Original Paper

NEPHRON

Nephron 1996;74:390–394

A Low-Nitrogen Low-Phosphorus Vegan Diet for Patients with Chronic Renal Failure

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Key Words
Vegan diet
Chronic renal failure

Abstract
The nutritional treatment of chronic renal failure with a low-protein low-phosphorus diet (conventional low-protein diet, CLPD) is effective in reducing uremic intoxication, slowing the progression of renal failure and preventing secondary hyperparathyroidism. Unfortunately, in some patients, the poor palatability and the high cost of the protein-free substitutes, together with difficulties in following the diet away from home, can make good compliance difficult, possibly causing low energy intake and malnutrition. Here the results are reported of an attempt we made to overcome these drawbacks, using a diet supplying only natural foods of plant origin in definite proportions to give an essential amino acid supply satisfying the recommended dietary allowance. This is possible thanks to an appropriate cereal-legume mixture, supplying proteins complementary for essential amino acids. Additional positive features of this special vegan diet (SVD) are the high ratio of unsaturated to saturated fatty acids, the absence of cholesterol, and the lower net acid production in comparison with a mixed diet. This study indicates that the results obtained with the SVD are similar to those obtained with the CLPD. Therefore the SVD can be a substitute for the CLPD in the management of patients with mild chronic renal failure. The SVD is the diet of choice when products made of starch are not available or poorly tolerated.

Introduction

It has been found in the past, and recently confirmed, that restriction of protein and phosphorus intake protects the residual renal function of patients with chronic renal failure [1–3]. It is also well established that these dietary restrictions relieve the signs and symptoms of chronic uremia and may prevent complications [4], and, finally, that protein malnutrition does not appear provided the energy requirement is satisfied and catabolic intercurrent conditions are removed [5, 6].

These positive aspects of the nutritional treatment of chronic renal failure are counteracted in part: (1) by the poor palatability of the protein-free substitutes such as bread and pasta made of starch that can make compliance difficult in some patients; (2) by the high cost of these substitutes, and (3) by the difficulties in keeping the diet when away from home. Inadequate energy intake may

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0028–2766/96/0742–0390$10.00/0

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Accepted:
February 1, 1996

result and malnutrition may appear, which is wrongly attributed to the low protein intake.

Here the results are reported of an attempt we made to overcome these drawbacks by utilizing a diet supplying only natural foods of plant origin [7] in definite proportions (special vegan diet, SVD), thus reducing the cost, improving palatability and making compliance easier, even when away from home.

The rationale of this attempt is that in many foods of plant origin the energy/protein and the energy/phosphorus ratios are higher than in foods of animal origin, which makes it possible to satisfy the energy requirement while maintaining a low nitrogen and phosphorus intake. An appropriate cereal-legume mixture [7] also makes a supply of essential amino acids (AAs) possible and very close to that supplied by the conventional low-protein diet (CLPD), satisfying the daily requirements of essential AAs [8] (table 1). In addition, the vegetarian diet can exert favorable effects in patients with renal disease as follows. First, the high ratio of unsaturated to saturated fatty acids and the absence of cholesterol can favorably affect lipid metabolism and renal disease [9, 10]. Second, the glomerular filtration rate, renal plasma flow and fractional clearance of albumin and IgG are lower on a vegetable protein than on an animal protein diet [11]. Third, at an equal protein intake level, the net acid production is lower using plant foods [12]. Fourth, the vegetarian diet can contribute to lowering blood pressure [13].

The aims of this study were: (1) to evaluate some of the metabolic effects of the SVD in patients with mild renal failure: (2) to evaluate the amount of nitrogen that escapes intestinal absorption in patients on the SVD; (3) to evaluate the risk of hyperkalemia, and (4) to detect signs (if any) of protein malnutrition after several months of SVD.

Patients and Methods

Twenty-two patients with mild renal failure [endogenous creatinine clearance (CRcl) ranging from 40 to 20 ml/min/1.73 m^2] entered the study: 11 patients (8 males, 3 females, aged 18–54 years) were shifted from an unrestricted-protein diet (UPD) to the SVD, whereas the other 11 patients (7 males, 4 females, aged 20–60 years) were shifted from the CLPD to the SVD. All the patients followed the SVD for at least 6 months.

Forty patients with severe renal failure (CRcl) <20 ml/min/1.73m^2) were studied for the acid base status: 15 were on the SVD, 15 were on the CLPD, and 10 were on a UPD for at least 3 months.

The nitrogen content of the feces was measured on 3 consecutive days during hospitalization, in 4 patients on the CLPD and in 4 patients on the SVD for several weeks.

Table 1. Mean daily intake (mg, calculated over a 12-day period) of the essential AAs supplied by the SVD or by the CLPD; the essential-AA requirements are adapted from Munro and Crim [8]

	CLPD	SVD	Requirement
Lysine	3,201	1,787	840
Histidine	1,099	1,023	–
Threonine	1,728	1,553	490
Valine	2,176	2,039	980
Leucine	3,102	3,431	980
Isoleucine	1,839	1,970	770
Methionine	1,076	717	–
Phenylalanine	1,753	2,275	–
Tryptophan	445	469	210
Phe + Tyr	3,163	3,403	1,100
Met + Cys	1,597	1,659	1,100

Table 2. Composition of the CLPD and of the SVD

	CLPD	SVD
Proteins, g/kg b.w.	0.6	0.7
Phosphorus, mg/kg b.w.	8.0	10.5
Potassium, mmol/kg b.w.	0.8	1.1
Energy supply, kcal/kg b.w.	>35	>35
From carbohydrates, %	61	57
From fats, %	31	34
From proteins, %	7	8

Excluded from the study were patients with nephrotic syndrome, secondary renal disease (LES, diabetes, myelome) or catabolic conditions (acute infections, steroid therapy).

All the studied patients were informed, before admission, of the experimental nature of the diet and all consented to participate. This study has been submitted for approval to the Ethical Committee of the University of Pisa, Italy.

The SVD is a pure vegetarian diet that supplies proteins, carbohydrates, fats, fibers and energy as reported in table 2.

The AAs supplied were those contained in the proteins of cereal and legumes, which were combined in such proportions as to utilize their complementarity in the essential-AA composition [7]. In fact, legumes have a low sulfur AA content and a relatively low content of valine and tryptophan, while the lysine content is high: this indicates that the proteins of legumes are complementary with those of cereals since the latter are rich in methionine and low in lysine [7]. This complementarity, when correctly utilizated, allows one to obtain mixtures of essential AAs that are not different, in biological value, from those of proteins of animal origin (table 1). To obtain the maximum benefit, the complementary proteins should be ingested together, as actually done by our patients. For a 70-kg patient, 36.4 g of proteins were supplied by cereals and 6.5 from legumes, so that the

Table 3. Serum (sCr) and urinary (uCr) creatinine, serum and urinary urea, serum inorganic phosphorus (sP_i) levels and CRcl in the 11 patients shifted from a UPD to the SVD, on the left, and in the 11 patients shifted from a CLPD to the SVD, on the right

	UPD	SVD	CLPD	SVD
Study period, months		14.1±5.0		12.8±5.7
sCr, mg/dl	2.1±0.7	2.3±1.0	3.5±1.4	4.1±0.9
uCr, mg/24 h	1,151±321	1,050±272*	997±281	916±309
CRcl, ml/min/1.73 m^2	41.1±19.0	36.8±20.7*	20.9±6.1	16.1±5.7[1]
sUrea, mg/dl	60±26	45±27*	86±43	84±30
uUrea, g/24 h	18.4±6.4	10.4±1.9***	10.1±3.1	9.9±2.7
sP_i, mg/dl	3.5±0.7	3.4±0.6	3.9±0.7	4.2±1.0

* $p < 0.05$, *** $p < 0.001$, vs. UPD.
[1] $p < 0.05$ vs. CLPD.

Table 4. Serum and urine biochemical parameters in patients with severe chronic renal failure on the SVD, CLPD or UPD, for at least 3 months

	SVD	CLPD	UPD
n	15	15	10
CRcl, ml/min	15.6±7.5	14.2±4.6	14.6±4.6
sUrea, mg/dl	73±34***	83±29***	132±33
uUrea, g/24 h	8.1±2.8***	8.3±2.3***	13.5±2.3
sP_i, mg/dl	3.8±0.7	4.0±1.0	4.4±1.2
uP_i, mg/24 h	457±121*	405±86**	561±114
sCa, mg/dl	9.0±0.8	8.6±0.7	8.6±1.2
sK^+, mEq/l	4.5±0.7	4.4±0.5	4.6±0.8
Capillary pH	7.36±0.04	7.37±0.04	7.34±0.06
HCO_3^-, mmol/l	20.3±2.9*	20.2±2.4*	17.6±3.4
Urinary pH	6.49±0.58**	5.99±0.86	5.50±0.47
TA, mmol/24 h	5.7±3.7***	9.1±5.0**	16.7±6.2
NH_4, mmol/24 h	3.4±1.4*	5.7±2.8	6.7±2.5
Total H^+, mmol/24 h	9.1±5.3**	14.8±7.1**	23.4±6.6

TA = Titratable acid.
*** $p < 0.001$, ** $p < 0.01$, * $p < 0.05$, vs. UPD.

Table 5. Body weight and some serum nutritional parameters in the 22 patients treated with the SVD for 13.4 ± 5.4 months

	Before SVD	During SVD
Body weight, kg	63.9±10.1	64.2±11.2
Serum total protein, g/dl	7.1±0.6	7.2±0.6
Serum albumin, g/dl	4.0±0.5	4.1±0.5
Serum transferrin, mg/dl	226±27	224±54
Serum complement C3, mg/dl	64±16	62±23
Serum complement C4, mg/dl	29±16	25±6

cereal-to-legume ratio, in terms of dietary protein source, was 5.6 to 1.

Several dishes very popular in Italy (e.g. pasta and beans, rice and pies) can be prepared with cereals and legumes cooked together. The fats are mostly supplied as oils from plant origin (mainly olive oil), obtaining a very high ratio of unsaturated/saturated fatty acids (4:1). Cholesterol was absent from the diet.

Calcium carbonate powder was given regularly at a daily dose of 2–5 g according to the calcium and phosphate plasma levels. Vitamin B_{12} and ferrous salts were also supplemented.

The serum and urinary biochemical parameters were evaluated using standard laboratory methods. Capillary blood was used for the determination of pH and bicarbonate. Urinary pH, titratable acid, and ammonium were determined on 24-hour urine samples collected with thymol as the preservative. Urinary ammonium was determined using a colorimetric procedure. The Kjeldahl procedure (Vapodest 36, Gerhardt, Bonn, Germany) was used for the measurement of total nitrogen in feces. The daily AA supply of the SVD and the CLPD were calculated over a 12-day period, using food composition tables [14].

Statistical evaluation was performed using the Student's t test for paired data and one-way analysis of variance. Differences were regarded as statistically significant when $p < 0.05$.

Results

The daily urinary excretion of urea in patients on the SVD was in keeping with the calculated protein intake, and quite similar to that of CLPD patients (table 3). The daily urinary excretion of creatinine decreased in subjects on the SVD, due to the lack of creatinine from an exogenous source. The CRcl values decreased from the baseline to the end of the SVD study periods (table 3). The amount of H^+ excreted daily in the urine was lower in the SVD patients than in those on the UPD, with the same residual renal function (table 4). This finding, together with higher

blood bicarbonate levels, confirms that the SVD induces a lower H^+ production.

Due to the low phosphorus content of the SVD, further reduced in some foods by boiling [15], and due to the binding action of the supplemented calcium on intestinal phosphate, plasma phosphorus concentrations remained within the normal limits even in the presence of severe renal failure (table 4). Hypercalcemia was never observed.

Total serum proteins, serum albumin, transferrin, C3 and C4 were normal at the baseline and unchanged at the end of the study period on the SVD; body weight was also unchanged (table 5). No clinical manifestation of malnutrition was detected.

The fasting serum K^+ levels never exceeded the value of 5.5 mEq/l even in the patients with very low residual renal function (table 4).

The SVD seems not to induce any change on triglycerides; plasma cholesterol, however, was reduced when the patients shifted from the UPD to the SVD (195 ± 55 vs. 172 ± 52 mg/dl, $p < 0.05$), whereas it was unchanged between the CLPD and the SVD (169 ± 32 vs. 169 ± 31 mg/dl).

Fecal nitrogen in the 4 patients on the SVD showed a trend higher than in the 4 patients on the CLPD (1,550 ± 524 vs. 1,164 ± 597 mg, respectively).

Discussion

The dietary treatment of chronic renal failure has its rationale in the use of minimal amounts of protein of high biological value to meet the energy requirement satisfied with fat and nitrogen-free substitutes [15] made of starch. Thus production and retention of waste metabolites may be reduced and protein malnutrition avoided due to the high biological value of the ingested proteins.

To advocate the use of foods of plant origin, which are known to contain proteins of low biological value, only appears contradictory. The biological value of individual proteins is indeed not relevant because the important factor is the composition of the AA mixture resulting from the digestion of all the proteins ingested. Indeed, the proteins supplied with plant foods (all together) may complement each other for their essential-AA content. Thus the biological value may be equivalent to that resulting from the digestion of protein of animal origin: this is what happens when the proteins of cereal foods and those of legumes are ingested together [7]. It is therefore not surprising that the studied parameters are not significantly different in the patients on the SVD and in the patients with similar renal failure on the CLPD almost exclusively ingesting proteins of high biological value. Also, the complete absence of signs of protein malnutrition, after 1 year of follow-up, demonstrates that the quality and quantity of the ingested proteins were adequate.

The amount of nitrogen that daily escapes the intestinal absorption in SVD patients seems to be higher than that lost by patients on the CLPD, but it is probably not relevant in terms of nitrogen balance.

The reduction of CRcl during the SVD periods (table 3) could be attributed both to the progression of the nephropathy and to the functional changes of glomerular hemodynamics induced by a vegan low-protein diet. Actually it is well known that the glomerular filtration rate decreases with the reduction of dietary proteins [16] as well as with the ingestion of proteins solely of plant origin [11, 17].

Although severe metabolic acidosis was not expected in the studied patients, the favorable effect of SVD on acid base status is demonstrated by the low values of the urinary H^+ output indicating that the net metabolic production of H^+ by patients on SVD is even lower than that of patients on CLPD (table 4).

The serum concentrations of inorganic phosphorus were normal before starting the SVD and did not change during 1 year of follow-up. This is accounted for by the low phosphate content of the SVD that was further reduced by boiling some foods [15]. Supplemented calcium carbonate is also important in this context, exerting a binding action on intestinal phosphate and thus increasing its fecal output. These normal plasma levels of phosphorus and calcium are certainly important in preventing soft-tissue calcifications and secondary hyperparathyroidism.

A favorable effect on serum total cholesterol was evident when the patients were shifted from UPD to the SVD, whereas no difference was detected comparing the SVD with the CLPD. This is in keeping with the cholesterol content and the fatty-acid composition of the diets.

Foods of plant origin are known to supply large amounts of K^+ and are regarded as extremely dangerous for patients with chronic renal failure. Undoubtedly the risk of hyperkalemia exists but it represents a real problem almost exclusively in patients with very low residual renal function, such as in those on dialysis. In the case of mild renal failure, the amount of K^+ taken in with food scarcely affects the plasma levels since the kidneys have an enormous capacity to excrete K^+ ions even in severe renal failure. The risk of hyperkalemia is serious, how-

ever, when intracellular K^+ shifts to the extracellular compartment due to tissue necrosis, catabolic conditions or use of drugs such as β-blockers or ACE inhibitors. It is evident, however, that the dietary supply of K^+ is not responsible for the possible hyperkalemia in these conditions. Indeed, hyperkalemia would appear even with a K^+-free diet.

In conclusion, the K^+ load from the SVD is not a serious problem in patients with a residual CRcl over 10 ml/min/1.73 m^2, provided the other causes of hyperkalemia are not present. Therefore when the risk of hyperkalemia appears, dialysis is indicated.

The observations made in this study indicate that the SVD may be regarded as a valid alternative to the CLPD for patients with moderate chronic renal failure. The problems of poor palatability, high cost and difficulties in maintaining the CLPD when away from home can be largely solved by the described vegan diet.

Acknowledgement

This study was supported in part by grant No. 277, 1994, from the Ministero dell'Università e della Ricerca Scientifica e Tecnologica, Italy.

References

1 Maschio G, Oldrizzi L, Tessitore N, D'Angelo A, Valvo L, Lupo A, Loschiavo C, Fabris A, Gammaro L, Rugiu C, Panzetta G: Effects of dietary and phosphorus restrictions on the progression of chronic renal failure. Kidney Int 1982;22:371–376.

2 Ihle BU, Becker GJ, Whitworth JA, Charlwood RA, Kincaid-Smith PS: The effect of protein restriction on the progression of renal insufficiency. N Engl J Med 1989;321:1773–1777.

3 Klahr S: Lessons from the modification of diet in renal disease study. J Nephrol 1994;7:136–137.

4 Barsotti G: Effects of dietary therapy on uremic symptoms and complication; in Giovannetti S (ed): Nutritional Treatment of Chronic Renal Failure. Boston, Kluwer Academic Publishers, 1989, pp 235–239.

5 Hara Y, May RC, Kelly RA, Mitch WE: Acidosis, not azotemia, stimulates branched-chain, amino acid catabolism in uremic rats. Kidney Int 1987;32:808–814.

6 Williams B, Hattersley J, Layward E, Walls J: Metabolic acidosis and skeletal muscle adaptation to low protein diet in chronic uremia. Kidney Int 1991;40:779–786.

7 Elfert G: Vegetarian diets; in Walser M, Imbembo AL, Margolis S, Elfert GA (eds): Nutritional Management. Philadelphia, Saunders, 1984, pp 31–35.

8 Munro HN, Crim MC: The proteins and amino acids; in Shils ME, Young VR (eds): Modern Nutrition in Health and Disease. Philadelphia, Lea & Febiger, 1988, pp 1–37.

9 Keane WF, Kasiske BL, O'Donnell MP: Lipids and progressive glomerulosclerosis. Am J Nephrol 1988;8:261–271.

10 Grundy SM: Management of hyperlipidemia of kidney disease. Kidney Int 1990;37:847–853.

11 Kontessis P, Jones S, Dodds R, Trevisan R, Nosadini R, Fioretto P, Borsato M, Sacerdoti D, Viberti GC: Renal, metabolic and hormonal responses to ingestion of animal and vegetable proteins. Kidney Int 1990;38:136–144.

12 Barsotti G, Agostini B, Cupisti A, Meola M, Morelli E: Metabolic acidosis and chronic renal failure: Effects of conservative dietary treatment. Ital J Miner Electrolyte Metab 1994;8:85–87.

13 Margetts BM, Beilin LJ, Vandongen R, Armstrong BK: Vegetarian diet in mild hypertension: A randomized controlled trial. Br Med J 1986;293:1468–1471.

14 Cok P, De Bernard B, Radillo O, Francescato MP: Synoptic Food Composition Tables. Padova, Piccin, 1987.

15 Giovannetti S: Low-protein diets for chronic renal failure; in Giovannetti S (ed): Nutritional Treatment of Chronic Renal Failure. Boston, Kluwer Academic Publishers, 1989, pp 179–190.

16 Klahr S, Levey AS, Beck GJ, Caggiula AW, Hunsicker L, Kusek JW, Striker G: The effects of dietary protein restriction and blood pressure control on the progression of chronic renal disease. N Engl J Med 1994;330:877–884.

17 Bosh JP, Saccaggi A, Lauer A, Ronco C, Belledonne M, Glabman S: Renal functional reserve in humans. Am J Med 1983;75:943–950.