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Partial Replacement Of Animal Protein by Soy Protein In The Diet Of Patients With Chronic Kidney Disease And its Positive Effect On Metabolic Acidosis

Research Article

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Abstract

Introduction: The diet has a strong influence on the formation of acidic load in the metabolism of patients with chronic kidney disease (CKD).
The aim of the study was to evaluate changes on parameters of acidosis in patients with CKD, after one week of partial replacement of dietary animal protein with plant protein (soybean).
Materials and Methods: Twenty-eight patients with CKD were selected for this experimental study. A nutritional intervention was carried out which consisted of including textured soy protein (TSP) in one of the main meals of the day for one week. The potential renal acid load (PRAL), (Remer, Manz., 1995), of the diet was calculated before and during the intervention. Anthropometric data and blood and urinary parameters of metabolic acidosis were taken before and after the intervention. Comparisons between pre- and post-intervention time-points were made by non-parametric Wilcoxon test.
Results: Twenty-eight patients of both genders participated in the study. There was a decrease in PRAL during intervention (median 37.9 vs 25.1mEq/d) and a significant increase in BIC (median 21.3 vs 23.5 mEq/L) and blood pH (7.29 vs 7.31), as well as changes in urinary pH (from Δ 0.21 X to Δ of 0.35) after one week of this changed diet. Most patients (67%) left the metabolic acidosis state, increasing on average 2.2 mEq/L in serum BIC.
Conclusions: In patients at CKD, the partial replacement of dietary animal protein with TSP for one week decrease the dietary acid load and improve metabolic acidosis parameters, even within this short time.

Keywords: Nutrition; Cronic Kidney Disease; Metabolic Acidosis; Soy Protein; Intervention.

Introduction

The acid-base balance in the intracorporeal environment is altered in chronic kidney disease (CKD) [1]. Such imbalance occurs through adaptive mechanisms that directly affect two main pathways of homeostasis: aminogenesis and bicarbonate regeneration, pathways for neutralizing H^+ ions [2, 3].

Due to this change, patients with CKD tend to accumulate acid load, a condition called metabolic acidosis [4] and which is present in 2.3 to 13% of patients in stage 3 of CKD and in 19 to 37% of those in stage 4 [5, 6].

Recent studies have suggested that patients might present acid retention in tissue interstitium that precedes the diagnosis of metabolic acidosis, called subclinical metabolic acidosis [7, 10].

Metabolic acidosis is diagnosed by low sérum bicarbonate (BIC) levels, which are directly associated with the activation of the ubiquitin-proteasome system [11, 12] and caspase-3 [13] that are the initial stimuli for cleavage of muscle proteins and their consequent degradationc [14]. Another important consequence of metabolic acidosis is the progression of kidney disease independent of CKD stage and other clinical, demographic, and socioeconomic factors [15].

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Acidosis regulation starts in the intestine with the excretion of alkali from pancreatic secretion, depending on the acidic dietary load [16]. The acidification or alkalinization depends on the amount of protein and micronutrients present in foods. Some amino acids, mostly from animal proteins, are classified as acidic because their metabolism generates hydrochloric acid (lysine, arginine and histidine) or sulfuric acid (cysteine and methionine). Plant proteins and fruits and vegetables are considered alkaline because they consume H^+ ions and produce citrate and malate [1].

Studies have investigated the association of metabolic acidosis with the potential acid load from the diet in patients with CKD. Ikzler et al. (2016) [17] reported a relationship between decrease in PRAL and improvement of metabolic acidosis.

Soy has a unique nutritional profile of amino acids, which differs from animal protein, providing a percentage of 30-40% protein. Its composition of micronutrients, specifically in the metabolism of phosphorus levels, which is present in soy in the form of phytate, which is less bioavailable to the body, directly affects the PRAL of the diet, making it less acidic [18-21].

The aim of this study was to evaluate changes in diet composition, on blood and urinary parameters of acidosis in patients with CKD, after one week of partial replacement of dietary animal protein with plant protein (soybean).

Methods

Overview of Study Design

The experimental study was planned in a one-week nutritional intervention. Patients treated at the Nephrology outpatient clinics, from March 2016 to February 2018, were invited to participate in the study.

Subjects

The number of patients for the study was estimated based on a pilot project, from which the sample size needed for a test with a power of 80 was calculated, considering the urinary pH variable. Patients older than 18 years diagnosed with CKD in stages 3 to 5 (K / DOQI 2012) (WHO,1998) and metabolic acidosis (serum BIC less than 22 mEq/L) [23], not treated for acidosis were invited to participate. Exclusion criteria were infectious and inflammatory diseases, patients not able to undergo anthropometric assessment or with neurological status that prevented daily measurement of acidosis and reliable food records, vegetarians or those who did not like the taste of TSP foods (based on a tasting session made at the time of study invitation).

Partial replacement of animal protein

Before the intervention, the patients were submitted to a food record, biochemical tests were performed, and anthropometry data were collected. PRAL, amount of total protein, and the proportion of dietary animal and vegetable protein were calculated. Participants were then instructed to include TS-based foods in one of the main meals of the day (lunch or dinner) for 7 days.

From the baseline data, through nutrition software, participants were informed of the amount of TPS protein (in cups and spoons) that they should consume, preserving the total average amount of protein consumed on a day, but changing the proportion of animal and vegetable protein for around 50% each.

To facilitate the patient's adherence to the study and the introduction of a new item to the dietary routine of participants, each participant received a kit that contained enough TSP for one week consumption by the whole family, a cookbook with TPS-based recipes, standard cups and spoons used to prepare the recipes, and herbs commonly used in TSP recipes (basil, marjoram, and fine herbs). The TSP was supplied in packs of 500g in the commercial form provided by the company Olvebra®. Patients were instructed to make food records (24) during the intervention days. In order to facilitate the food records, semi-structured sheets of food records were distributed with the division of periods of the day (morning, afternoon, night, dawn) and the patient was instructed on homemade measures to take the notes, for example: a full soup spoon or half american glass.

During the initial consultation, the patient was also instructed to self-measure the urinary pH of first-morning urine and last-night urine, using pH colorimetric strips (Kasvi brand commercial presentation). After 7 days, the participant delivered the food records, urine pH records, and underwent biochemical and anthropometry assessments.

Clinical, biochemical and anthropometric data

Clinical data were taken from patients' records and included age, gender, CKD stage, and medications. Biochemical examinations were performed at the General Laboratory of the Clinical Hospital and included urea, creatinine, sodium, potassium, phosphorus, venous blood gas analysis, albumin, total proteins, total calcium, and uric acid. Weight and height were measured in a previously tested and regulated scale and stadiometer, from which body mass index (BMI) was calculated for classification according to cutoff points of the World Health Organization for patients younger than 60 years [22] and of the Pan American Health Organization for patients 60 years and older [25].

Potential Renal Acid Load (PRAL)

The methodology developed by Remer and Manz (1995) [20] for the calculation of PRAL uses a formula that combines daily intake of protein, phosphorus, potassium, magnesium, and calcium and is based on average cation and anion absorption and in the urinary excretion rate of organic acids, considering the intestinal absorption rate of nutrients:

PRAL (mEq / d) = 0.49 x protein (g/d)

+ 0.037 x phosphorus (mg/d)
- 0.021 x potassium (mg/d)
- 0.026 x magnesium (mg/d)
- 0.013 x calcium (mg/d)

When PRAL is below zero, the food/diet is considered alkaline and above zero, acidic (REMER; MANZ, 1995) [20]. Dairy foods have a PRAL of zero and are considered neutral. All TSP recipes had negative PRAL. The 7-day mean PRAL was calculated for

each participant and diets classified as acidic (above 1), neutral (between -1.0 and 1), and basic (below -1).

Statistical Analysis

Sample characteristic data were reported as mean ± standard deviation. The remaining data were reported as medians, minimum, and maximum. Delta (Δ), the difference between values before and after the intervention, was used to evaluate the changes of parameters.

Comparisons between pre- and post-intervention time-points were made by non- parametric Wilcoxon tests. Graph Pad Prisma 8® was used for all analyzes and a $p < 0.05$ was considered statistically significant.

Results

A total of 296 medical records were analyzed and 45 pre-selected patients, all were invited to the study, but only twenty-eight patients, 53.5% in CKD 3 (3 individuals in 3a and 12 in 3b), 12 in CKD 4 and 1 in CKD 5,completed according to the methodology.

The average age was 56 years, ranging from 26 to 77 years and 57% were female. Most patients (67%) had hypertension and 11 (39.2%) had hypertension and diabetes. Only 1 patient did not use any medication. The interaction drug-nutrient and availability of supplements were not included in the calculations.

The average BMI was 27.1 ± 4.2, with 71% classified as overweight and the rest as eutrophic. Weight and BMI significantly decreased, but without clinical relevance, from a median of 71.95 kg (minimum of 44.7, maximum of 98.3) to 70.7kg (45.8 - 95.7) and from 27.35 kg/m^2 (19.6 - 36.4) to 27.15 kg/m^2 (19.9 - 34.7), respectively.

At baseline, regarding energy intake, 23 patients were within the recommended range, 4 below, and 1 above (from 20 to 35 kcal/kg/day). Energy intake did not change significantly. However, the values of carbohydrate (CHO) and plant protein (PTN) were significantly higher. Almost all patients had a protein intake above the recommended for conservative treatment of CKD, with average 1.6 ± 0.6 g protein/kg body weight, except for 1 patient, who had an average intake of 0.7 g/kg of body weight. In 27 patients the intake of animal protein was higher than plant protein, with average of 83.8 ± 10.5%. Only 1 patient had animal/plant protein intake rate of 1:1.

The qualitative evaluation of the diets showed that all patients had consumption of processed foods and animal proteins, except dairy, at least twice a day. The consumption of milk and dairy products appeared in 35.7% of the sample. Legumes appeared in 82.14% of patients once a day. Fruit consumption was verified in only 17.8% of the study participants, once a day and of vegetables in 96.4%, also once a day.

During the intervention, the quality of the diet changed little in relation to the consumption of processed foods and fruits. Qualitative consumption of greens and vegetables showed an increase in the frequency of consumption, with 25% of patients consuming this variety twice a day and the consumption of milk and dairy products during the intervention was once a week in 12 patients.

Based on the PRAL, 92.8% of participants had an acidic diet, with an average of 40.3 ± 26.5; 1 patient had a basic diet and 1 patient had a neutral diet.

After one week, the PRAL value was significantly lower, with an average decrease of 15.2 mEq/day. A decrease of 28.3 mEq/day was observed in 67.8% and in the remaining patients an increase of 12 mEq/day was found. The highest decrease in PRAL was from 126 to 51 mEq/day.

For a better analysis of the change that occurred in the intervention, Table 2 shows the difference in nutritional composition between TSP and the main protein sources reported on the patients' usual days.

Magnesium increased significantly, increasing the basic potential of the diet, according to PRAL. The average level of metabolic acidosis markers, serum BIC and pCO_2, significantly increased after the intervention. Serum BIC decreased in 3 participants and did not vary in 2 of them.

Table 1. Nutritional composition of diets before and during the intervention.

	Before intervention	During intervention	Delta	p valor
Kilocalorie/day	1719.39 (571.38 — 2789.9)	1778.20 (785.98—2781.61)	13.1	
Kilocalorie/kg weight /day	23.1 (12.7—51.8)	25(12.3—43.3)	0.27	
Carbohydrate* (g)	198.18 (78.79 — 335.82)	238.31 (104.88—334.7)	28.6	0.048
Total Proteins (g)	118.69 (35.04 — 277.72)	93.8(49.33—161.42)	-18.1	
Animal Protein (%)*	88.5 (50 — 96.4)	44 (24.2—57.9)	-41	0.03
Plant Protein (%)*	11.4 (3.58 — 50)	55.6 (43.6—75.8)	40.7	0.0002
Protein/kg body weight /day (g)	1.65 (0.7 — 3.5)	1.4(0.6—2.5)	-0.21	
Fat (%)	38.79 (11.74 — 78)	44.33(7.81—157.01)	8.3	
PRAL*	37.99 (-4.39 — 126.9)	25.1 (-6.1—51.3)	-15.2	0.033
P/PTN	10.78 (4.20 — 17.38)	12.24 (3.14—18.12)	0.23	

Data are reported as medians, minimum, and maximum values. *p<0.05. PRAL: potential renal acid load, P/PTN: phosphorus/protein ratio. Delta: Difference between before and during intervention.

The mean increase in serum BIC was 2.2 mEq/L. A median increase of 3 mEq/L occurred in 25 participants, of whom 18 (64.2%) were without metabolic acidosis.

Participants with the lowest PRAL value after the intervention were 57% of the sample and included the patients who left the metabolic acidosis state. Eleven patients did not show pH changes and 14 patients presented increased pH (by 1 unit in 11 and 2 units in 3). Only 3 patients had a pH decreased by 1 unit, and these were the same patients who increased dietary PRAL.

Discussion

The inclusion of TSP in one of the daily meals of patients with CKD may have contributed to changes in the diet, such as the adjustment of the animal/vegetable protein ratio, decreasing the PRAL influencing the improvement in the metabolic markers of acidosis.

Energy consumption was 23.9 kcal/kg of current weight, which was below the recommendation for CKD patients of 30 to 35 kcal/kg of body weight/day [23].

Regarding the manufactured foods consumption in the diet the analysis showed that it was the same before and during the intervention, which can be related to its consumption always in the intermediate snacks (afternoon snack), thus, we can consider that

Table 2. Centesimal composition data of textured soy protein and most frequent protein sources on the usual day of the evaluated group.

Protein (100g)	Kcal	Protein g	Phosphorus mg	Potassium mg	Magnesium mg	Cálcium mg	PRAL	
							(mEq/d)	P/PTN
Textured Soy Protein	449.3	33.3	572	740.5	241	232	12.6	17.1
Raw Beef	204.9	26.7	164	256	17	4	13.2	6.1
Raw Pork	272	28.9	229	366	25	34	13.8	7.9
Raw Chicken	150.5	32	295	387	18	5	17.9	9.2
Raw Egg	141	15.3	284	139	11	49	14.1	18.5
Raw Fish	117.8	17.4	278.1	221.4	28.3	47	12.8	15.9
Canned Sardines	208	24.6	490	397	39	382	15.8	19.92

Data in absolute values per 100g of food. Kcal: Kilocalorie. PRAL: potential renal acid load, P/PTN: phosphorus/protein ratio.

Table 3. Micronutrients used in the PRAL calculation before and during the intervention.

	Before intervention	During intervention	Delta
Total Protein (g)	118.69 (35.04 — 277.72)	93.8(49.33—161.42)	-18.1
Phosphorus (mg/d)	1271.3 (219—2228)	1089.2 (225.1— 2318.2)	-185.1
Potassium (mg/d)	2424.4 (542 —4355.2)	2675.2 (421.3 — 5494.1)	-250.8
Magnesium (mg/d)* (p=0,019)	198.9 (67.7—460.4)	339.6 (51.5 — 629.7)	104.07
Calcium (mg/d)	485.3 (66.6 — 11256.8)	608.2 (255.7 — 1637.8)	103.8
P/PTN	10.78 (4.20 —17.38)	12.24 (3.14 —18.12)	0.23

Data are reported as medians, minimum, and maximum values. *p<0.05. PRAL: Potential renal acid load, P/PTN: phosphorus/protein ratio. Delta: Difference between before and during intervention.

Table 4. Biochemical parameters before and after the intervention.

	Pre-intervention	Post-intervention	Delta	Reference values
Urea	77.5 (29—176)	74 (20—160)	-4.3	10 to 50 mg/dL
Creatinine	2.36 (1.34—5.2)	2.31 (1.52—5.35)	-2.7	0.7 to 1.5 mg/dL
Sodium	138.5 (126.9—1.6)	138.05 (124.7—143.)	-0.5	135 to 145 mmol/dL
Phosphorus	3.75 (2.4—5.3)	3.8 (2.2—9.6)	0	2.5 a 5.6 mg/dL
Potassium	5 (4—5.9)	5 (3.5—5.9)	0	3.5 to 5 mmol/L
Bicarbonate* (p=0,029)	21.3 (17.6—22.5)	23.15 (17.4—28)	2.2	22 to 26 mEq/L
pCO2* (p= 0,036)	45.45 (33.7—53.8)	46.35 (35.6—57.2)	2.5	35 to 45 mmHg
pH* (blood) (p=0,034)	7.29 (7.25—7.39)	7.31 (7.25—7.39)	0	7.35 to 7.45
pO_2	22.25 (15.3—96.5)	20.05 (13.5—100.6)	-2.6	>60 mmHg
Albumin	4.35 (3—4.7)	4.25 (3.4—4.6)	0	3.5 to 4.8 g/dL
Total Proteins	7 (6.3—8.1)	7 (5.9—20.4)	-0.4	6.5 to 8.1 g/dL
Total Calcium	9.5 (8.3 —11)	9.65 (8.2—10.8)	0	8.4 to 10.5 mg/dl
Uric Acid	7.2 (3.9—17.1)	7.14 (3.8—10.7)	-0.6	2 to 5 mg/dL
Proteinuria	525.2 (27.5—618)	670.8 (37.5—6038.3)	217	>300 mg/day

Data are reported as medians, minimum, and maximum values. *p<0.05. PRAL: Potential renal acid load, P/PTN: phosphorus/protein ratio. Delta: Difference between before and after intervention.

the influence of processed foods on the value of PRAL was the same before and during the intervention.

This consumption pattern reflected in the predominantly acidic PRAL value of the study patients. SCIALLA; ANDERSON (2013) [26] showed that contemporary diets are high in industrialized and protein-based products and low in fruits and vegetables, characteristics of an acidic diet. SEBASTIAN et al., (2002) [27] estimated that the acid burden of an ancestral diet averaged -88 mEq per day compared to an average of +48 mEq per day of the current American diet, very close to the value found in our study. Half of the patients was eutrophic according to BMI and 42.8% was overweight. However, due to the short intervention time, the clinical relevance of weight change cannot be assured.

Many intervention studies with the pre-dialytic CKD population propose BIC supplementation for metabolic acidosis control [28-30]. However, disadvantages and adverse effects of such supplementation are a challenge for patient compliance: BIC tablets are associated with impeding a proper control of hypertension, causing water overload [31], abdominal discomfort and edema resulting from the generation of carbon dioxide in the intestine are also reported [32].

In addition, the nutritional interventions for CKD conservative treatment have two objectives: control the underlying causes of CKD and control disease progression and its side effects. TSP is a food that has been widely studied in patients with CKD because it meets the

two main goals of CKD conservative treatment [21, 33, 34]. The strategy to use soy protein can decrease animal proteins ingestion, while maintaining the protein level with less phosphorus content [35, 36].

The data showed that an animal/vegetable ratio close to 50/50 was achieved with the intervention, with no significant change in the total amount of protein consumed, which was reflected in the average PRAL decrease in 57% of the sample.

CUPISTI et al., (2017) [37] evaluated diets of CKD patients that were in accordance to guidelines (0.8 g protein/kg a day) and found that the values of vegetarian and vegan diets were significantly more alkaline that regular diets. The average PRAL value for the vegetarian diet was - 26.9 mEq/day compared to an average + 3 mEq/day for the usual diet. Similar results were found by STRÖHLE; HAHN; SEBASTIAN (2010) [38] who confirmed that PRAL becomes progressively more positive, i.e. more acidic, as the ratio of plant protein/animal protein becomes disproportionate elevated. In addition, our results showed that magnesium, which reflects the formation of a basic load, increased significantly with inclusion of TSP in meals, which may explain the decrease in PRAL during the intervention.

Comparing TPS with animal proteins, we can see that the micronutrients that reflect the negative charge, (REMER; MANZ, 1995) [20] potassium, magnesium and calcium, present higher values in TPS than in protein of animal origin in natura. The factor that may explain the decrease in PRAL during the intervention is the micronutrient magnesium, which increased significantly with the inclusion of TPS in a meal.

Regarding the micronutrient phosphorus, it is known that its value is high in animal protein, and also in the phosphorus / protein ratio. The consumption of proteins with these characteristics is not recommended for patients with CKD, which is to offer foods with a low value for this reason [35, 36]. In soy, phosphorus is in the form of phytate, making it less bioavailable. This condition is not corrected by the PRAL calculation methodology used by REMER; MANZ (1995) [20].

Significant increases were seen in the BIC and pH values. It is well known that reducing animal protein ingestion can lead to benefits by reducing the acid load from animal protein metabolism [39, 40]. However, our results were consistent with the findings of SCIALLA et al., (2011) [41] in which serum BIC was more strongly associated with dietary acid load than with protein intake alone, probably because the protein level per kg of weight was maintained and only the proportions between animal and plant protein were adjusted, which improved markers of metabolic acidosis.

In our study, the mean urinary pH increased, becoming more alkaline after the intervention week. Similar results were found in a study by WELCH et al., (2008) [42] that showed that a more alkaline diet was associated with a more alkaline urinary pH before and after adjustments for age, BMI, physical activity, and smoking. Markers of kidney function, like urea and creatinine, were not altered by the intervention, which can be explained by the short study time.

Potassium also did not change significantly. The inclusion of TSP in the diet a could be an option for treatment hyperkalemia as it did not alter the serum phosphorus. To alkalinize the diet, it is recommended to increased consumption of fruit and vegetables [20, 41]. However, there is an important barrier, since such foods are the main sources of potassium [41]. In previous studies that linked vegetarian diets to CKD, consumption of soy, grains, such as nuts, is encouraged as a source of vegetable protein with low amounts of potassium [43].

Since this is the first study to use TSP to alkalize the diet, some limitations were encountered. First, the methodology for calculating PRAL depends on dietary records and urinary pH was also based on the subjective evaluation of the color scale by participants thus is

subjected to bias. The fact of not having a control group and the short intervention time, may have limited the observation of other effects.

Conclusion

Our study showed that the inclusion of TSP in the daily diet may have contributed to the decrease of dietary PRAL and increase of the proportion of protein from plant sources, without increasing the total daily protein intake. These changes may have positively affected the metabolic acidosis markers, even in this short period of time of the study. Future investigations require PRAL corrections, for the bioavailability of phosphate sources, which may better clarify the relationship between dietary intake and metabolic acidosis markers in this group of patients.

Improving studies with PRAAL can can consolidate protocols of dietary interventions focused on the metabolic acidosis control and other beneficial effects on the clinical condition of this group of patients.

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