolled after written informed consent was obtained. Participants were anonymized on datasets for analysis.

Study design, sampling and participants

This nested study formed part of a randomised controlled trial (RCT) (trial number: Pan African Trial Registry: PACTR202002892187265), investigating the effect of a prebiotic on uremic toxins, CKD outcomes and the gut microbiome. Participants were enrolled at their routine doctor's appointment at a pre-dialysis clinic in Cape Town, South Africa, provided they were older than 18 years and presented with stage 3–5 CKD. This before and after sub-study investigated the effect of simplified dietary advice on the nutritional status, uremic toxins and dietary adherence of CKD participants, representing the run-in period of the main trial. A control group was not assigned owing to all of the participants having to follow the diet during the run-in period. All participants were educated and placed on the simplified dietary regime and outcomes were measured before and after four weeks of the dietary advice. Participants were excluded if they met the following criteria: taking antibiotics, prebiotics or probiotics, active gastrointestinal conditions (such as severe diarrhoea, constipation and abdominal cramping, inflammatory bowel disease or Crohn's disease), malignant hypertension, crescentic glomerular nephritis, diabetes, coeliac disease or any infectious diseases that would affect nutritional status. Measurements were performed at enrolment (Baseline) and after four weeks (Week 4).

Sample size

The sample size was calculated for the main clinical trial using a two-sample t-test using the Power Analysis Sample Size software (PASS program) based on previous study outcomes.[22] A power of 90% was used. The total number of participants needed for the main trial was 46, but, owing to expected attrition, 70 participants were enrolled. Eleven participants were lost to follow-up.

Diet advice and assessment

The study dietitian provided individual dietary counselling based on CKD guidelines to all participants using simplified advice.[8,9] The older guidelines were used because the updated KDOQI guidelines were only released after the study was conducted. Therefore, protein was restricted to 0.8 g/kg and no specific energy guidelines were given. All participants also received the following simplified key guidelines that were part of the infographic: limiting of additives, processed foods, salt and salty foods, high-phosphate meats and encouraging low-fat proteins, wholegrains and an adequate intake of fruits and vegetables. Additional tips on cooking, alcohol and fluid intake were included. These guidelines were conveyed to the participants as an infographic, which was developed based on scientific evidence, together with predetermined protein exchanges.[21] At the end of the study the participants were asked about the ease of use of the infographic and whether it assisted them in making dietary changes.

A 160-item interviewer-administered quantified food frequency questionnaire (QFFQ) was adapted from a previous QFFQ[23] to assess dietary intake at both visits. The QFFQ was adapted for suitability in CKD to include a wider variety of potassium-, sodium- and phosphate-containing foods. The following foods were added to the original QFFQ: a wider variety of fruits and vegetables for their potassium content, processed and crumbed protein containing foods and dark cold drinks for their phosphate content, as well as added salt for sodium content. The QFFQ contained food items from various food groups so that energy, macronutrients and micronutrients could be analysed. The QFFQ was tested for face validity with patients with CKD and content validity with specialist dietitians and changes made accordingly, before being finalised. Household food utensils and food models were used to estimate portion sizes. The recorded food portions were quantified using a food quantities manual and entered into a database, coded and calculated to grams per daily intake. Dietary intake was analysed for its nutrient content by a statistician from the South African Medical Research Council using the SAFOODS Database.[24] An adapted dietary adherence score sheet was also developed to determine whether participants were adhering to the diet and was completed at Week 4. The adherence score sheet was adapted for CKD from the PREDIMED adherence score sheet.[25] There were 12 questions on dietary changes from various food groups with a set of criteria (Appendix A). The criteria were selected based on information advised in the infographic and the dietary advice given. These included five questions on adhering to protein allowance, sufficient fruit and vegetable intake, healthy cooking methods and wholegrain intake, seven questions on the avoidance of processed food high in additives including fizzy cool drinks, 'fast' foods, alcohol intake, salt and salty foods and high-phosphate

meats. A score of 1 was allocated if they were adhering to the criteria. The scores were totalled, and adherence was calculated as a percentage out of 12.

Anthropometric assessments

Anthropometric measurements included: weight and height, waist circumference, triceps skinfold and mid-upper arm circumference (MUAC) using standard measuring techniques.[26] A calibrated Seca scale (Seca GmbH, Hamburg, Germany) was used to measure weight, while a Seca stadiometer was used to measure height, a plastic measuring tape was used for the waist circumference and MUAC and a Harpenden Caliper (Baty International, Burgess Hill, UK) was used to measure triceps skinfold. Three measurements were performed, and the average was recorded. The body mass index (BMI) was calculated by dividing the weight by the height squared. The BMI and waist circumference were interpreted according to World Health Organization (WHO) guidelines.[27] Mid-upper arm circumference was interpreted using standard measures.[28] Triceps skinfold was recorded.

Biochemistry and uremic toxin assessments

Routine blood results such as kidney function and electrolytes were obtained from clinic records and blood was drawn by the clinic nurse for additional biochemistry such a full lipid profile, uremic toxins and C-reactive protein (CRP) and analysed by the National Health Services (NHLS) laboratory. The blood samples for uremic toxin analysis were delivered directly to the NHLS laboratory onsite for further analysis.

For the determination of uremic toxins, venous blood was collected at baseline and Week 4 in K-EDTA tubes (9 ml). Blood was immediately centrifuged at 2100 × g for 10 minutes at 4°C. Plasma was aliquoted on ice at 500 µl in sterile tubes. Plasma was stored at −80°C. The NHLS laboratories were used to store the blood samples for uremic toxins analysis. Plasma was sent on dry ice to the Nephrology Laboratory of the Ghent University Hospital in Belgium for batch analysis. Liquid chromatography and fluorescence detection determined total and free concentrations of *p*CS, IxS, *p*CG and IAA as previously described.[29] In brief, plasma samples were deproteinized by heat, centrifuged and filtered through an Amicon Ultra 0.5 µl (Merck Merck Millipore Ltd. Tullagreen, County Cork, Carrigtwohill, Ireland) (molecular weight cut-off off 30 kDa Filters) for the quantification of the total toxin concentrations. For the free fraction quantification, Amicon filters were used to first filter the untreated plasma. The ultrafiltrate was transferred into an autosampler vial, and fluorescein was added as an internal standard. Analysis was performed by ultra-performance liquid chromatography with an Agilent 1290 Infinity device (Agilent, Santa Clara, CA, USA): IxS (λex: 280 nm, λem: 376 nm), *p*CS and *p*CG (λex: 264 nm, λem: 290 nm), IAA (λex: 280 nm, λem: 350 nm). Fluorescein (λex: 443 nm, λem: 512 nm) was detected by an Agilent G1316C fluorescence detector.

Clinical measurements

Blood pressure was measured by the clinic nurse and recorded. Ankle oedema was assessed by the dietitian by applying pressure on the tibia of the ankle with thumb and releasing after five seconds. The oedema was graded according to the time it took to rebound.[30] The severity was based on a Likert scale from 1 to 4 with one being no oedema and four being severe oedema.

Statistical analyses

IBM SPSS® version 27 (IBM Corp, Armonk, NY, USA) was used for statistical analysis. Data were checked for normality using Shapiro–Wilk, histograms and skewness values. Means were reported for normally distributed data and medians and interquartile ranges for non-normal distributed data. Frequencies were reported for categorical data. Normally distributed data were compared from Baseline to Week 4 using paired *t*-tests, while non-normal data were compared using Wilcoxon tests. Categorical variables were compared using Mcnemar tests. A *p*-value of < 0.05 was considered significant.

Results

Sociodemographics

Fifty-nine participants completed the study. The sociodemographic information is presented in Table 1. This predominantly female group (57.6%) were fairly young (41 ± 11.6 years). Half of the participants were employed, and the income earned was less than US$126 per month for most participants. The main cause of kidney failure as documented in the medical files was hypertension, and most participants were in stage 5 CKD.

Dietary intake

Table 2 shows the comparison of the dietary intake between Baseline and Week 4. There were highly significant reductions in all macronutrients and micronutrients including potassium, phosphate and sodium between the two visits, except for total sugar.

Anthropometry

A significant decrease occurred in the weight ($p < 0.006$), BMI ($p < 0.006$), MUAC ($p = 0.001$) and waist circumference ($p < 0.001$) over the four-week period as shown in Table 3. Although these were small differences, the maximum loss in weight was 3.5 kg and 13.3 cm in waist circumference. Of note was that some participants' weights remained stable (11.9%), most lost weight (68%) and a few gained weight (18.6%). A majority of participants (68%) were overweight and obese (Figure 1) and abdominal obesity was present in 59% of participants at baseline.

Table 1: Sociodemographic data of study participants ($n = 59$)

Item	Factor	*n* (%)
Age (years) (Mean ± SD)		41.0 ± 11.6
Gender	Male	25 (42.4)
	Female	34 (57.6)
Income (per month)	$0–$126	24 (40.7)
	$127–$316	16 (27.1)
	$317–$633	13 (22.0)
	$634–$949	4 (6.8)
	> $949	2 (3.4)
Employment	Employed	29 (49.2)
	Unemployed	30 (50.8)
Cause of kidney failure	Polycystic kidneys	3 (5.1)
	Hypertension	29 (49.2)
	Glomerular disease	13 (22.0)
	Other	14 (23.7)
GFR categories (ml/min/1.73 m^2)	30–59	19 (32.2)
	15–29	16 (27.1)
	< 15	24 (40.7)

Abbreviations: GFR = glomerular filtration rate.

Table 2: Dietary intake changes between Baseline and Week 4

Nutrients	Baseline Mean ± SD Median (IQR) *n* = 59	Week 4 Mean ± SD Median (IQR) *n* = 59	*p*-value
Energy (kcal/kg) Total kJ	27 8 018.2 (6 101.0, 10 114.0)	19 5 710.0 (4 480.0, 6 982.0)	< **0.001**
Total protein (g/kg) Total protein (g)	1.0 72.5 ± 26.9	0.7 51.9 ± 20.5	*< **0.001**
Plant protein (g)	24.7 (17.0, 30.1)	16.6 (14.0, 21.1)	< **0.001**
Animal protein (g)	43.9 (32.0, 55.0)	31.6 (22.4, 39.6)	< **0.001**
Total fat (g)	74.7 (53.0, 100.3)	50.0 (35.1, 60.8)	< **0.001**
Saturated fat (g)	22.8 (14.9, 31.0)	13.05 (9.6, 18.8)	< **0.001**
Total trans-fat (g)	0.5 (0.3, 0.9)	0.3 (0.1, 0.6)	**0.001**
Cholesterol (mg)	249.8 (167.6, 345.2)	148.0 (114.0, 228.5)	< **0.001**
Carbohydrate (g)	244.7 ± 90.3	186.0 ± 68.9	*< **0.001**
Added sugar (g)	37.4 (22.4, 56.0)	27.5 (13.7, 44.5)	< **0.001**
Total sugars (g)	69.0 (49.0, 81.9)	60.0 (47.0, 76.0)	0.097
Dietary fibre (g)	19.4 (13.8, 28.5)	17.6 (14.1, 21.3)	**0.005**
Phosphate (mg)	942.2 (668.9, 1229.5)	735.6 (523.0, 939.7)	< **0.001**
Sodium (mg)	1 829.2 (1 290.4, 2 584.8)	1 037.0 (673.5, 1 445.0)	< **0.001**
Potassium (mg)	2 525.9 (1 942.7, 3 304.6)	1 923.0 (1 553.5, 2 405.4)	< **0.001**

Statistical tests: Wilcoxon tests, *paired *t*-tests. Bold if $p < 0.05$.

Biochemistry

There were significant reductions in serum sodium ($p < 0.001$), serum total cholesterol ($p = 0.045$) and serum triglycerides ($p = 0.017$), while serum potassium slightly increased ($p = 0.046$) from Baseline to Week 4 as shown in Table 4. Serum urea, creatinine and phosphate tended to decrease. The plasma levels of the uremic toxins remained stable between Baseline and Week 4. There were 4 missing samples at Week 4, therefore only 55 samples were analysed.

Clinical changes

Most of the participants had no oedema Table 5. There was a significant reduction in the moderate and severe categories with more participants shifting to the mild category at week 4. Blood pressure did not change significantly.

Dietary adherence scores

Participants reported overall adherence scores of 88.6% to the dietary guidelines advised. Of the individual adherence score categories, only 47.5% of participants adhered to the fruit criteria of 2–3 servings of fruit a day, 69.5% to the vegetable criteria of 2–4 servings a day and 81.5% of participants to the wholegrain servings criteria of more than 2 servings a day. The salt and processed food category as well as the other food categories were adhered to in more than 90% of participants (Figure 2).

Table 3: Anthropometrical changes between Baseline and Week 4

Measurement	Baseline Mean ± SD *n* = 59	Week 4 Mean ± SD *n* = 59	*p*-value
Weight (kg)	76.4 ± 21.1	75.7 ± 20.7	**0.006**
BMI (kg/m^2)	28.6 ± 6.7	28.3 ± 6.6	**0.006**
Waist (cm)	91.5 ± 15.6	89.6 ± 15.0	< **0.001**
MUAC (cm)	31.0 ± 5.5	30.2 ± 5.1	**0.001**
Triceps skinfold (mm)	21.4 ± 8.9	21.4 ± 9.0	0.913

Abbreviations: BMI = body mass index; MUAC = mid upper-arm circumference. Statistical tests used: paired *t*-tests. SD = standard deviation. Bold if $p < 0.05$.

Usefulness of infographic

All participants indicated they found the infographic useful, understood it and that it assisted them in making dietary changes.

Discussion

The simplified dietary advice suggests improved nutritional parameters and adherence to dietary guidelines over the short term.

Low-protein diets are effective in improving outcomes in CKD,[31] but dietary adherence remains poor. Dietary education for CKD is usually complex and time consuming, owing to multiple dietary restrictions[7] and particularly in South Africa there are extensive exchange lists for CKD complicating dietary education.[21] Additionally, in resource-limited settings, dietary education from dietitians is limited. Pisani *et al*.[32] reported promising improvements in metabolic parameters and dietary adherence by using simplified dietary guidelines in CKD.

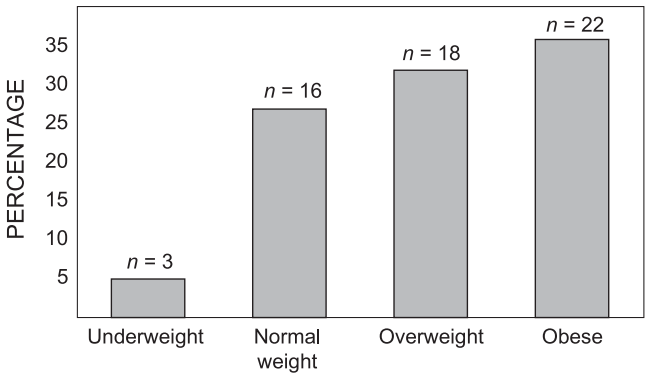

Figure 1: BMI categories of participants (%) at baseline.

Table 4 : Biochemical changes between Baseline and Week 4

Biochemical value	Normal ranges	Baseline Mean ± SD Median (IQR) *n* = 59	Week 4 Mean ± SD Median (IQR) *n* = 59	*p*-value
Urea (mmol/l)	2.1–7.1	14.4 (10.3, 25.0)	14.2 (9.1, 28.6)	0.775
Creatinine (umol/l)	64.0–104.0	269.0 (178.0, 447.0)	232.0 (175.0, 461.0)	0.804
GFR (ml/min.1.73m^2)	> 60	20.0 (11.0, 35.0)	20.0 (11.0, 35.0)	0.822
Potassium (mmol/l)	3.5–5.1	4.8 ± 0.6	4.9 ± 0.7	***0.046**
Sodium (mmol/l)	136.0–141.0	141.0 ± 2.9	139.3 ± 2.6	***< 0.001**
Phosphate (mmol/l)	0.78–1.42	1.3 (1.1, 1.5)	1.16 (1.0, 1.5)	0.174
Total cholesterol (mmol/l)	< 4.5	4.9 ± 1.2	4.7 ± 1.1	***0.045**
LDL (mmol/l)	< 2.5	2.7 ± 1.0	2.6 ± 1.0	*0.143
HDL (mmol/l)	> 1.2	1.1 (0.9, 1.4)	1.1 (0.9, 1.3)	0.055
TG (mmol/l)	< 1.7	1.9 (1.2, 2.6)	1.6 (1.2, 2.4)	**0.017**
CRP (mg/l)	< 10.0	5.0 (1.0, 9.0)	4.0 (2.0, 8.0)	0.329
Uremic toxins		*n* = 55	*n* = 55	
Total IxS (mg/l)	0.53	4.47 (1.90, 8.47)	3.96 (1.55, 10.27)	0.560
Free IxS (mg/l)	ND	0.10 (0.05, 0.29)	0.09 (0.03, 0.27)	0.131
Total *p*CS (mg/l)	1.90	5.77 (3.02, 9.84)	5.69 (2.86, 10.37)	0.597
Free *p*CS (mg/l)	0.08	0.14 (0.06, 0.25)	0.14 (0.06, 0.30)	0.267
Total *p*CG (mg/l)	–	0.09 (0.03, 0.23)	0.11 (0.03, 0.26)	0.199
Free *p*CG (mg/l)	–	0.09 (0.02, 0.18)	0.09 (0.02, 0.20)	0.506
Total IAA (mg/l)	0.50	0.70 (0.49, 1.55)	0.80 (0.50, 1.33)	0.855
Free IAA (mg/l)	–	0.13 (0.09, 0.27)	0.12 (0.08, 0.25)	0.913

Abbreviations: GFR = glomerular filtration rate, LDL = low-density cholesterol, HDL = high-density cholesterol, TG = triglycerides, CRP = C-reactive protein, ND = not detectable; IxS = indoxyl sulfate, *p*CS = *p*-cresyl sulfate, *p*CG = *p*-cresyl glucuronide, IAA = indole-3-acetic acid. Statistical tests: Wilcoxon tests,*paired *t*-tests. Bold if $p < 0.05$.

Dietary pattern studies show that whole foods focusing on a prudent diet rich in fish, poultry, fruit, vegetables and legumes showed no association with albuminuria, while GFR remained unchanged compared with those consuming a more Westernised diet rich in processed foods, sugar and salt, resulting in microalbuminuria and a decline in the glomerular filtration rate (GFR).[14] Similarly, the current study also showed a stable GFR by following simplified dietary advice. In addition, there was an improvement in other nutrition outcomes such as anthropometry, dietary intake and lipid values, while uremic toxins also remained stable.

The usefulness of the infographic reported by the participants may explain why the dietary adherence was high; this is much higher than reported in other studies, although this may be owing to the shorter duration of the present study. It could also be owing to the individual counselling the participants received at the start of the study. Studies have shown that patients with CKD have an adherence of 70% with intensive counselling compared with a 48% adherence with standard counselling.[33] This shows that more intensive counselling has a positive effect on dietary adherence. The improvement in the adherence in this study may therefore relate to the simplified nature of the dietary education allowing more variety, as well as the individual counselling participants received. However, in resource-limited settings, individual counselling is not always available. The simplified infographic may still have some benefits in this instance, as it is easy to follow.

There was a significant decline in protein intake in the four-week period, from 1 g to 0. 7 g/kg of ideal bodyweight. This is within the KDOQI recommended guidelines of 0.6–0.8 g in pre-dialysis patients.[8] However, this guideline has recently been revised and the current recommendation is 0.55–0.6 g/kg per day.[11] Low-protein diets reduce the progression of CKD.[4] The six tips diet intervention study used simplified

Table 5: Clinical changes between Baseline and Week 4

Clinical Factor		Baseline Median (IQR) *n* = 55	Week 4 Median (IQR) *n* = 55	*p*-value
Systolic blood pressure (mmHg)		141.0 (130.0, 159.0)	142.0 (128.3, 168.3)	*0.336
Diastolic blood pressure (mmHg)		79.0 (70.0, 89.0)	80.0 (72.0, 92.8)	*0.205
		Baseline *n* (%) *n* = 59	Week 4 *n* (%) *n* = 59	*p*-value
Oedema	None	35 (59.3)	37 (62.7)	**0.008**
	Mild	14 (23.7)	18 (30.5)	
	Moderate	7 (11.9)	3 (5.1)	
	Severe	3 (5.1)	1 (1.7)	

Statistical tests: *Wilcoxon and Mcnemar tests. Bold if $p < 0.05$.

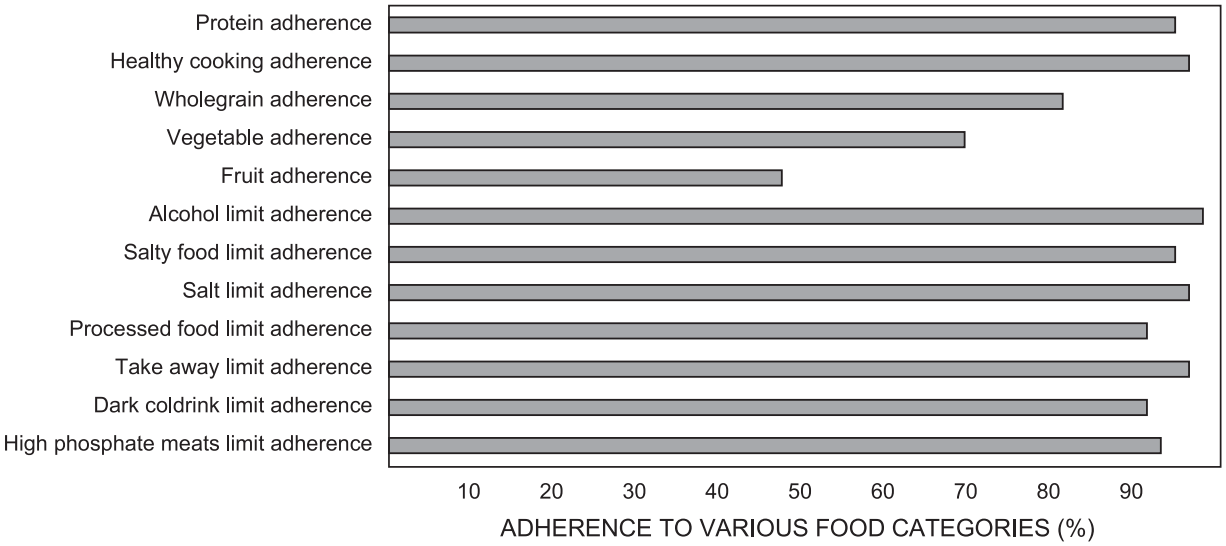

Figure 2: Adherence to various food categories (%).

written dietary suggestions (6TD) versus a standard low-protein diet (LPD) to improve dietary adherence in CKD patients over six months with follow-up at one, three and six months.[32] They showed a significant reduction in protein intake after three and six months in the 6TD group, with a reduction in serum urea only at six months in the 6TD group. This could explain why in the present study no difference in serum urea levels was observed after four weeks. The stabilising of kidney function in the present study is similar to the findings of Morales *et al*.,[34] who found no significant difference in GFR in patients on a weight-loss diet despite losing weight, whereas it declined by 8% in the control group.

A meta-analysis on the effect of weight-loss interventions on kidney outcomes in non-surgical weight-loss patients suggests that weight loss does not seem to affect GFR.[35] Although weight loss was not one of the goals of this present study, there was a significant although small reduction in the mean weight, BMI and waist circumference in participants, and most participants lost weight. Although participants were not advised on a specific energy allowance, there was a significant reduction in energy intake and all other macronutrients, which may explain the weight reduction. The weight loss is beneficial especially in this group where overweight and obesity prevalence was very high. The prevalence of obesity in this population has been reported[36,37] and has been associated with negative outcomes.[5] Weight should be monitored over a longer duration to see if the effect of weight loss will be sustained. Since malnutrition has commonly been reported in the CKD population,[38] caution should be advised in undernourished patients not to reduce overall energy intake drastically while following simplified dietary advice to prevent further weight loss. Reassuringly, in the current study the underweight participants did not lose weight by following the simplified guidelines.

The present study had a reduction in all fats, carbohydrates and sugar intake from Baseline to Week 4, which may have resulted in the significant effects on lipid values. Other studies do not report on all the dietary analyses from baseline to the intervention period, making comparisons difficult. Although the effect of saturated fat increasing low-density lipoprotein (LDL) has mainly been studied, the results are ambiguous. In a review comparing the relationship of sugar and saturated fat's effect on cardiovascular disease, it was shown that diets should focus on the elimination of refined sugar, rather than advising on reducing saturated fat to reduce cardiovascular disease risk.[39] A high sugar intake increases uric acid and insulin resistance. This increases the conversion of glucose to fructose through the polyol pathway; this pathway has been implicated as contributing to CKD progression.[40] Nonetheless, total fat and favouring plant-based unsaturated fat should still be important components of CKD dietary advice.

As expected, the concentrations of the uremic toxins were higher than the normal ranges for healthy individuals.[41] However, there were no significant differences in uremic toxins concentrations from Baseline to Week 4. This finding may in itself be a positive finding as the uremic toxins stabilised and did not increase. Although the diet changed significantly in most nutrients, the fibre intake was marginally reduced, which may have influenced this result. Fibre is important to maintain a healthy gut microbiome, enhancing saccharolytic bacteria and reducing proteolytic bacteria, which are mainly responsible for the production of the precursors of uremic toxins.[42] Although participants were advised to increase wholegrains, fruits and vegetables, the fibre intake did not increase. This may relate to the overall reduction in energy between baseline and Week 4. The fruit and vegetable intake categories were adhered to by fewer participants in the present study according to the adherence score sheet, with fruit intake adherence being the lowest. Socioeconomic status may have contributed to low fruit and vegetable intake, because half of the participants were unemployed, and most were in the low-income range. Low fruit and vegetable intake has been found in socioeconomically disadvantaged communities in South Africa.[43] In addition, it was reported that a third of South Africans consume two or fewer portions of fruit and vegetable per day.[44] Participants may also have been hesitant to increase their fruit and vegetable intake owing to potassium limitations advised on the traditional CKD diet in the past.

While dietary protein intake dropped significantly in the present study there was only a trend for a decrease in levels of total and free IxS. Other studies have shown a reduction in IxS levels on a very low-protein diet of 0.3 mg/kg supplemented with keto-analogues,[45] compared with the present study which was at 0.7 g/kg. Guida *et al*.[20] reported an increasing trend in *p*CS over a one-month period in their control group (CKD 3–4)

compared with their intervention group taking a synbiotic in haemodialysis patients, in which *p*CS was significantly reduced. It seems that dietary supplements such as prebiotics, probiotics or synbiotics may be necessary to reduce uremic toxins significantly, whereas the diet seems to stabilise it. A cross-sectional dietary pattern study evaluating plant-based diet quality with uremic toxins and gut microbiota in haemodialysis patients showed that the quality of the diet, particularly plant-based foods, either suppressed or promoted certain microbes, which in turn links to the concentrations of uremic toxins.[46] Ultimately the quality of the diet affects the generation of gut-derived uremic toxins.[46]

Limitations of the study

This study did not have a control group because the study represented the baseline dietary education run-in period before the main trial. However, participants were compared with their baseline values before and after the simplified dietary advice was given, hence serving as their own controls. The assessment of fluid status is a subjective measure, and this may have impacted on the accuracy of the adjusted bodyweight. The dietitian was, however, standardised in these measurements, thereby minimising error. This study was also of a short duration of four weeks and did not impact on variables that need a longer time to change, such as kidney function. Highly accurate information can be obtained with an QFFQ; however, methodological flaws remain.[47] The adherence score sheet revealed high adherence in the short term; this also aligns with what was reported on the QFFQ, but there may be under-reporting involved with both the QFFQ and the adherence score sheet.

Recommendations

Randomised controlled trials investigating the effect of simplified dietary advice using a longer study period should be performed in CKD pre-dialysis patients. Dietetic counselling and education should be offered to all pre-dialysis CKD patients, rather using simplified advice with some graphics to explain the diet, focusing on the whole diet. A concerted effort to increase dietary fibre intake should be considered in future intervention studies to at least recommended levels, possibly by providing supermarket vouchers to purchase fruit and vegetables for those unable to afford these. Encouraging vegetable gardens may also be a solution. This would need to be considered at government level where policies are put in place to uplift all communities, not only specific to the CKD population.

Conclusion

In conclusion, the simplified dietary advice and counselling by the dietitian suggest favourable effects on many nutritional outcomes, including BMI, waist circumference, oedema, MUAC, dietary variables, serum cholesterol and triglycerides. Kidney function and uremic levels were stabilised over the four-week period. Diet adherence was high, allowing participants to improve their food choices. The dietitian is an integral part of the multidisciplinary team caring for CKD patients. This study emphasises the important and feasible role of simplified nutrition education in improving the nutritional status of CKD participants, especially in resource-limited settings.

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Appendix A

Question	Criteria for 1 point
1. Do you follow your protein allowance daily portions or with each main meal?	Yes
2. How many high-phosphate meats do you eat in a day, i.e. eggs, liver, kidney, cheese?	1
3. How many dark cold drinks do you consume in day?	< 1
4. How many takeaway foods do you consume in a week? E.g. burgers, chips, fried chicken	1
5. How many burgers, polonies, sausages, viennas, crumbed boxed items, packets of soups do you eat in a week?	< 2
6. How many pieces of fruit do you eat in a day?	2–4
7. How many vegetables do you eat in a day?	2–4
8. How many wholegrain foods do you eat in a day? E.g. wholewheat or brown bread or crackers, oats, all-bran, any other high-fibre cereal, wholewheat pasta	> 2
9. Do you add salt to your cooking (more than ¼ tsp per serving) or add at the table?	No
10. How many other salty foods do you eat in a day, e.g. salted chips, popcorn, packets of soups, sauces, biltong, readymade gravies	> 1
11. How many servings of alcohol do you have in a day?	< 1
12. Do you steam, grill, boil, braise your foods daily?	Yes

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