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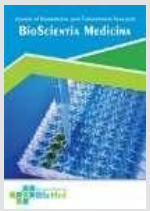

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The Role of Nutritional Therapy in Inhibiting the Progression of Chronic Kidney Disease: A Narrative Literature Review

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A B S T R A C T

The need for proper nutrition and diet is fundamental in every stage of chronic kidney disease. The principle of nutritional therapy is slowing the progression of chronic kidney disease, delaying patients with CKD (chronic kidney disease) from getting kidney replacement therapy. In CKD patients, there is a disturbance of protein homeostasis, disturbance in metabolism protein, acid-base disorders, and hormonal dysfunctions. As the progression of CKD increases, nitrogen-containing products accumulate, causing a decrease in appetite. In CKD patients, intestinal absorption is also impaired because uremia causes microbiota disturbance and damage to the intestinal epithelium. These various things cause nutritional status to become often irregular, and protein energy wasting frequently occurs, thus requiring dietary adjustments in patients with CKD. In conclusion, each individual with CKD has a different nutritional therapy approach depending on the disease conditions and nutritional status of the individual. Appropriate nutritional therapy in CKD patients can reduce disease progression.

1. Introduction

The need for proper nutrition and diet is fundamental in every stage of chronic kidney disease. The principle of nutritional therapy is slowing the progression of chronic kidney disease, delaying patients with CKD (chronic kidney disease) from getting kidney replacement therapy. In patients with kidney disease who have received dialysis therapy, nutritional therapy functions to prevent the patient's condition from worsening. Nutrition therapy should be started from the early stages of kidney disease, end-stage renal disease (ESRD) who have not received renal replacement therapy, to patients who have received hemodialysis, peritoneal dialysis, and kidney transplantation. Patients with diabetic kidney disease and nephrolithiasis also require a different nutritional approach.[1]

In CKD patients, there is a disturbance of protein homeostasis, disturbance in metabolism protein, acid-base disorders, and hormonal dysfunctions. As the progression of CKD increases, nitrogen-containing products accumulate, causing a decrease in appetite. In CKD patients, intestinal absorption is also impaired because uremia causes microbiota disturbance and damage to the intestinal epithelium. These various things cause nutritional status to become often irregular, and protein energy wasting frequently occurs, thus requiring dietary adjustments in patients

with CKD. However, in addition to dietary adjustments, nutritional therapy can help manage uremia, as well as other complications such as electrolyte and acid-base imbalances, water and salt retention, and mineral and bone disturbances.[2,3]

Dietary interventions can be used for conservative management of uremia or as a way to delay or avoid dialysis therapy. It is possible, although not conclusively proven, that nutritional interventions may slow disease progression independent of uremia management. Given that approximately 10% of the adult population worldwide has chronic kidney disease and given the very high cost and burden of maintenance dialysis therapy and kidney transplantation, dietary intervention may be increasingly selected as a management strategy for chronic kidney disease.[4,5]

In patients with CKD stage 5, food restrictions containing sodium, potassium, phosphate, and amino acids are quite important. Dietary interventions in CKD include regulating the intake of protein, energy, phosphate, sodium, potassium, and calcium and regulating fluid intake, vitamins, and minerals. Nutritional intake depends on the stage of CKD and in patients undergoing dialysis, depending on the type of dialysis being undertaken. Before giving nutritional therapy, an assessment of nutritional status must be carried out first. Assessment of nutritional status in CKD patients cannot use just one parameter but includes several parameters such as anthropometry, biochemistry, clinical, food recall, and malnutrition inflammation score (MIS). Malnutrition indicators were: SGA, serum albumin <3.8 g/dl, serum creatinine 25 <10 mg/dl, BMI <20 kg/m, cholesterol <147 mg/dl, serum prealbumin <30 mg/dl.[6]

Patients who received nutritional therapy from nutritionists who had experience and knowledge of chronic kidney disease had better outcomes than participants who did not receive nutritional therapy. Participants who received nutritional therapy at stages 3 and 4 CKD experienced slower progression to ESRD and better laboratory evaluation results than participants who received nutritional therapy at CKD stage V. Often, patients who were referred for nutritional therapy at CKD stage V experienced symptoms of uremic and nutritional therapy is only preferred to minimize these symptoms.[7]

Nutritional status worsens as CKD progresses, but it is still debatable whether nutritional status is affected by uremia or poor diet. Symptoms of uremia are usually the reason patients start dialysis. A high BUN level is indicative of poor kidney health, so a normal BUN level will not be seen at the start of dialysis and may be an indication that the patient is not on a good diet. Patients with CKD receiving nutritional therapy have normal albumin levels at the start of dialysis. Malnutrition and low serum albumin have good prognostic significance in CKD patients, including inpatients and mortality rates.

Protein

Protein is a complex molecule and has a large molecule. Protein is an important nutrient in living things and plays a role in many processes in life. Increased protein intake has been shown to affect renal hemodynamics and contribute to kidney function and tissue damage. A low-protein diet has an important role in the treatment of chronic kidney disease (CKD), especially chronic kidney failure. Protein is a molecule that is not much excreted in urine. The normal amount of protein in the urine is <150 mg/day. Most of the protein is a result of a viscous glycoprotein secreted physiologically by tubular cells, which is called "Tamm-Horsfall protein". Low protein diet therapy has been known for a long time and is applied to CKD. A low-protein diet is beneficial in reducing the accumulation of uremic toxins, thereby reducing uremia symptoms, reducing proteinuria, and slowing the initiation of renal replacement therapy. There are two types of low protein therapy in CKD, namely a low protein diet (0.6-0.8g/kg per day) and a very low protein diet (0.3-0.4g/kg per day). In various prospective studies, a very low protein diet can significantly reduce the progression of chronic kidney disease, but the risk of malnutrition increases in patients. GFR limits for

starting a low-protein diet have not been established. Most nephrologist recommends that a low-protein diet be started when GFR <60 ml/min/1.73 m (CKD stage 3). This reduction must be carried out progressively based on the stage of CKD and the amount of protein intake of each patient. With the application of a low protein diet, especially a very low protein diet, it is advisable to supplement the patient with α-ketoacid or essential amino acids to avoid malnutrition. α-ketoacid supplements are more effective than essential amino acids in slowing the course of kidney disorders. Keto acids are amino acids that undergo deamination with a carbon chain that does not contain an amino group. Keto acids don't contain nitrogen and don't produce nitrogen, so they don't overload the kidneys. Keto acids are used as substitutes for non-nitrogen-containing amino acids in various disorders involving nitrogen retention or protein intolerance. The transamination of most amino acids to their keto analogs is reversible. This circumstance makes use of possible α–keto analogs of branch-chain amino acids or branched-chain keto acids (BCKA) as a substitute for dietary amino acids in uremia patients. In the clinic, these mixtures are given together with dietary protein restrictions to improve patient compliance and increase amino acid intake essential. Thus nitrogen-free analogs of some amino acids essential it can completely replace its amino acid in the diet and is able to maintain nutrition when given on a very low protein diet in the long term. Recent research concluded that long-term use of keto/amino acids in patients receiving low-protein diet therapy and rEPO significantly improves protein metabolism, and lipid metabolism, reduces proteinuria, and can also slow down the decline in GFR in CKD patients. Although the mechanism is not clear, researchers suggest that low-protein diet therapy, EPO, and keto acid supplements can be used in conservative therapy for CKD.[8,9]

With the application of a low protein diet, especially a very low protein diet, it is advisable to supplement the patient with α-ketoacid or essential amino acids to avoid malnutrition. α-ketoacid supplements are more effective than essential amino acids in slowing the course of kidney disorders. Benefits of a low protein diet with α-ketoacid therapy: improve azotemia and metabolic acidosis, provide essential amino acids and improve protein metabolism, reduce insulin resistance, and improve carbohydrate metabolism. Increase lipase activity and improve fat metabolism, reduce phosphorus levels and increase calcium levels, reduce symptoms of secondary hyperparathyroidism, and reduce urinary protein excretion and inhibit the course of CKD.[10]

When a low-protein diet is given, patient compliance and nutritional status need to be considered carefully to avoid malnutrition. Monitoring must begin when the GFR is below 60 ml/minute because CKD patients tend to experience malnutrition at this stage. If a low-protein diet is administered, monitoring should be carried out more frequently, i.e., once a month at the start of therapy or in malnourished, then every 2 or 3 months.

Sodium and liquid

The relationship between sodium intake and increased blood pressure was found in people who consumed foods high in sodium (> 4 g sodium per day) with risk factors for having previously suffered from hypertension or aged over 55 years. In patients with chronic kidney disease, dietary sodium restriction is always recommended to control fluid retention and hypertension and to improve the cardiovascular risk profile. However, it's not clear whether a sodium chloride restriction diet can slow down the progressivity of chronic kidney disease. This is because cardiovascular studies and studies involving dietary sodium restriction often include patients with renal disease as exclusion criteria, so relevant intervention data are limited for these patients. Reducing sodium intake enhances the effect of a low-protein diet and angiotensin-modulating therapy in reducing intraglomerular pressure and may also reduce proteinuria and delay the progression of chronic kidney disease. Some studies show no association between dietary sodium intake and the

development of kidney disease, and other studies show a positive association. The study, which involved serial 24-hour urine collection from 3939 patients with chronic kidney disease, showed that the highest quartile of urinary sodium excretion (≥4.5 g per day), compared with the lowest quartile (<2.7 g per day), was associated with a 45% higher mortality and a 54% higher risk of developing the disease. Worsening cardiovascular conditions were observed when dietary sodium intake exceeded 4 g per day. Dietary sodium intake higher than 5 g per day and intake lower than 3 g per day is associated with an increased risk of cardiovascular disease and death.[11,12]

Although a daily sodium intake of less than 2.3 g (<100 mmol) is often recommended for patients with cardiovascular disease, there is no evidence that patients with kidney disease would benefit from this very low level of sodium restriction. Therefore, a daily dietary sodium intake of less than 4 g (<174 mmol) is recommended for all patients with chronic kidney disease, with a sodium intake of less than 3 g (<131 mmol) recommended for Specific management of symptomatic fluid retention or proteinuria. However, adequate fluid intake can reduce the risk of kidney disease, patients with renal insufficiency commonly experience isosthenuria. This is the basis for the recommendation that patients with stage 3 chronic kidney disease should limit fluid intake to less than 1.5 liters per day to avoid hyponatremia. Adjustment of these limits for hot climates and other conditions associated with insensible water loss (IWL) is very important. Complementary therapy with loop diuretics is frequently prescribed, especially for patients who are predisposed to symptomatic fluid retention or hyponatremia. Given the association of these conditions with chronic kidney disease, it has poor outcomes.[13]

Potassium

Potassium intake is an electrolyte intake to watch out for in CKD patients. In CKD, there is a disruption of the mechanism of excretion, secretion, and reabsorption of potassium. This causes an increased risk of hyperkalemia in CKD patients which increases the risk of mortality. Many potassium-rich foods, such as fresh fruit and vegetables, are considered healthy choices for most people, given their high fiber and vitamin content and low acidity. A higher potassium diet with lower sodium intake reduces the incidence of hypertension, stroke, nephrolithiasis, and kidney disease. Therefore a relatively high daily intake of potassium, 4.7 g (120 mmol), is recommended for healthy adults, including those at high risk of developing kidney disease.[14]

High potassium intake is associated with an increased risk of kidney disease progression. The study showed that in patients with chronic kidney disease, high potassium intake was associated with 2.4 times increased risk of death, which the results of this study were independent of plasma potassium level measurements. In another study, moderately low (<4.0 mmol per liter) and high (>5.5 mmol per liter) plasma potassium levels were associated with accelerated progression of chronic kidney disease. Dietary potassium restriction is often recommended in patients with hyperkalemia, especially those with advanced CKD. However, an excessive dietary restriction may expose the patient to a less heart-healthy and more atherogenic diet, which may actually lead to higher intestinal absorption of potassium.

Although the risk of hyperkalemia is greater as kidney disease worsens, several studies have examined the effects of dietary potassium restriction or potassium extraction methods during food preparation and cooking. At present, there has not been researching found whether potassium binding agents can allow more free dietary potassium intake so that CKD patients can consume potassium-rich foods, which are generally healthier. In patients with a tendency to hyperkalemia (>5.5 mmol potassium per liter), potassium intake of fewer than 3 grams per day (<77 mmol per day) is recommended, provided that the intake of fruits and vegetables is high in fiber and balanced and should not be reduced.

Phosphate

High plasma phosphate levels are associated with an increased risk of incident CKD. Marked hyperphosphatemia is rare in stages 1, 2, and 3 of chronic kidney disease, given the high circulating and urine levels of parathyroid hormone and fibroblast growth factor (FGF-23). This encourages the excretion of phosphorus through the urine. Increased parathyroid hormone and FGF-23 levels can cause renal bone disease, left ventricular hypertrophy, vascular calcification, and accelerated kidney disease progression due to vascular and tubulointerstitial injury. Dietary phosphorus management is important, even if no overt hyperphosphatemia is found. Although a low-protein diet also lowers phosphorus intake, the amount of phosphorus varies depending on the type of protein. For example, the phosphorus-protein ratios of egg white and yolk (which have 3.6 and 2.7 g of protein per egg, respectively) are 1 to 2 mg and 20 to 30 mg per gram.[15]

The absorption of phosphorus through the digestive tract is lower from vegetable sources (along with fiber) than from animal sources (30-50% versus 50-70%). In addition, consumption of processed foods has higher levels of phosphorus. A limitation of dietary phosphorus intake to less than 800 mg per day (26 mmol per day) is recommended for patients with moderate to advanced kidney disease, and processed foods with a high phosphorus-protein ratio should be minimized. However, in patients with stage 5 chronic kidney disease who are receiving dialysis therapy or who are at high risk of protein-energy wastage, excessive protein intake restriction to control hyperphosphatemia is not recommended.

Calcium and vitamin D

Renal bone disease is a disease that is quite common in patients with CKD. In patients with CKD, there is a decrease in levels of 1,25-dihydroxy vitamin D caused by renal insufficiency reduces the absorption of calcium from the gastrointestinal tract. However, passive diffusion of ionized calcium continues and can lead to a positive calcium balance but is exacerbated by reduced urinary calcium excretion due to secondary hyperparathyroidism. Increased release of calcium from bones in renal bone disease (increased bone resorption due to secondary hyperparathyroidism) promotes a positive calcium balance and can cause vascular calcification. Intestinal calcium absorption varies because of differences in dissociation and content of the different types of calcium. For example, calcium citrate is more easily absorbed than calcium acetate. Elemental calcium intake of 800 to 1000 mg per day (20 to 25 mmol per day) can produce stable calcium balance in people with stage 3 or 4 chronic kidney disease. Therefore, the recommended calcium intake for people without kidney disease is 1000- 1300 mg per day (25 to 32 mmol per day). In patients with chronic kidney disease stages, 2 to 5, 800 to 1000 mg per day of calcium from all food sources should be sufficient in patients with CKD.[16]

Native vitamin D supplementation (cholecalciferol or ergocalciferol) can be given to patients with chronic kidney disease. In several studies, the administration of vitamin D analogs resulted in reduced proteinuria and healing of renal osteodystrophy. Despite inconsistent data on the need for and effect of vitamin D on sub-population in certain patients with chronic kidney disease, including black Americans, who have lower total vitamin D levels and higher parathyroid hormone levels than white Americans, hydroxylated vitamin D agents may be needed in addition to native vitamin D to control progressive secondary hyperparathyroidism.

Carbohydrates and fats

Carbohydrate intake makes up half of the daily energy intake, and the proportion may be higher on a low-protein diet. In patients with kidney disease, carbohydrates should be consumed, preferably complex carbohydrates with a high fiber content (e.g., whole wheat bread, cereal multigrain, oatmeal, and fruit and vegetable blends) to help reduce dietary phosphorus and protein and reduce the formation of urea and creatinine. Such diets are also thought to

improve microbiota performance which has more beneficial effects and less constipation.

Unsaturated fat is the recommended fat. In CKD patients, it is recommended to replace butter with linseed, canola, or olive oil, which are rich in n−3 fatty acids. A study suggests that n-3 fatty acid supplementation in patients with diabetes and hypertriglyceridemia can reduce albuminuria and maintain kidney function. There is currently no evidence that the low-fat diet, which some guidelines recommend, slows down the progressivity of Kidney illness. In a low-protein diet, fats and carbohydrates must together cover more than 90% of the daily energy intake requirement of 30 to 35 kcal per kilogram to avoid protein-energy wastage. However, in patients with diabetic kidney disease, proper glycemic control must be maintained, but adequate energy intake is required to reduce the risk of protein-energy wasting and hypoglycemia, which increases with worsening renal function.[17]

Vitamins and trace elements

Patients with chronic kidney disease often experience multiple imbalances in trace elements and vitamins. Inadequate food intake can lead to a lack of consumption of antioxidant vitamins, including vitamins C and E, and carotenoids. In addition, in patients with chronic kidney disease, folic acid, vitamin K, and calcitriol become deficient. Micronutrient imbalance in patients with kidney disease can lead to increased oxidative stress, inflammation, and increased risk of cardiovascular disease. Among various trace elements, iron deficiency is the most common. This is due to the high frequency of gastrointestinal blood loss in patients with chronic kidney disease. Zinc deficiency, copper, and selenium may occur, while aluminum and magnesium levels may increase. One study showed that 800 μg of folic acid per day with enalapril, slow progressive CKD compared to enalapril alone. Vitamin K supplementation can slow vascular calcification. Daily intake of other vitamins and trace elements at conventional doses is often recommended both for people at high risk for CKD and for those who already have CKD.[18-20]

2. Conclusion

Individualized nutritional intake management is an important aspect of care for individuals diagnosed with any stage of CKD. Each individual with CKD has a different nutritional therapy approach depending on the disease conditions and nutritional status of the individual. Appropriate nutritional therapy in CKD patients can reduce disease progression.

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