Nutritional support in chronic renal failure: systematic review
Zarazaga A, Garcia-De-Lorenzo L, Garcia-Luna P P, Garcia-Peris P, Lopez-Martinez J, Lorenzo V, Quecedo L, Del Llano J

Authors' objectives
To locate and assess the quality of scientific evidence, in order to establish graded recommendations based on the efficacy and effectiveness of nutritional support prescribed in patients with chronic renal disease. In addition, to answer the following two questions.

1. What effect does nutritional therapy have on the course of chronic renal failure (CRF) in the general population and in diabetic patients?
2. What effect does nutritional support have on patients with CRF in dialysis?

Searching
MEDLINE, EMBASE, HealthSTAR and the Cochrane Library were searched from 1989 to January 1999. CCOHTA and HTA were also consulted. The MeSH terms and keywords used were: 'nutritional support', 'kidney-failure-chronic', 'diabetic nephropathies', 'quality of life', 'diet', 'nutrition', ‘protein restriction’, ‘renal failure’ and ‘kidney failure’.

Study selection
Study designs of evaluations included in the review
The review included: systematic reviews; randomised controlled trials with large or small sample sizes; prospective, non-randomised concurrent or non-concurrent studies; and cohort studies. Case-controlled studies, clinical series, descriptive studies, expert committee reports and single cases were excluded.

Specific interventions included in the review
Studies of the administration of nutritional support with amino acid or ketoacid supplements, with or without restriction of the protein intake were eligible for inclusion. The included studies compared protein- or phosphate-restricted diets with control diets, which were either unrestricted or had a higher protein content (measured).

Participants included in the review
The inclusion criteria for the participants were: non-diabetic patients with CRF in dialysis or pre-dialysis; insulin-dependent diabetic patients with CRF in dialysis or pre-dialysis state; and patients aged 2 to 65 years. Studies that included patients with systemic immune diseases, urinary tract infections, or cardiovascular or respiratory diseases were excluded.

Outcomes assessed in the review
The selected studies had to include data collected on various renal function parameters, anthropometric and nutritional measurements, degree of compliance with the diet, and measures of quality of life or patient satisfaction.

How were decisions on the relevance of primary studies made?
Two independent reviewers selected the studies for inclusion by assessing the level of quality of each study. Any differences were resolved by discussion.

Assessment of study quality
It appears that the studies were selected, analysed and classified based on aspects of study design, and were graded for the level of evidence (see Other Publications of Related Interest); the authors referred to this as a methodological quality assessment. Study methodology-based search terms were used to filter out the excluded study types. Two independent reviewers assessed the level of quality of each study, and any differences were resolved by discussion.
Data extraction
The authors do not state how the data were extracted for the review, or how many of the reviewers performed the data extraction.

The following data were extracted: study identification; sample size; the type of diet; control; the duration of treatment; outcome measures; conclusions; and level of evidence.

Methods of synthesis
How were the studies combined?
The results of the included studies were summarised for each population in each question. No statistical pooling was undertaken.

How were differences between studies investigated?
Differences between the studies were not investigated.

Results of the review
Forty-six studies (n=7,476) were included. There were 20 studies (n=6,192) in 17 publications of nutritional support in CRF patients in pre-dialysis, 7 studies (n=1,004) in CRF patients in haemodialysis, and 19 studies (n=280) in patients with insulin-dependent diabetes.

One systematic review, 3 meta-analyses, 25 randomised controlled trials and 14 other study designs were included in the review.

Effects of nutritional therapy on the progression of renal function in 'general population' CRF.

Ten of the 13 studies concluded that protein- and phosphate-restricted diets slowed deterioration of renal function, retarded the rate of fall of glomerular filtration rate and delayed the onset of end-stage renal failure (deferring the patient's entry into a dialysis programme).

Effects of nutritional therapy on nutritional status in 'general population' CRF.

Six studies performing anthropometric measurements concluded that protein restriction, both in low-protein and very low-protein diets associated with specific enteral supplements, allowed weight and lean body muscle mass (mid-arm circumference) to be maintained or even improved. Six studies also concluded that with both types of diets, albumin levels were maintained and transferrin and cholesterol levels were lowered.

Effects of nutritional therapy on the progression of renal function in diabetic patients.

Fifteen studies concluded that protein-restricted diets reduced nocturnal microalbuminuria and delayed the onset or progression of nephropathy. This effect was noticeably greater in hyperfiltrating patients. The benefit in these patients appeared to be independent of glycaemic control. The beneficial effect of diet was evident even before the onset of nephropathy.

Effects of nutritional therapy on nutritional status in diabetic patients.

All 19 studies confirmed good metabolic tolerance to protein restriction, with a reduction in hyperglycaemia and decreased insulin requirements (in some cases, due partly to an undesirable reduction in caloric intake). The majority of the studies confirmed that anthropometric parameters (weight, mid-arm circumference and triceps skinfold) were preserved. No change or a slight improvement was seen in albumin, triglyceride and cholesterol levels. Some studies confirmed the beneficial effect of these diets in lowering urinary losses of albumin and immunoglobulin G.

Effects of nutritional support on patients with CRF in dialysis (energy supplements).

Energy supplements improved weight in 2 cohort studies; the amino acid profile was also improved in one of these...
studies, although there was no demonstrable nutritional benefit. In one cohort study, supplementation with a high-calorie, low-phosphate diet containing 0.6 g of protein was well-tolerated.

Effects of nutritional support on patients with CRF in dialysis (low-calorie, low-protein, liquid diet as a supplement).

One cohort study of a very low-protein diet supplemented with essential amino acids and ketoacids found it to be associated with malnutrition in 50% of the patients. One small trial compared two low-phosphate, high-calcium liquid diets providing 1.25 g protein and 35 kcal/kg per day to a control diet with a higher phosphate content, concluded that enteral products as sole sources of nutrition were well-tolerated by patients in haemodialysis and that preparations specifically designed for these patients have advantages over standard preparations. Two other studies looked at the benefit of protein-restricted diets to defer initiation of dialysis: one pointed out a slower deterioration of renal function; the other confirmed delayed initiation of dialysis, with a subsequent beneficial effect on mortality.

Effects of nutritional support on patients with CRF in dialysis (disease progression).

Supplemented very low-protein diets appeared to be useful in the pre-dialysis phase to slow the progression of end-stage renal failure, and in one study they reduced mortality during the first 2 years of dialysis treatment. When these diets were tested for their ability to reduce dialysis to once per week, it was found that although urea levels were maintained, there was a loss in clearance capacity and above all, a deterioration of nutritional status.

Effects of nutritional support on patients with CRF in dialysis (nutritional effects).

Both energy supplements and the different diets tested allowed weight to be maintained. Very low-protein diets caused a worsening of the anthropometric parameters studied. Supplementation with a calorically dense, low-phosphate liquid diet providing 0.6 g protein improved weight and triceps skinfold thickness. The study comparing 3 diets, which contained 1.25 g protein and 35 kcal/kg per day, found that they were well-tolerated and that compliance was adequate. Albumin and pre-albumin levels were maintained. An increase in triglycerides and a decrease in cholesterol was seen. The low-phosphate diets allowed good control of plasma phosphorus and an improvement in calcium metabolism, avoiding the need to administer phosphorus binders and thus reducing constipation.

Authors’ conclusions

Very low and low-protein diets associated with specific enteral supplements are indicated in the incipient phases of diabetic nephropathy and in most patients with CRF, in order to slow disease progression and improve the patient's overall condition, thus contributing to improved survival in these patients. In patients with renal failure in dialysis, the studies reviewed do not support the prescription of a very low-protein diet with the aim of reducing the frequency of dialysis sessions. Although the level of evidence was low, improvements in nutritional parameters were seen when specific diets were given.

CRD commentary

The review question seems fairly clear. The study inclusion criteria relating to the participants, interventions and outcomes were explicit, and it would appear that the review’s authors used study methodology-based search filters to find studies of randomised, controlled or cohort design. The literature search appears reasonable, although there seems to have been no attempt to locate unpublished studies. In addition, it is unclear whether the search was restricted to English language articles. The included studies were assigned a level of evidence based on some aspects of study design, but this does not constitute a full validity assessment. The recommendations for practice were based on the levels of evidence, but these have not been reproduced in this abstract. Details of the included studies and of the review process were supplied.

It is unclear how the data were summarised from the results of the included studies. The authors' conclusions should therefore be treated with some caution.

Implications of the review for practice and research

Practice: The authors state many indications for practice based on levels of evidence assigned to the included studies.
Research: The authors state that controlled clinical trials on the use of specific enteral supplements, both in CRF patients in pre-dialysis and in haemodialysis patients, are needed so that their use can be definitely validated. They also recommend that studies to assess the quality of life and the costs should be carried out.

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