Contributions to Nephrology
Editors: G.M. Berlyne, Brooklyn, N.Y.; S. Giovannetti, Pisa

Reprint
Publisher: S. Karger AG, Basel
Printed in Switzerland

Guarnieri G, Panzetta G, Toigo G (eds): Metabolic and Nutritional Abnormalities in Kidney Disease. Contrib Nephrol. Basel, Karger, 1992, vol 98, pp 149–156

Dietary Treatment of Type I Diabetic Nephropathy with Renal Insufficiency

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Diabetic nephropathy is a late complication of insulin-dependent diabetes mellitus (IDDM), which appears in about 25–50% of patients [1], 20 or 30 years after the onset of diabetes [2].

Diabetic nephropathy must be regarded as a rapidly progressive nephropathy. Although a strict blood glucose control [3] and an aggressive management of arterial hypertension [4] can slow the progressive fall of glomerular filtration rate, several papers show that the end-stage renal failure is reached 5–7 years after the appearance of dipstick-positive proteinuria, and that the mean decline of glomerular filtration rate ranges from 10 to 25 ml/min/year [5, 6].

In recent years, several uncontrolled trials have demonstrated that an adequate dietary protein (0.6 g/kg/day or less) and phosphorus (600 mg/day or less) restriction can reduce the rate of progression of renal insufficiency and exert other beneficial effects in patients with chronic renal failure of various etiology [7–9]. Recently, a controlled, prospective, randomized trial on the effect of a 0.6 g/kg/day protein intake on the progression of renal insufficiency confirmed these results [10]. More recently, a similar protective effect of low-protein and low-phosphorus diets has been reported also in chronic renal failure due to diabetic nephropathy, by clinical, uncontrolled [11–13] and prospective, controlled, randomized trials [14].

The main aim of the present investigation was to evaluate the long-term effect of two different low-protein, vegetarian diets, supplemented with a mixture of essential amino acids and their ketoanalogues in patients with chronic renal failure due to diabetic nephropathy.

Table 1. The supplemented diets

For patients with mild renal failure (C_{Cr} > 20 ml/min/1.73 m²)	
Energy	30–35 kcal/kg/day
Proteins	0.7 g/kg/day, only from plant foods
Carbohydrates	62–65% of total energy supply, mainly from normal pasta and bread
Lipids	25–28% of total energy supply, only plant origin
Cholesterol	negligible
Phosphorus	600–700 mg/day
For diabetics with severe renal failure (C_{Cr} < 20 ml/min)	
Calories	30–35 kcal/kg/day
Proteins	0.35 g/kg/day, from plant foods and EAAs supplements
Carbohydrates	65–70% of total energy supply, mainly from nitrogen-free, starch-made foods
Lipids	28–32% of total energy supply, plant origin only
Cholesterol	negligible
Phosphorus	350–400 mg/day

Supplements: EAAs + KAs mixture. $CaCO_3$, Vitamin B_{12}, iron.

Patients and Methods

We submitted to the dietary treatment 23 insulin-dependent diabetics (16 males and 7 females) aged 24–69 years (mean 48.5 years). The duration of diabetes was 19.6 ± 6.3 years, and the mean duration of diabetic nephropathy 5.9 ± 1.9 years. The mean creatinine clearance (C_{Cr}) at the beginning of the study was 24.1 ± 19.8 ml/min. The prevalence of diabetes complications was: retinopathy 88%, neuropathy 56%, arteriopathy 40%; 36% of patients had retinopathy and arteriopathy, and 28% retinopathy, arteriopathy and neuropathy.

We used a 0.3 g/kg/day protein diet for patients with severe chronic renal failure, having a C_{Cr} lower than 20 ml/min, and a 0.7 g/kg/day protein for patients with less severe chronic renal failure. In both diets the protein source was from foods of vegetable origin only. The phosphorus supply was approximately 350–400 and 600–700 mg/day, respectively. The diets were supplemented with a mixture of essential amino acids and keto-analogues in tablets, as it is reported in table 1.

These diets were defined as supplemented diets (SD). The rate of decline of C_{Cr} during the SD period was compared with the rate observed in a previous period on free and uncontrolled diet (UD). The follow-up on UD ranged from 8 to 24 months, and on SD from 8 to 58 months. The rate of decline of C_{Cr} on UD was retrospectively evaluated in 18 out of the 23 studied diabetics.

Before and at the end of the SD period, we evaluated: C_{Cr} and its rate of decline, mean arterial pressure (MAP), daily urinary protein loss (uPR), serum total protein (sPR)

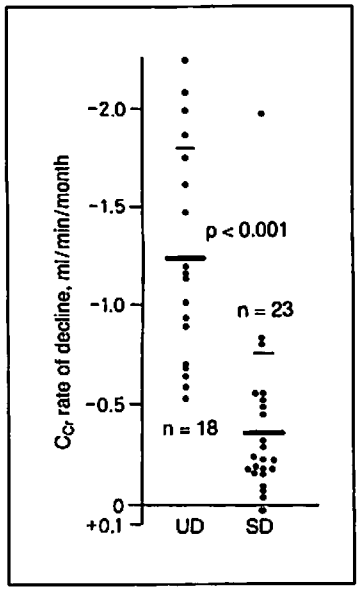

Fig. 1. The rate of decline of C_{Cr} observed on UD (18 patients) and on SD (23 patients) (mean ± SD).

and serum albumin (sAlb), fasting serum glucose (sG) levels, daily insulin requirement (IR), serum calcium (sCa), serum inorganic phosphorus (sPi) and parathyroid hormone (middle molecule fragment) (sPTH M-M).

The statistical analysis of the results was performed with a personal computer, by using IBM Epistat software. The results were expressed as mean ± standard deviation. For the evaluation of the statistical significance we calculated the Student t test for paired data, and the statistical significance was considered when $p < 0.05$.

Results

The C_{Cr} rate of decline on UD was 1.21 ± 0.62 ml/min/month, significantly different from the mean rate of decline observed on SD (0.39 ± 0.31 ml/min/month) (fig. 1). The MAP on UD was significantly higher than on SD: 116.7 ± 1.7 and 113.1 ± 1.9 mm Hg, respectively ($p < 0.01$).

uPR significantly decreased on SD, from 4.6 ± 2.1 to 2.9 ± 1.9 g/day ($p < 0.01$, fig. 2), while sPR increased (fig. 2). sAlb also increased, but not significantly, on SD (fig. 2).

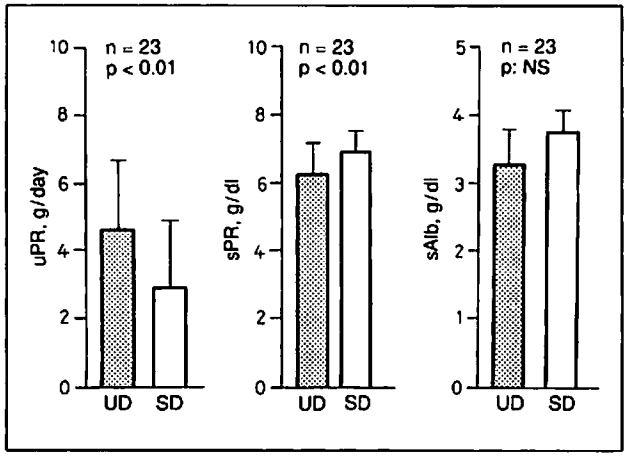

Fig. 2. The behavior of daily uPR, sPR, and sAlb, observed in 23 type I diabetics who changed from UD to SD (mean ± SD).

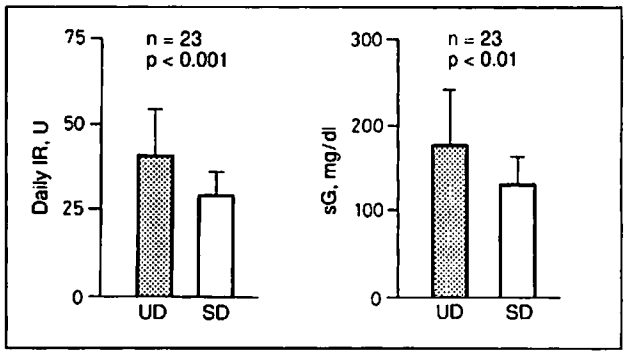

Fig. 3. Daily IR and sG levels on UD and SD (mean ± SD).

In spite of high carbohydrate intake on SD, the daily IR significantly decreased (from 41.6 ± 11.8 to 28.9 ± 7.6 units, respectively, $p < 0.001$) (fig. 3) together with fasting sG levels (from 178.8 ± 64.4 to 132.6 ± 31.2 mg/dl, $p < 0.005$) (fig. 3).

sPTH M-M decreased from 2.7 ± 1.6 to 1.3 ± 0.7 ng/ml on SD ($p < 0.001$, fig. 4). sPi decreased from 5.2 ± 0.7 mg/dl on UD to 4.1 ± 0.5 mg/

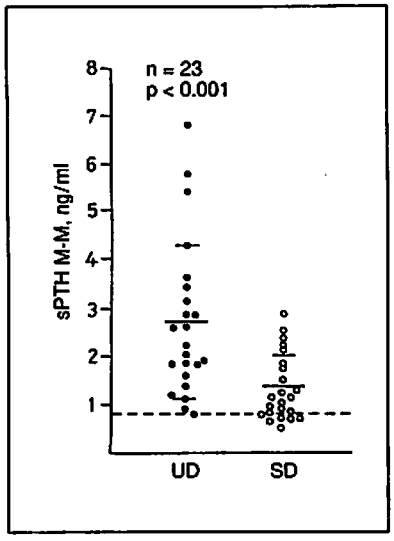

Fig. 4. The lowering effect on sPTH M-M observed in 23 type I diabetics with chronic renal failure who changed from UD to SD (mean ± SD).

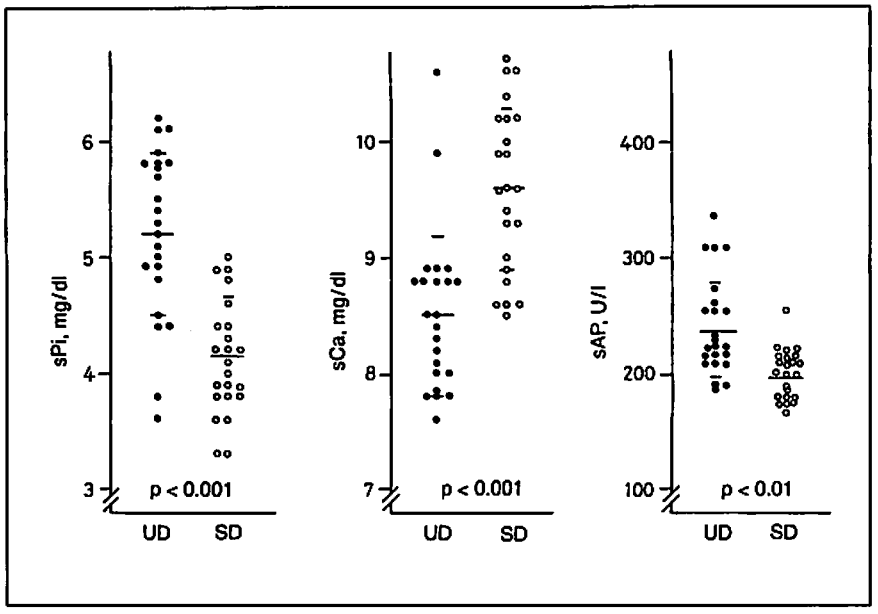

Fig. 5. The fall of sPi, serum alkaline phosphatase (sAP) and the increase of sCa levels following the change from UD to SD (mean ± SD).

dl on SD ($p < 0.001$; fig. 5). sAP also decreased from 239 ± 42.3 to 200 ± 21 U/l ($p < 0.01$, fig. 5) while sCa increased from 8.5 ± 0.7 to 9.6 ± 0.7 mg/dl ($p < 0.001$; fig. 5).

Discussion

The lowered rate of decline of C_{Cr} observed in our patients shifted from UD to SD may be a consequence of the correction of several factors which may negatively affect the progression of diabetic nephropathy. A significant role is probably played by the decrease of glomerular hypertension [15] and of hyperfiltration in remnant nephrons [16]. The better control of arterial hypertension observed on SD is another important factor for the protection of residual renal function in IDDM with chronic renal failure [17]. Because heavy proteinuria negatively affects the outcome of glomerular diseases [18, 19], the decrease of urinary protein loss may be of some importance for the lower rate of decline of C_{Cr} on SD.

The lowering effect of low-protein diets on daily urinary protein loss is far from being clarified, but the hemodynamic changes at the glomerular level and the correction of hyperfiltration surely play an important role [20, 21].

The decrease of daily insulin requirement on SD may be partly accounted for by the improvement of insulin sensitivity and glucose tolerance induced by low-protein and low-phosphorus diets [22], and by the correction of secondary hyperparathyroidism [23] which may be easily explained by the fall of sPi and the increase of sCa levels due to low-phosphorus intake and to the calcium carbonate supplementation [24].

In conclusion, the dietary restriction of protein and phosphorus of SD can slow down the rate of progression of chronic renal failure in patients with diabetic nephropathy. SD seems to be a safe, effective and inexpensive therapeutic measure and we think it should be recommended early in the course of type I diabetic nephropathy.

Acknowledgements

This study was supported by grant No. 67/C from the Dipartimento Sicurezza Sociale, Regione Toscana. The authors thank Farma Biagini SpA, Castelvecchio Pascoli, Lucca, for the generous supply of essential amino acids and ketoacids mixture in tablets.

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