Nutritional status in dialysis patients: a European consensus

Francesco Locatelli¹, Denis Fouque², Olof Heimburger³, Tilman B. Drüke⁴, Jorge B. Cannata-Andia⁵, Walter H. Hörli⁶ and Eberhard Ritz⁷

¹Department of Nephrology and Dialysis, Azienda Ospedale di Lecco, Ospedale A. Manzoni, Lecco, Italy, ²Department of Nephrology, Hôpital Edouard Herriot, Lyon, France, ³Division of Renal Medicine, Department of Clinical Science, Karolinska Institute, Huddinge University Hospital, Stockholm, Sweden, ⁴Department of Nephrology and Inserm U507, Necker Hospital, Paris, France, ⁵Bone and Mineral Research Unit, Instituto Reina Sofia de Investigación, Hospital Central de Asturias, Universidad de Oviedo, Oviedo, Spain, ⁶Department of Nephrology and Dialysis, Department of Medicine III, University of Vienna, Vienna, Austria, and ⁷Department of Nephrology, University of Heidelberg, Heidelberg, Germany

Abstract

Background. Malnutrition is common in dialysis patients and closely related to morbidity and mortality. Therefore, assessment of nutritional status and nutritional management of dialysis patients play a central role in everyday nephrological practice.

Methods. Achieving a consensus on key points relating to pathogenesis, clinical assessment, and nutritional management of dialysis patients.

Results. The assessment of nutritional status should be based on clinical assessment and biochemical parameters, including history of weight loss, percent standard weight, body mass index, muscle mass, subcutaneous fat mass, and plasma albumin, creatinine, bicarbonate and cholesterol. Co-morbid conditions should be assessed and C-reactive protein (CRP) measured—as a marker of inflammation—as there is a close relation between malnutrition, on one side, and co-morbid conditions and inflammation on the other. For a more detailed assessment, subjective global assessment of nutritional status is a well-validated tool, and dual-energy X-ray absorptiometry (DEXA) is a useful method for routine assessment of lean body mass. Anthropometric methods are also useful. They are cheap and easy to apply, although less precise than DEXA. The recommended daily protein intake is at least 1.2 g/kg standard body weight and the energy intake 35 kcal/kg standard body weight (BW), in patients <60 years, and 30 kcal/kg standard BW in patients >60 years. The standard bicarbonate level should be at least 22 mmol/l. If CRP is >10 mg/l, it is important to seek and treat the underlying cause.

Conclusion. Malnutrition assessment and treatment is a great challenge for nephrological care. Achieving evidence-based consensus can help in implementing the progress of knowledge in clinical practice.

Keywords: acidosis; catabolism; dietary counselling; dietary supplements; dietician; inflammation; lean body mass; malnutrition; nutritional status

Introduction

The dietary approach in the different phases of chronic renal insufficiency (CRI) is one of the most important, and yet controversial, topics in the whole history of nephrology. Since the time (35 years ago) when dialysis facilities were not yet easily available and a low protein diet was the only means to delay the occurrence of uraemic symptoms [1,2].

In the subsequent decades of the dialysis era, low protein diets (varying from 0.85 to 0.3 g/kg/day with supplementation of essential amino acids and ketone analogues) were given emphasis, in order to slow the
progression rate of CRI, until two large prospective randomized controlled clinical trials published in the early 1990s, one Italian [3] and the other American [4], showed that dietary protein restriction had little effect on the progression rate of CRI [5]. Even more disturbingly, the American trial showed that the development of malnutrition could be a possible drawback of protein-restricted diets.

Nevertheless, a recent meta-analysis of randomized trials has shown that a low protein diet is effective in reducing the number of 'renal deaths' (defined as the need for starting dialysis, the death of a patient or kidney transplant during the trial) [6].

Both malnutrition, defined by insufficient protein-calorie intake, and cachexia, defined by defective food assimilation or utilization in the presence of hypercatabolism and systemic inflammation, are highly prevalent in dialysis patients from the very beginning of substitutive treatment. They are due to uraemia itself (loss of appetite), dialytic treatment (loss of amino acids and proteins, bio-incompatibility of treatments, quality of the dialysate), as well as the premature ageing of dialysis patients and the increased burden of co-morbidity factors [7], with consequent patient invalidity and inflammatory triggers.

While much progress has been made in recent years in recognizing the link between malnutrition, inflammation, cardiac disease, and increased mortality [8], no consensus has yet been reached concerning the best assessment and management of nutritional status in dialysis patients.

This paper presents an analysis of the major unresolved issues concerning nutritional status in dialysis patients. The accord reached on key points is provided.

The pathogenesis of malnutrition in dialysis patients: are there two types of malnutrition in CRI?

Dialysis patients with malnutrition often have signs of inflammation, characterized by an increase in plasma C-reactive protein (CRP) and an imbalance between pro-inflammatory and anti-inflammatory cytokines [9,10]. Markers of both malnutrition and inflammation predict mortality in dialysis patients, the majority of whom die from cardiovascular disease. There is a close relationship between malnutrition, inflammation, and atherosclerosis in patients with renal disease. It has been suggested recently that pro-inflammatory cytokines represent a common link between malnutrition, inflammation, and atherosclerosis (MIA syndrome) in patients with chronic renal disease [9,10].

Therefore, it has been suggested that there may be at least two fundamentally different types of malnutrition in patients with CRI [10]. The first is related to low protein and energy intake. In this context, co-morbid conditions are uncommon and serum albumin may be normal or only slightly decreased. This type of malnutrition may be amenable to adequate nutritional and dialysis support. In contrast, the second type of malnutrition is associated with inflammation and atherosclerotic cardiovascular disease (MIA syndrome). Co-morbid conditions are common and serum albumin levels are usually decreased. This type of malnutrition is much more difficult to reverse with nutritional support and dialysis therapy, unless the underlying co-morbid conditions and chronic inflammatory response are adequately treated [10]. Obviously, these two types of malnutrition are often combined in the clinical setting.

The causes of both malnutrition and inflammation are numerous in CRI patients with elevated serum levels of CRP and pro-inflammatory cytokines. Patients may not ingest sufficient amounts of food because of loss of appetite. Anorexia can be caused by factors such as the retention of uraemic toxins and chronic metabolic acidosis, which, moreover, is an important catabolic factor. In this regard, inadequacy of dialysis treatment may be an important cause of malnutrition. Renal replacement therapy per se causes a loss of nutrients. During a haemodialysis (HD) session, a considerable quantity of amino acids may be lost (4–9 g in the fasting state and 8–12 g post-prandially). In contrast, protein losses are negligible, unless multiple re-use of dialysis filters is practised. Peritoneal dialysis (PD) causes a loss of peptides, ~9 g of total protein and 6 g of albumin daily, and even much more during episodes of peritonitis [11]. Both HD and PD can cause a loss of vitamins, particularly water-soluble vitamins. Endocrine and metabolic disturbances of uraemia, in particular insulin resistance, can reduce protein anabolism and favour catabolism. The role of psychological factors (depression) and socio-economic factors (loneliness, invalidity, poverty) should never be neglected, considering that at present the majority of the dialysis population is composed of elderly patients. Acute concurrent illnesses can also contribute to malnutrition. Finally, inadequate dietary prescription, due to the traditional physician’s preference of prescribing nutritional restriction rather than providing nutritional counselling, can further worsen malnutrition.

The pathogenesis of chronic systemic inflammation in dialysis patients, which is associated with hypercatabolism and body wasting, is complex and not yet fully understood. Serum IL-1, IL-6, and TNF-α levels are increased in patients with CRI already before the start of dialysis [12,13], suggesting that renal failure per se is a contributing factor. Other non-dialysis related causes of elevated CRP include co-morbid conditions, e.g. chronic heart failure with oedema [14] and the atherosclerotic process [15]. Moreover, various chronic infections, such as Chlamydia pneumoniae [16] and dental or gingival infections may also contribute. Systemic inflammation due to infection can be of major importance in PD patients, due to recurrent peritonitis episodes and it is not negligible in HD patients, as infections and sepsis are the second most common cause of death in this population. Furthermore, it has been suggested that factors related to the
dialysis procedure itself may contribute to maintaining chronic systemic inflammation, e.g. bio-incompatibility [17], the use of non-sterile dialysate [18], and back-filtration [19]. However, although HD with ultra-pure dialysate and biocompatible membranes is able to reduce serum CRP, it does not normalize it, reinforcing the importance of non-dialysis related factors in triggering the inflammatory response [20].

In order to prevent and treat malnutrition in dialysis patients, it is important to assess appropriately the nutritional status and to identify patients at risk.

**Methods to assess nutritional status in dialysis patients**

The authors do not believe that there is a single best nutritional marker in patients with CRI, but that several nutritional markers should be evaluated together. The assessment of nutritional status should be based on a combination of clinical parameters with biophysical and biochemical parameters. Malnourished dialysis patients often have protein energy malnutrition with a reduction of both fat mass (FM) and lean body mass (LBM). Therefore, clinical assessment of subcutaneous FM and muscle mass and a history of weight loss are important parts of routine nutritional assessment. Percentage of standard weight and body mass index (BMI) are also important and easy to measure, although BMI is more useful for assessment of obesity than of malnutrition. Most dialysis patients with malnutrition also have co-morbid diseases, in particular cardiovascular disease and inflammation, and the assessment of co-morbid conditions is an important part of the nutritional assessment of dialysis patients [10].

The most commonly used laboratory parameters for routine assessment of nutritional status are plasma concentrations of albumin, pre-albumin, transferrin, and other liver-derived proteins. Although serum albumin is by far the most commonly used nutritional marker in dialysis patients, its value has been questioned as low serum albumin levels not only reflect poor nutritional status, but also albumin losses in urine (and/or dialysate) and, as albumin is a negative acute phase protein, the presence of an inflammatory process [21–23]. Therefore, other visceral proteins have been used, including pre-albumin, transferrin, and retinol-binding protein [23]. For these proteins in general, there is considerable overlap between malnourished and well-nourished patients [21]. Pre-albumin has a shorter half-life than albumin, has a close relationship with nutritional status and is a good predictor of clinical outcome [24]. Therefore, it is likely that in the near future pre-albumin will be established as a valuable additional marker for routine assessment of nutritional status in dialysis patients. However, it should be noted that pre-albumin is a negative acute phase protein as well [21]. Measurement of CRP is important for the assessment of inflammatory co-morbid conditions, as well as for the interpretation of albumin and pre-albumin levels. Additional biochemical nutritional markers, with low values indicating poor nutrition and poor outcome, include serum creatinine and total cholesterol [21]. The creatinine level before dialysis is a strong predictor of low muscle mass and poor outcome. Serum total cholesterol is a less sensitive nutritional marker, but is cheap and easily available. Acidosis is a strong catabolic factor in uraemia and serum bicarbonate monitoring is recommended for routine follow-up of the acid–base status.

During recent years, subjective global assessment of nutritional status (SGA) [25] has been used increasingly to assess nutritional status in many studies of dialysis patients (mainly cross-sectional studies) [26–28] and in patients with CRI at start of dialysis therapy [29]. SGA correlates well with other nutritional markers in patients with CRI [21,26–28]. Furthermore, it has a high predictive value for mortality in these patient groups [29]. However, one potential problem with SGA is its subjective nature, which may reduce its reproducibility, thus small differences in SGA score must be interpreted with great caution.

**Assessment of LBM**

As protein malnutrition with loss of muscle mass is particularly common in patients with CRI, various methods have been applied for objective monitoring of muscle mass or LBM, e.g. anthropometrics, creatinine kinetics (CK), bioimpedance, and dual-energy X-ray absorptiometry (DEXA). Of these methods, DEXA seems to be the most reliable [21,30,31]. With DEXA, one can estimate bone mineral, fat, and LBM distribution directly, without making assumptions about the two-compartment model [32]. DEXA is considered to be superior to other non-invasive methods for determining body composition in renal failure [33], and has been widely applied for studies of body composition in dialysis patients [21,33]. However, it must be kept in mind that, although the state of hydration does not affect the estimate of FM with DEXA, it does affect that of LBM, and ideally, for assessment of body cell mass, it should be combined with estimation of the extra-cellular fluid volume with tracer dilution technique.

With anthropometric methods, the sum of skinfold thickness values at four sites can be used to calculate body density, e.g. using the equations of Durnin and Womersley [34]. FM and LBM can then be obtained from body density and body weight. Although the use of anthropometric methods is an indirect and rather insensitive means of evaluation, with several inherent errors including the influence of hydration status, the results agree reasonably well with results obtained by DEXA [21]. As the use of anthropometric methods is easy and cheap to apply, it can be recommended for routine assessment of nutritional status, bearing its limitations in mind.
CK has also been used to calculate LBM from creatinine excretion in the urine and dialysate, in particular in PD and pre-dialysis patients, as suggested by Keshaviah et al. [35]. However, the estimated LBM from CK is usually markedly lower than with other methods such as total body potassium [36], anthropometry [21,22], bioimpedance [22], or DEXA [21]. Furthermore, LBM estimates based on CK are influenced by the creatinine content of foods (mainly related to meat content), and metabolic creatinine degradation [36,37]. Finally, the variation of LBM with repeated measures of LBM using CK is unacceptably high [36]. Therefore, CK cannot be recommended for LBM assessment in CRF.

Single-frequency and multi-frequency bioelectrical impedance (BIA) has recently been used in many studies of nutritional status of dialysis patients. However, it is not clear to what extent the measured impedance really contributes to the results, as it has been suggested that height and body weight are major sources of variance in BIA prediction models [38]. Furthermore, the technique has not been appropriately validated against more specific methods, and BIA does not measure FM and LBM accurately in patients with a body composition that differs from young healthy adults with normal BMI [39,40]. Therefore, BIA cannot be recommended presently for routine use.

**Optimal protein and energy intake for patients on maintenance dialysis**

A number of descriptive studies have reported energy intakes to be as low as 22–24 kcal/kg body weight (BW)/day in patients on routine HD treatment. There is no metabolic or pathological reason for not giving a standard energy intake to stable adult maintenance dialysis patients. Indeed, their metabolic needs, based on resting energy expenditure, are similar to those of normal adults, i.e. 35 kcal/kg BW/day. Energy balance studies, mainly in PD patients, confirmed that a positive nitrogen balance could only be attained with energy intakes >30 kcal/kg/day [41].

Although a level of ~0.7–0.8 g of protein/kg BW may be sufficient to permit a neutral nitrogen balance in pre-dialysis stable adults, the dialysis procedure itself increases protein needs. The Dialysis Outcome Quality Initiative (DOQI) guidelines in nutrition have proposed that, based on nitrogen studies in HD and PD patients, a minimum of 1.2 in HD and 1.3 g of proteins/kg BW in PD represent the minimum daily intake to ensure a neutral protein balance [42]. Half of this intake should be made by proteins of high biological value from animal origin, e.g. meat, fish, or dairy products.

These intakes may not be easily met for the following reasons. First, patients may be anorectic during the weeks or months preceding the start of dialysis, particularly if they were under-managed. Secondly, changes in lifestyle may have psychological effects and patients may not want to change their whole behaviour, including food habits. This is especially important since any delay in providing adequate intake will induce a loss of energy stores and protein mass, which are not easily regained afterwards. In this regard, we believe that a nutritional survey including the setting of a care plan should be performed no later than 1–2 weeks after the start of dialysis, and should be repeated periodically by means of a food questionnaire to be recorded by the patient in his or her routine environment. The optimal duration of the food report should be at least 3 days and possibly up to 1 week. Ideally, dietary monitoring should be performed by the renal dietitian or the nephrologist if no specialized dietitian is available for this task.

Food intake may vary considerably, depending on the dialysis schedule. It is believed that the intake may be spontaneously reduced in the last hours preceding the dialysis session, and this may be more pronounced during the weekly 3-day interval off dialysis. Reducing the interval between dialysis sessions may improve the food intake pattern. In a pilot study in eight HD patients, the body composition alterations that were present during a standard dialysis of 3 weekly sessions improved when patients were switched to short sessions of 2 h daily, thus allowing a more regular food and beverage intake, an increase in energy and protein by 13 and 24%, respectively, and a rapid improvement in nutritional indices [43]. Another important fact is the decreased number of meals that occur when patients are hospitalized, for numerous reasons such as fasting before and after procedures or surgical interventions, post-dialysis fatigue, sepsis, pain and frequent changes in dialysis schedule. In our experience, these events may lead to a reduction of ~20% in meals and, hence, result in an energy debt of ~2800 kcal during a full week of hospitalization [44].

**Dietary supplements**

Supplements are often proposed to dialysis patients, after having checked that their regular food intake does not meet the recommended optimal daily intake and having ruled out any treatable disease. In a cross-sectional analysis of three university hospital dialysis units, it was shown that, among over 100 HD patients, almost 50% of patients were prescribed oral supplements. The energy and protein intake, respectively, gained through these daily supplements were between 1500–2200 kcal and 110–160 g protein weekly (D. Fouque et al., personal communication). Only 25% of supplement withdrawals were due to patients’ personal choice. Despite taste, financial limitations, and lassitude, this approach, largely sustained by the renal dietitian, appears to be worth proposing to moderately malnourished patients. A wide variety of products are currently available providing protein-calorie supplementation with high biological value proteins.
**L-Carnitine supplementation**

In an attempt to correct abnormal serum levels of carnitine, L-carnitine supplementation has been suggested to correct or improve many symptoms in HD patients. Indeed, there are many causes for carnitine depletion during maintenance dialysis. Low animal protein intake, particularly from meat and cheese, and increased losses into the dialysate during regular dialysis, possibly in association with high-flux techniques, may be responsible for low serum or tissue carnitine. Furthermore, abnormal metabolism also occurs with the accumulation of carnitine by-products, such as acyl- and acetyl-carnitine derivatives. These compounds, which are normally cleared by the kidney, may accumulate during CRI. Unfortunately, they cannot be specifically measured by a routine technique that allows the determination of total and free carnitine only. Therefore, increasing serum carnitine by providing greater amounts of L-carnitine, either orally or by the i.v. route, may not be sufficient to correct abnormal carnitine metabolism and symptoms in dialysis patients. A meta-analysis of all randomized controlled clinical trials of the effects of L-carnitine in HD patients did not allow the demonstration of an effect of L-carnitine supplementation, either orally, i.v. or added into the dialysate, on serum total cholesterol and triglyceride profiles [45]. In contrast, there seemed to be a positive effect on anaemia control and sparing of erythropoietin (EPO) when patients randomly received L-carnitine. This finding should be confirmed in a larger, well-designed clinical trial. The effects of L-carnitine on muscle weakness, asthenia, and cardiovascular symptoms could not be reliably assessed, due to an insufficient number or quality of trials. Again, they deserve further study.

**Vitamins and trace elements**

There are many reasons for abnormal vitamin and trace element metabolism in maintenance dialysis patients. Among them, abnormal renal metabolism, insufficient intake and/or intestinal absorption, and dialysis losses can account for frequent deficiencies. The most frequently observed vitamin disturbances concern water-soluble vitamins. Folate levels have been reported to be reduced in serum and red blood cells and, before the era of EPO, abnormal production of red cell precursors could be improved by folic acid supplements. It is not clear at present if large amounts of folate should be given when EPO treatment is started, as folate stores may last for months before deficiency occurs. However, over the long term, because of impaired intestinal absorption, the interference of medications and dialysate losses, it is recommended that 1 mg of folic acid should be given daily. The question of whether folate should be prescribed in order to lower plasma homocysteine levels and improve cardiovascular morbidity and mortality is still open. For this purpose, the administration of 5–10 mg folic acid has been shown to reduce plasma homocysteine levels by about two-thirds, although this dose, and even higher doses, was not able to normalize them [46,47].

There is also evidence that vitamin B6 (pyridoxine) is low in the plasma and red cells of patients undergoing maintenance dialysis [48,49]. A daily supplement of 10 mg of pyridoxine hydrochloride may be recommended, as it has been shown to normalize the transamination activation index of stable maintenance HD patients [49].

In addition to frequently reduced intakes of vitamin C (ascorbic acid), substantial amounts are lost into the dialysate during the dialysis session, and mild signs of scurvy have been reported in patients with very low serum vitamin C levels. However, as vitamin C is converted to oxalate in the body, high doses are not recommended in dialysis patients, who are already at risk for hyperoxalaemia. Currently, a routine daily supplement of 50 mg vitamin C may be recommended. Vitamin E (tocopherol) is a strong antioxidant compound that has been shown to reduce cardiovascular morbidity in some studies in patients without renal impairment. A recent randomized, controlled trial has addressed the potential benefit of high-dose vitamin E supplementation in high cardiovascular risk dialysis patients. After 2 years of a daily supplement of 800 IU of alpha-tocopherol, there was a statistically significant 50% decrease in a cardiovascular composite index as compared with the placebo group [50]. According to this evidence, it may be worth considering treating selected high-risk dialysis patients with vitamin E.

Although thiamine (vitamin B1) deficiency has rarely been described in dialysis patients, and may be confused with other neurologic symptoms (such as confusion or encephalopathy), infection, surgery, and a large quantity of glucose infusion may increase the need for thiamin. The common dietary intake of 0.5–1.5 mg/day can be supplemented with a daily oral dose of 1–5 mg of thiamin hydrochloride.

To date, data are lacking to indicate if routine supplementation with other vitamins is needed in maintenance dialysis patients. On an individual basis, however, selected vitamins may be lacking and be replaced.

Dietary requirements for trace elements are not well defined in dialysis patients. Because of the major role of the kidney in trace element clearance, it is possible that accumulation may occur. Moreover, as trace elements are strongly bound to serum proteins, small quantities of trace elements contained in the dialysate may be taken up against an apparently unfavourable concentration gradient. Iron deficiency is not uncommon in CRI patients. EPO may rapidly deplete iron stores by enhancing erythropoiesis. Therefore, before starting EPO therapy body iron stores should be checked and iron supplements administered, if required. Ferrous sulfate, 300 mg, may be given orally three times a day, 30 min after meals to reduce gastric discomfort. Some patients may present with nausea, constipation, anorexia, or abdominal pain. Ferrous
fumarate, gluconate, or lactate may be better tolerated. I.v. iron supplements are generally required in HD patients; they should be used after a first test dose in order to prevent intolerance reactions.

Zinc deficiency may be present in CRI [51]. It has been associated with anorexia, diarrhoea, negative nitrogen balance, acrodermatitis, and impotence. Reports indicate that dysgeusia and impotency may be improved by giving patients zinc supplements. Moreover, a recent randomized study in maintenance dialysis patients has shown that the daily intake of a 2.2 mg zinc sulfate supplement was able to correct serum zinc levels to normal values, and this was associated with an increase in normalized protein nitrogen appearance (nPNA) [52]. In maintenance dialysis patients, selenium levels have been reported to be reduced in serum, but to be in the range of healthy adults when measured in plasma [53], associated with reduced serum glutathione peroxidase activity. Selenium deficient patients have shown evidence of muscle pain and weakness and, more importantly, cardiomyopathy that may progress to severe intractable cardiac failure [54]. Because selenium is a strong antioxidant compound and might be involved in the prevention of cancer, cardiovascular disease and sub-fertility, the issue of selenium supplementation is of particular importance and deserves further study [55]. In the case of proven selenium deficiency, a trial of selenium supplementation can be recommended.

Role of the dietitian in setting a nutritional care plan in selected patients

For decades, renal patients have followed dietary advice, which should be adapted to the degree of renal dysfunction (Figure 1). Present research data indicate that the optimal energy intake is 35 kcal/kg BW/day. However, the optimal protein intake may vary from 0.6 g/kg BW/day in stable pre-dialysis patients to 1.3–1.5 g/kg BW/day on selected occasions, such as the immediate post-transplant period or acute illness during maintenance dialysis. In addition, individual disturbances of potassium and calcium–phosphate metabolism may further complicate dietary prescriptions. Renal diets include a specific selection of foods, and there is ample evidence at every stage of CRI that a sufficient energy intake should always be a major goal. Therefore, it is mandatory that the majority of patients, if not all of them, be trained and followed by a renal dietitian. Since in the authors’ experience, ~30–50% of patients entering dialysis may have never met a dietitian, the renal care plan should start as soon as possible in order to treat a potential state of malnutrition within 2 weeks of the start of dialysis. Every lost day of optimal intake will need weeks or months of effort to reach an adequate nutritional status. By tailoring the food choice, the dietitian will encourage the patient to actively select palatable diets and not to be afraid of hyperkalaemia or fluid overload. This advice should be strongly enforced by the medical team, particularly when patients still have diuresis, maybe via improved dialysis techniques that allow individual profiling of the dialysis session. Recent examples of daily dialysis programmes show that an almost free diet can be administered to patients who are switched from a standard 3-weekly session programme to a short, 2-h daily session programme. Using such a treatment schedule, weight gain and body composition rapidly improve in response to a dramatic increase in food intake, that is an increase in energy and protein intakes by 13 and 24%, respectively [43]. Although daily dialysis cannot be recommended for every patient, it may be advisable as a rescue therapy in selected severe situations.

The dietitian will gather important nutritional information at least three times yearly, including food reports (which is currently the only means of estimating energy intake), anthropometric measures and, in co-ordination with the medical staff, verify the nPNA, serum albumin, pre-albumin and total cholesterol, calcium phosphorus status, inter-dialytic weight gain, and salt intake. For reasons of work overload, it is unlikely that all patients will benefit from this optimal care plan. However, in the coming years, major efforts should be made to propose an optimal dietary survey for every CRI patient.

Management of catabolic factors

Metabolic acidosis is an important stimulus for net protein catabolism in patients with CRI. In non-dialysed patients with CRI, the correction of metabolic acidosis improves nitrogen balance [56], and acidosis, rather than uraemia, increases protein catabolism in uraemic rats [57]. The catabolic effect seems to be mediated by the stimulation of skeletal muscle branched-chain keto acid decarboxylation, resulting in increased catabolism of the branched-chain amino acids. A slightly decreased pre-HD blood standard bicarbonate level has been reported to correlate with
low intracellular valine concentration in muscle, indicating that even slight and intermittent acidosis may have stimulated the catabolism of valine in muscle, resulting in valine depletion that may be a limiting factor for protein synthesis. Correction of slight acidosis has also been reported to decrease whole body protein degradation, as determined from leucine kinetics [58]. However, the relationship between standard bicarbonate and nutritional status in dialysis patients is generally poor and no large study has demonstrated clearly beneficial nutritional effects of the correction of acidosis. Nevertheless, the standard bicarbonate level should be at least 22 mmol/l, mainly based on opinion and clinical experience.

There is a close relationship between malnutrition, on one side, and co-morbid conditions and inflammation on the other. If the serum CRP is > 10 mg/l, it is important to seek for and treat (if possible) the cause. The causes of inflammation in CRI include inflammatory diseases and persistent chronic infections such as Chlamydia pneumoniae, Cytomegalovirus, and gingival and dental infections. Cardiovascular diseases, in particular ischaemic heart disease and chronic heart failure, are common in CRI patients and may also be important factors behind systemic inflammation. Both inflammation and malnutrition may predict outcome and patients with the complete MIA syndrome have the worst prognosis.

The HD procedure

There is no definite evidence of the amount of dialysis that is needed for the preservation or improvement of nutritional status in HD patients. Adequate dialysis (at present a Kt/V > 1.2 for HD) should be provided. Whether a higher Kt/V can improve nutritional status is not established at present. More information on this issue will be available with the results of the HEMO study [59]. Although no definite evidence is available for the importance of water quality for nutritional status and clinical outcome, there are indications that bacterial and pyrogen contamination of the dialysate may contribute to the inflammatory reaction during HD [60]. Better nutritional status with more biocompatible dialysis membranes has been suggested in some studies, but this has not been confirmed in others. At present, the role of the biocompatibility of the dialysis membrane is not clear and no specific recommendations can be made.

Dietary management of hyperphosphataemia

There are numerous ways to achieve the control of hyperphosphataemia in CRI patients. They include dietary management in terms of low protein intake, the prescription of various phosphate-binding drugs and an intensification of the dialysis procedure.

The avoidance of hyperphosphataemia and the subsequent development of secondary hyperparathyroidism by reducing dietary protein intake has long been advocated and shown to be efficacious, in particular in the experimental animal and the patient with advanced renal failure [61].

In a well-conducted study in patients with advanced renal failure, lasting 12 months, Lafage-Proust et al. have shown that a very low protein diet, together with a low phosphorus diet, led to a decrease in plasma intact PTH and in bone formation rate [62]. In a subsequent long-term study lasting 5 years, these authors demonstrated that the ingestion of same type of restricted protein and phosphorus diet induced a normal or even low bone turnover state in 13 out of 16 uraemic patients [63]. It must be pointed out, however, that results such as this can only be obtained in an extremely favourable environment with regular dietary counselling by devoted dieticians and under close medical supervision, in order to avoid the risk of malnutrition. In fact, it is now clear that too strong a dietary limitation in phosphorus intake will also reduce protein intake. Indeed, the phosphorus/protein ratio is quite constant, namely 10–13 mg phosphorus/g protein. Based on an optimal protein intake, the daily amount of ingested phosphate will be ~ 1000 mg. Therefore, although the amount of phosphorus absorbed in the intestine is only 40–80% of that ingested, a regular HD session generally clears only 600–1000 mg of phosphorus, mostly during the first 2 h of dialysis. In addition, phosphorus clearance decreases when haematocrit rises under EPO treatment. Thus, if dialysis patients have an adequate protein intake, most of them will need oral phosphate binders to prevent a rise in serum phosphorus and a concomitant increase in serum parathyroid hormone.

Figure 2 shows the challenge of controlling the bone status and parathyroid function, in the face of an adequate nutrient intake during the different phases of CRI. As phosphorus and protein are combined in nutrients, and a minimal intake of protein is absolutely required, all possible efforts should be made in order to increase phosphorus clearance and binding.

In addition, dietary counselling can play an important role in an integrated treatment approach of hyperphosphataemia. In fact, food selection can help patients to choose nutrients low in phosphorus. For example, white soft cheese will provide less phosphorus than Gruyère or Beaufort cheese. Sausages that have added phosphate for taste enhancement will need oral phosphate binders to prevent a rise in serum phosphorus and a concomitant increase in serum parathyroid hormone.

In summary, a patient entering maintenance dialysis should be ‘nutritionally investigated’ and counselled as soon as possible. His/her intakes should be checked and improved towards optimal needs. The nutritional order of importance appears to be: (i) protein, (ii) energy, (iii) water and salt, (iv) potassium, and (v) phosphorus.
Final accord

After intensive discussion, the panel reached a consensus on the following key points.

- There are at least two fundamentally different types of malnutrition in patients with CRI. The first type of malnutrition is related to low protein and energy intake. In this case, the decrease in serum albumin may be small and malnutrition may be reversed with adequate nutritional and dialysis support. In contrast, the second type of malnutrition is associated with inflammation. This type is generally much more difficult to reverse with nutritional support and dialysis therapy, unless the underlying co-morbid conditions and chronic inflammatory response can be adequately treated.
- A close correlation has been noted between malnutrition (in particular malnutrition type II), cardiovascular disease and inflammation. In particular, in CRI patients chronic systemic inflammation, as characterized by high serum CRP levels, is generally associated with malnutrition and cardiovascular risk and mortality. However, the panel concluded that it was currently difficult to determine if the inflammation was the cause or the consequence of cardiovascular disease.

Routine assessment of nutritional status

- The assessment of nutritional status should be based on clinical evaluation and biochemical markers.
- Valuable clinical parameters for routine assessment of nutritional status are history of weight loss, percentage of standard weight, BMI, clinical evaluation of muscle and subcutaneous FM, and assessment of co-morbid conditions.
- Valuable biochemical parameters for routine assessment of nutrition are serum albumin, creatinine, bicarbonate, and total cholesterol in combination with CRP for the assessment of inflammation.

More detailed assessment of nutritional status

- SGA of nutritional status is a well-validated tool for assessment of nutritional status.
- DEXA is a useful method for more detailed assessment of body composition.
- Anthropometric methods for the assessment of body composition are also useful (but less precise than DEXA) because they are easy to apply.
- BIA is not recommended for routine assessment of nutritional status.
- CK are not recommended for assessment of body composition.

Management of catabolic factors in CRI

- Protein intake should be at least 1.2 g/kg standard BW, to be on the safe side for almost all patients.
- Energy intake should be 35 kcal/kg standard BW in patients < 60 years of age, and 30 kcal/kg standard BW in patients > 60 years of age.
Role of dietary counselling

The panel agreed that the renal dietitian plays a pivotal role in the unit and should supervise nutrient intake, including supplements and micro-nutrients.

It was agreed that there is a strong conflict between the need for adequate protein intake and phosphate intake restriction, so that in dialysis patients it is very difficult to control hyperphosphataemia with dietary measures alone while avoiding the risk of malnutrition. Nevertheless, dietary counselling was felt to be useful, together with the use of phosphate binders and adequate dialysis, in integrated management of hyperphosphataemia.

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