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ORIGINAL ARTICLE

# 6-tips diet: a simplified dietary approach in patients with chronic renal disease. A clinical randomized trial

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**Abstract**
*Background* The beneficial effects of dietary restriction of proteins in chronic kidney disease are widely recognized; however, poor compliance to prescribed low-protein diets (LPD) may limit their effectiveness. To help patients to adhere to the dietary prescriptions, interventions as education programmes and dietary counselling are critical, but it is also important to develop simple and attractive approaches to the LPD, especially when dietitians are not available. Therefore, we elaborated a simplified and easy to manage dietary approach consisting of 6 tips (6-tip diet, 6-TD) which could replace the standard, non-individualized LPD in Nephrology Units where dietary counselling is not available; hence, our working hypothesis was to evaluate the effects of such diet vs a standard moderately protein-restricted diet on metabolic parameters and patients' adherence.
*Methods* In this randomized trial, 57 CKD patients stage 3b-5 were randomly assigned (1:1) to receive the 6-TD (Group 6-TD) or a LPD containing 0.8 g/kg/day of proteins (Group LPD) for 6 months. The primary endpoint was to evaluate the effects of the two different diets on the main "metabolic" parameters and on patients' adherence (registration number NCT01865526).
*Results* Both dietary regimens were associated with a progressive reduction in protein intake and urinary urea excretion compared to baseline, although the decrease was more pronounced in Group 6-TD. Effects on serum levels of urea nitrogen and urinary phosphate excretion were greater in Group 6-TD. Plasma levels of phosphate, bicarbonate and PTH, and urinary NaCl excretion remained stable in both groups throughout the study. 44 % of LPD patients were adherent to the dietary prescription vs 70 % of Group 6-TD.
*Conclusions* A simplified diet, consisting of 6 clear points easily managed by CKD patients, produced beneficial effects either on the metabolic profile of renal disease and on patients' adherence to the dietary plan, when compared to a standard LPD.

**Keywords** Adherence · Chronic kidney disease · Low-protein diet · Protein intake

## Introduction

Dietary restriction of proteins and sodium is a cornerstone in the treatment of chronic kidney disease (CKD) for its ability to reduce the work load of surviving nephrons and to lessen the signs and symptoms of uraemia, as well as for its positive metabolic impact. Moreover, the reduction in dietary sodium intake contributes to reduce hypertension in advanced CKD [1–7]. Although the dietary treatment does not reduce the decline in glomerular filtration rate (GFR), it delays renal death sparing patients with CKD from dialysis

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by 1–2 years [8–10] and may also be considered a cost-effective therapy [11].

Dietary adjustments in subjects with CKD, however, are complex and imply a major change in lifestyle. Furthermore, low-protein diets (LPDs) are considered tedious, unpalatable and expensive, and are therefore often associated with a low patients' compliance in the long term [12, 13]. Since poor dietary adherence nullifies the advantages of such treatment, a better compliance to this therapeutic approach is a critical issue to reach and represents a leading challenge to healthcare professionals [14].

A key process to obtain adequate adherence to LPDs is to provide individualized dietary programmes and specific periodic counselling by skilled renal dietitians, possibly joined with intensive educational programmes [15]. These strategies, however, need dedicated personnel and are time and money consuming [16].

In Nephrology Units devoid of such possibilities [16], the usual practice is to prescribe to CKD patients standard, non-individualized LPDs (with no counselling), or even to maintain their usual diet, thus renouncing to the benefits of LPDs. To overcome these difficulties, we have elaborated an easy dietary plan, consisting of 6 written suggestions, which could replace the use of the standard LPDs (6-tip diet, 6-TD, Table 1). These "tips" are based on the same principles that regulate usual LPDs but are more easily understood and memorized by patients.

Therefore, the aim of the present study was to evaluate, in patients with CKD, the ability of the 6-TD to reduce protein, phosphate and sodium intake, and the degree of compliance to this dietary plan in comparison with standard LPDs.

## Subjects and methods

### Patients

This prospective, randomized study was carried out in the CKD Unit of the University Federico II of Naples, Italy, where 61 consecutive patients (stage 3b-5 CKD), admitted in our Unit for a clinical assessment of chronic renal failure, were screened from March 2010 to December 2012. Inclusion criteria for the study were age >18 years, estimated GFR (eGFR) ≤45 ml/min/1.73 $m^2$, and dietary protein intake 0.7–0.9 g/kg/day stable throughout their hospital stay. Exclusion criteria included inability to perform correct 24 h urine collections, malignancies, treatment with immunosuppressive drugs, pregnancy, congestive heart failure (NYHA class III–V), or proteinuria >3.5 g/24 h.

Withdrawal from the study was considered in case of malnutrition (loss of body weight >5 % in 1 month or BMI <20 kg/$m^2$ with serum albumin levels <3.2 g/dl), need to start dialysis (eGFR ≤6 ml/min, $K^+$ >6.0 mEq/L, intractable hypertension), development of other serious clinical conditions, or death.

The study was approved by the Local Ethics Committee and was in adherence with the Declaration of Helsinki. Informed written consent was obtained from each patient.

**Table 1** The six-tip diet

1. Do not add salt at table and for cooking
2. Food to avoid: any kind of salami, sausages, cheese and dairy products or canned food
3. Replace noodle or bread with special hypoproteic food
4. The second course (meat, fish and eggs) are allowed once a day in the usual quantity
5. 4–5 servings/day of fruits or vegetables are suggested
6. Once or twice a week the main course may be of "normal" noodle with legumes instead of the second course, with fruit and vegetables

### Study design and procedures

Accordingly to our inclusion/exclusion criteria, 57 patients were enrolled in the study and were randomly assigned (1:1) to receive the 6-TD or a standard LPD; the randomization list was generated by means of a computer and kept concealed with the use of numbered, sealed envelopes opened in sequence by administrative staff personnel not involved in patients care.

The first arm received, by the nephrologist, a list of six items indicating how to modify their dietary habits at time of discharge (Group 6-TD; Table 1); all the items were thoroughly explained and discussed with the patients. In particular, the patients and their partners were advised to eat portions of the single foods similar as those of the hospital (defined as "usual" in the diet scheme); moreover, all the patients were encouraged to eat fruit and vegetables during the 3 daily meals. No food list nor specific frequencies for any food were suggested.

Patients of the second arm received a written, standard diet containing 0.8 g of proteins/kg of desirable body weight/day, which contained at least 30 kcal/kg/day (25 in overweight patients), 3 and 6 g NaCl/day, and included hypoproteic noodle and bread (Group LPD). Such a diet, not customized to patients' dietary habits, was carefully explained to the patients by the nephrologist and included a list of allowed foods.

No further nutritional counselling was provided thereafter in both groups.

All the patients were followed up for 6 months, with three further clinical, nutritional, and laboratory controls after one (T1), three (T3), and 6 months (T6), beyond

baseline (T0). At each time point, blood was withdrawn to determine the main laboratory data; urinary urea nitrogen (UUN), sodium, potassium, phosphate, and protein excretion were also determined in samples from 24 h collections. Standard laboratory procedures were used for blood and urine measurements.

During their hospital stay, patients were prescribed pharmacological therapies in order to achieve the therapeutic targets suggested by K/DOQI guidelines for stage 3b-5. All the therapies were maintained throughout the follow-up period.

Renal function was expressed as eGFR, calculated by MDRD equation [17]. Dietary protein intake was estimated by daily UUN excretion and non-ureic nitrogen faecal or urinary loss or according to Maroni formula [18]. Changes in estimated protein intake defined adherence to prescribed diet over time. As in our previous study [19], the adherence to LPD was defined by a constant protein intake between 0.7 and 0.9 g/kg BW/day throughout the study; any patient out of this range during the follow-up period was considered "non-adherent." The same interval was arbitrarily considered as synonymous of compliance also in patients of Group 6-TD. The adherence to caloric prescription was indirectly verified by body weight variation.

### Endpoints

The primary efficacy end point of the study was to compare the effects of the two different diets, (6-TD and LPD) on protein intake, UUN excretion, serum urea nitrogen, urinary phosphate excretion, and serum phosphate concentration during a follow-up period of 6 months. As secondary endpoints, we also evaluated patients' adherence to the prescribed diet, and the effects of both diets on several additional metabolic (sodium, potassium, bicarbonate, parathyroid hormone) and nutritional parameters (BMI, serum albumin).

### Statistical analysis

The primary outcome measure with respect to efficacy was the mean decrease in protein intake from baseline to 6 months which was compared between two groups. Assuming a clinically significant difference of 0.15 g/kg/day in mean decrease between groups with a standard deviation (SD) of the differences equal to 0.2 g/kg/day, a power of 80 %, and 2-sided significance level of 5 %, a minimal sample size of 58 subjects (29 for each group) was calculated.

Analysis of change from baseline for the primary endpoints was performed using separate ANCOVA models with dietary regimen as a between group factor, time (1, 3, 6 months) as within factor and baseline values of dependent variable as covariates. Results from the ANCOVA models are expressed as estimated marginal means with 95 % CI both for the mean change from baseline within each dietary regimen as well as for the difference in mean change from baseline between groups. For each group and for each time point, the change from baseline was deemed significant, at a significance level of 0.05, if the estimated 95 % CI do not cross the zero values with no adjustment for multiplicity. The effect of dietetic therapy on patients' compliance, defined by a constant protein intake between 0.7 and 0.9 g/kg BW, measured at 1, 3, and 6 months, was evaluated by Chi-Square test.

Statistical analyses were performed with the statistical computing environment R (version 3.0.1; R Foundation for Statistical Computing, Vienna, Austria).

## Results

### Baseline data

As shown in Fig. 1, 57 of 61 patients assessed for eligibility were randomized to the two different diets: 28 to 6-TD (Group 6-TD) and 29 to LPD (Group LPD). Moreover, three patients (2 in Group LPD, 1 in Group 6-TD) developed a proteinuria >3.5 g/24 h during the follow-up and were excluded from the study; accordingly, the statistical analysis was performed on 54 patients ($n = 27$ in each group), who completed the study (Fig. 1).

The characteristics of these patients are summarized in Table 2. At baseline, the two groups were comparable for age, sex, body weight, eGFR (and distribution of CKD stages), and concomitant treatments. Moreover, blood pressure did not differ among patients of both groups (data not shown). Baseline laboratory data are reported in Table 3; no difference was detected between the two groups.

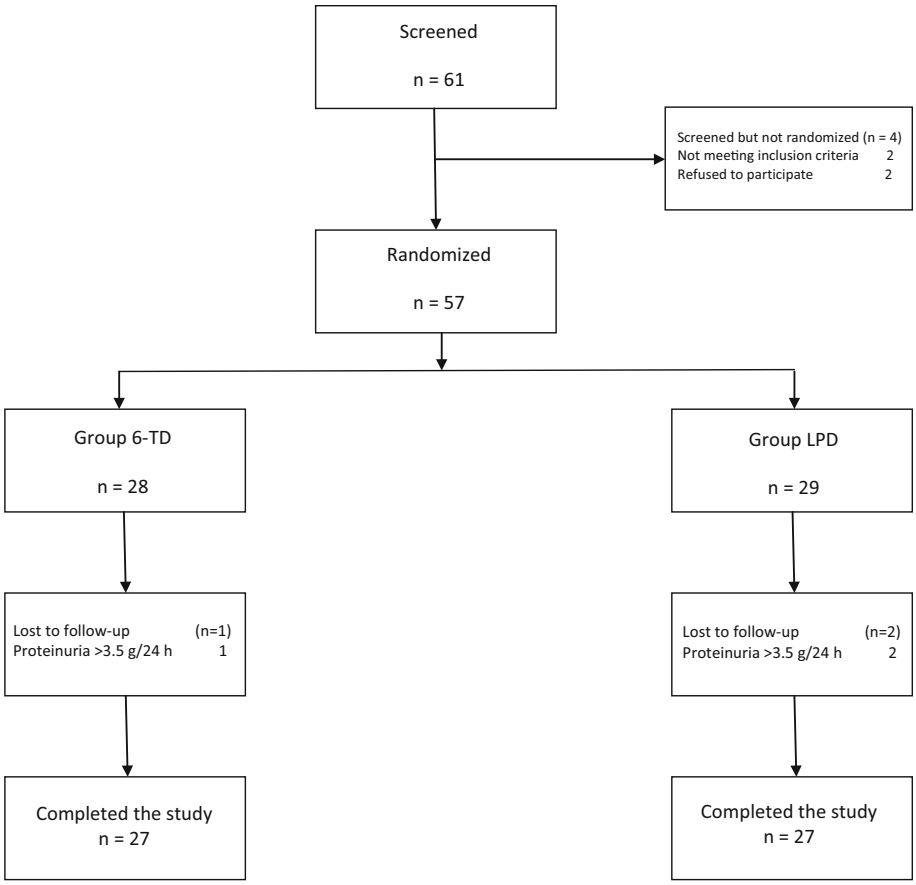
It is noteworthy that in both groups, the main laboratory data were in the desired range, mostly considering the severely reduced eGFR. Both groups, however, started from values of daily protein intake slightly higher than expected, considering that all the patients were prescribed a moderately protein-restricted diet during their hospital stay (0.7–0.8 g/kg/day of proteins and 6 g/day of NaCl).

### Follow-up data

The complete data (T0–T6) of main blood and clinical parameters of both groups of patients are reported in Table 4.

Both dietary regimens were associated with a progressive and significant reduction in UUN excretion compared to baseline since the first month of study (T1), although to a

**Fig. 1** Patient disposition




different extent (Table 5). Starting from the third month of diet (T3), the differences in UUN excretion in the two groups under study became statistically significant (mean difference between groups: −1.8 g/day, 95 % CI −3.0 to −0.6, $p = 0.005$), and such difference persisted at T6 (mean difference between groups: −1.5 g/day, 95 % CI −2.6 to −0.4, $p = 0.008$) (Table 5; Fig. 2a).

Daily phosphate excretion showed a divergent pattern in the two groups (Table 5; Fig. 2b); in fact, patients of the Group 6-TD showed a decrease in phosphate excretion compared to baseline, statistically significant since the first month of study, which progressively decreased until T6. In the Group LPD, conversely, daily phosphate excretion remained stable throughout the study. Starting from T3, the differences in phosphate excretion between the groups under study became statistically significant (mean difference between groups: −102.9 mg/day, 95 % CI −197.1 to −8.7, $p = 0.033$), and such difference persisted at T6 (mean difference between groups: −137.6 mg/day, 95 % CI −231.0 to −44.2, $p = 0.005$) (Table 5; Fig. 2b).

This discrepancy, however, did not influence serum phosphate concentrations that remained quite stable and in the normal range throughout the study in both groups (Tables 4, 5).

The decreased urinary excretion of urea and phosphate mirrored the significant reduction in protein intake in both groups during the follow-up period, observed since the third month of study (Fig. 2c; Tables 4, 5). However, starting from T3, the treatment effect became more pronounced in the Group 6-TD (−0.13 g/kg/day, 95 % CI −0.24 to −0.02, $p = 0.022$) and such difference persisted at T6 (difference between groups: −0.11 g/kg/day, 95 % CI −0.21 to −0.01, $p = 0.040$).

In partial agreement with such data, a significant difference was also detected in serum urea nitrogen (SUN) levels, that remained stable in Group LPD, but progressively decreased in Group 6-TD (difference between groups: −19.6 mg/day, 95 % CI −34.8 to −4.4, $p = 0.012$) (Table 5; Fig. 2d).

Conversely, and quite unexpectedly, the reduction in nutrients intake was not associated with a concomitant decline in urinary sodium chloride excretion, which was substantially high at baseline (Table 3) and was not modified during the follow-up (Table 5).

Only marginal variations were detected in bicarbonate levels in both groups with respect to baseline, with no significant change between the groups throughout the 6-month follow-up period (Fig. 2e; Tables 4, 5).

**Table 2** Demographic characteristics of the two groups under study at baseline

| | Group 6-TD ($n = 27$) | Group LPD ($n = 27$) |
|---|---|---|
| Gender (% female) | 48 | 48 |
| Age (years) | 58.8 ± 12.06 | 56.1 ± 12.06 |
| BMI (kg/m$^2$) | 25.9 ± 6.99 | 27.15 ± 4.05 |
| eGFR (mL/min/1.73 m$^2$) | 21.2 ± 7.4 | 20.9 ± 8.3 |
| CKD stage (%) | | |
| Stage 3b (30–45 mL/min/1.73 m$^2$) | 11 | 11 |
| Stage 4 (15–30 mL/min/1.73 m$^2$) | 59 | 59 |
| Stage 5 (<15 mL/min/1.73 m$^2$) | 30 | 30 |
| Renal disease (%) | | |
| GN | 29 | 26 |
| DM | 22 | 25 |
| ADPKD | 20 | 18 |
| Urological causes | 3 | 5 |
| Other/unknown | 26 | 24 |
| Drug treatments (%) | | |
| Antihypertensive drugs | 90 | 88 |
| Phosphate binders | 36 | 38 |
| Lipid lowering agents | 41 | 39 |
| Bicarbonate supplements | 78 | 74 |
| Diuretics | 9 | 10 |
| Vitamin D analogues | 5 | 6 |
| Iron supplements | 34 | 33 |
| ESA | 28 | 30 |

**Table 3** Main laboratory data of the patients of the two diet groups at baseline

| | Group 6-TD ($n = 27$) | Group LPD ($n = 27$) |
|---|---|---|
| Serum parameters | | |
| Serum creatinine (mg/dL) | 3.3 ± 1.32 | 3.3 ± 1.28 |
| Serum urea (mg/dL) | 105 ± 29 | 113 ± 32 |
| Serum potassium (mEq/L) | 5.06 ± 0.47 | 5.18 ± 0.66 |
| Serum phosphate (mg/dL) | 3.97 ± 0.7 | 3.98 ± 0.82 |
| Serum calcium (mg/dL) | 9.5 ± 0.5 | 9.4 ± 0.3 |
| Serum bicarbonate (mEq/L) | 23.4 ± 2.4 | 24.1 ± 3.5 |
| Serum albumin (g/dL) | 4.47 ± 0.23 | 4.42 ± 0.29 |
| Intact-PTH (pg/mL) | 155 ± 138 | 136 ± 84 |
| Total cholesterol (mg/dL) | 179 ± 36 | 187 ± 34 |
| Triglycerides (mg/dL) | 138 ± 85 | 125 ± 49 |
| Hb (g/dL) | 11.4 ± 1.2 | 11.2 ± 1.1 |
| Transferrin (μg/dL) | 305.4 ± 76.3 | 298.7 ± 95.4 |
| CRP (mg/dL) | 0.9 ± 0.3 | 1.1 ± 0.5 |
| Urinary parameters | | |
| Proteinuria (g/day) | 1.6 ± 1.7 | 1.5 ± 1.4 |
| UUN excretion (g/day) | 9.2 ± 3.3 | 9.5 ± 2.3 |
| Phosphate excretion (mg/day) | 619.3 ± 158.8 | 606.9 ± 214.6 |
| NaCl excretion (mEq/day) | 159.3 ± 53.5 | 174.4 ± 58.3 |
| Protein intake (g/kg/day) | 0.94 ± 0.21 | 0.96 ± 0.2 |

**Table 4** Main laboratory and clinical data of patients of LPD and 6-TD groups throughout the follow-up period

| | Protein intake (g/kg/day)[a] | | SUN (mg/dL) | | Phosphate (mg/dL) | | Bicarbonate (mEq/L) | | Albumin (g/dL) | | BW (kg) | | GFR (mL/min/1.73 $m^2$) | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | LPD | 6-TD | LPD | 6-TD | LPD | 6-TD | LPD | 6-TD | LPD | 6-TD | LPD | 6-TD | LPD | 6-TD |
| T0 | 0.96 (0.2) | 0.94 (0.21) | 113.1 (32.2) | 105.2 (28.9) | 4 (0.8) | 4 (0.8) | 24.1 (3.3) | 23.5 (2.4) | 4.4 (0.2) | 4.5 (0.2) | 78.2 (13.9) | 76.2 (15.7) | 21 (8.3) | 21.2 (7.4) |
| T1 | 0.88 (0.25) | 0.81 (0.22) | 114.1 (45.7) | 98.6 (41.3) | 4.1 (0.8) | 3.7 (0.8) | 25.2 (3.6) | 24.4 (2.6) | 4.3 (0.3) | 4.5 (0.2) | 78 (14.0) | 75.5 (15.6) | 20.8 (8.8) | 21.3 (8.2) |
| T3 | 0.86 (0.23) | 0.73 (0.19) | 111.3 (37.4) | 96.7 (23.9) | 4.2 (0.9) | 3.9 (0.9) | 23.4 (3.7) | 25 (2.2) | 4.4 (0.3) | 4.5 (0.3) | 77.4 (13.9 | 75.3 (15.4) | 19.3 (9.0) | 21.3 (8.6) |
| T6 | 0.86 (0.21) | 0.75 (0.17) | 115 (43.5) | 89.6 (24.6) | 4.2 (0.9) | 3.9 (0.8) | 24.7 (2.6) | 25.3 (3.6) | 4.4 (0.3) | 4.4 (0.3) | 77.2 (14.0) | 75.4 (15.6) | 18.7 (9.3) | 21.2 (9.3) |

Data are expressed as mean ± SD

*SUN* serum urea levels, *BW* body weight, *GFR* glomerular filtration rate

[a] The amount of protein was calculated according to the desired body weight

No modification was observed throughout the study period in the other laboratory data, including serum albumin (Table 4), haemoglobin, sodium, potassium, PTH and urinary protein excretion, and BP in both groups (data not shown).

Last, although the progression of renal failure was not an outcome of the trial, patients of Group LPD experienced a slight but significant decrease of eGFR starting from the third month of follow-up, while renal function remained remarkably stable in Group 6-TD (Fig. 2f; Table 4).

According to the protocol, patients were maintained at the same pharmacological therapies throughout the follow-up period.

### Compliance data

Following our arbitrary definition of "dietary adherence", i.e., daily protein intake never exceeding the range 0.7–0.9 g/kg/day in each time point of the study, 19 patients (70 %) of Group 6-TD were considered adherent to our prescription, compared to only 11 patients of Group LPD (44 %), although such difference did not achieve statistical significance. No patient had a protein intake below 0.7 g/kg/day throughout the follow-up period.

Conversely, since BW remained stable in both groups during the entire study period, the caloric intake was considered acceptable in both in LPD and 6-TD patients.

## Discussion

The key finding of our randomized trial is that a simplified diet, consisting of 6 clear points easily managed by patients with CKD, produced beneficial effects either on the metabolic profile of renal disease and on patients' adherence to the dietary plan, when compared to a moderately low-protein diet (0.8 g/kg/day).

Although the beneficial metabolic effects of LPDs are widely recognized, diet efficacy is hampered by the low patients' adherence [21]. Clinical trials generally employ extensive dietary counselling and close clinical monitoring in selected patients to enhance dietary compliance; nevertheless, adherence to LPDs continues to be poor [22–25] and is even worse in current medical practice, if patients benefit of less intensive care either in terms of education and of periodic dietary counselling. Therefore, it seems crucial to develop easier and more flexible approaches to LPDs able to join metabolic efficacy and better acceptance [20], as also recently suggested by Piccoli et al., who allowed 1–3 unrestricted meals/week and a tailored control policy in patients prescribed 0.6 g/kg/day, reaching an average protein intake of 0.7 g/kg/day [26].

**Table 5** Mean changes from baseline for all study variables

| | T1 | | | T3 | | | T6 | | |
|---|---|---|---|---|---|---|---|---|---|
| | 6TD | LPD | *p* value° | 6TD | LPD | *p* value° | 6TD | LPD | *p* value° |
| UUN (g/day) | −1.7 (−2.5 to −0.9)* | −1 (−1.8 to −0.2)* | 0.220 | −2.7 (−3.6 to −1.9)* | −0.9 (−1.8 to −0.1)* | 0.005 | −2.8 (−3.6 to −2)* | −1.3 (−2.1 to −0.5)* | 0.008 |
| Phosphate excretion (mg/day) | −97.2 (−168.5 to −25.8)* | −51.1 (−122.5 to 20.2) | 0.364 | −133.3 (−199.9 to −66.7)* | −30.4 (−97 to 36.2) | 0.033 | −165.3 (−231.3 to −99.2)* | −27.6 (−93.7 to 38.4) | 0.005 |
| Serum phosphate (mg/day) | −0.3 (−0.5 to 0.0) | 0.1 (−0.1 to 0.3) | 0.054 | 0 (−0.4 to 0.3) | 0.2 (−0.1 to 0.5) | 0.259 | −0.1 (−0.3 to 0.2) | 0.2 (0 to 0.4) | 0.093 |
| NaCl excretion (mEq/day) | −12.4 (−32.1 to 7.4) | −9.3 (−29 to 10.5) | 0.825 | −16.2 (−35 to 2.6) | −5 (−23.8 to 13.8) | 0.405 | −18.2 (−40 to 3.6) | 4.5 (−17.3 to 26.2) | 0.148 |
| Protein intake (g/kg/day) | −0.14 (−0.22 to −0.06)* | −0.08 (−0.16 to −0.00)* | 0.266 | −0.22 (−0.3 to −0.15)* | −0.09 (−0.17 to −0.02)* | 0.022 | −0.2 (−0.28 to −0.13)* | −0.1 (−0.17 to −0.03)* | 0.040 |
| SUN (mg/dL) | −6.65 (−18.97 to 5.67) | 1.65 (−10.67 to 13.97) | 0.345 | −9.55 (−18.18 to −0.91)* | −0.71 (−9.35 to 7.92) | 0.154 | −16.63 (−27.3 to −5.96)* | 2.96 (−7.71 to 13.64) | 0.012 |
| Bicarbonate (mEq/L) | 0.69 (−0.44 to 1.83) | 1.21 (0.08 to 2.35)* | 0.518 | 1.22 (0.05 to 2.39)* | −0.45 (−1.62 to 0.72) | 0.055 | 1.63 (0.55 to 2.7)* | 0.72 (−0.35 to 1.8) | 0.241 |
| GFR (ml/min/1.73 $m^2$) | 0.12 (−1.21 to 1.45) | −0.14 (−1.47 to 1.2) | 0.785 | 0.15 (−1.23 to 1.52) | −1.68 (−3.05 to −0.3)* | 0.066 | 0.24 (−1.03 to 1.51) | −2.28 (−3.55 to −1.01)* | 0.007 |

Data are expressed as means (95 % CI) variations from baseline. *T1*, *T3*, *T6*: 1, 3, and 6 months of follow-up, respectively

*UUN* urinary urea excretion, *SUN* serum urea concentration, *GFR* glomerular filtration rate

* Significantly different from 0 at p = 0.05

° Between-group *p* values estimated by ANCOVA models adjusted by baseline values

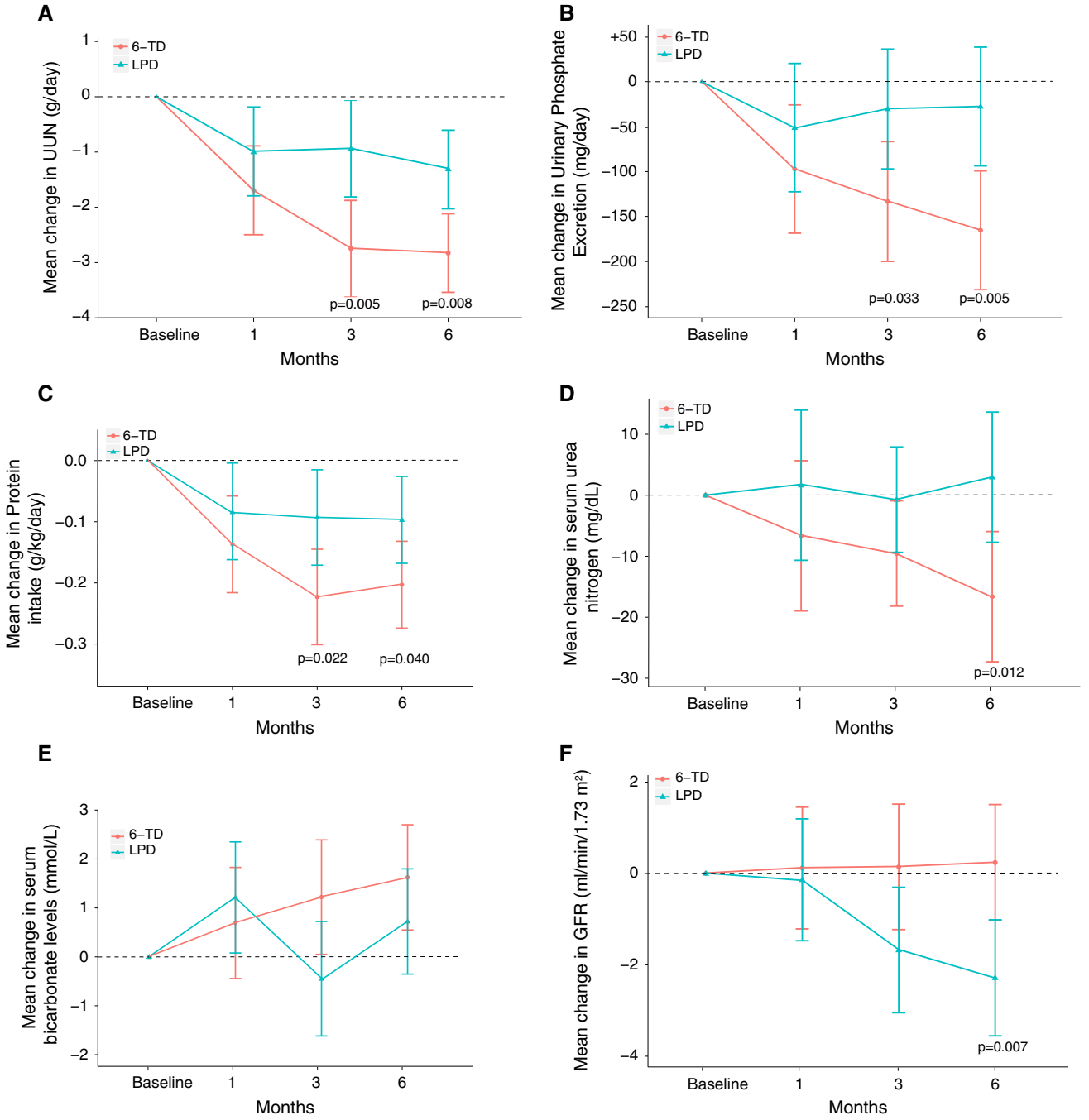



**Fig. 2** Mean changes in UUN excretion (**a**), urinary phosphate excretion (**b**), protein intake (**c**), serum urea nitrogen (**d**), bicarbonate (**e**), and GFR (**f**) for Group 6-TD (*circles*) and Group LPD (*triangles*). *Error bars* represent 95 % CIs as estimated by ANCOVA models for repeated measures with baseline values as covariates. *UUN* urinary urea nitrogen, *GFR* glomerular filtration rate

These considerations induced us to develop a new, simplified and easy to manage dietary plan to improve patients' acceptance and adherence when dietary counselling is not available; hence, our working hypothesis was to evaluate the effects of such diet compared to a standard, moderately protein-restricted diet on metabolic parameters and patients' adherence.

Although KDOQI guidelines still recommend diets containing 0.6 g/kg/day of proteins, we chose to prescribe a 0.8 g/kg/day diet, a low-normal protein diet, since there is evidence in the literature that such intake still positively influences metabolic parameters and may be reached in the majority of CKD patients [20].

Our data demonstrate that the 6-TD was associated with a better metabolic pattern compared to standard LPDs, as primary efficacy end point. In fact, despite both diets were associated with a significant decrease in protein intake compared to their respective baseline intake during the 6-month follow-up, such reduction was more pronounced in patients with 6-TD. Accordingly, even urinary urea excretion and serum urea nitrogen decreased significantly more with 6-TD than with LPD.

Also phosphate excretion decreased significantly more in 6-TD patients than in Group LPD; this difference, however, did not influence phosphate plasma levels that remained similar and in the normal range in both groups throughout the study. It is possible that LPD patients ingested a greater amount of "hidden phosphorus" in prepared foods, which may significantly contribute to the phosphorus burden in CKD patients [25]; the use of phosphate binders probably allowed plasma phosphate concentration to remain in the normal range.

In both groups, the intake of NaCl averaged 10 g/day, far exceeding that recommended at baseline (point #1 of our 6-TD), and remained quite stable throughout the study. This was not surprising, since adherence to salt restriction is likely the most difficult to achieve in CKD patients, and even the use of very low-protein diets (VLPDs) in adherent patients allows just a small reduction in salt intake [7]. In our setting, moreover, the peculiar dietary habits of Southern Italy, characterized by high salt ingestion and the increased intake of sodium bicarbonate in most patients of both Group LPD and 6-TD (74 and 78 %, respectively), further contributed to this result. These data suggest that a greater effort should be made to strengthen the concept of limiting salt intake with either diet, of minimizing the use of specific foods and also of avoiding particular sauces or preserved food.

As second end point of the study, we also evaluated patients' adherence to both diets, a critical issue in CKD patients. We have previously reported that patients' compliance to a diet containing 0.6 g/kg/day of protein did not exceed 20 % during the 1 year follow-up, despite dietary counselling [13]; the better compliance observed in MDRD study [23] using a similar dietary regimen, (35–46 % in study A and B, respectively) merely reflected the wider 'adherence range' for protein intake (±30 %), far higher than ours (±12 %). Better results in terms of adherence were obviously obtained with higher intakes of nutrients (and proteins): 53 % of patients assigned to a 0.8 g/kg/day diet were able to follow our prescription during a 18-month follow-up, and such percentage raised to 76 % including also patients prescribed a very strict protein intake (0.55 g/kg/day) that did not exceed 0.8 g/kg/day [20]. Unfortunately, the dietary adherence in Group LPD of the present study was very low: only 44 % of patients, in fact, remained in the desired range of protein intake, much less than expected on the basis of our previous experience [13, 20]. It is possible that the lack of dietary counselling, which represented a key point of our previous studies, has consistently contributed to a worse result. It is well known that a multidisciplinary approach results in an improved metabolic pattern, with positive influences on quality of life and in better adherence. A recent, randomized study by Paes Barreto shows that intensive dietary counselling in CKD patients prescribed a LPD, determined a satisfactory level of adherence (69 %) compared to patients with standard counselling, in whom adherence averaged 48 %, quite similar as in our study [15]. Most patients of Group 6-TD (70 %), conversely, remained in the desired range of protein intake than in Group LPD, despite this difference was at limit of statistical significance ($p > 0.05$), likely due to the limited power of our study to detect a true difference between the groups. These data, however, clearly suggest that the 6-TD, beyond its metabolic efficacy, is certainly better accepted than the usual diet, probably for its simplicity (no food to weight, large selection of meals) and for its easiness to be memorized. Moreover, the relative stability of body weight observed in all the patients also suggests that caloric intake was adequate in both groups.

We used 6 tips in our diet, since we considered them the most important points to face when prescribing a diet. Specific subsets of patients could have requested some additional tips about a correct energy intake, like diabetic patients, or the need to increase water ingestion and avoid caffeine intake, like ADPKD patients. We did not consider these points in 6-TD, however, assuming that these patients had their diagnosis years before the onset of renal failure and, therefore, were certainly aware of the peculiar problems linked to their condition. It seems useful, however, in ADPKD patients, to stress these advices not considered in the written diet.

Last, no difference was detected between the groups in the other metabolic parameters, all maintained in a satisfactory range according to our targets.

The major limit of the study resides in the small number of patients enrolled in the protocol and the short follow-up period that do not allow to evaluate patients outcomes. Moreover, patients of both groups started the experimental study in good clinical and metabolic conditions and therefore are not representative of the general CKD population, although it seems reasonable that the beneficial effects of 6-TD on patients' adherence and on metabolic profile may be extended to all CKD patients. Another limit of the study is that the 6-TD mostly reflects the dietary habits of Southern Europe and, although it could be easily adapted to Western people, cannot certainly be prescribed to Eastern populations due to obvious differences in selection of nutrients and in meals schedule. Last, no questionnaire was performed throughout the study period to ascertain the

quality of patients' diets, the biologic level of proteins or the daily amount of fruit/vegetables they really ingested.

In conclusion, the adoption of the 6-TD was characterized by a better metabolic pattern (decreased intake of protein, decreased excretion of phosphate) and a higher adherence rate than LPDs; in fact, the greater flexibility in quantity and quality of food selection and the easiness in realizing these tips encourage patients to follow the dietary restriction.

However, despite these beneficial effects of 6-TD, we continue to emphasize the need of dietitians and of a continuous dietary counselling in clinical practice, mostly when we must prescribe a "real" LPD (0.55–0.60 kg/day) or a VLDP (0.3 g/kg/day) and we need a good adherence to the dietary plan [27]. The 6-TD, therefore, may represent a valid alternative to a standard low-protein diet, mostly when a dietary counselling is not available.

**Compliance with ethical standards**

**Conflict of interest** All the authors declare that no conflict of interest exists.

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