REVIEW

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Nutritional therapy in autosomal dominant polycystic kidney disease

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Abstract

CKD-related nutritional therapy (NT) is a crucial cornerstone of CKD patients' treatment, but the role of NT has not been clearly investigated in autosomal dominant polycystic kidney disease (ADPKD). Several clinical studies have focused on new pharmacological approaches to delay cystic disease progression, but there are no data on dietary interventions in ADPKD patients. The aim of this paper is to analyze the evidence from the literature on the impact of five nutritional aspects (water, sodium, phosphorus, protein intake, and net acid load) in CKD-related ADPKD extrapolating—where information is unavailable—from what occurs in CKD non-ADPKD patients Sodium intake restriction could be useful in decreasing the growth rate of cysts. Although further evidence is needed, restriction of phosphorus and protein intake restriction represent cornerstones of the dietary support of renal non-ADPKD patients and common sense can guide their use. It could be also helpful to limit animal protein, increasing fruit and vegetables intake together with a full correction of metabolic acidosis. Finally, fluid intake may be recommended in the early stages of the disease, although it is not to be prescribed in the presence of moderate to severe reduction of renal function.

Keywords ADPKD · CKD · Nutritional therapy · Fluid intake · Sodium intake · Protein intake · Phosphorus intake · Metabolic acidosis

Background

Autosomal dominant polycystic kidney disease (ADPKD) is an inherited disorder caused by mutations of polycystin 1 (PKD1) and polycystin 2 (PKD2) genes. As a result, multiple

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cystic formations grow into kidney parenchyma causing compression and disruption of functional kidney tissue leading to chronic kidney disease (CKD) and ultimately to end-stage renal disease (ESRD) in almost 50% of patients older than 50 years old. Cysts and aneurysms can also develop in several tissues and organs such as the liver, pancreas and blood vessels (especially encephalic and aortic ones). Arterial hypertension and left ventricular hypertrophy are quite prevalent in ADPKD patients [1, 2]. Some clinical studies have focused on new pharmacological approaches to slow down ADPKD progression, but few of them have dealt with nutritional and dietary aspects in ADPKD patients. The aim of this paper is to analyze the evidence from the literature on the impact of five nutritional aspects (water, sodium, phosphorus, protein intake, and net acid load) in CKD-related ADPKD, extrapolating the information, where unavailable, from what occurs in CKD non-ADPKD patients.

Water intake

High fluid intake represents an appealing therapeutic strategy due to the pathophysiological background and to the

lack of severe side effects; on the other side, this approach is not always accepted by patients. The recommended fluid intake in ADPKD patients is still an open debate within the scientific community. The rationale is linked to the attempt to suppress anti-diuretic hormone (ADH) secretion and consequently both adenylyl cyclase and cyclic adenosine monophosphate (cAMP) production through vasopressin V2 receptor activation, since adenylyl cyclase and cAMP secretion induces renal cysts growth [3, 4]. Several studies show that an increased fluid intake, with consequent ADH suppression, induces regression of cysts growth and also reduces kidney disease progression [5, 6].

Nagao et al. evaluated the consequences of increasing fluid intake in rats: by increasing fluid intake from 3.5 to 8.2-fold for 10 weeks, a 68% reduction in arginine vasopressin urinary excretion and a urine osmolality up to 290 mOsm/kg occurred. A significant reduction (29.8 and 27% in male and female mice, respectively) in kidney weight and serum urea (from 38 to 26 mg/dl) was found. Therefore, a 54 and 28% reduction in cystic area and kidney/body weight ratio was also observed [7].

Hopp et al. reported that over-hydration had protective effects in an ADPKD rat model [8]. Water intake reduced urinary vasopressin and cAMP levels together with delaying disease progression in PKD rats. Rats assigned to the experimental arm also presented higher phosphodiesterase activity, lower cAMP levels and they were less sensitive to cystogenic effects of arginine-vasopressin [8]. In another study in 13 ADPKD patients, water intake higher than 7 Ls/day for a week led to urine osmolality reduction but it did not affect urinary cAMP excretion [9]. In a non-randomized trial performed on 30 ADPKD patients (17 with high water intake and 13 with unforced water intake) no changes were observed at 1-year follow-up, despite higher diuresis rates. Osmolality reduction was observed only in the higher water intake ADPKD patients during the follow-up period, as well as a reduction in estimated glomerular filtration rate (eGFR) ($p = 0.011$) and an increase in kidney volume [10]. Two years later, Amro et al. demonstrated that a 12-month hypo-osmolality and high water intake diet led to a significant reduction in copeptin (an arginine-vasopressin surrogate biomarker) and urine osmolality [11].

An updated survey has highlighted that, although 61% of patients had water intake higher than 2 Ls/day, only 4% had a fluid intake higher than 4 Ls/day [12]. To date, it is still unclear what patients mean by "high fluid intake" and no evidence about the efficacy has been published: randomized clinical trials are probably needed [13]. Data on over-hydration as a method to delay and reduce the cystogenic pathway are still ineffective at present. However, over-hydration is often recommended in ADPKD patients, especially in the early phases of the disease. But a common complication in ADPKD is renal calculus, and in these cases hydroponic therapy is useful. Therefore, the use of such therapy, as there are no papers showing a deterioration of residual renal function after hydroponic therapy, is not to be excluded *a priori*, but rather should be carefully evaluated case by case [14, 15].

The use of vasopressin V2-receptor antagonists (Tolvaptan) to slow the increase in total kidney volume has recently been demonstrated by a major phase 3 multicenter double-blind placebo-controlled study [16]. In fact, the TEMPO 3:4 trial demonstrated, in 1445 patients aged 18–50 years, that the use of Tolvaptan led to a reduced increase in kidney volume, of 2.8% compared to 5.5% per year ($p < 0.001$) in controls [16]. Tolvaptan antagonizes the V2 receptors in the collecting duct of the kidney, causing an elimination of electrolyte-free water (aquaresis) and a consequent increase in plasma sodium. The action of Tolvaptan regarding the 24-h urinary volume increase is dose-dependent and appears to affect the same mechanisms as high water intake action in antagonizing the V2 receptors in the collecting duct and suppressing ADH secretion and consequently both adenylyl cyclase and cAMP production [17].

Sodium intake

HALT PKD is a perspective randomized double-blind study designed to verify whether intensive blood pressure control, through a combination of angiotensin converting enzyme inhibitors (ACEi) and angiotensin receptor blockers (ARBs), can delay kidney disease progression compared to monotherapy with ACEi only, in ADPKD patients [18]. A post-hoc analysis of HALT PKD was performed to assess if lowering urine osmolality by a reduction of sodium intake (< 2.4 g/day) could lead to better results than over-hydration [19]. Torres et al. analyzed data from 558 ADPKD patients with normal renal function (study-A with eGFR 91 ml/min on average) and 486 stage 3 CKD patients (study-B with eGFR 48 ml/min on average) both on low sodium diet. Patients showed a mild urinary sodium reduction from 178 to 166 mmol/die (study A) and from 177 to 152 mmol/die (study B). In the study A cohort, changes in urinary sodium excretion were significantly associated with kidney volume growth (0.43 and 0.09%/year respectively, for each 18 mEq of urinary sodium excretion). At the same time, changes in urinary sodium excretion were not associated with a delay of renal function loss (− 0.07 ml/min/1.73 m^2/year for each 18 mEq of urinary sodium excretion). In the study B cohort, urinary sodium excretion was related to composite end-points (hazard ratio 1.08 for each 18 mEq urinary sodium excretion) and to progression of kidney disease (–0.09 ml/min/1.73 m^2/year for each 18 mEq of urinary sodium excretion). Torres et al.'s findings suggest that dietary sodium restriction may play a beneficial role in ADPKD patients [19].

Amro and coll. [11], as already mentioned, have demonstrated that a reduced dietary intake of sodium can produce a significant reduction in vasopressin secretion in patients with ADPKD, in the same way as an increased intake of water. This finding has also been confirmed by Taylor et al. [20]. Based on these reported findings, dietary sodium intake restriction may be helpful in the clinical management of ADPKD patients, as well as in essential hypertensive patients and/or non-ADPKD CKD patients [21, 22].

Phosphorus intake and role of phosphorus level in ADPKD patients

A cross-link between phosphorus levels and cardiovascular mortality in a non-CKD population has been reported [23–25], as well as in CKD and ESRD patients on renal replacement therapy [26, 27]. However, there is no prospective randomized or retrospective study investigating the effect of phosphorus intake and cardiovascular and renal outcomes in patients with ADPKD. On the other hand, there are no data actually reported in the literature that link the dietary phosphorus intake and ADPKD progression.

A very recent paper [28] has highlighted, in a pediatric population with ADPKD and preserved renal function, the presence of hypophosphatemia and suppressed bone formation. The study showed that although there was no difference with respect to controls in the high fibroblast growth factor 23 (FGF23) levels the level should nevertheless be considered inappropriate given the concomitant hypophosphatemia

[28]. The pathophysiology and potential clinical consequences of aspects such as FGF23 and fractional phosphorus excretion need to be further investigated in patients with ADPKD.

We must therefore use experimental data drawn from randomized prospective studies designed for other purposes. We used the Independent study [29, 30] to investigate a general population with CKD to search for data to evaluate the phosphorus level in ADPKD patients and mortality. Obviously, such analysis allows only to generate hypotheses, which would then need to be confirmed by prospective randomized prospective studies. In the Independent–HD study, 33 ADPKD patients are enrolled [29]. Table 1 shows baseline data based on phosphorus serum levels according to the following tertiles: the 1st tertile was 3–4.6 mg/dl (parathormone [PTH] 145 ± 95 pg/ml and creatinine 9 ± 2 mg/dl); the 2nd tertile was 4.6–5.5 mg/dl (PTH 261 ± 98 pg/ml and creatinine 10.3 ± 3 mg/dl) and the 3rd tertile was 5.5–6.8 mg/dl (PTH 284 ± 110 pg/ml and creatinine 12.3 mg/dl). Kt/V did not differ among the three groups. In the follow-up period, 12 patients died due to cardiovascular disease, as shown in Fig. 1—the mortality rate according to serum phosphorus levels was 8% in the lowest tertile, 34% in the medium tertile, and 58% in the highest tertile ($p < 0.001$).

We also evaluated data of the Independent-CKD study [30]: 15 ADPKD patients were found (7 patients with P < 4.5 mg/dl and 8 with P > 4.6 mg/dl) (Table 2) with medium eGFR 34 ± 6 ml/min. Of these 15 patients, 9 died from cardiovascular disease and/or started renal replacement

Table 1 Baseline data of 33 Independent—HD study ADPKD patients [24]

	All	1st tertile	2nd tertile	3rd tertile	p
Number	33	11	11	11	NA
Male	12	3	3	6	NA
Age (years)	66.7 ± 7.7	67.8 ± 7.5	70.0 ± 3.6	62.2 ± 9.4	NS
BW (kg)	69 ± 14	70 ± 13	63 ± 11	74 ± 16	NS
SBP (mmHg)	142 ± 23	150 ± 20	140 ± 21	136 ± 27	NS
DBP (mmHg)	80 ± 9	82 ± 11	78 ± 10	79 ± 12	NS
HR (b/min)	73 ± 10	73 ± 12	71 ± 9	73 ± 9	NS
Creatinine (mg/dl)	10 ± 3	9 ± 2	10 ± 3	12 ± 3	0.043
Na (mmol/l)	141 ± 4	140 ± 4	142 ± 4	140 ± 5	NS
K (mmol/l)	5.4 ± 0.7	5.4 ± 0.6	5.0 ± 0.7	5.7 ± 0.8	NS
Ca (mg/dl)	9.2 ± 0.9	9.0 ± 0.6	9.1 ± 0.8	9.5 ± 1.2	NS
P (mg/dl)	5.1 ± 1.0	4.0 ± 0.5	5.1 ± 0.2	6.2 ± 0.4	0.001
PTH (pg/ml)	231 ± 116	146 ± 95	261 ± 98	284 ± 110	0.007
Hb (g/dl)	11.2 ± 1.4	10.8 ± 1.0	11.7 ± 1.8	11.1 ± 1.1	NS
Serum albumin (g/dl)	3.8 ± 0.5	3.7 ± 0.4	3.8 ± 0.5	4.0 ± 0.6	NS
CRP (mg/dl)	9 ± 9	8 ± 14	13 ± 10	6 ± 3	NS
Total cholesterol (mg/dl)	172 ± 47	160 ± 58	182 ± 34	173 ± 48	NS
Kt/V	1.22 ± 0.13	1.22 ± 0.10	1.17 ± 0.13	1.26 ± 0.16	NS

BW body weight, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *HR* heart rate, *PTH* parathormone, *HB* hemoglobin, *CRP* C-reactive protein
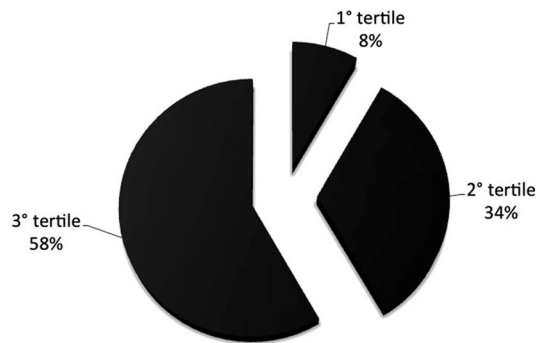
Fig. 1 Deaths due to cardiovascular causes by tertile of phosphorus in APKD patients who participated in the Independent-HD study (data from [23])

Table 2 Baseline data of 15 Independent—CKD ADPKD patients [25]

	All	P < 4.5	P > 4.6	p
Number	15	7	8	NA
Male	9	4	5	NA
Age (years)	56.1 ± 8.7	54.9 ± 8.4	56.9 ± 9.5	NS
BW (kg)	67 ± 15	72 ± 12	63 ± 16	NS
SBP (mmHg)	140 ± 13	147 ± 12	134 ± 11	NS
DBP (mmHg)	76 ± 10	78 ± 10	75 ± 11	NS
HR (b/min)	69 ± 12	66 ± 8	71 ± 14	NS
Creatinine (mg/dl)	4.5 ± 0.9	4.3 ± 0.6	4.6 ± 1.1	NS
Na (mmol/l)	139 ± 2	139 ± 3	139 ± 2	NS
K (mmol/l)	5.3 ± 0.9	5.6 ± 0.5	5.1 ± 1.1	NS
Ca (mg/dl)	9.0 ± 0.5	9.1 ± 0.6	9.0 ± 0.3	NS
P (mg/dl)	5.04 ± 1.65	3.62 ± 0.59	6.11 ± 1.33	0.001
PTH (pg/ml)	242 ± 153	271 ± 187	220 ± 131	NS
Hb (g/l)	11.1 ± 1.0	11.4 ± 1.3	10.8 ± 0.8	NS
Serum albumin (g/dl)	3.7 ± 0.3	3.7 ± 0.3	3.7 ± 0.3	NS
CRP (mg/dl)	12 ± 20	6 ± 5	16 ± 27	NS
Total cholesterol (mg/dl)	153 ± 48	130 ± 28	170 ± 60	NS
Triglyceride (g/dl)	156 ± 67	134 ± 75	173 ± 60	NS

BW body weight, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *HR* heart rate, *PTH* parathormone, *HB* hemoglobin, *CRP* C-reactive protein

therapy: 2 (28%) had P < 4.5 mg/dl and 7 (87%) had P > 4.6 mg/dl.

Post-hoc analyses involving 33 and 15 patients cannot provide scientific proof; however, the results mentioned above suggest that hyperphosphatemia could be accountable for a higher mortality risk also in ADPKD-ESRD patients. To date, it still remains to be demonstrated that a reduction of phosphorus serum levels can impact on cardiovascular mortality in ADPKD patients: this could represent a new challenge to be faced in the coming future.

Protein intake

Experimental data have highlighted that an early restriction of protein intake can delay CKD progression in non-ADPKD patients, and it has been repeatedly shown that the reduction of protein intake must be accompanied by an energy intake of 30–35 kcal/kg/BW/day to avoid dangerous episodes of caloric-protein malnutrition [31, 32]. Back in 1992, Aukema et al. showed a lower increase of cystic volume, namely a 46% reduction in cyst area in mice on low protein intake (LP) compared to mice with normal protein intake, or casein and sunflower seed oil (SO) and fish oil (FO) [33]. The authors also demonstrated that a vegetable protein-enriched diet led to a 28% reduction in kidney weight (p = 0.0037), a 37% reduction (p = 0.0089) in cyst score (cystic area % x relative body weight) and a 25% reduction in kidney water content (p = 0.0144) compared to an animal protein-enriched diet [34].

Lower protein intake (6 vs. 17.4 g %) was associated with a 30% reduction of kidney weight (p = 0.001), a 25% reduction in cyst score (p = 0.0327) and a 35% reduction in kidney water content [34]. Similar results were reported by Tomobe et al. in a 105 day follow-up period with vegetable protein intake in mice [35]. In a small sample study on genetic polycystic rats, a reduction in the protein intake caused a reduction of kidney and glomerular volume, but it did not affect size and/or growth of the kidney cysts [36].

Finally, Ogborn et al. evaluated two dietetic schedules (with the same protein intake) administered to mice during a period of 6 weeks comparing casein vs. soil seeds. The authors found a cystic volume reduction (from 7 to 4.3 ml/kg) associated to vegetable protein intake (p < 0.001), together with a reduction of epithelial cells (from 21 to 15.7 cells/mm, p < 0.001), of macrophage infiltration (from 43.5 to 25.3, p < 0.001) and of fibrosis (from 1.06 to 0.6 ml/kg, p < 0.001) [37].

More recently, Yamaguchi et al. did not find any clinical benefit in Pkd2WS25 mice (ADPKD mice) after 13 weeks of soil protein nutrition compared to casein intake in the control population [38]. In ARPKD (autosomic *recessive* polycystic kidney disease) mice, an animal protein-based diet led to an increase of kidney and liver weight together with an increase of kidney water content and cystic area [38]. Kidney and liver histology did not improve but lower proteinuria and higher urine pH suggested that a soil seeds diet could be favorable in the long-term period, independently of its effects on cystogenesis [38].

Another paper reported that food restriction may delay ADPKD progression in experimental models [39]. Cyst volume was reduced by moderate food restriction (10–40%), while renal fibrosis and inflammation were not affected [39]. Molecular and biochemical investigations showed that food restriction improves ADPKD progression

by suppression of the rapamycin pathway and liver B1/AMP kinase activation [39].

Kipp and coll reported that a 23% food restriction is able to impact on polycystic disease progression [40]; without affecting physiological growth or causing malnutrition or other side effects, it can postpone the disease's progression [40]. In fact, the relative increase in kidney weight was 41 vs. 151% and cystic proliferation was 7.7 vs. 15.9% compared to controls [40].

Food restriction was able to preserve renal function in experimental PKD models suggesting that polycystic kidneys are susceptible to food and calorie restrictions [40, 41].

The above-mentioned experimental data were not confirmed in a human population [42, 43]. Klahr et al. evaluated 200 ADPKD patients from the MDRD study: CKD progression was faster in ADPKD patients than other patients; disease progression was found to be related to the disease *per se*, to higher serum creatinine levels (independently of GFR), to higher proteinuria and to higher mean blood pressure [42]. Therefore, in ADPKD patients with GFR between 25 and 55 ml/min/1.73 m^2, neither lower protein intake, nor lower blood pressure levels significantly delayed renal disease progression [42]. On the other hand, in stage 4–5 CKD patients (GFR between 13 and 24 ml/min/1.73 m^2), patients with a lower mean arterial pressure showed the fastest decline in GFR values. However, faster GFR decline did not appear to be related to the anti-hypertensive treatment. Reduced protein intake, but not keto-analogues prescription was associated to the slowest CKD progression [42].

In a retrospective study enrolling 109 ADPKD patients, Choukroun et al. demonstrated a weak positive relationship between eGFR changes and mean arterial blood pressure; no relation with dietary protein intake (r = 0.10; p = 0.33) or proteinuria was found (r = 0.10; p = 0.28) [43]. The authors' conclusion was that lower CKD progression rate in ADPKD patients is mainly linked to genetic predisposition, female sex and aging, while blood pressure control and protein intake have no effect on CKD progression rate in ADPKD patients with advanced renal disease [43].

More recently, the role has been investigated of branched chain amino acids (BCAA: 0.2 g isoleucine, 0.4 g leucine, and 0.2 g valine) on cyst growth in an experimental model. The results showed that BCAA stimulated the cyst growth by cellular proliferation and mTOR/cAMP pathway activation [39]; however, it is important to underline that the BCAA group had a 10% higher protein intake with respect to controls (977 vs. 885 mg/day) [44].

In summary, no clear evidence concerning the role of a low-protein diet in delaying ADPKD progression is available at present. At the same time, nephrologists can only provide some recommendations on low-protein intake based on what occurs in non–ADPKD CKD patients.

A correct nutritional therapy has to take into consideration a proper intake of sodium, phosphate, protein (quantity and quality), amino acid supplements, and fluid intake [39] to ensure a better control of CKD signs and symptoms. This nutritional support has been described in a feasibility study by Taylor and coll [20]. including 12 ADPKD patients. Patients consumed their standard diet for a week and then shifted to a low sodium and protein diet together with higher fruit, vegetables and water intake for 4 weeks [20]. As a consequence, the patients enrolled consumed 36% sodium, 28% proteins and 99% amino acid precursors and increased by 42% fruit and vegetables intake. Urinary sodium, urea, net acid excretion and osmolality decreased by 20, 28, 20 and 15%, respectively; urinary volume increased by 35% [44]. Based on these preliminary findings, an interventional study protocol needs to be designed. Obviously, also in ADPKD the protein restriction has to be prescribed whilst at the same time maintaining an adequate energy intake, although experimental data do not exist in the literature.

Net acid load

In recent years, metabolic acidosis complications have been extensively studied in CKD patients. Consequently, correction of acid–base imbalance with sodium bicarbonate administration and/or vegetables and fruit intake is a mainstay of CKD treatment [13, 44–48].

Although this topic is crucial for CKD patients, no randomized controlled trial actually exists for ADPKD [44].

Our group has designed a prospective multicenter randomized controlled study to evaluate the effects of metabolic acidosis correction on CKD progression and renal death (UBI study, ClinicalTrials.gov Identifier: NCT01640119); definitive data will soon be available [49]. The UBI study included 84 ADPKD patients, 38 in the experimental group and 46 in control group. Eleven patients dropped out or were lost to follow-up. Table 3 shows the baseline data of the 73 active patients. Baseline bicarbonate levels did not differ between the experimental (22.0 ± 1.9 mmol/l) and control groups (22.3 ± 2.6 mmol/l). During the 3-year follow-up, bicarbonate levels increased in the experimental group: from 25.4 ± 2.6 at 1 year, to 26.4 ± 2.6 at 2 years, and 26.3 ± 1.8 mmol/l at 3 years, whereas no changes were observed in the control group. Twenty-four hour urinary urea, potassium and phosphate excretion were used to calculate the potential renal acid load (PRAL) and net endogenous acid production (NEAP). NEAP represents the non-volatile acid load derived from diet, estimated by the production of non-volatile acids and bases produced during digestion, calculated by the known nutritional content. PRAL and NEAP were calculated as previously described [45] by the Remer and Manz formula and the Frassetto formula, respectively [50, 51]. Figures 2 and 3 show changes in NEAP and PRAL

Table 3 Baseline data of 73 UBI study ADPKD patients [44]

	All	Control group	Sodium bicarbonate group	p
Number	73	42	31	NA
Male [n (%)]	53 (72)	29 (69)	24 (77)	NA
Age (years)	51.19 ± 9.14	51.26 ± 10.04	51.11 ± 8.05	NS
BW (kg)	74.5 ± 10.8	74.0 ± 10.9	75.2 ± 10.7	NS
SBP (mm Hg)	130 ± 20	126 ± 17	132 ± 23	NS
DBP (mm Hg)	75 ± 8	75 ± 8	74 ± 9	NS
Serum urea (mg/dl)	91 ± 45	92 ± 47	90 ± 71	NS
Serum creatinine (mg/dl)	2.14 ± 0.83	2.13 ± 0.93	2.15 ± 0.71	NS
Na (mmol/l)	140 ± 3	139 ± 3	141 ± 4	NS
K (mmol/l)	5.0 ± 0.8	5.0 ± 0.9	5.1 ± 0.5	NS
Ca (mg/dl)	9.3 ± 0.7	9.2 ± 0.8	9.5 ± 0.9	NS
P (mg/dl)	4.18 ± 0.84	4.10 ± 0.82	4.28 ± 0.87	NS
Bicarbonate (mmol/l)	22.1 ± 2.2	22.0 ± 1.9	22.3 ± 2.6	NS
PTH (pg/ml)	123 ± 77	118 ± 76	128 ± 80	NS
Hb (g/dl)	12.3 ± 1.6	12.2 ± 1.8	12.3 ± 1.5	NS
Serum albumin (g/dl)	3.91 ± 0.50	3.95 ± 0.49	3.87 ± 0.51	NS
CRP (mg/l)	3.1 ± 2.8	2.8 ± 2.5	3.4 ± 3.2	NS

BW body weight, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *HR* heart rate, *PTH* parathormone, *HB* hemoglobin, *CRP* C-reactive protein
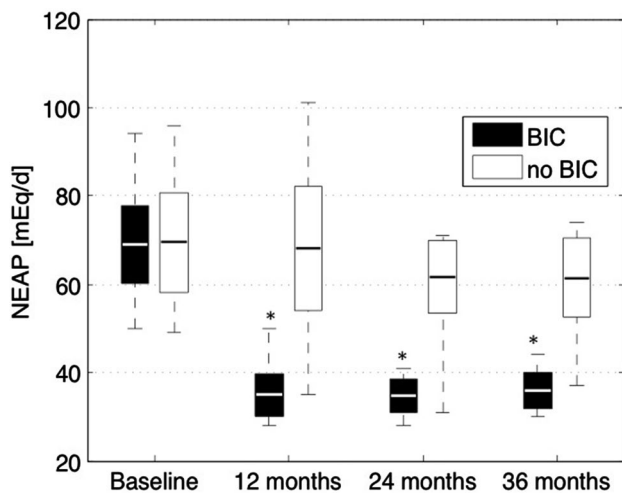

Fig. 2 Variation of net endogenous acid production (NEAP) in ADPKD subjects who participated in the UBI study and underwent oral administration of sodium bicarbonate compared to the control group. The plot box represents the mean ± SD, the dotted lines the maximum value and the minimum value. *p < 0.001 vs. NO-bicarbonate use
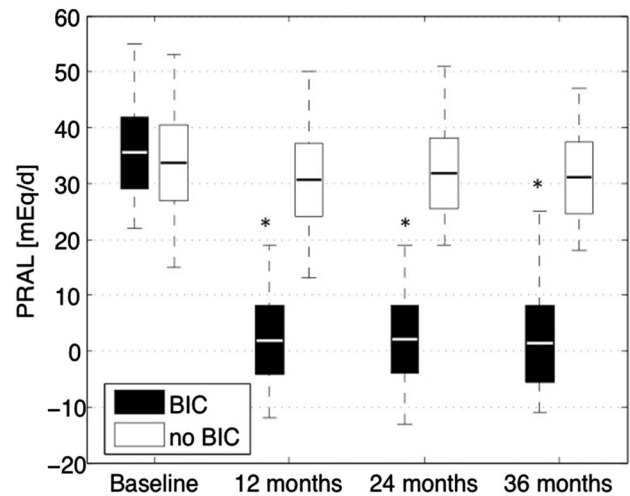

Fig. 3 Variation of potential renal acid load (PRAL) in ADPKD subjects who participated in the UBI study and underwent oral administration of sodium bicarbonate, compared to the control group. The plot box represents the mean ± SD, the dotted lines the maximum value and the minimum value. *p < 0.001 vs. NO-bicarbonate use
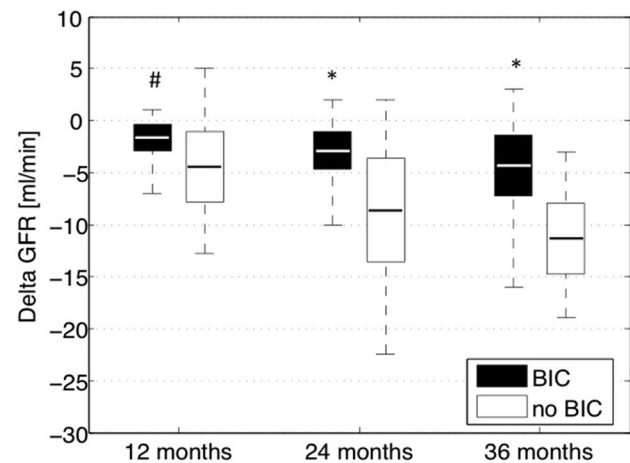

Fig. 4 GFR loss during the 36-month follow-up of patients with ADPKD who participated in the UBI study. The plot box represents the mean ± SD, the dotted lines the maximum value and the minimum value. #p < 0.01 vs. NO-bicarbonate use. *p < 0.001 vs. NO-bicarbonate use

in the ADPKD patients taking sodium bicarbonate orally vs. the control group [Fig. 4 shows changes in eGFR for both groups: eGFR declined during 36 months of follow-up by 1.5 ml/min/year in the experimental ADPKD group vs. 3.3 ml/min/year in the ADPKD control group (p < 0.001)]. In the control group, 19% of patients doubled their serum creatinine in the follow-up period vs. 9.6% of patients in the experimental group. Renal replacement therapy had to be started in 24% of control patients vs. 10% in the experimental group, while 2 patients (one for each group) died.

Sodium bicarbonate administration represents one of the treatments of metabolic acidosis in CKD patients; our group [45] has already reported that a vegetarian low-protein diet makes possible a 50% decrease of administered sodium bicarbonate, in line with Goraya et al.'s data [46]. In 1998, Tanner demonstrated, in experimental models, that potassium citrate administration improved eGFR levels in PKD mice and he concluded that further data are needed to better understand the role of nutritional interventions in ADPKD models and patients [52]. Four years before, Torres had demonstrated a renal acidification defect following ammonium chloride load in ADPKD patients without renal insufficiency in comparison to healthy subjects [53].

Conclusions

Evidence exists that dietetic interventions cannot modify the ADPKD course with the exception of sodium intake reduction. At the same time, we cannot renounce the provision of nutritional support to ADPKD patients [54]. Dietary support makes it possible to prevent and treat several signs, symptoms and complications closely linked to renal insufficiency progression which are addictive effects of conventional pharmacological treatment. A dietary support could improve metabolic, nutritional and clinical conditions of CKD and ADPKD patients together with their quality of life, postponing the need for renal replacement treatment.

In conclusion, even though data on nutritional therapy in ADPKD are scant, common sense can be a guide in suggesting that sodium intake restriction may be useful to decrease cyst growth rate [17]; although further evidence is needed, a restriction of phosphorus and protein intake restriction represent cornerstones of the dietary support in renal patients. It could be also helpful to limit animal protein, increasing the intake of fruit and vegetables together with a full correction of metabolic acidosis. Finally, fluid intake may be recommended in the early stages of the disease, but it is not to be prescribed in the presence of a moderate to severe reduction of renal function. In conclusion, there is currently little evidence testifying the importance of nutritional treatment as a therapy to slow the growth of the volume of the kidneys and the progression of CKD in ADPKD subjects. Therefore, studies focused on this issue need to be performed in coming years [55, 56].

Compliance with ethical standards

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