Efeitos a curto prazo da dieta com proteína da soja em pacientes com glomerulopatias proteinúricas

Short-term effects of soy protein diet in patients with proteinuric glomerulopathies

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Submitted on: 11/20/2010
Accepted on: 03/24/2011

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The present study was conducted at the Glomerulopathies Section of the UNIFESP.

Authors declare no conflict of interest.

ABSTRACT

Introduction: It has been suggested that soy protein can slow renal disease progression by decreasing plasma cholesterol and proteinuria in patients with nephropathies. This study was designed to evaluate the effect of soy protein on proteinuria and dyslipidemia, in patients with proteinuric glomerulopathies. **Patients and Methods:** Patients were divided into three groups: Control Group (n = 9) received diet with 0.8 g/kg/day of animal protein; Study Group 1 (n = 9), 0.8 g/kg/day of soy protein; and Group 2 (n = 9), 0.8 g/kg/day of soy protein plus fibers. The study period corresponded to eight weeks. During the baseline period and by the end of the study, patients were submitted to laboratorial and anthropometric evaluation. **Results:** There was no statistically significant difference between baseline and post-diet periods among the three groups in anthropometric parameters or body composition, neither in proteinuria levels (Control: 0.7 ± 0.6 *versus* 0.8 ± 0.6; Group 1: 2.0 ± 1.7 *versus* 1.9 ± 1.8; Group 2: 2.0 ± 1.4 *versus* 2.1 ± 2.0). However, a slight decrease in triglycerides (244.8 ± 275.9 *versus* 200.5 ± 34.0), total (234.0 ± 59.4 *versus* 181.2 ± 110.3) and LDL (136.0 ± 59.1 *versus* 104.1 ± 39.4) cholesterol in Group 1 was observed, although not significant. **Conclusion:** We have not observed beneficial effects when using soy protein instead of animal protein with the aim of attenuating proteinuria and hyperlipidemia, but we have shown that soy protein has not caused deleterious changes in body composition, ensuring an adequate nutritional state.

Keywords: glomerulonephritis, soy foods, proteinuria, diet.

RESUMO

Introdução: Há indícios de que a proteína da soja poderia contribuir para reduzir a velocidade de progressão da doença renal, diminuindo colesterol sérico e proteinúria em pacientes com nefropatias. Este estudo foi desenvolvido para avaliar o efeito da dieta com proteína da soja sobre proteinúria e dislipidemia, em pacientes com glomerulopatias proteinúricas. **Pacientes e Métodos:** Os pacientes foram divididos em três grupos: o Grupo Controle (n = 9) recebeu dieta com 0,8 g/kg/dia de proteína animal; o Grupo de Estudo 1 (n = 9) recebeu dieta com 0,8 g/kg/dia de proteína da soja e o Grupo 2 (n = 9), dieta com 0,8 g/kg/dia de proteína da soja mais fibras. O período de estudo foi de oito semanas. Durante o período basal e no final do estudo, os pacientes foram submetidos à avaliação laboratorial e antropométrica. **Resultados:** Não foram observadas diferenças estatisticamente significantes entre os períodos pré e pós-intervenção em nenhum dos grupos estudados, nos parâmetros antropométricos ou na composição corporal entre os três grupos, nem nos níveis de proteinúria (Controle: 0.7 ± 0.6 versus 0.8 ± 0.6; Grupo 1: 2.0 ± 1.7 versus 1.9 ± 1.8; Grupo 2: 2.0 ± 1.4 versus 2.1 ± 2.0). No entanto, observou-se discreta diminuição nos níveis triglicérides (244.8+-275.9 versus 200.5+-34.0), colesterol total (234.0+-59.4 versus 181.2+-110.3) e LDL (136.0+-59.1 versus 104.1+-39.4) no Grupo 1, embora sem atingir significância estatística. **Conclusão:** Não foram detectados efeitos benéficos com a substituição da proteína animal pela proteína da soja em relação aos objetivos de reduzir proteinúria e hiperlipidemia; porém, constatou-se que a dieta de proteína da soja não causou alterações deletérias na composição corporal, mantendo um estado nutricional adequado.

Palavras-chave: glomerulonefrite, alimentos de soja, proteinúria, dieta.

Introduction

Proteinuric glomerulopathies are chronic kidney diseases, which prognosis is particularly related to the levels of persistent urinary protein excretion. As the nephrotic condition is an extreme of the manifestations' spectrum of the glomerular diseases, associated with more severe metabolic changes, it illustrates the context in which a nutritional therapeutic approach (evaluated in the present study) could contribute to the management of proteinuric glomerulopathies.

The hallmark of nephrotic syndrome (NS) is the increased glomerular permeability to proteins, which leads to proteinuria. Homeostatic mechanisms are unable to cope with such urinary protein losses, and the resulting hypoalbuminemia frequently leads to edema.[1,2] The glomerular damage that is characteristic of NS can also result in urinary loss of lipids and other plasma proteins, including some of the apolipoproteins.[3]

Another important feature of the NS is hyperlipidemia characterized by increased plasma concentrations of very-low-density (VLDL), intermediate-density, low-density lipoproteins (LDL) and, as the disorder progresses, also by hypertriglyceridemia and decreased concentrations of high-density lipoproteins (HDL). Such lipid abnormalities may predispose to more rapid progression of the renal disease.[4] Therefore, correction of lipid abnormalities or their prevention when possible, in patients with nephrotic syndrome, could be a protective factor against its progression.

It is noteworthy that persistent proteinuria is one of the most relevant prognostic factors determining progression of glomerular diseases. Therefore, reduction of proteinuria and maintenance of serum proteins levels are important goals in the treatment of NS, as the protein traffic decrease would protect the kidney from the pro inflammatory consequences of the protein tubular overload determined by protein reabsorption.[5,6]

Considering all these factors, it has been proven that individuals with NS and proteinuria need a special diet, and protein is the nutrient that deserves a particular emphasis in the nutritional management of these patients.[7]

There is abundant evidence that changing the amount of diet protein exerts a profound influence on renal function and course of renal disease. High protein intake has long been known to aggravate renal injury and accelerate the progression of chronic kidney disease, whereas low protein intake produces the opposite effects.[4,8-10]

According to Azadbakht *et al*.,[11] an usual diet prescribed for NS and proteinuria has 0.8 g/kg of body weight, per day, with 70% of animal protein in its composition. In addition, there is evidence that changing the source or type of dietary protein may have a beneficial effect on renal function and renal disease.[8,12-14] The protein of animal origin, for example, seems to exert a deleterious effect on renal function.[15] This is supported by nutritional intervention studies in animals and humans, showing that the replacement of animal protein with vegetable protein in the diet reduces proteinuria and preserves renal function.[3,8,12-14]

Meal studies indicate that soy protein does not alter post-prandial renal blood flow or glomerular filtration rates, whereas the animal one significantly increases these indexes. Long-term intakes of soy-protein diets were associated with lower renal blood flow, glomerular filtration rate, and fractional clearance of albumin than those of animal-protein diets. Of interest in this area, vegan and lactoovovegetarian subjects without renal disease had lower glomerular filtration rates and less urinary albumin excretion than omnivores.[16]

Long-term studies also indicate that soy-protein intake protects kidneys, whereas excessive animal-protein intake may be harmful to kidneys. In animal models of kidney diseases, rats fed with soy protein had much slower progression of renal disease than did rats fed with casein. Human studies have not been optimally controlled, but they suggest that substituting soy protein for animal protein decreases proteinuria in individuals with chronic glomerular disease.[16]

Soy protein is a vegetable protein that sustains adequate growth rate in rats and infants. It has an amino acid profile that meets the requirement for each one in humans and rats to growth and maintenance. Therefore, soy protein is considered to be a complete protein, with a protein digestibility-corrected amino acid score of 1; it also has a high arginine/lysine ratio, which is associated with lower insulin secretion compared to protein of animal origin. Afterwards, soy protein contains isoflavones, which act as weak estrogens, inhibiting tyrosine kinase-dependent signal transduction processes and functioning as cellular antioxidants.[3] Anderson *et al*.,[17] in a meta-analysis, showed that the consumption of soy protein significantly decreased serum concentrations of total cholesterol, LDL cholesterol, and triglycerides (TG) with a larger decrease in subjects with moderate or severe hypercholesterolemia.

Considering recent evidence related to the beneficial effects of soy protein on proteinuria reduction, as

well as on hyperlipidemia correction, more detailed studies are necessary to better evaluate such improving effects in patients with the NS. An additional application of the soy protein prescription may be proteinuric glomerular diseases in which antiproteinuric drugs could not be administered.

Therefore, the aim of the present study was to evaluate whether soy protein decreases proteinuria and hyperlipidemia in patients with proteinuric glomerulonephritis in short-term.

Patients and methods

Subjects

We have evaluated 27 adult patients (23 of them were female), with proteinuria and normal or slightly altered renal function, from the Glomerulopathy Section of Universidade Federal de São Paulo – Escola Paulista de Medicina, in Brazil.

The inclusion criteria involved the diagnosis of: primary glomerulopathy, and serum creatinine < 2.0 mg/dL (and creatinine clearance > 50 mL/minutes) by the time of the first nutritional evaluation. The selected patients could be in the course of a treatment for proteinuric glomerulonephritis, without response, or they could initiate treatment by this dietitian approach. In the first condition, immunosuppressive drugs were interrupted when results were considered inadequate; then, two months after total drug withdrawal, the patient became eligible to participate in the present study. Nevertheless, the use of antiproteinuric medication, as angiotensin converting enzyme (ACE) inhibitors, and angiotensin receptor blockers, could be maintained during the study both by their renoprotective or antihypertensive actions. Failure of such antiproteinuric treatment was defined when, after three different proteinuria determination separated by one month interval, no decrease of proteinuria levels was observed. Besides, during this study, it was not permitted to increase the dosage of such drugs; patients should be under adequate blood pressure control by the time of inclusion in the study, but in case of uncontrolled hypertension during the study period, other drugs were utilized to control blood pressure levels.

Patients were excluded of the study if a secondary glomerulopathy was diagnosed and in the event of noncompliance (especially if related to the oriented diet).

Study protocol

A prospective, randomized, controlled, clinical study was performed. After meeting the inclusion criteria and providing the informed written consent, all patients were instructed to eat an animal protein diet (APD) during one month. At the initial period of observation, after admission to the study, patients maintained their previous treatment and were submitted to a clinical evaluation, the laboratory exams were performed (24-hour proteinuria, urinalysis, 24-hour urinary urea, creatinine clearance, hemoglobin, hematocrit, serum iron, transferrin, albumin, calcium, phosphorus, cholesterol, TG, serum and urinary potassium, sodium and phosphorus).

After this period, patients were randomly allocated to three groups. The groups were as follows: Control, APD; Group 1, vegetable protein diet (VPD) that received *Previna* (nutritional composition in Appendix A); and Group 2, VPD with fiber (VPD + F) that received *Sanavita* (nutritional composition in Appendix B).

During the period of study, after the initial phase, patients were submitted to a complete physical examination of anthropometric parameters, measures of body composition, and a food diary of three days.

Diet

The patients were carefully instructed by a skilled dietitian about the corresponding diet. The APD diet consisted on 0.8 g/kg/d of animal origin protein, patients assigned to VPD and VPD+F Groups were prescribed a 0.8 g/kg/d of vegetal origin protein diet. For all groups, energy prescription was 30 kcal/kg of ideal body weight/day, with 60% of high biological value proteins, and reposition of 1 g/day of protein for each gram of nutrient lost by the urine.

Nutritional assessment

Dietary assessment

Energy, macronutrients (protein, carbohydrate and lipids) and micronutrients (calcium, phosphorus, iron and cholesterol) intake were estimated from a three-day food diary (not at the week end), using a computer software developed at UNIFESP and at the United States of America Department of Agriculture[18] table as the nutrient data base. Protein intake was also estimated from the normalized protein equivalent of nitrogen appearance (nPNA), determined according to the formula of Sargent e Gotch,[19] using a 24-hour urinary urea excretion.

Anthropometric data and body composition

The following anthropometric parameters were evaluated: body weight and height. Body mass index (BMI) was calculated as body weight divided by squared height. The cutoff points used were as recommended by the World Health Organization.[20] Body

composition was also evaluated using bioelectrical impedance analysis (BIA), which was performed using a single frequency tetrapolar technique (800A, 50 kHz, BIA 101 Quantum, RJL Systems, Detroit, USA). The software Fluids & Nutrition (version 3.0), provided by the manufacturer, was used to estimate the body composition.

Laboratory data

The patients had blood drawn under fasting conditions. Twenty-four urine collection were obtained to measure urinary protein excretion and to evaluate glomerular filtration rate, using standard creatinine clearance corrected for the body surface area (1.73 m^2). These and the following parameters were measured on a monthly basis, and also after two months: urinary urea, phosphorus and sodium, serum creatinine, urea, albumin, cholesterol and TG, sodium and potassium, hemoglobin, hematocrit, and transferrin. Laboratory tests were performed in the Central Laboratory of the Nephrology Division of UNIFESP.

Statistical analysis

Nonparametric tests were applied. The Wilcoxon test was used to compare the results obtained after animal and soy diet (post-diet period) *versus* baseline period (pre diet) within the same group. It was used the statistical software Sigma-Stat, version 2.0. Results were shown as mean and standard deviation (X ± SD). Statistical significance was defined as $p < 0.05$.

Results

Twenty-seven patients with proteinuric glomerulopathies were evaluated, with a mean age of 46 ± 12 years-old.

Table 1 shows the means of the ingestion of calories, macronutrients (protein, lipids and carbohydrates) and micronutrients (calcium, iron, sodium and potassium) in baseline and post-diet periods in the three groups. It was observed a significant decrease in the energetic intake from the baseline to the post-diet period in the three groups (30.6 ± 6.7 *versus* 21.7 ± 6.0; 30.4 ± 5,6 *versus* 24.6 ± 4.3 and 28.8 ± 7.8 *versus* 24.9 ± 4.2 kcal/kg/d, respectively). The same behavior was observed in lipids (48.4 ± 11.2 *versus* 42.6 ± 13.5; 52.3 ± 23.1 *versus* 30.5 ± 14.6 and 43.5 ± 17.4 *versus* 26.9 ± 6.5 g/d, respectively), and proteins (1.3 ± 0.3 *versus* 1.0 ± 0.4; 1.2 ± 0.2 *versus* 1.0 ± 0.3 and 1.2 ± 0.4 *versus* 0.9 ± 0.2 g/kg/d, respectively) ingestion in the three groups. But the carbohydrate ingestion revealed a significant decrease only in the Control Group (279.7 ± 115.1 *versus*. 165.7 ± 48.5 g/d). Nevertheless, in opposition to what was observed through the food diary, when the

Table 1 Intake of calories, macronutrients and micronutrients in baseline and post-diet periods in the three groups (Control, Soy and Soy + Fibers)

Intake	Control Group (Animal protein) (n = 9)		Study Group 1 (Soy) (n = 9)		Study Group 2 (Soy + Fibers) (n = 9)	
	Pre	Post	Pre	Post	Pre	Post
Energy (kcal/d)	1,859 ± 571	1,287 ± 319*	1,753 ± 383	1,412 ± 270*	1,609 ± 315	1,412 ± 216*
Energy (kcal/kg/d)	30.6 ± 6.7	21.7 ± 6.0*	30.4 ± 5.6	24.6 ± 4.3*	28.8 ± 7.8	24.9 ± 4.2*
Protein (g/d)	77.5 ± 23.7	61.4 ± 21.7*	72.3 ± 17.4	60.1 ± 16.4*	70.5 ± 23.3	53.6 ± 14.9*
Protein (g/kg/d)	1.3 ± 0.3	1.0 ± 0.4*	1.2 ± 0.2	1.0 ± 0.3*	1.2 ± 0.4	0.9 ± 0.2*
PNA	0.9 ± 0.3	0.9 ± 0.2	0.8 ± 0.3	0.8 ± 0.1	0.7 ± 0.2	0.7 ± 0.1
Lipids (g/d)	48.4 ± 11.2	42.6 ± 13.5*	52.3 ± 23.1	30.5 ± 14.6*	43.5 ± 17.4	26.9 ± 6.5*
Carbohydrate (g/d)	279.7 ± 115.1	165.7 ± 48.5*	250.3 ± 65.1	229.7 ± 51.0	236.9 ± 58.8	243.8 ± 41.9
Iron (mg/d)	14.9 ± 5.1	9.4 ± 3.2	12.0 ± 2.9	13.5 ± 1.7	13.5 ± 4.5	15.7 ± 3.9
Calcium (mg/d)	603.2 ± 121.3	581.5 ± 115.5	756.3 ± 431.0	925.9 ± 179.0	640.4 ± 299.2	352.0 ± 128.5*
Phosphorus (mg/d)	1009.5 ± 258.9	864.7 ± 198.8	1093.2 ± 331.1	908.4 ± 199.0	1072.6 ± 317.9	1029.1 ± 254.5
Cholesterol (mg/d)	167.4 ± 61.1	155.9 ± 70.4	146.0 ± 58.7	74.2 ± 113.9*	185.2 ± 62.3	78.2 ± 93.3*

X ± SD, *$p < 0.05$ *versus* pre; PNA: equivalent of protein nitrogen appearance.

protein ingestion was evaluated by PNA, no group showed significant decrease. Considering micronutrients, a significant decrease in calcium ingestion was observed only in the Study Group 2 (640.4 ± 299.2 *versus*. 352.0 ± 128.5 mg/d). The cholesterol ingestion presented a significant decrease in the Study Groups 1 and 2 (146.0 ± 58.7 *versus*. 74.2 ± 113.9 and 185.2 ± 62.3 *versus* 78.2 ± 93.3 mg/d).

The Table 2 shows the means of the anthropometric parameters and body composition of the patients in the Control, Soy, and Soy + Fibers Groups. It was not observed any statistical difference related to the anthropometric parameters between baseline and post-diet periods in all the groups. As concerned to body composition, it was not observed any difference between muscle mass and fat mass between baseline and post-diet periods in all groups. The Study Group 2 presented a significantly lower body water value in post-diet period than in the baseline (34.4 ± 6.9 *versus* 33.3 ± 6.7 kg).

Table 3 shows the means of laboratory parameters of the three groups' patients. It was not observed any statistical difference of protein excretion levels between baseline and post-diet periods in all groups. The other laboratory parameters were not statistically different between baseline and post-diet periods, except for hemoglobin and serum urea in the Soy Group, which presented a significant decrease (14.1 ± 1.5 *versus* 13.4 ± 1.4 g/dL and 36.8 ± 13.5 *versus* 31.7 ± 15.2 mg/dL), and serum sodium that presented a significant increase (137.2 ± 2.3 *versus* 139.2 ± 1.8 mEq/L). A slight decrease of TG, total and LDL cholesterol was observed at the post-diet period *versus* baseline in the Study Group 1, although this difference has not been significant.

The Figures 1, 2, 3 and 4 show the individual values of the 24-hour proteinuria, total and LDL cholesterol and TG of the patients in the three groups, respectively, where each point represents a patient.

Discussion

We have chosen to evaluate soy diet in the present study, because it is considered a unique food, and contains several nutrients (complex carbohydrates, vegetal protein, soluble and insoluble fibers, oligosaccharides, fitochemistries – especially isoflavones, and minerals). The oligosaccharides present in soy are responsible by part of its peculiar profile, as they are not hydrolyzed in the bowel, being fermented to short chain fatty acids that inhibit the cholesterol synthesis. Besides, soy is considered one of the main sources of soluble fibers, which decrease significantly serum cholesterol and glucose, and of the insoluble fibers that contribute to the gastrointestinal function.

Different studies have shown that the use of soy protein may slow progression of chronic renal disease[8,21] by decreasing hyperfiltration and proteinuria.[22]

In the present study, aiming to evaluate the short-term effect of "soy protein", with the intention of reducing proteinuria and dyslipidemia in patients with proteinuric glomerulopathies, we compared a diet with protein of animal origin (0.8 g/kg/day, a conventional diet) to a diet with soy protein (0.8 g/kg/day).

When energetic and macronutrients ingestion was evaluated, through the food diary of three days in

Table 2 Intake of calories, macronutrients and micronutrients in baseline and post-diet periods in the three groups (Control, Soy and Soy + Fibers)

Variables	Control Group (Animal protein) (n = 9)		Study Group 1 (Soy) (n = 9)		Study Group 2 (Soy + Fibers) (n = 9)	
	Pre	Post	Pre	Post	Pre	Post
Age (years)	46.0 ± 12.1		41.8 ± 12.7		43.1 ± 15.2	
Weight (kg)	70.5 ± 18.4	69.4 ± 17.9*	60.5 ± 14.7	58.3 ± 12.1	57.8 ± 22.5	61.0 ± 11.5
BMI (kg/m²)	26.7 ± 5	26.1 ± 5.1	24.1 ± 5.7	23.1 ± 4.8	24.8 ± 3.2	24.4 ± 3.1
Body water (kg)	33.4 ± 4.5	33.1 ± 3.7	33.3 ± 6.7	33 ± 6	34.4 ± 6.9	33.3 ± 6.7*
Body water (%)	51.9 ± 5.3	52 ± 5.7	57.7 ± 7.1	57.0 ± 5	55.4 ± 7.7	54.9 ± 5.7
Fat-free mass(kg)	45.7 ± 5.9	45.1 ± 5.3	45.6 ± 9.2	45.0 ± 8.2	46.8 ± 9.4	45.5 ± 9.3
Fat-free mass (%)	70.7 ± 7.5	71.1 ± 8.1	76.3 ± 8.1	77.9 ± 6.5	75.9 ± 10.2	74.8 ± 7.4
Fat mass(kg)	19.0 ± 5.7	18.7 ± 6.3	14.8 ± 7.2	13.3 ± 5.5	15.5 ± 8	15.4 ± 5.8
Fat mass(%)	29.2 ± 7.5	28.9 ± 8.11	23.7 ± 8.1	22.1 ± 6.5	24.1 ± 10.2	24.9 ± 7.9

BMI: body mass index; X ± SD, *p < 0.05 *versus* pre.

Table 3 Comparison of laboratory data among the three groups (Control, Soy and Soy + Fibers)

Laboratory data	Control Group (Animal protein) (n = 9)		Study Group 1 (Soy) (n = 9)		Study Group 2 (Soy + Fibers) (n = 9)	
	Pre	Post	Pre	Post	Pre	Post
Hemoglobin (g/dL)[b]	13.9 ± 1.5	14.6 ± 0.8	14.1 ± 1.5	13.4 ± 1.4*	13.2 ± 1.2	13.1 ± 1.9
Hematocrit[b]	42.7 ± 4.8	44.1 ± 2.4	41.8 ± 4.5	40.1 ± 4.4	40.2 ± 3.8	40.3 ± 5.8
Sodium (g/d)[b]	139.0 ± 1.7	138.2 ± 2.6	137.2 ± 2.3	139.2 ± 1.8*	137.3 ± 2.4	138.1 ± 1.8
Potassium (mEq/d)[b]	4.4 ± 0.4	4.4 ± 0.3	4.5 ± 0.4	4.4 ± 0.1	4.4 ± 0.6	4.1 ± 0.4
Phosphorus (mEq/L)[b]	3.7 ± 0.3	3.7 ± 0.4	3.6 ± 0.5	3.8 ± 0.8	3.8 ± 0.5	3.6 ± 0.8
Albumin (g%)[b]	4.3 ± 0.3	4.3 ± 0.3	3.9 ± 0.7	3.9 ± 0.7	3.9 ± 0.7	3.9 ± 0.6
Triglycerides (mg/dL)[b]	140.0 ± 80.6	127.1 ± 67.7	244.8 ± 275.9	181.2 ± 110.3	175.3 ± 145.5	163.4 ± 104.2
Cholesterol (mg/dL)[b]	200.9 ± 30.8	202.2 ± 29.4	234.0 ± 59.4	200.5 ± 34.0	240.9 ± 79.9	236.2 ± 80.2
HDL (mg/dL)[b]	55.5 ± 11.4	54.6 ± 14.1	67.1 ± 23.0	60.0 ± 20.3	58.5 ± 17.6	57.7 ± 19.6
VLDL (mg/dL)[b]	28.0 ± 16.0	25.5 ± 13.5	31.9 ± 20.6	36.4 ± 21.8	30.5 ± 18.2	32.62 ± 20.7
LDL (mg/dL)[b]	117.3 ± 24.1	122.1 ± 25.5	136.0 ± 59.1	104.1 ± 39.4	147.8 ± 73.3	145.9 ± 71.4
Iron (mg/d)[b]	79.5 ± 12.4	89.6 ± 22.6	85.2 ± 18.3	91.7 ± 24.8	79.7 ± 13.8	70.9 ± 20.7
Transferrin (mg/dL)[b]	249.4 ± 36.6	258.4 ± 32.4	228 ± 51.7	247.0 ± 41.4	240.3 ± 40.6	242.1 ± 39.9
Creatinine (mg/dL)[b]	1.1 ± 0.2	1.2 ± 0.3	1.0 ± 0.1	1.0 ± 0.1	1.1 ± 0.3	1.1 ± 0.3
CrCl (mL/min)	75 ± 27.1	79.1 ± 22.7	74.5 ± 27.3	73.6 ± 9.8	64.9 ± 17.4	67.6 ± 17.2
Urea (mg/dL)[b]	35.7 ± 12.7	35.6 ± 15.3	36.8 ± 13.5	31.7 ± 15.2*	36.4 ± 16.6	34.3 ± 11.2
Urea clearance (mL/min)	42.9 ± 19.1	37.9 ± 14.1	33.5 ± 13.8	39.9 ± 13.6	35.4 ± 12.0	34.4 ± 13.1
Proteinuria (g/24-hour)	0.7 ± 0.6	0.8 ± 0.6	2.0 ± 1.7	1.9 ± 1.8	2.0 ± 1.4	2.1 ± 2.0
Urinary sodium (mEq/L)	201.5 ± 46.8	189.4 ± 78.1	151.9 ± 66.0	182.4 ± 77.7	162.4 ± 44.5	137.9 ± 37.0
Urinary phosphorus (mEq/L)	658.1 ± 320.0	658.1 ± 298.7	551.3 ± 344.1	503.6 ± 234.8	530.9 ± 172.3	511 ± 157.6

X ± SD, *p < 0.05 *versus* pre; [b:] blood determination.

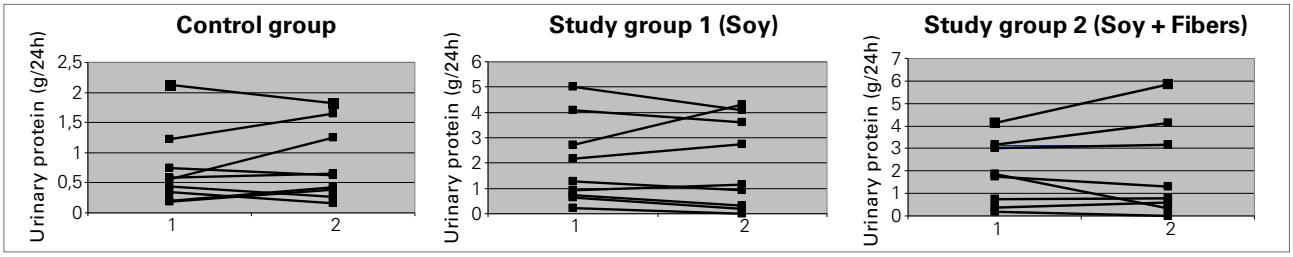

Figure 1. Urinary protein in baseline and post diet periods in the three groups (Control, Soy and Soy + Fibers)

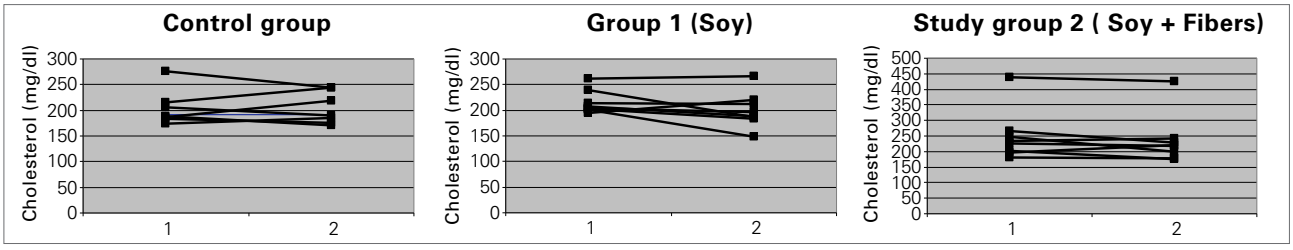

Figure 2. Total cholesterol in baseline and post diet periods in the three groups (Control, Soy and Soy + Fibers)

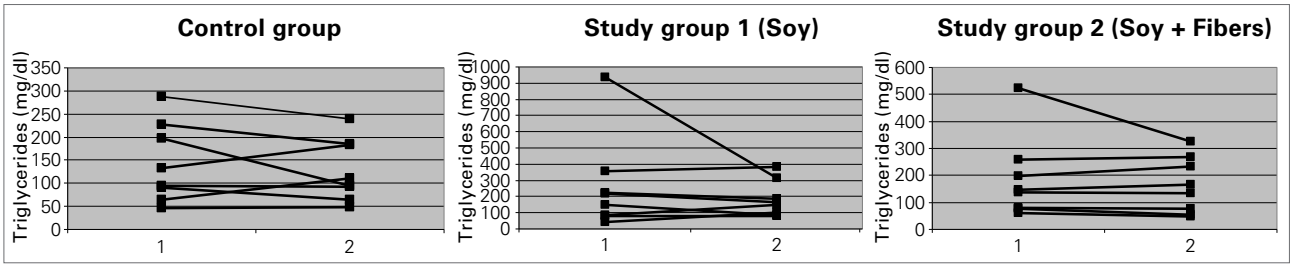

Figure 3. Triglycerides in baseline and post diet periods in the three groups (Control, Soy and Soy + Fibers)

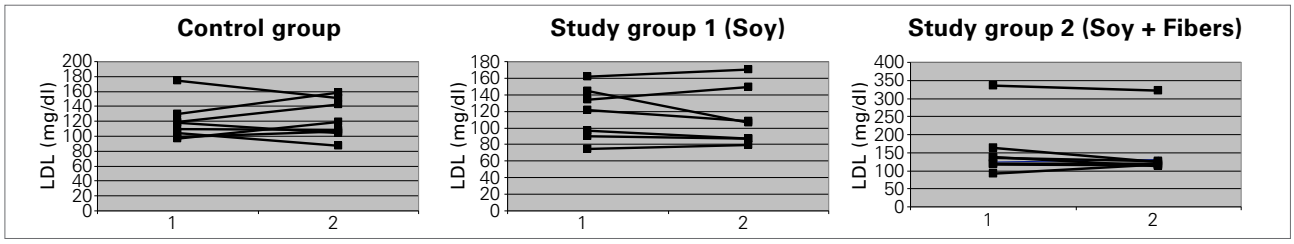

Figure 4. LDL in baseline and post diet periods in the three groups (Control, Soy and Soy + Fibers)

order to establish whether the patients were following correctly the prescribed diet, a significant decrease in the energetic, lipids and protein intake in the three groups was observed. Although the food diary evaluation has suggested an expressive decrease in food ingestion, according to the patients' report during the period of study, significant changes were not observed in three groups when weight, BMI and body composition (body fat-free mass plus fat mass) were evaluated, suggesting that the patients had an adequate diet ingestion during the period of study, and had not reported their true food ingestion by the time of fulfilling the food diary. When protein ingestion was evaluated by PNA, there was no significant decrease of intake in all groups; besides, the ingested amount was in accordance with the prescribed amount, reinforcing the assumption that the patients have maintained an adequate protein ingestion during this study.

We also demonstrated that soy protein diet was safe to maintain the nutritional state (weight, BMI and body composition) of patients with proteinuric glomerulopathies, as well as APD in short-term. The ability of soy protein to warrant a good nutritional state can be justified by the fact that it is classified as a protein of high biological value, as it has all essential amino acids in its composition similarly to the animal proteins.[23]

In rats, it seems to be well-established the ability of soy protein to reduce proteinuria and, consequently, to lower the progression of renal disease.[4,24] Tovar *et al*.[3] observed, in male Wistar rats that were receiving a soy protein diet (20%), a considerable recovery of creatinine clearance and a significant decrease in proteinuria compared with rats that were fed with casein (20%). Some investigators[14,24,25] have shown lower renal damage and proteinuria in rats fed with soy protein than those with casein.

On the other hand, although the effect of soy protein is already well-established in rats, this statement is not true for humans. In humans, this issue was not yet carefully investigated, and there is a lot of controversy about it. Some studies show positive results[12,25-28] and others show negative.[12,29,30]

Studies performed in healthy subjects have demonstrated that substituting the APD by one of vegetal origin was efficient to prevent the proteinuric and hyperfiltration related effects of meat, which could be very advantageous in the treatment of subjects with chronic renal disease.[13,31] On the contrary, Kitazato *et al*.[30] have evaluated the effect of a diet with elevated amount of vegetal protein and reduced content of animal protein and vice versa in healthy subjects, and they have not observed any difference of those diets on renal function and 24-hour urinary albumin excretion.

Soroka *et al*.[29] have evaluated the effect of a low-protein diet with vegetal protein compared to a low-protein diet with animal protein in subjects with chronic renal failure, in a period of six months, and observed that although the vegetal protein diet had warranted better blood urea nitrogen levels, lower protein catabolic rate and lower 24-hour urinary levels of creatinine and phosphate, the urinary excretion of protein was similar in both diets. Serum levels of transferrin, albumin, and cholesterol were also similar.

Some studies have suggested that the source of protein may affect the excretion of protein in subjects with diabetic nephropathy.[32,33] Jibani *et al*.[32] have compared the renal function in diabetic subjects with proteinuria, using a diet with animal protein *versus* a diet with vegetal protein. The last one has not affected glomerular filtration rate, but it has caused a significant decrease in albumin excretion. Azadbakht *et al*.[11] have evaluated the effect of soy protein in comparison with animal protein on renal function, proteinuria, plasma cholesterol and TG, and they have observed that the soy diet was associated with significant decreases in the levels of cholesterol, TG, and proteinuria. On the contrary, Anderson *et al*.[12] have compared the effect of soy protein *versus* the animal one on renal function and proteinuria in type 2 diabetic subjects, and they verified that the soy protein diet determined a significant decrease only in cholesterol and TG concentration.

As previously mentioned, if we take in account that nephrotic patients develop numerous changes in the lipid profile, it would be very interesting to evaluate the effect of soy protein, specifically in subjects with NS, not only due to its possible action on protein loss, but also due to the possibility of lowering cholesterol and TG levels. Nevertheless, in the present study, when the effect of soy diet on the urinary excretion of protein and on serum total and LDL cholesterol levels and TG was evaluated, we have not observed significant changes in none of the groups between the baseline and post-diet periods. In opposition to the results found in this study, some investigators have observed that the soy protein was efficient to decrease proteinuria and plasma cholesterol in nephrotic syndrome.[4,34,35] Gentile *et al*.[34] and D'Amico *et al*.[4] have observed that a eight-week soy protein diet decreased the proteinuria and hyperlipidemia in nephrotic patients with severe proteinuria.

Nevertheless, it should be emphasized that, in this study, it was not possible to determine if the favorable effect on proteinuria was due to the change of animal origin protein by soy protein or this effect was due to a significant decrease in the amount of protein ingested by the patients that received vegetal diet. In all these studies, the effect of soy protein on proteinuria in subjects with severe proteinuria was evaluated. Herein, proteinuria was mainly evaluated in patients with low proteinuria levels. It is possible that the baseline low levels of proteinuria have prevented significant changes in the urinary excretion of proteins, after ingestion of soy protein diet. In the present study, no marked decrease in cholesterol or TG levels was seen; it is also noteworthy that most of patients presented baseline and post-diet lipid levels within the range of reference values or very close to them.

Finally, in the present study, no beneficial effects were observed when substituting animal protein by soy one for attenuating the glomerular injury, proteinuria and hyperlipidemia, but we concluded that the soy protein did not cause deleterious changes in body composition, warranting an adequate nutritional status. Certainly, more studies involving short-term ingestion of soy protein in a higher number of patients are necessary to investigate the role of soy protein in proteinuric glomerulopathies. Although no beneficial effect was demonstrated in the groups evaluated, it was evident that the soy protein has adequately substituted the animal protein diet. The low number of cases could have explained the negative results related to the targets of this study. Besides, it would be more likely to find a positive effect of dietetic intervention with long-term use of soy protein, which will be analyzed in future studies.

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APPENDIX A

NUTRITIONAL INFORMATION
Portion of 40g

Quantity by portion		% VD (*)
Energy	150 kcal	6%
Carbohydrate	21 g	6%
Protein	10 g	20%
Total fat	3 g	4%
Saturated fat	0 g	0%
Cholesterol	0 mg	0%
Fiber	5 g	17%
Calcium	32 mg	4%
Iron	3 mg	21%
Sodium	0 mg	0%
OTHER MINERALS		
Phosphorus	260 mg	35%
Magnesium	64 mg	20%
Zinc	2,2 mg	15%
Copper	0,32 mg	10%
Mn	2,1 mg	40%
VITAMINS		
B1	0,3 mg	20%
B2	0,15 mg	10%
Niacine	1,2 mg	6%
A	136 mg	20%
D	2,5 mg	50%

*VD: daily reference values based on a diet with 2,500 calories. Ingredients: Soy, Oat, wheat germ, brown sugar, cashew nut, raisin, and sesame.

APPENDIX B

NUTRITIONAL INFORMATION
Portion of 30g

Quantity by portion		% VD (*)
Energy	110 kcal	4%
Carbohydrate	10 g	3%
Protein	17 g	34%
Total fat	0 g	0%
Saturated fat	0 g	0%
Cholesterol	0 mg	0%
Fiber	0 g	0%
Calcium	360 mg	45%
Iron	3 mg	20%
Sodium	85 mg	3%
OTHER MINERALS		
Phosphorus	290 mg	40%
Magnesium	30 mg	10%
Zinc	1 mg	7%
Copper	0,3 mg	10%
Mn	0,3 mg	6%

*Daily reference values based on a diet with 2,500 calories. Ingredients: soy protein, low fat powder milk, and calcium carbonate.