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THE ROLE OF PROTEIN RESTRICTION IN THE PROGRESSION OF CHRONIC KIDNEY DISEASE

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ABSTRACT

Even though nephrology has made much progress, reducing the progression of the chronic kidney disease remains, in fact, one of the biggest challenges. Long before the renal replacement therapy (RRT), it was known that limiting the protein could help almost all uremia symptoms. Although it was proposed as early as the 1960s, it only became widely used in the 1980s. By lowering the urea and other nitrogen wastes and lowering the metabolic acidosis, oxidative stress, and insulin resistance, limiting the amount of protein in your diet can help improve uremic symptoms. Also, limiting the protein in the diet positively controls the cardiovascular complications, including the arterial blood pressure and proteinuria reduction, which are risk factors for CKD progression. This mini-review examines the impact of protein restriction on the possibility of slowing CKD progression in depth.

Keywords: protein in diet, chronic kidney disease, progression, proteinuria

INTRODUCTION

Chronic kidney disease (CKD) is a progressive disease. It causes damage to and loss of some nephrons, followed by increased glomerular filtration (GF) in the intact nephrons. Most of the evidence comes from experimental studies in animals. Intact nephrons undergo hemodynamic changes like increased plasma flow and hydrostatic pressure, leading to increased glomerular permeability, proteinuria, and glomerulosclerosis. The continuous repetition of this vicious cycle illustrates the progression toward the end-stage CKD. Due to the kidney's important role in amino acid and protein metabolism, including the breakdown and excretion of protein metabolites, the amount of protein in the diet significantly affects the kidney's metabolic processes and kidney function. A high-protein diet may induce kidney injury through an increased intraglomerular pressure, glomerular hyperfiltration, and the accumulation of toxic protein metabolites. In contrast, a low-protein diet (LD) provides numerous clinical benefits for patients with renal insufficiency. Less accumulation of protein waste products ameliorates the clinical symptoms of uremia even in very advanced stages of CKD, and the LPD may be used effectively to postpone the initiation of dialysis therapy. Low protein diet and VLPD

supplemented with essential amino acids (AAs) and keto analogs (KAs) of nitrogen-free AAs together with salt restriction have been shown to be effective in modifying the natural history of CKD. In this review, we aim to summarize the role of diet, with a focus on protein restriction, as well as the use of supplements with AAs and KAs, in delaying the progression of CKD and preserving the nutritional status of patients with and without diabetes and CKD.

MECHANISMS THROUGH WHICH DIETARY PROTEIN RESTRICTION POTENTIALLY PROTECTS THE KIDNEY

Since the early 1900s, people have argued about whether the amount and/or quality of the protein you eat makes you more likely to get kidney disease. Although it was proposed as early as the 1960s, protein restriction was recognized as an intervention and became widely used around the 1980s [1,2]. It has been indicated that people with high blood pressure or diabetes lose more protein when they eat a high-protein diet, but the effect on the kidneys needs to be fully understood. Animal experiments have shown that eating protein raises intraglomerular pressure by dilating the afferent arteriole [3], where glomerular hyperfiltration (following dilatation of the afferent arteriole), over time leads to glomerular damage [4]. The evidence of more pronounced sclerotic lesions and higher proteinuria in animal experiments with CKD and high protein intake, compared to those with low protein intake [5], supports the idea that protein restriction in subjects with CKD can slow the progression and postpone the start of renal replacement therapy (RRT).

The decrease in protein consumption is associated with vasoconstriction of the afferent arteriole, which leads to an incremental decrease in intraglomerular pressure, which in the long term, results in a decrease of glomerular damage and improvement or stabilization of the renal function. The reduction in intraglomerular pressure causes a reduction in transforming growth factor (TGF-) expression via attenuation of the signal from the mesangial cells, resulting in a reduction in the interstitial fibrosis. Dilatation of the efferent arteriole has also been observed after reducing the protein consumption in the diet (synergistically with angiotensin-converting enzyme inhibitors (ACEi), angiotensin receptor blockers (ARB), and salt in the diet), with an additional effect of lowering the intraglomerular pressure [6]. In an attempt to explain the antiproteinuric and renoprotective effect of the protein restriction in the diet, some authors implicate the decrease in the activity of the renal renin-angiotensin system (RAS) [7,8]. Figure1 illustrates a simplified view of the mechanisms involved in renoprotection and reduction of proteinuria.

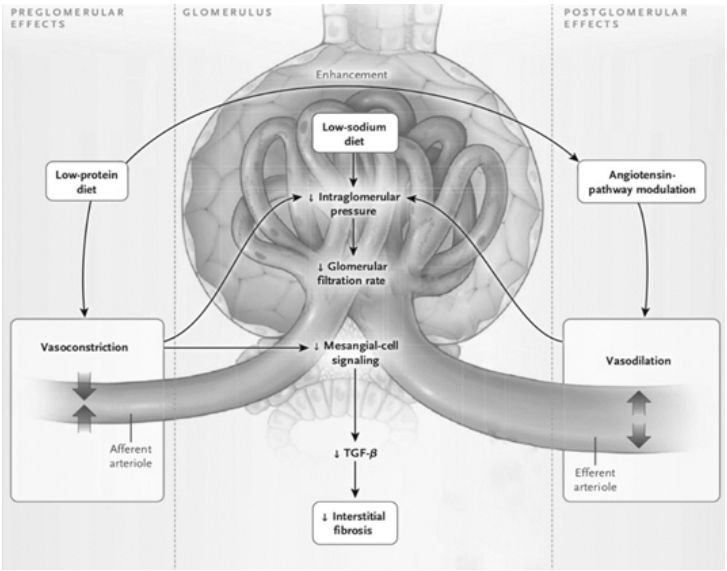


Figure 1. *Mechanisms involved in renoprotection and proteinuria reduction*

Furthermore, protein restriction was referred to reduce uremia symptoms and improve related factors like arterial pressure, water overload, metabolic acidosis, and phosphate levels, negatively affecting the quality of life and potentially causing the onset of RRT [9].

Types of protein restricted diets

A protein-restricted diet in a subject with CKD usually refers to a specific protein intake (see below) and applies to non-nephrotic patients with no co-morbidities (co-morbidities would be associated with hypercatabolism) [10], where ½ of the proteins are of high biological value (of animal origin and from dairy products), to provide the intake of essential amino acids [10].

The various studies conducted to test the safety and efficacy of dietary protein restriction in subjects with CKD generally include three types of diets described below:

1. Low protein diet (LPD) with 0.6-0.8 g of protein /kg body weight/day;

2. Very low protein diet (VLPD) with 0.3-0.4 g protein /kg body weight/day supplemented with a mixture of essential amino acids (EAA) or ketoanalogues/ketoacids (KA);

3. Primarily vegetable proteins (VPD) supplemented with EAA or KA.

The protein intake in the above regimens provides < 10% of the total daily calories (compared to 15-25% in normal or high protein regimens) [11]. For this reason, to avoid malnutrition, in subjects undergoing dietary regimes with protein restriction, a mandatory caloric intake of 25-35 kcal/kg body weight/day is advised [12,13]. To achieve VLPD, some centers prescribe vegetarian diets [14]. Dietary counseling is a must for patients to understand how to achieve adequate daily caloric intake while taking LPD/VLPD. Compliance can be tested by measuring 24h urine nitrogen and calculating protein consumption through the Maroni formula (6.25 X [urinary urea nitrogen x 0.03 body weight in kg]) [15].

THE EFFECTS OF DIETARY PROTEIN RESTRICTION ON CKD PROGRESSION-RESULTS OF CLINICAL STUDIES

MDRD study

The MDRD study (Modification of Diet in Renal Disease Study) is the largest controlled, randomized study of LPD in patients with CKD. It was conducted in 840 patients with CKD stages 3-5 (including patients with APKD) to test the hypothesis that protein restriction slows the progression of CKD (Study A: 585 patients with LPD = 0.58 g/kg body weight/day versus normal dietary protein intake NPD = 1.3 g/kg body weight/day. A significant limitation of this study was the fact that the real amount of protein consumed in the diet (estimated by nitrogen excretion) was higher than the target in the group with LPD (0.73 g/kg body weight/day versus the target 0.58 g /kg body weight/day) and lower than the target in the NPD group (1.11 g/kg body weight/day versus the target 1.3 g/kg body weight/day). Despite the significant limitations, such as the low amount of protein consumed, the small number of subjects, and the short follow-up period, the MDRD study found that LPD had a minor, non-significant effect on CKD progression [16].

Studies in nondiabetic subjects.

In nondiabetic patients with CKD, dietary protein restriction may help delay the onset of RRT and reduce proteinuria. A randomized controlled trial compared LPD with supplemented VLPD in these patients. This study showed that people in the supplemented VLPD group started dialysis much later than those in the LPD group [17]. VLPD maintains a stable and improved metabolic status in patients with very low GFR (<12 ml/min), maintaining a good nutritional status until the time of dialysis initiation [18]. A delay of dialysis initiation of approximately one year was

observed in a study on elderly, nondiabetic, stage 5 CKD patients treated with supplemented VLPD [19]. Also, this delay in starting dialysis was not linked to a higher rate of morbidity and mortality [19]. In a systematic review of the literature published initially in 2000, updated in 2006, in 2009 [20], and 2020 [21], the data were as follows: in 2009, ten randomized controlled trials (RCT) were used to study the effects of dietary protein restriction on the reduction of renal death (defined as the start of chronic dialysis or a kidney transplant) and death in nondiabetic patients with stages 3–5 CKD [20]. 1022 subjects treated with a dietary regimen of 0.3-0.6 g protein/kg body weight/day were compared with 998 subjects treated with a higher protein diet, which constituted the control group. The results showed that patients treated with LPD had a relative risk reduction (RRR) of 32% for renal death compared to the control group [20]. The authors searched the Cochrane Kidney and Transplant Register of Studies until September 7, 2020, in the 2020 update of this meta-analysis, aiming to determine the efficacy of dietary protein restriction in preventing the natural progression of CKD toward the end stage and the efficacy in delaying the time to onset of RRT. Seventeen randomized controlled trials with 2.996 adults, and nondiabetic subjects with stage 3-5 CKD were included in this systematic literature review. Subjects were randomized to receive VLPD (0.3 - 0.4 g protein/kg body weight/day) supplemented with EAA or KA compared to LPD (0.5 - 0.6 g protein/kg body weight/ day) or LPD compared to a normal protein diet (≥ 0.8 g protein/kg body weight/day) and were followed for 12-50 months. Studies in which subjects received EAA or/and KA were included in this systematic review, provided that the total nitrogen intake differed between treatment groups. According to the findings of this systematic review, the authors concluded that VLPD compared with LPD and NPD, probably reduces the number of patients with CKD who progress to RRT (RR 0.65). LPD compared to the normal diet does not make a difference in the progress toward RRT. VLPD and LPD were not associated with changes in mortality. Adverse effects of protein-restricted diets were uncommon, although these data were limited [21]. In clinical practice, the onset of RRT may be a better predictor of CKD progression than GFR since the onset of RRT is influenced more by uremic symptoms and cardiovascular complications than by the GFR value itself [1]. In the previous systematic review [21], the authors did not find any differences in GFR between those with VLPD and those with LPD, even though the way they progressed to RRT was different. According to the authors, this finding suggests that the positive effects of protein restriction, rather than a direct effect on the kidneys, might be attributed, to some extent, to the correction of metabolic acidosis, reduction of phosphate retention, and maintaining a well-nourished status [21,22].

Studies in diabetic subjects

The data of the randomized controlled studies on CKD patients with DM (so-called diabetic kidney disease-DKD) are contradictory. A similar effect has been seen in people with type 1 diabetes as in people who do not have diabetes. So, cutting back on protein intake, even though it does not change the rate of GF decline, it is linked to a 77% lower risk of death from kidney disease in the long term effect [23]. Two meta-analyses that looked at dietary protein restriction in diabetic patients and had a large number of patients, randomized controlled trials, and composite events like GFR and albuminuria, not just renal death, are worth pointing out. In populations of patients with DM (type 1 & 2), in one of the meta-analyses, a positive effect of protein restriction was found, both in type 1 and in type 2 DM [24], while in the other, this positive effect was found only in type 1 DM, but not in type 2 [25]. It is important to note that the studies were very different in terms of the type of diabetes, the stage of CKD, and the type of diet, how long it was followed, and how well it was followed.

In conclusion, limiting the protein in the diet delays the start of RRT in people with CKD who do not have diabetes. A similar effect can be observed in type 1 diabetic patients, while in type 2, the data are unclear [24, 26].

EFFECTS OF DIETARY PROTEIN RESTRICTION ON PROTEINURIA-RESULTS OF CLINICAL STUDIES

The positive effects of LPD on the reduction of proteinuria have been observed in nephrotic and non-nephrotic patients, while the association of the degree of proteinuria with the progression of CKD in diabetic and nondiabetic patients has been clearly demonstrated [23–29].

Effects on non-nephrotic proteinuria.

Secondary analysis of a sub-study of the MDRD trial showed that LPD reduced the rate of increase of protein excretion over a follow-up period of 2.2 years [30]. This result is quite significant, considering the important limitation of this study, which was mentioned above (exceeding protein intake beyond the target amounts in both groups).

A study by Chauveau et al., carried out in stage 4-5 CKD patients with proteinuria > 1 g/day, aimed to observe the long-term effects of VLPD supplemented (0.3 g protein/kg/day + EAA+ KA) on proteinuria. After three months, this treatment plan was linked to less protein in the urine and more albumin in the blood (see Table 1). These effects lasted the whole two years of the study, no matter how much protein was in the urine at the start or if ACE inhibitors were used [31].

Another study compared the safety and efficacy of LPD versus VLPD in nondiabetic patients, with GFR < 30 ml/min/1.73 m2 and proteinuria < 1 g/day. At the end of the 15-month study, there was a trend toward less protein in the urine, but there were no significant differences between the two groups [17]. This suggested that both LPD and VLPD are just as good at reducing protein in the urine.

Effects on nephrotic proteinuria

The first study of this type was carried out with a limited number of 9 subjects [32] and showed a decrease in proteinuria after protein restriction in the diet. This study was followed by several other studies, also conducted in a relatively small number of nephrotic patients with CKD, followed for short-term periods. Table 1 summarizes the data of these studies, including the number of subjects, the amount of protein in the diet, the stage of CKD, the duration of the study, and the results [17, 30-36]. Most of these studies have found that proteinuria goes down, and some have found that serum albumin goes up. One of the studies [36] compared the effects of LPD versus a moderate protein diet (MPD) and found no significant difference in proteinuria and serum albumin compared to the baseline levels. The problem with this study is that the LPD goal, which was measured by the amount of nitrogen excreted, still needs to be met.

A positive effect of the protein restriction was observed in patients with steroid-resistant proteinuria in the early stages of CKD. Thus, in a 1-year randomized controlled trial carried out in 108 patients with stage 3-5 CKD, the urinary protein excretion was significantly reduced at 6, 9, and 12 months after the initiation of a protein-restricted diet (0.6 g/kg/day), supplemented with KA compared to the normal diet (1.0g/kg/day) [37]. When dietary protein restriction is combined with renin-angiotensin system blockade (with ACE inhibitors or ARBs), the effect is synergistic. In a study in patients with CKD and proteinuria above 3g/24h, it was observed that the use of LPD in subjects under treatment with ACE inhibitors had an additional effect in reducing proteinuria [38]. The study noted that the most pronounced effect was observed in patients with the best adherence.

Effects on proteinuria in diabetic subjects

Studies in diabetic patients have found somewhat conflicting data. Meta-analyses are hard to do because studies vary in many ways, such as follow-up time, clinical records, primary disease, stage of CKD, other diseases, compliance, etc. In a study of 74 type 2 DM patients with stage 3 CKD followed up for three years, a significant decrease in proteinuria was observed, with no changes in serum albumin [34].

In a meta-analysis by Pan Y.et al., which included eight randomized, controlled trials, with a total of 519 types 1 and 2 diabetic patients with diabetic nephropathy, a significant decrease in proteinuria with the use of LPD was reported [27]. Meanwhile, a later meta-analysis by Nezu U. et al. [24], which included 12 studies with 634 patients with type 1 and 2 DM, showed no significant difference in proteinuria after LPD.

In conclusion, evidence suggests that dietary protein restriction reduces the proteinuria in nondiabetic patients with CKD and possibly in diabetic patients. More specific studies in larger populations are necessary to clarify the effect on diabetic patients (type 1 and 2).

SAFETY OF DIETARY PROTEIN RESTRICTION AND ASSOCIATED MODIFICATIONS

When figuring out how dietary protein restriction works, it is essential to consider whether it is safe and well-tolerated and if it does not make the patient's nutritional status worse. In the MDRD study, dietary protein restriction was linked to a slight drop in body weight and increased serum albumin after 2.2 years of follow-up [16]. This

shows that nutritional status did not get worse. In a randomized study of 423 patients with CKD under LPD, followed for 2.5 years, only three patients developed malnutrition [36].

In another study, nutritional, anthropometric, and biochemical parameters were assessed at the beginning and end of the study in 207 patients with advanced CKD (GFR < 30ml/min) who were treated with LPD or supplemented VLPD. At the end of the study, the anthropometric and biochemical parameters stayed the same from the beginning [17]. In another study, people with advanced CKD who took VLPD with AAE kept the same body weight and BMI [33]. Two studies evaluating the long-term effects of LPD and AAE-supplemented VLPD confirmed stable, even improved levels of serum albumin, lipids, transferrin, and improved nitrogen balance [39,40].

It has been demonstrated that patients with uncomplicated CKD, regardless of the stage (including patients with GFR < 20 ml/min/1.73 m2), adapt efficiently to dietary protein restriction (0.6 g/kg body weight/day), through the same mechanisms as normal subjects [41]. As part of these mechanisms, protein breakdown rates and amino acid oxidation slow down, and amino acids are used more for protein synthesis.

Short-term and long-term metabolic adaptation with a daily dietary protein intake of 0.8g/kg body weight was studied in nephrotic, non-diabetic, non-obese, and well-nourished patients, as well as in patients with advanced CKD on VLPD (0.28 g/kg weight/day) supplemented with KA or EAA [42-44].

One of the studies suggested that proteinuria may serve as an additional stimulus for inhibiting amino acid catabolism [43]. However, when insufficient protein intake, adaptive responses may not sufficiently compensate, leading to negative nitrogen balance and loss of lean body mass [45]. Also, it should be emphasized that the state of metabolic acidosis or concomitant hypercatabolic diseases should be treated with care about the recommendations for dietary protein restriction, for they have a higher risk of catabolism and malnutrition [46,47].

In diabetic patients with CKD, the debate on the efficacy and safety of LPD remains open, as there are study data that in people with diabetes, adaptive responses cannot be activated, as stated above [24, 27].

Italian researchers and doctors, on the other hand, support the use of LPD with KA in people with DM. They say that these diets are safe to maintain nutritional status and improve DKD [48, 49]. These diets improve uremia and diabetes, while the nutritional impact is the same in non-diabetic patients [49]. According to the "Italian Standard of Care in DM", LPD is recommended for the treatment of all diabetic patients with CKD, provided that they are under strict clinical control and nutritional follow-up [48]. In a recent study, involving 299 patients with stage 4 CKD, 98 of which were diabetics, followed from January 2010-March 2018, in collaboration with an experienced nutritionist, Baragetti et al. compared LPD (0.6 g protein/kg body weight/day) versus controlled protein intake (0.8 g protein/kg body weight/day) versus an unrestricted protein diet. GFR in the group with LPD and unrestricted diet was < 20 ml/min/1.73 m2. The authors concluded that LPD, which is recommended by nephrologists working closely with nutritionists, delays the start of dialysis and keeps the nutritional status of people with advanced CKD [50].

In a 2020 meta-analysis, a systematic review of the literature was done to find out how LPD affects the renal function and nutritional status. The investigators analyzed PubMed, Embase and Cochrane Library data up to January 2019. There were 29 studies with 3,566 people who were treated with LPD (1,784 people) and NPD (1,782 people). The results were positive in terms of renal disease progression, but nutritional status parameters were found to be worsened. Thus, the authors concluded that LPD significantly improves nephropathy but is associated with malnutrition. To confirm what has been found so far, the authors say that high-quality, randomized, and controlled trials need to be done [51].

Nutritional status was also assessed in the above-mentioned meta-analysis [21], which analyzed data through a search of the Cochrane Kidney and Transplant Register of Studies up to 7 September 2020 (2,996 adults, non-diabetic, with stage 3-5 CKD). In this meta-analysis, 12 of the 17 randomized controlled trials included did not report any evidence of protein-energy wasting (PEW) malnutrition. 3 studies reported low rates of PEW (in each of the VLPD, LPD and NPD groups). 2 studies did not have sufficient data to judge malnutrition, and the quality of life was not formally assessed in either study. It is necessary to note that people who have had a nephrectomy,

have diabetes, arterial hypertension, or have a polycystic kidney (although ADPKD is a bit of a gray area) may also benefit from a low-protein diet because it lowers intraglomerular pressure [52].

Based on the best, updated information, the Kidney Disease Outcomes Quality Initiative (KDOQI) and the Academy of Nutrition and Dietetics, to make this information available and applicable to clinical decision-making, carried out the latest update of the "KDOQI Clinical Practice Guideline" for Nutrition in CKD on 2020 [13]. According to this clinical guideline, the following is recommended in patients with stage 1-5D CKD.

Protein restriction in non-diabetic CKD patients not on dialysis.

In adults with stage 3-5 CKD, who are metabolically stable, dietary protein restriction with/without KA supplements is recommended to reduce the risk of end-stage renal disease/death (1A) and to improve quality of life (2C):

– LPD = 0.55-0.60 g of protein/kg body weight/day or

– VLPD = 0.28-0.43 g/protein/kg body weight/day supplemented with KA/EAA to meet protein needs (0.55-0.60 g/kg weight/day).

Table 1. *Summary of clinical studies on antiproteinuric effect of low protein diets*

Author/year	No of subjects/ follow-up	Diagnosis	Protein regimes	Proteinuria Starting serum albumin	Proteinuria Ending serum albumin
Kaysen et al./ 1986 [32]	9 / 2 weeks with each regime	St 2-4 CKD, nephrotic proteinuria	1.6g/kg/day then *0.8 g/kg/day*	Proteinuria decreased by 3.78g/day after regime change (p<0.01) Serum albumin increased by 0.21 g/dl after regime change (p< 0.005)	
Levey et al./ 1999 [30]	A Study 585 pts B Study 255 pts / 2.2 years	A Study: st 3-4 CKD B Study: st 4-5 CKD	A Study 1.3g/kg/day vs *0.58g/kg/day* B Study 0.58g/kg/day vs *0.28g/kg/day*	There were not reached dietary targets (see text)	
Aparicio et al. / 2000 [33]	239 pts/ 29.6 months	st 4-5 CKD	Vegetarian VLPD (0.3g/kg/day) + EAA/KA	5.7 ± 2.8g/day 33.8 ± 6.4 g/L	3.0 ± 2.1g/day (p< 0.001*) 37.8 ± 5.4 g/L (p<0.002*)
Chaveau et al/ 2007 [31]	78 pts/24 months	st 4-5 CKD Proteinuria >1g/day	Vegetarian VLPD (0.3g/kg/day) + EAA/KA	2.7 ± 1.9 g/day 37.7 ± 4.9 g/L	1.5 ± 1.3 g/day (p<0.001*)/ 39.3 ± 4.1 g/dL(p< 0.05*)
Cianciaruso et al 2009 [36]	423 pts/48 months	st 4-5 CKD	0.55 g/kg/day versus *0.8 g/kg/day*	1.53 ± 2.22 g/day versus *1.79 ± 2.44 g/day* 4.0 ± 0.6 g/dL versus *3.9 ± 0.7g/dL*(NS**)	No significant change in proteinuria 4.2 ± 0.4 g/dL versus *4.1 ± 0.4 g/dL* (NS**)
Giordano et al 2014 [34]	74 old age patients / 36 months	T2 DM st 3-4 CKD	0.7 g/kg/day versus *1 mg/kg/day*	2.4 ± 0.5 versus *2.3 ± 0.9 g/day* 3.5 ± 0.3 versus *3.6 ± 0.2 g/dL*	1.1 ± 0.2 (p< 0.05*) versus *2.4 ± 0.8 g/day (NS*)* 3.4 ± 0.3 g/dL (NS *) versus *3.4 ± 0.2 g/dL (NS*)*
Garneata et al/2016 [17]	207 pts/ 15 months	st 4 CKD	0.6 g/kg/day versus *0.3 mg/kg/day vegetarian*	0.88 vs *0.88 g/day (NS***)*/ 4.1 versus *4.1 g/dL (NS***)*	0.67 versus *0.78 g/day* (p=0.06***) 4.1 versus *4.1 g/dL (NS***)*

NS- non-significant. *compared to basic levels, ** compared to basic and in between groups levels, *** compared between groups

Protein restriction in diabetic patients with CKD (not on dialysis)

In adults with stage 3-5 CKD, it is reasonable to prescribe a protein intake of 0.6-0.8 g/kg body weight/day, to maintain a stable nutritional status and to maintain good glycemic control (Opinion).

In all cases, a very careful clinical supervision is recommended. Regarding the type of protein (vegetable vs. animal), there is no clear evidence for the superiority of either, regarding nutritional status, calcium, phosphorus or lipid profile (1B).

The guideline advises to increase the number and training of specialized renal dietitians, who will be able to implement safely and efficiently LPD and VLPD.

The story of dietary protein restriction, like many stories in medicine and nephrology, remains a story of 'belief and disbelief' [53]. The application of dietary protein restriction in patients with CKD varies in different countries. In the USA and Canada these diets are not used frequently [10], based on the "so-considered" negative results of the MDRD study, while LPD are more popular in Europe and especially in Italy [48].

A recent study in France referred that even in elderly CKD patients the protein content is higher than recommended, they are mostly spontaneous in diet and indicates there is a need for nutritional care for this population [54].

Therefore, educating patients on the significance of LPD/VLPD dietary therapy for treating CKD and supervising its incorporation into their food practices is crucial. Identifying and selecting the appropriate CKD candidates and providing intensive dietary counseling are strategies to improve adherence to low-protein diets. Since undernutrition exacerbates the risk for malnutrition and atrophy, an alternative, graduated approach could gradually reduce the recommended protein intake while maintaining an adequate energy status [55].

CONCLUSION

In managing chronic kidney disease (CKD), a low protein diet (LPD) or very low protein diet (VLPD) supplemented with specific amino acids and ketoacids (KAs), along with salt restriction, has been shown to be effective in delaying the decline of glomerular filtration rate (GFR) and reducing proteinuria. The synergistic effect of LPD and renin-angiotensin system blockade in CKD management is supported by scientific evidence. While LPD can be a helpful intervention for diabetic and non-diabetic CKD patients, its application must be tailored to each patient's unique needs and challenges. However, LPD must be individualized and carefully monitored to ensure its safety, tolerability, and nutritional adequacy, and challenges such as medical assessment, professional renal dietitians, and patient adherence must be addressed to ensure its feasibility and effectiveness as a CKD intervention.

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Резиме

УЛОГАТА НА ОГРАНИЧУВАЊЕТО НА ПРОТЕИНИТЕ ВО ПРОГРЕСИЈАТА НА ХРОНИЧНАТА БУБРЕЖНА БОЛЕСТ

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И покрај постигнатиот голем напредок во нефрологијата, намалувањето на прогресијата на хроничната бубрежна болест (ХББ) останува сè уште еден од најголемите предизвици. Долго пред започнување со реналната заместителна терапија (РЗТ) беше познато дека ограничувањето на протеинскиот внес може да помогне за речиси сите симптоми на уремија. Иако ова беше предложено уште во раните 1960-ти, тоа стана широко користен пристап дури во 1980-тите. Со намалувањето на уреата и на другите азотни отпадоци, како и намалувањето на метаболната ацидоза, оксидативниот стрес и инсулинската резистенција, ограничувањето на количината на протеини во исхраната може да помогне во подобрување на уремичните симптоми. Исто така, ограничувањето на протеините во исхраната позитивно ги контролира кардиоваскуларните компликации, вклучително и артериски крвен притисок и намалувањето на протеинуријата, кои се фактори на ризик за прогресијата на ХББ. Овој мини-преглед го евалуира влијанието на ограничувањето на протеините врз можност за забавување на прогресијата на ХББ.

Клучни зборови: протеини во исхраната, хронична бубрежна болест, прогресија, протеинурија