

Low-Protein Diet for CKD

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The epidemiology of chronic kidney disease (CKD) shows increasing trends in prevalence and mortality and has become the leading health problem worldwide. Reducing the amount of proteins ingested from rice is an easy way to control the total intake of proteins, saving energy sources, particularly in rice-eating countries.

low-protein rice

processed low-protein brown rice

CKD

dietary therapy

lactobacillus

1. Increasing Trends of CKD in the World

In addition to cardiovascular diseases and cancer, chronic kidney disease (CKD) contributes to increased mortality in many industrialized countries ^{[1][2][3][4]}. The prevalence of CKD is estimated to be 8–16% worldwide ^{[5][6][7]}. CKD leads to kidney failure, requiring hemodialysis or renal transplantation. Recently, 20–40% of diabetic patients have developed CKD as a late complication ^{[8][9][10]}. Adequate interventions are necessary ^{[11][12][13]}.

In Japan, peritoneal dialysis and hemodialysis are the most current treatments for advanced renal failure, and transplantation is rare. The medical cost is enormous ^{[14][15]}: 96% of dialyzed patients receive hemodialysis, and only 3–4% undergo peritoneal dialysis ^{[16][17]}. The number of patients treated with hemodialysis in Japan exceeded 344,640 in 2019, including 40,885 newcomers.

To improve patients' quality of life and decrease medical costs, it is essential to delay the onset of conditions necessary for hemodialysis.

2. Effects of a Low-Protein Diet on CKD

In 1918, von Noorden W. and Volhard F. reported that a protein-reduced diet (Homburg diet) had suppressed uremic symptoms ^[18]. Since then, many studies have shown that a low-protein diet (LPD) reduced uremia symptoms, delayed the progression of renal failure, and extended life expectancy ^{[19][20]}. In 1963, Giordano reported that a low-protein diet could improve uremic patients' azotemia and shifted the nitrogen balance from negative to positive ^[21]. In 1964, Giovannetti also defined a diet whereby animal proteins and energy sources were provided by cereals ^[19].

In 1983, Brenner reported that excess protein intake imposed a load on glomerular hemodynamics and caused glomerular disorders ^[22]. After that, the mechanisms of renal damage due to excessive protein intake were rapidly elucidated ^[23]. Early intervention through LPD could decrease proteinuria in CKD ^{[24][25][26][27][28]}.

For 50 years, a LPD has been employed to treat chronic renal failure in Japan. It is now recognized that a LPD is almost certainly effective [\[29\]\[30\]](#). However, large-scale studies conducted by Locatelli et al. did not detect the same effect of a LPD inhibiting renal disease progression [\[31\]](#). Although low-protein diets have proven very effective for CKD patients, many physicians have failed to control renal dysfunction in RCT; they fail to ensure patients keep to a LPD and maintain their energy intake simultaneously [\[32\]\[33\]\[34\]\[35\]](#). A recent meta-analysis of RCT showed inconclusive results, and the appropriate protein intake is still an issue of debate [\[36\]](#).

Even though excess protein intake promotes glomerular overfiltration and adversely affects renal function, the Japanese guidelines for CKD patients recommend as standard a daily protein intake of 0.8 to 1.0 g/kg for stage G3a and 0.6 to 0.8 g/kg normal weight/day for stage G3b and later [\[37\]](#). This dose does not seem to be effective, as described below. An extreme LPD was poorly judged to reduce the various risks involved and more work is needed to confirm efficacy and safety in future studies.

3. Adequate Amount of Protein Intake by CKD Patients

Historically, the first recommendation on protein intake was 118 g/day/person in the so-called essential diet by German physiologist Professor Voit in 1881 [\[38\]](#). Professor R.H. Chittenden (Yale University) took a different position. He began to experiment with reduced protein intake in November 1902 on his own body. He first quit breakfast, had only a light lunch, and had a regular supper for seven months until June 1904 [\[39\]](#). In that time, his intake of protein was progressively reduced. After carefully analyzing nitrogen in his food and urine, Chittenden proved that taking 30–35 g of protein a day was sufficient to maintain his nitrogen balance. This diet also helped Chittenden control rheumatoid arthritis and mild nonspecific complaints.

Different results had been reported, but from almost all studies, it appeared that simultaneous intake of the right balance of energy and protein seemed to be difficult. In Japan, the dietary reference intake (DRI) uses the reference value of 0.8 g/kg body weight for healthy people. The average protein intake of Japanese people is 0.65 g/kg/day. Adding two standard deviations yields a figure of 0.87 g/kg/day. So, the Japanese DRI was set at 60 g daily for healthy men and 50 g for women [\[40\]](#). In 1973, the FAO Protein Requirement Committee reported that the minimum physiological input was 0.35 g/kg body weight. So, the lowest acceptable protein intake would be 0.3 to 0.4 g/kg body weight. The experience of Chittenden practicing on his own body and getting better with 30 g a day was substantial evidence in the age of personalized nutrition. After all, Zen priests used to remain healthy with a minimal intake of protein!

4. Effect of Prolonged Intake of Low-Protein Diet

Many physicians did not adopt LPD therapy, especially after the Evaluation of Modification of Diet in Renal Disease Study (MDRD), in which a LPD resulted in a worse prognosis [\[41\]](#). Those regimens failed to maintain an adequate energy intake, so malnutrition seemed to worsen the prognosis.

We carried out a case study to confirm the effect of more than six years of treatment with a LPD. We enrolled ten patients with LPD and hemodialysis patients (0.39 g/kg in CKD and 0.55 g/kg in the hemodialysis group, respectively) or families of the patients and supportive dietitians [42]. The daily protein intake of families was 1.17 g/kg and 1.25 g/kg in the dietitian groups, respectively. The recommended protein intake during hemodialysis was 1.2–1.5 g/kg body weight in the guideline, but 0.55 g/kg was enough to maintain body weight and serum protein. Important was the energy intake, being 32 kcal/kg body weight.

Intake of vitamins and minerals was less than half of the DRI, but none of the patients showed signs of deficiency. Study groups did not show any significant difference either in tests using dual-energy X-ray absorptiometry (DEXA), bone mineral density, and non-fatty tissue weight. CKD patients did not complain of sarcopenia, osteoporosis, hyperkalemia, hypo-phosphatemia, or high uric acid. Even lower intakes could reduce the frequency of dialysis in some cases [43].

In another retrospective analysis on 241 CKD patients who participated in the “Low-Protein Diet Practice for advanced CKD” program [44], patients started with serum creatinine levels around 5 mg/dL. Proteinuria improved within a relatively short period, with urinary protein output decreasing by 1.1 g/day after reducing protein intake to 0.5 g/kg body weight. Thus, we recommended LPD protocols, starting with a low-protein diet (0.5 g/kg body weight) from the earliest stage of the disease (eGFR < 60 mL/1.73 m²). Blood urea nitrogen (BUN) is a good index for healthy people based on how much they eat protein. A target value was under 15 mg/dL in our population-based cohort study. The substitution of meat with vegetable proteins improved the prognosis in diabetic renal disease [45].

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