Nutrition support in renal disease

Topic 15

Module 15.2

Nutrition support in chronic kidney disease (CKD)

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Learning Objectives

- To understand the metabolic abnormalities in patients with CKD;
- To know the determinants of nutritional state and the causes of malnutrition in CRF;
- To learn how to evaluate nutritional status in CRF;
- To know the nutritional requirements in CRF;
- To be aware of the aims of nutritional support and the type and composition of diets in CKD;
- To learn how to manage PN and EN.

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Key Messages

- Adequate nutritional screening and monitoring can influence long-term prognosis in CKD;
- Insufficient nutritional care and metabolic disturbances mainly due to metabolic acidosis, hormonal disturbances, chronic inflammation and partially loss of nutrients in heavy proteinuria are considered as the main causes of malnutrition;
- Other factors which may contribute to malnutrition are low social status and poverty, altered dentition and impaired digestion;
- Protein-energy wasting (PEW) leads to loss of body weight, a fall in body mass index below 20kg/m2, reduced muscle mass, and decreased serum albumin and transferring, all of which influence morbidity and mortality in CKD;
- PEW, chronic inflammation and metabolic disturbances (mainly lipid, carbohydrate and Ca-P product) can accelerate atherosclerotic processes (MIA syndrome);
- In patients with mild malnutrition linked to insufficient spontaneous intake, dietary counselling and nutritional supplements are worth trying first;
- In patients with severe malnutrition, enteral tube feeding may be necessary in addition to dietary counseling;
- In patients with severe malnutrition with a spontaneous intake less than 20 kcal/kg/day and/or the stress response (e.g. severe infection, surgery) daily nutritional support becomes necessary. Whenever possible, enteral is preferred to parenteral nutrition.

1. Introduction

Nutritional impairment and nutritionally related metabolic changes in patients with renal failure have been the subject of in-depth studies for many years.

Uraemic patients are especially sensitive to the effects of malnutrition and of nutritional support, both of which can affect the natural course of the disease and influence quality of life, morbidity, mortality and the rate of progression of the disease.

In clinical nutrition, kidney disease is unique among other clinical conditions in that dietary treatment helps to control most of the disease consequences and has therefore the same importance as other aspects of medical treatment.

The uraemic syndrome leads to malnutrition. The causes are summarized in Table 1:

Table 1 Causes of malnutrition in CKD

Reduced oral intake-restrictive diet
Metabolic disorders in uraemic toxicity
Metabolic acidosis
MIA syndrome (microinflammation)
Hormonal derangements
Insulin, PTH, erythropoietin, leptin, etc.
Gastrointestinal disease

The strategy of nutritional intervention in CKD patients is determined by specific metabolic alterations:

- Insulin resistance;
- Abnormal plasma lipid clearance;
- Metabolic acidosis;
- Hypocalcaemia and hyperphosphataemia;
- Secondary hyperparathyroidism, uraemic bone disease;
- Impairments of vitamin D3 activation;
- Hyperkalaemia;
- Renal anaemia;
- Chronic inflammatory reaction;
- Activation of protein catabolism due to intercurrent acute illness, acidosis and inflammation.

2. The aim of nutrition in CKD

The main aims of nutritional intervention can be summarized as follows:

- Avoid malnutrition;
- Reduce metabolic disorders;
- Delay progression.

In fact the history of advances in nephrology has followed closely developments in nutritional therapy for kidney disease.

An exhaustive overview and complete guidelines on nutrition in renal disease are complicated by the fact that the term "renal disease" embraces a number of clinical conditions whose common features are a decrease in glomerular filtrate, accumulation of toxic uraemic products, or some derangement in kidney physiology.

Moreover, the cut-off point between early and advanced renal failure, as well as the optimal time to start dialysis treatment are ill- defined.

3. Evaluation of nutritional state in CKD

It has been repeatedly shown that the much feared complication of protein-energy wasting (PEW) in dialysis patients may be partially caused by inadequate nutritional management and by protein and/or energy deficiency occurring in the predialytic phase, causing the patients to enter dialysis in a malnourished state (1-7).

For these reasons, nutritional status must be carefully monitored in all CKD patients from the time of diagnosis. Nutritional deficiencies should be detected and accurately identified before they become clinically relevant. No single parameter on its own provides reliable information on the overall nutritional status. Moreover, nutritional assessment should encompass all body compartments and functions. Combined evaluations of dietary intake and compliance, as well as of anthropometric measurements, biochemical determinations, serum and cell-mediated immune responses, and more in-depth assessment of body compartment status are recommended. Subjective global assessment (8, 9) or other combined nutritional indices (10, 11), if used appropriately, can be useful tools for the nutritional assessment of uraemic patients.

3.1 Assessment of dietary intake and compliance

This is of crucial importance in all uraemic patients. Direct investigation by a skilled dietitian (by dietary interviews, by three day recalls or by food diaries) is recommended (12, 13, 14), since there is no other simple way of determining total energy, lipid or CHO intake. In contrast, objective methods for measuring protein and phosphorus intake are well established. Urea nitrogen appearance, "protein catabolic rate", urea nitrogen urinary excretion and blood urea levels are directly related to protein intake in stable uraemic patients. Phosphaturia is also related to the dietary intake of phosphorus, but the correlation is less close, since it also depends on P absorption, the use of oral phosphate binders, and the degree of Vitamin D deficiency and secondary hyperparathyroidism (11, 15, 16).

3.2 Anthropometry

These measurements may be influenced by a number of factors unrelated to nutrition.

3.2.1 Body weight

From this and the measurement of height, the body mass index (BMI, Wt in Kg/ Ht in metres squared). This in turn can be compared with tables of the normal range of values for the relevant population. Weight is, of course, affected by fluid balance as well as by changes in solid tissue. Indeed short term changes are the best measure of water balance. Longer term changes are helpful in monitoring gain or loss of real tissue. Serial measurements and recording of weight are therefore of clinical value, providing these factors are understood and national and regional variations in body composition and Body Mass Index are taken into account.

3.2.2 Skinfold thickness and arm muscle circumference (AMC)

If oedema or important body water changes are not present, skinfold thickness is related to total body fat (13, 18-21,). Reproducible information is best given by measurements from multiple locations. Arm muscle circumference is a reliable index of total body proteins and lean body mass, particularly if triceps skinfold thickness is first subtracted from it. Only gross changes can be distinguished and results are influenced by overhydration. Again serial measurements are a useful monitoring tool, although skinfold thickness is subject to considerable observer error and repeat measurements should be made by the same observer. AMC is a bit more robust.

3.3 Plasma proteins

Plasma proteins are indices of protein synthesis, mainly by the liver. **Serum albumin** levels have recently been identified as prognostic indices (1, 22-25,) in chronic uraemia. However, the albumin concentration in plasma is raised by fluid losses andlowered by the diluting effects of fluid retention. It is also reduced by redistribution due to the increase in capillary permeability which accompanies injury and inflammation. Albumin has therefore been described as a "negative acute phase protein". **Serum transferrin** due to its short half-life time (9 days), this protein is a sensitive marker of PEM; iron status, infections and inflammation, however, influence its concentration independently from nutritional status. Short half-life proteins (Retinol-binding protein, prealbumin, ribonuclease) should be useful to monitor short-term nutritional changes: unfortunately, because of

their low molecular weight, they are normally filtered by the kidney, and thereafter they are of small value in non-dialyzed renal insufficiency. **Cholinesterase, fibronectin and IGF-1**, which may also be useful in assessing nutritional status, are not measured routinely(26-29).

3.4 Other biochemical determinations

Plasma creatinine is roughly related to muscle mass. The value of creatinine/height index is however diminished in stable uraemic patients; also by tubular and gut excretion. Plasma urea, potassium and phosphate levels are indices of dietary intake and/or actual protein status. Low serum cholesterol (<150 mg/dl) is a sign of protein energy wasting. Urinary 3-methylhistidine (3-MH) correlates with muscle mass and protein catabolic rate (some Authors have found a different 3-MH turnover in different proteins). In uraemia, its usefulness is limited by reduced excretion rates.

3.5 Immune function

The immune system is often deranged in renal failure but the relative contribution to its impairment of toxicity, drugs, malnutrition, or other deficiencies is not known. Levels of C3, C3a, Clq are reduced in uraemic patients, and the total lymphocyte count is often low. PMN metabolism and function are also impaired.

3.6 Nitrogen balance

Nitrogen balance (including nitrogen output in faeces) studies are traditionally used to assess the adequacy of protein intake, but nitrogen balance is sensitive also to the amount of other nutrients (e.g. energy (8)). If properly performed, nitrogen balance studies can be very accurate and precise, but they are time consuming and do not give any information concerning the mechanisms of nitrogen depletion or gain. I It must also be pointed out that, in malnourished populations as in uraemic patients, nitrogen balance can be achieved with less protein or at the expense of a reduced body protein pool and therefore may be of limited value in assessing nutritional adequacy (18, 30-35).

3.7 Amino acids

The pattern of fasting levels of plasma amino acids in patients with renal failure shows characteristic abnormalities that can be dependent on the uraemia itself or on nutritional abnormalities and deficiencies. Such abnormalities can be partially corrected by modified amino acid formulae.

3.8 Body composition

The increasing complexity of available technologies allows greater accuracy in measuring body composition. Body impedance analysis for total body water, intracellular water and lean body mass or dual-energy X-ray absorptiometry for bone or soft tissue assessment are widely used. Other more sophisticated instruments to determine total body potassium, nitrogen, or other elements, although giving more accurate measurement of composition and the response to nutritional interventions, are not available in most centers.

Two levels of nutritional assessment of CKD patients can be proposed:

- **A simpler level, for clinical purposes,** including the following:
  - Dietary history, estimation of protein intake (from Urea Nitrogen Appearance, Protein Catabolic Rate, etc.);
  - Anthropometry: weight (BMI, Ideal BW, Relative BW, Usual BW, Dry BW), skinfold thickness for body fat (multiple locations), arm muscle circumferences reflecting muscle and fat;
  - Visceral proteins: in relation to their half life (albumin, transferrin); small molecular weight proteins are of little value;
  - Creatinine, urea, potassium, phosphate, cholesterol in serum. Urea, creatinine and phosphate urinary excretion;
  - Lymphocyte count, complement protein concentration.

- **A more complex level, for scientific work, including the following:**
  - Nitrogen balance studies, if properly designed, are among the most precise methods for investigating N needs and equilibrium;

- BIA gives easy, accurate and reproducible measurements of total water, fat mass and fat-free mass. DEXA gives measurements of bone and fat mass and lean body mass;
- Neutron activation analysis gives the most reliable measurement of subtle modifications of body composition at molecular level (36-42);
- The best insights into intracellular metabolic events can be gained by a direct approach to single tissues (e.g. muscle biopsy) (31), by NMR studies, or by using isotopes (radioactive or stable) to measure total body or individual organ/tissue protein, amino acid or other substrate metabolism (synthesis, degradation and oxidation);
- Immunological and muscle functions.

4. Prevalence of PEW in chronic kidney disease (CKD)

Evidence of wasting and malnutrition is unfortunately found also in CDK receiving conservative treatment. (43-46).

Several year ago, Bajardi (47) found a 40% prevalence of PEW in kidney patients with advanced renal failure at the beginning of their of HD treatment. Because of the high percentage of uncontrolled patients in CKD (up to 30%) the prevalence of PRW is still high. Signs of malnutrition are found in 10-70 % at the beginning of HD treatment and in 18-51% of those undergoing CAPD (48-53).

Severe derangements of protein metabolism have been found in the skeletal muscle of CKD patients, who seemed clinically well nourished (11, 16). Unfortunately there appeared to be no direct link between measured nutritional parameters and muscle mass (41, 42, 54, 55).

The characteristics of PEW in uraemic patients differ widely, and large variations in the involvement of different body compartments have been described (18), with the body fat stores and visceral proteins being most frequently compromised. On the other hand, even obese chronic renal failure patients may be malnourished, mainly due to chronic inflammation (2, 56-60).

More sophisticated and sensitive methods are often required for the early diagnosis of malnutrition. In the early phase of chronic renal failure subclinical modifications of nutritional status were found only at the cellular level (19). Measurement of body cell mass by determination of total body potassium has revealed a mean 10% reduction in patients entering MHD and 6% in those entering CAPD programmes (34, 53, 55, 61).

5. Effects of PEW on morbidity, mortality and quality of life

5.1 PEW effect on morbidity and mortality

PEW in chronic renal failure is related to poor clinical outcome and mortality. Unfortunately, the causes of PEW are multiple and it is difficult to identify a single or specific nutrition-related cause of morbidity or mortality.

A low serum albumin has been found to be the strongest predictor of death risk in CKD patients (1), but this correlation does not indicate a causal relationship, because hypoalbuminaemia may merely reflect the severity of associated inflammatory illness. Albumin levels <30 g/L and particularly <25 g/l are associated with the worst prognosis. Besides albumin, other nutritional variables are also be related to mortality (anthropometry, body weight, transferrin, lymphocyte count, plasma amino acids, serum creatinine, etc.) with TBN > 80%) (1, 22, 27, 29, 32).

The most obvious way for malnutrition to induce worsening of morbidity and mortality rates is through immunodeficiency, which increases infectious complications by lowering serum and cellular immune response.

5.2 Effects of PEW on renal function

Besides its metabolic effects and its influence on outcome, PEW itself has some negative effects on renal functions (frequently associated with metabolic acidosis): it impairs the kidney's ability to eliminate an acid and a salt load, and it reduces the renal plasma flow, the GFR and the urine concentrating capacity.

6. Mechanisms responsible for malnutrition

6.1 Two types of malnutrition in CKD

The pathogenesis of PEW in patients with kidney failure is multifactorial. The principal causes involved are poor dietary intake (due to anorexia, nausea, disgeusia, protein, salt or water intolerance or to excessive dietary intake), abnormal lipid and carbohydrate metabolism, amino acid imbalances, abnormal hormonal response, losses of nutrients and metabolic acidosis causing catabolism (malnutrition type1 according to Stenvinkel).

In many complicated CKD patients the main reason for PEW is chronic inflammation (malnutrition type 2).The main initial goal in these patients is to reduce or eliminate inflammation by treating any chronic inflammatory disease, any intercurrent illness, or the severe form of nephrotic syndrome. It has been repeatedly confirmed, that the most damaging processes are linked to the severity of metabolic acidosis (7, 44, 45, 46, 61, 62).

6.2 An important cause of malnutrition is inadequate nutrient intake

A large percentage of CKD patients are in negative energy balance with an intake of 25-30 kcal/kg/day compared with the recommended 35 kcal/kg/day (11, 22, 23). There are similar deficits in protein and other nutrients. A spontaneous reduction in protein intake is usually associated with the pre-uraemic state of CKD and other metabolic disorders (mainly metabolic acidosis and renal anaemia) and should be addressed by appropriate nutritional management (18, 23, 33, 54, 63, 64).

Role of acidosis in protein catabolism

A key role for **metabolic acidosis (MA)** as a cause of malnutrition has been demonstrated: MA is a mediator of protein breakdown and amino acid oxidation (25) and proteolysis is related to its severity. Cortisol increases in MA, as well as BCKA dehydrogenase activity. Intracellular valine is directly related to blood pH. Acidosis stimulates ubiquitine (26) mediated proteolysis and the m-RNA for ubiquitine and proteasome. MA also impairs insulin activity and glucose utilization, and its correction improves nitrogen balance and lowers the 3-MH/creatinine ratio in urine (34, 61, 64, 65).

7. Management of nutritional care in CKD

"Protein restriction has been the traditional mainstay of the non-dialytic conservative treatment of CRF."

It was in fact the only treatment for irreversible uraemia until chronic dialysis became available. The principle remains essentially unchanged. Accumulation of urea, other nitrogen waste products, phosphates, potassium, and organic acids is diminished by lowering protein intake with a consequent reduction in and uaremic symptoms such as fatigue, anorexia and itching. However, a prolonged period of such protein restriction (exceeding 3-6 weeks and protein intake below 0.6-0.8 g of protein/kg body wt), may result in PEW.

Finally, it is important to remember that malnutrition in advanced CKD (stages 4-5) is multifactorial and not just a product of reduced nutrient intake. As well as trying to improve intake it is important to treat other causes of PEW, such as acidosis and hyperparathyroidism in the best possible way and also to improve dialytic treatment (based on Kt/V urea).

As in other conditions, nutritional treatment in uraemic patients should aim to maintain optimal body composition and function to achieve more rapid recovery and the best possible quality of life (Subjective Global Assessment-SGA).

8. Conservative nutritional treatment in CRF patients (CKD 3-5)

8.1 Low protein diets

8.1.1 Conventional low-protein diet

0.6-0.8 g protein/kg ideal body weight/day is the minimum protein requirement for CRF patients without proteinuria exceeding 1.5 g/day. This intake equals the requirements of normal healthy individuals. If proteinuria exceeds 1,5 g/day, an equivalent amount of protein should be given as an additional dietary supplement (35, 66-70).

All CRF patients treated with 0.6 -0.8g/kg IBW/day should be carefully monitored and the nutritional status regularly assessed. This amount of protein is normally considered safe in stable clinical conditions and can maintain nitrogen balance and body composition. Serum urea levels can be easily maintained at the recommended level up to 25 mmol/l.

Protein intake must be calculated per kg of ideal body weight and, to ensure an adequate intake of essential amino acids, should contain 50-75% protein of high biological value. Meticulous attention to acidosis and fluid and electrolyte disturbances is required.

With this amount of protein, phosphate intake can also be easily reduced to 800mg/day. In metabolically instable patients protein intake should be adjusted to serum level of albumin. When the serum albumin falls below 30g/l, nutritional supplements are necessary. In some cases administration of keto amino acids can also be helpful (71-74).

8.1.2 Supplemented very low-protein(VLPD) diet

In more advanced CRF (CKD stages 4-5) VLPD supplemented with keto amino acids (KA) may be prescribed: 0.28-0.30 g protein/kg/day + KA according to ESPEN Consensus, 0.3-0.4 + KA according to National Kidney Foundation (3).

Such a diet has some advantages:

- The sum of protein and amino acid intake does not exceed 0.7 g/kg/day, which is sufficient, in steady state patients, for nitrogen balance. Thanks to the administration of keto-and hydroxy forms of essential amino acids, the serum urea level decreases;
- It usually improves compliance, by increasing the variety of foods;
- It maintains a neutral nitrogen balance and a good nutritional status provided **that an adequate energy intake is maintained.**

Keto or hydroxy acids, analogues of leucine, isoleucine, valine, methionine and phenylalanine plus tyrosine, threonine, lysine and histidine can be given as supplements to VLPD. They can be provided as calcium salts or salts of ornithine, lysine and histidine. Besides better control of urea production, and of nitrogen balance, an improvement has been reported in hyperphophatemia, hypocalcemia, metabolic acidosis and glucose metabolism (14, 75, 76, 77).

8.2 Energy requirements

A crucial role in determining the nutritional adequacy of LPD and VLPD in CRF patients on conservative treatment is linked to adequate energy intake. Even in physiological conditions the optimal utilisation of minimal quantities of protein requires a good energy supply (30). It has been shown that higher energy intakes - in the range of 35-45 kcal/kg/day- are associated with better nitrogen balance in predialysis patients on LPD (0.6g/kg/day), with gain in body weight and improved body composition. On the other hand, the energy requirements of CRF patients are not reduced and are similar to those of normal populations, so that the low energy intake, often described in CRF patients, is probably one of the main reasons for abnormal body composition and malnutrition. 35kcal/kg BW/day is recommended, with adaptation (±20%) to individual needs (severe malnutrition or overweight/obesity) (33, 69, 78 – 81).

Other recommendations for the general population are also valid for patients with CRF: 30% or less of energy as fat with saturated fats <10% of total calories, cholesterol <300 mg/day, and simple sugars 10% is a reasonable goal for all uraemic patients. If an overt dyslipidaemia is present, further

modifications are recommended, but because of the need for appropriate energy intake, the dietary treatment of uraemic dyslipidemia can be difficult.

8.3 The role of the dietitian

As a general rule, successful dietary treatment requires close cooperation between a trained physician and a skilled dietitian. It also requires thorough education of the patients and their families. It is important to recognize the limitations of dietary treatment alone in the management of CRF. Once nutritional deficiencies are identified or terminal uraemic symptoms have developed, then the management strategy should be changed and more aggressive treatment, including dialysis, should be started.

Conclusions

- Closely supervised low protein diets provide a safe and cheap treatment for the early stages of uraemia in renal failure. The treatment should maintain nutritional status, but if nutritional status is threatened and supportive measures are ineffective, dialysis should be contemplated without delay;
- Close monitoring of nutritional status and nutrient intake is mandatory.

9. Positive effect of nutritional therapy on progression of renal insufficiency

The adequacy and efficacy of dietary treatment in controlling some of the uraemic metabolic disturbances of LPD or supplemented VLPD is well established. On the other hand, it has not yet been established whether protein (and phosphate) restriction in CRF patients, during conservative treatment, is able to slow down the progression of renal failure. The reasons for this uncertainty are many: heterogeneous populations, different kidney disease, low dietary compliance, difficulties in measuring progression and nutritional adequacy, different end-points, co-existence of other factors responsible for progression, different dietary composition (quality of protein, type of energy supply, etc.).

It remains less clear whether patients with GFR >60ml/min and progressive renal failure benefit from protein restriction.
According to some experimental studies, a low protein diet is effective in reducing microalbuminuria and proteinuria in diabetic nephropathy. This beneficial effect is much more evident in patients with early renal insufficiency than in patients with more advanced renal failure.
In diabetic patients with more severe renal damage (heavy proteinuria, more advanced renal failure) the results are less unequivocal (65, 77, 82–85).

But other factors are involved in the control of progression of nephropathy, mainly:

- Hypertension
- Proteinuria
- Hyperlipoproteinemia
- Hyperglycemia and
- Calcium and phosphorus metabolic disorders

The role of dietary phosphate may be independent from that of protein, and may be mediated by abnormal intracellular calcium metabolism. A low daily phosphorus intake is generally achieved in patients who comply b with a VLPD + KA diet, and this allows an improvement in divalent ion metabolism, PTH functions and hyperparathyroidism. A high Ca4 x PO4 product and hyperparathyroidism might be responsible for a state of cellular calcium toxicity (86-91).

Conclusions

There is some good evidence that protein restriction may reduce the rate of decline in renal function. The optimal time to start LPD is difficult to establish. Worsening of nutritional status in the late phases of CRF can be an important indication for beginning dialysis treatment, i.e. a policy of dialysis accompanied by the more liberal feeding which that allows.

Many other factors responsible for progression of renal failure are likely to be important. Predominant roles are attributed to proteinuria, to the type of disease causing the nephropathy, and to hypertension and its genetic determinants.

10. Guidelines for nutritional treatment of CKD on conservative treatment.

10.1 Protein and Energy intake

- CKD stage 1 (normal renal function)-protein intake as for general population, not exceeding 1-1.2g /kg iBW/day, energy intake up to 35 kcal/kg iBW/day, in obese patients restriction of energy intake up to 25-30 kcal/kg iBW/day;
- CKD stage 2-(GFR over 60-70ml/min/1.73 m2)-protein intake 0.8-1.0g/kg/ iBW, vegetable proteins and fibres, energy intake up to 35 kcal/kg, in obesity energy restriction up to 25-30 kcal/kg iBW/day iBW/day;
- CKD stage 3-(GFR 30-60 ml/min/1.73 m2)-protein intake 0.8 g/kg iBW/day, vegetable proteins and fibres, energy intake up to 35 kcal/kg, in obese energy restriction up to 25-30 kcal/kg iBW/day, in proteinuria over 1.5g/day, add protein loss;
- CKD stage 4-(GRF 15-30 ml/l/1.73m2)-protein intake 0.6 g/kg iBW/day or 0.5-0.6g +keto amino acids (100 mg/kg iBW/day), energy intake 35 kcal/kg, animal:vegetable protein ratio 1:1,add protein loss;
- CKD stage 5-(GFR below 15 ml/min/1.73 m2)- 0.28-0.30 g protein/kg/day + KA according to ESPEN Consensus, 0.3-0.4 + KA according to National Kidney Foundation (3) .energy intake 35 kcal/kg iBW/day. Animal: vegetable protein ratio 1:1, add protein loss.

10.1.1 Meticulous nutritional monitoring is mandatory for points 3, 5

Animal proteins are necessary to increase the biological value of LPD. In VLPD with KA, the biological value, because of KA supplements, is less important, and more vegetable proteins can be allowed. The long-term nutritional adequacy of vegetarian LPD is not proven.

Most active patients, with body weights in the range ±10% DBW, need 35kcal/day. Overweight (>120% of the standards) or malnourished patients may need adjustment of daily energy intake. Normal percent distribution between lipid and carbohydrate (30% and 55-60% respectively) is suggested, **with emphasis on fiber, complex carbohydrates and unsaturated fatty acids.** If hypertriglyceridaemia is present, avoid simple sugars and ethanol. If hypercholesterolaemia is present: dietary cholesterol <300 or 200 mg/day, saturated fatty acid <10%, monounsaturated fatty acid > 10%.

In malnourished patients, if anorexia inhibits a higher energy intake, supplements can be given.

10.2 Phosphates

Different intakes of phosphates can be achieved by more or less severe exclusion of phosphate rich foods of animal origin (dairy products, egg yolks, meat). Also vegetable foods can be chosen according to their phosphate content. The foods (meat, fish, and vegetables) can be boiled in large amounts of water so as to eliminate as much phosphate as possible. By following this recommendation a phosphate intake between 5 and 10 mg/kg/day can be achieved (70, 74, 92).

10.3 Calcium

Low-protein, low-phosphate diets are, as a rule, low in calcium because of a low intake of dairy products. Vegetarian diets cause even more risk of calcium deficiency, because of the poor calcium bioavailability in vegetable foods, due to poor intestinal absorption. Calcium supplementation, to achieve a total calcium intake of 1.5-2.0 g/day is recommended: it is efficient in preventing secondary hyperparathyroidism and its metabolic and clinical consequences (66, 92).

Calcium carbonate contains a higher proportion of calcium in comparison with other salts, and is effective in helping to control l acidosis. Calcium salts of the ketoanalogues of essential amino acids also provide large amounts of calcium. These calcium supplements are sometimes responsible for hypercalcaemia.

10.4 Vitamins

10.4.1 Water soluble vitamins

In the long term, LPD or VLPD are associated with a risk of water-soluble vitamin deficiency. Low levels of riboflavin (B2) and to a minor extent of thiamine (Bl) were found after 6 months' diet giving 0.6 g/kg/day of protein. Functional tests indicate an even greater deficiency of pyridoxine, regardless of treatment but increasing with time. Therefore supplements of 5 mg/day of pyridoxine in predialysis patients are recommended. Cyanocobalamin (B12) levels are normal in CRF, and supplements are required neither for this vitamin nor for folic acid, unless specific reasons for deficiency are present. Ascorbic acid is often low in CRF patients in conservative or dialytic treatment and a supplement of 100 mg is generally suggested in all uraemic patients. Higher amounts are not recommended because of the risk of secondary oxalosis (93-96).

As a general rule, patients treated with VLPD plus supplements of KA+EAA must be supplemented with water soluble vitamins. Patients treated with long term vegetarian diets (e.g. nephrotic patients) are also at risk of developing water-soluble vitamin deficiency.

10.4.2 Fat soluble vitamins

The plasma levels of Vit A are directly related to serum creatinine and are frequently high in CRF, but the signs of hypervitaminosis are generally not evident, possibly because of high levels of carrier proteins. Supplements of fat soluble vitamins A, E and K are not recommended. Deficiency of active Vit D metabolites develops progressively as the GFR falls and symptoms of hyperparathyroidism and osteodystrophy appear. For this reason, long term oral supplements of 1-25 $(OH)_2$ D3 are recommended. The initial dose of 0.25microg/day can be increased by 0.25 µg/day, until an optimal correction of hypercalcaemia has been obtained. Plasma levels of calcium must be monitored to avoid hypercalcaemia, especially in patients receiving calcium carbonate supplements (93, 97).

10.5 Iron

Iron needs should be assessed by changes in the ferritin plasma concentration, rather e than by iron and transferrin values (9). In predialysis patients, iron deficiency is rare but supplementation may t be necessary in patients on VLPD supplemented with KA and/or EEA and in patients on a long term vegetarian diet. In patients on dialysis the prevalence of iron deficiency is higher, because of the larger blood losses.

Phosphate binders reduce iron absorption and should therefore be taken separately. During EPO therapy, iron supplements may be necessary to obtain a better response to erythropoietin. On the other hand, blood transfusions and reduced erythrocyte life span may cause iron overload.

10.6 Trace elements

If the macro-nutrient intake and dietary adequacy are suboptimal, there is a risk of developing trace element deficiency. However, continuous supplementation of trace elements is not recommended routinely in CRF patients (68). **Zinc** deficiency can worsen some uraemic symptoms (18), such as ageusia, impaired olfactory acuity; anorexia, delayed wound healing, sexual dysfunctions, and impaired PMN leukotaxis). In renal failure Zn deficiency can also be caused by decreased intestinal absorption, deranged tubular transport, urinary loss associated with heavy proteinuria, or diminished carrier proteins. Selenium is important for the activity of glutathione peroxidase that protects cells against oxidative damage. Low selenium levels have been found in CRF patients with cardiovascular complications and both zinc and selenium deficiency may be due to chronically low protein intake or to diminished plasma levels of carrier proteins. These last problems can be corrected by enhancing protein intake or correcting low levels of such transport proteins. High blood copper levels occur in CRF, but do not appear to cause clinical symptoms or to worsen the symptoms of uraemia (95, 98, 99, 100).

Current practices

These vary between different centres and countries, according to culture, nutritional habits, dialysis facilities, and economic circumstances. Some centres use dietary restriction from a very early stage, while others limit the use of LPD and VLPD to advanced renal failure, in patients who have developed uraemic symptoms. Some tend to dialyse early and others delay until a later stage of the disease.

11. CKD patients and need for parenteral nutrition (PN) and enteral nutrition (EN)

Conservatively treated patients with CKD seldom need PN. Potential indications for PN in CKD patients are similar to those in non-renal patients. Malnourished CKD patients requiring nutritional support should only be considered for PN when ONS and/or EN are impossible or inadequate to reach nutritional goals Special attention should be given to CKD patients requiring PN during perioperative periods.

The goals of PN in CKD patients are:

- to prevent or treat undernutrition leading to cachexia;
- to ensure the provision of optimal levels of energy, essential nutrients and trace elements;
- attenuation of disease (CKD) progression through protein or phosphate restriction.

In nutrition of non-dialyzed CKD patients there is a delicate balance between causing toxic effects from an excess of nitrogen – containing compounds and pro-oxidants and causing undernutrition by providing too little energy and/or protein. In this regard, low protein diets should be accompanied by strict monitoring of energy intake and nutritional status.

Because no hard data is available on disease-specific PN formulae, standard PN solutions should be used if PN is indicated (C). In patients receiving PN without any oral or enteral intake, vitamins and trace elements should be administered intravenously (C). If the patients has to continue PN for more than, accumulation of vitamin A and trace elements should be considered (C).

PN may be useful as an initial supplementary short-term nutrition strategy in patients with inadequate oral intake in order to 'kick-start' the refeeding process. Periods of PN are also useful in conservatively treated CKD patients that cannot achieve adequate nutritional goals through normal dietary intake or enteral feeding, or in whom the enteral route is compromised by severe gastro-intestinal complications. A decision tree for nutritional support in conservatively treated CKD patients with signs of malnutrition is suggested as follows:

Is the gastro intestinal tract functioning normally?
If the answer is yes:

- Increase dietary intake by augmenting energy and protein. The use of oral supplements is recommended;
- If the patient's nutritional status keeps worsening, start tube feeding. Oral intake can be maintained in combination with oral supplements;
- If the patient's nutritional status still keeps worsening, start PN.

If the answer is no:

- Start PN. The PN can be:
  - Peripheral PN: in cases requiring short term supplementary feeding, with or without fluid restriction depending on concomitant complications;
  - Central PN: in cases needing long term feeding, with fluid restriction.
- When the gastrointestinal tract is working again, PN should be tapered gradually and, if possible, withdrawn in favour of normal oral intake with or without ONS and/or enteral tube feeding. The important thing is that the total intake from all sources should at all times meet the patient's nutritional requirements.

Summary

Patients with CKD are prone to malnutrition. Adequate nutritional support not only improves the quality of life, morbidity, and mortality, but may also have beneficial effects on the underlying disease and on the progression of renal failure. Evaluation and monitoring of nutritional status, dietary and supplement intake, and compliance are of crucial importance. Evidence of wasting and malnutrition (PEW) is also found also in CKD patients receiving conservative treatment as well as those on dialysis. The pathogenesis of PEW is multifactorial: poor dietary intake, abnormal metabolism of amino acids, proteins, lipids and carbohydrates, and metabolic acidosis causing

catabolism (malnutrition type 1). Many CKD patients also suffer from chronic or intercurrent inflammation whose catabolic effects increase the risk of PEW (malnutrition type 2).

The basic composition of the diet in CKD stages 1-5 is as follows:

- CKD stage 1 (normal renal function): protein intake as for general population, not exceeding 1-1.2g /kg iBW/day; energy intake up to 35 kcal/kg iBW/day, in obesity restriction of energy intake up to 25-30 kcal/kg iBW/day;
- CKD stage 2-(GFR over 60-70ml/min/1.73 m2): protein intake 0.8-1.0g/kg/ iBW, vegetable proteins and fibres; energy intake up to 35 kcal/kg, in obesity energy restriction up to 25-30 kcal/kg iBW/day iBW/day;
- CKD stage 3-(GFR 30-60 ml/min/1.73 m2): protein intake 0.8 g/kg iBW/day, vegetable proteins and fibers; energy intake up to 35 kcal/kg, in obesity energy restriction up to 25-30 kcal/kg iBW/day; in proteinuria over 1.5g/day, add protein loss;
- CKD stage 4-(GRF 15-30 ml/l/1.73m2): protein intake 0.6 g/kg iBW/day or 0,5-0.6g +keto amino acids (100 mg/kg iBW/day); energy intake 35 kcal/kg; animal: vegetable protein ratio 1:1,add protein loss;
- CKD stage 5-(GFR below 15 ml/min/1.73 m2)- 0.28-0.30 g protein/kg/day + KA according to ESPEN Consensus, 0.3-0.4 + KA according to National Kidney Foundation (3); energy intake 35 kcal/kg iBW/day. Animal: vegetable protein ratio 1:1, add protein loss.

Conservatively treated patients with CDK seldom need parenteral nutrition, which is only indicated when oral and/or enteral nutrition are unable to achieve nutritional goals, although it may be used as an initial refeeding 'kick-start' in patients who are already severely malnourished.

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