Malnutrition in Patients Undergoing Hemodialysis: Is Intradialytic Parenteral Nutrition the Answer?

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Abstract and Introduction

Abstract

Patients with end-stage renal disease often experience malnutrition as a result of decreased dietary intake; inadequate dialysis; loss of nutrients into the dialysate; abnormal protein, carbohydrate, and lipid metabolism; and concomitant diseases, which may contribute to an increase in morbidity and mortality. Intradialytic parenteral nutrition (IDPN) is being used to improve nutritional status, in conjunction with other methods of nutritional supplementation. The biggest advantage of IDPN is probably its convenience since it is administered during dialysis treatment and thus does not require additional clinic visits or prolonged dialysis time. Although IDPN has several disadvantages, its ability to improve nutritional status and reduce morbidity and mortality in patients with end-stage renal disease is promising. Well-designed, large-scale, prospective studies are required to confirm its beneficial effects.

Introduction

Maintenance of adequate nutrition in patients with end-stage renal disease (ESRD) is frequently a challenge. Chronic renal failure results in abnormal protein, carbohydrate, and lipid metabolism. As a result, many patients have protein wasting and protein-calorie malnutrition. Malnutrition may be present in patients undergoing hemodialysis if their predialysis serum albumin and creatinine concentrations are less than 3.4 g/dl and 8 mg/dl, respectively; weight loss exceeding 10% of their ideal body weight, or greater than 20% of their usual body weight; clinical examination consistent with malnutrition; and decreased intake of dietary protein (< 0.8 g/kg) and calories (< 25 kcal/kg). In the Hemodialysis (HEMO) study, the largest study to date to delineate the nutritional status of patients undergoing long-term hemodialysis, 290 (29%) of the 1000 patients studied had serum albumin concentrations less than 3.5 g/dl. In addition, dietary energy intake was less than 28 kcal/kg/day in 760 (76%) patients, and protein intake was less than 1 g/kg/day in 610 (61%) patients. These findings indicate that most patients with ESRD had protein and energy intake levels below the National Kidney Foundation Kidney Disease Outcomes Quality Initiative (NKF-K/DOQI) guidelines. Inadequate nutritional intake is an important cause of suboptimal nutritional status in many patients with renal failure, and may contribute to the increased morbidity and mortality commonly seen in these patients. A growing body of data shows that the extent of malnutrition correlates with increased morbidity and mortality.

Etiology of Malnutrition

Decreased dietary intake is one of the most important causes of malnutrition in patients undergoing hemodialysis. These patients often have anorexia due to reduced sense of taste and food palatability as a result of dietary sodium and water restrictions. In addition, they may experience psychosocial problems, such as depression and loneliness, that may contribute to the development of malnutrition.
Many patients receiving long-term dialysis may have received suboptimal dialysis, which may result in uremic symptoms, such as lethargy, drowsiness, nausea, vomiting, and anorexia. Thus, frequent monitoring of the dosage of delivered dialysis, urea removal, and plasma urea levels is needed to ensure adequate treatment and minimize development of uremia and risk of malnutrition.\(^{10, 11}\)

The risk of developing malnutrition is increased during dialysis through the loss of nutrients such as amino acids,\(^{12}\) glucose,\(^{13}\) and water-soluble vitamins\(^{14}\) into the dialysate. An average of 8 g of amino acids is estimated to be lost into the dialysate during hemodialysis using conventional cellulosic membranes.\(^{12}\) A greater amount of amino acids is lost with high-flux polysulfone membranes or increased reuse of the membranes.\(^{15}\) In addition, about 25 g of glucose is removed by the dialysate during each hemodialysis session.\(^{16}\) These amounts may represent only a small proportion of daily requirements, but together they assume increasing importance when dietary intake is marginal.

Abnormal metabolism of nutrients, minerals, and hormones also occurs in patients undergoing hemodialysis as their renal function declines. For example, insulin degradation is reduced with chronic renal insufficiency.\(^{17}\) In addition, resistance to the hypoglycemic effects of insulin has been observed in patients with advanced renal failure. The abnormality in insulin metabolism may in turn lead to abnormalities in patients' lipid profiles.\(^{18}\)

Next, the decreased response to growth hormones and insulin-like growth factors in these patients may lead to an increase in catabolism and promote protein wasting.\(^{10, 19}\) Also, hyperparathyroidism that occurs in patients with chronic renal failure may increase metabolism of muscle proteins and amino acids and further worsen the wasting syndrome in patients with ESRD.\(^{20}\)

Metabolism of amino acids is also affected by renal insufficiency, leading to an abnormal plasma amino acid profile and impaired protein synthesis.\(^{10}\)

Metabolic acidosis, which is common in patients with ESRD, may increase catabolism and promote protein breakdown. This may in turn further impair nutritional status.\(^{21}\) The hemodialysis treatment is often catabolic and can promote wasting.\(^{22-25}\) In addition, bioincompatibility of the dialysis membrane results in cytokine production, which causes an increase in protein breakdown.\(^{24}\)

Concurrent illnesses and acute or chronic conditions, such as inflammation, infection, liver disease, and cancer, may compromise the nutritional status of patients with ESRD. In addition, diabetes mellitus, one of the major causes of ESRD, may be associated with gastroparesis, uremic gastritis, and esophagitis, further discouraging optimal dietary nutrient intake.\(^{26, 27}\)

**Markers of Malnutrition**

The ideal method for assessing nutrition in patients undergoing hemodialysis would be one that is readily available, easy to perform, sensitive, reproducible, and validated in patients with ESRD.\(^{28}\) Currently, no single test is available to detect and define the presence of malnutrition accurately. Thus, various methods are used to assess the nutritional status of patients undergoing maintenance hemodialysis.

Assessment commonly involves determining serial changes in anthropometric parameters, such as body weight, and obtaining serum albumin concentrations. Other nutritional markers are serum phosphorus, creatinine, urea, transferrin, and prealbumin concentrations, as well as body composition, which is determined with dual-energy x-ray absorptiometry (DEXA), nuclear magnetic resonance (NMR), and bioelectric impedance.

Serum albumin concentration is commonly used as a nutritional index, but the value may be affected by concomitant illnesses, such as liver disease, nephrotic syndrome, infection, or inflammation, and hence may not accurately reflect the nutritional status of the patient. Its relatively long half-life of 21 days also explains why it may not ideally reflect the effects of acute nutritional intervention.

Prealbumin, on the other hand, has a shorter half-life and may be a more sensitive indicator of changes in nutritional status. However, prealbumin levels might be elevated in patients with renal disease as a result of altered degradation by the kidneys.\(^{29, 30}\) In addition, a decrease in the breakdown of retinol-binding protein, which is bound to prealbumin, in renal failure may indirectly be responsible for the elevated prealbumin levels.\(^{29}\)

More precise methods for calculating body composition, such as DEXA, NMR, and bioelectric impedance, require equipment that is expensive and complicated to use. As such, these methods may not be readily available for routine clinical use.

Subjective global assessment is a simple, reliable method that is commonly used for comprehensive nutritional assessment.\(^{31, 32}\) It combines evaluation of the patient's medical history (weight or weight change, dietary intake, gastrointestinal problems, functional
capacity, and other comorbidities) and physical examination (body fat stores, signs of muscle wasting, edema, and ascites). An overall rating is determined subjectively based on the clinical and professional judgment of the practitioner. Subjective global assessment takes into consideration different factors that might affect nutritional status. Also, it is noninvasive and relatively simple to use. However, it may not be as precise as other measures of nutritional status.\[31\]

Management of Malnutrition in Patients Undergoing Hemodialysis

To develop an effective nutritional management strategy, a comprehensive nutritional assessment should be performed and an individualized care plan developed for each patient. In addition, this plan should be updated frequently based on the patient's clinical condition and nutritional status and requirements.

The current NKF-K/DOQI guidelines recommend protein intake of 1.2 g/kg/day, as well as a daily caloric intake of 35 kcal/kg for patients younger than 60 years, and 30-35 kcal/kg for those aged 60 years or older.\[3\]

When a patient with ESRD is diagnosed with malnutrition, it is essential to identify and correct the cause of malnutrition. Assessment of the patient's dietary intake, and aggressive treatment of any concurrent medical conditions that may contribute to development of malnutrition, such as metabolic acidosis or infection, is necessary. Therapy with drugs that may cause loss of appetite or aggravate malnutrition should be minimized or avoided.

Administering an optimal dialysis prescription is also an important component of an effective nutritional management strategy. Routine monitoring of dialysis adequacy with the fractional urea clearance of one hemodialysis session (Kt/V) or the urea reduction ratio, as well as appropriate modification of the dialysis prescription, is necessary to treat any intensification of the patient's uremic state possibly caused by superimposed illness and increased protein intake. The Kt/V is a measure of urea removal, which is represented by the amount of plasma cleared of urea divided by the urea distribution volume.

Some patients cannot meet their protein and energy requirements with food for an extended period. For these patients, dietary and nutritional counseling and nutritional support with oral, enteral, or parenteral supplementation may be required to satisfy their nutritional needs and to improve their status. However, the increased intake should not overwhelm the capability of the kidneys to eliminate waste products and thereby promote development of uremia.

Dietary Counseling

The patient and caregivers should be given a list of foods, with recommended daily intake, as well as information on restricted food items, to help them design a nutritional plan that the patient will like and adhere to. Counseling and dietary advice should be provided regarding the importance of appropriate nutritional intake with the aim of increasing the quantity, quality, and palatability of the food the patient consumes.\[33\]

Oral Supplements

Oral supplementation with special-formula preparations containing high-quality proteins, essential amino acids, carbohydrates, and fats may be added to the patient's diet.\[20\] These are available as solid foods, powders, and liquid formulations. Unfortunately, patients with malnutrition often have a decreased appetite and do not tolerate increased oral intake, which may make oral supplementation difficult. As a result, patient compliance with the recommended regimens may be a problem; in addition, many patients may not be able to afford the cost of these products.\[34\]

Enteral Tube Feeding

Patients who cannot consume the required amounts of nutrition orally may receive enteral tube feeding, which has several advantages. For example, it can be administered daily and can provide optimal quantities of essential nutrients; in addition, it may be useful for patients with anorexia.

Specialized formulas for patients with renal failure are commercially available. These are designed as renal supplements for patients receiving potassium, phosphorus, and fluid-restricted diets. Other nutritional products also may be useful for patients with renal disease. These are calorically dense and volume sparing, thus providing patients with energy and nutrition requirements in a smaller volume. Depending on the patient's medical conditions and energy, protein, and fluid requirements, a combination of such products may be given to provide adequate nutrition and prevent fluid and electrolyte imbalance.
Enteral tube feeding also has some disadvantages, such as increased risk of aspiration and resultant infection, and possible intolerance of nasogastric and percutaneous enterogastric administration.[35] In addition, enteral formulas are not reimbursed by the Medicare end-stage renal disease program and thus may be too costly on a long-term basis.[35-37] Their efficacy for prevention or treatment of malnutrition in adult patients receiving maintenance dialysis remains unsubstantiated.[38]

**Anabolic Agents**

Androgenic steroids, such as nandrolone decanoate, have improved nutritional parameters through their anabolic effects, hence increasing lean body mass and improving nitrogen balance.[39-41]

Recombinant human growth hormone has well-established anabolic properties. It promotes protein synthesis, decreases protein degradation, enhances lipolysis, and increases food conversion.[42-44] Although the exact mechanisms by which it exerts its metabolic effects are not clearly understood, these properties are mediated in part through induction of the anabolic hormone insulin-like growth factor-1.[45]

Based on several preliminary studies, the use of anabolic steroids and growth factors for treatment of malnutrition may be promising.[39-41, 46-50] However, whether use of these agents will result in long-term improvement in nutritional indexes, morbidity, and mortality must be clarified by further studies.

**Total Parenteral Nutrition**

Total parenteral nutrition involves the use of an indwelling catheter to provide intravenous feeding. An important advantage of total parenteral nutrition is that it can provide patients with their complete daily nutritional needs. However, it is expensive and carries the risk of catheter-related sepsis in patients receiving dialysis who are more susceptible to systemic infection due to uremia.[20] Also, there are concerns regarding overuse and depletion of potential arterial venous dialysis access sites with total parenteral nutrition.[1]

**Intradialytic Parenteral Nutrition**

Administration of nutrients such as amino acids, glucose, and lipids during hemodialysis was first explored in 1975.[51] Intradialytic parenteral nutrition (IDPN) is administered through an infusion pump that can overcome venous pressure in the dialysis blood lines. The fluid is then mixed with the patient's venous blood and returned to the body through the venous access.[52]

Intradialytic parenteral nutrition should be given until the patient's nutritional status is improved, as evident by weight gain and increased concentrations of serum albumin and creatinine to 3.8 g/dl or greater and 10 mg/dl, respectively, and increased oral intake of calories and protein to 30 kcal/kg and more than 1.0 g/dl, respectively. Oral nutritional supplementation will then be sufficient for maintenance.[1] However, if improvement is not seen after several months, or if significant adverse effects or complications are apparent, IDPN should be discontinued.

**Advantages**

Because IDPN is administered during dialysis, convenience is probably its most important advantage. Additional vascular access is not required, and IDPN administration obviates the need for prolonged dialysis or additional trips to the clinic.

Electrolyte imbalance and fluid overload are common concerns when patients are adminis-tered parenteral nutrition. With IDPN, the content of the solution can be adjusted with relative ease according to the patient's clinical or metabolic requirements. Electrolytes, multivitamins, trace elements, and drugs such as insulin can be added whenever necessary.[53] Since the patient is undergoing hemodialysis, the amount of ultrafiltration may be adjusted according to the need for fluid removal.[54] In addition, frequent, routine patient monitoring by dialysis center staff reduces the risk of electrolyte and mineral imbalance.[55]

Patients receiving dialysis who experience catabolic complications or other debilitating conditions may be given IDPN in short courses to restore nutritional status to a level at which oral or enteral feeding might again be successful.[1]

**Disadvantages**

Intradialytic parenteral nutrition is considered a nonphysiologic means of providing nutrition because it bypasses the gastrointestinal
tract. Hence, its use may reduce the benefits of direct nutrient contact with the intestinal mucosa, such as maintenance of gut integrity, stimulation of gut hormones, minimization of bacterial and endotoxin translocation, and prevention of systemic complications.

Patients often receive IDPN 3 times/week, during the hemodialysis sessions; this may not be sufficient to provide enough protein and calories to support the patient's nutritional needs for the other days of the week.\[^{53, 55}\] This probably explains why nutritional improvements are usually not seen until IDPN has been administered for several months.\[^{51, 53, 57-62}\] In addition, IDPN has not been shown to improve patients' oral intake.\[^{63}\]

Intradialytic parenteral nutrition may alter glucose metabolism and induce lipid intolerance, which may require immediate clinical intervention.\[^{64}\] For example, rapid infusion of high-osmolality solutions may cause pain in the extremities. At the end of the glucose infusion, reactive hypoglycemia may occur, especially when the dialysate also contains a significant glucose concentration. As such, a patient may need to be fed immediately after dialysis.\[^{65}\]

Intake of excessive glucose and carbohydrate calories over a long period may result in liver function abnormalities. In addition, rapid lipid infusions may cause alterations in immune function.\[^{66}\] Patients who have received IDPN after undergoing prolonged periods of fasting or starvation are susceptible to development of refeeding syndrome. This syndrome is characterized by hypophosphatemia, hypokalemia, and hypomagnesemia, due to the rapid intracellular shift of electrolytes required for anabolism.\[^{64, 65}\] Finally, the cost of IDPN therapy is high and may not be covered by Medicare unless specific criteria are met (Table 1).\[^{37}\]

With these considerations in mind, and in conjunction with the recommendations for use of IDPN by the American Society for Parenteral and Enteral Nutrition,\[^{63}\] one can conclude that oral and enteral nutritional supplementation are preferred for patients with functional gastrointestinal tract since that is the most physiologic site of nutrient absorption. Intradialytic parenteral nutrition should be considered only if the oral and enteral methods fail, are contraindicated, or are not tolerated, or if significant adverse effects are present.\[^{5}\]

**Review of Studies Evaluating Intradialytic Parenteral Nutrition**

A study published in 1975 first treated 18 mildly malnourished patients with IDPN containing 2 g of nitrogen (as essential amino acids) and 100 g of oral protein for 60 weeks.\[^{51}\] The patients reported an improvement in appetite, and increases in serum albumin, total protein and transferrin concentrations were observed. Since then, numerous studies have evaluated the use of IDPN to improve nutritional status in patients undergoing hemodialysis (Table 2).\[^{4-9, 12, 26, 34, 35, 46, 51, 54, 57-62, 67-80}\]

**Effects on Protein and Energy Homeostasis**

One study examined the effects of IDPN on protein and energy homeostasis in seven patients undergoing long-term hemodialysis who received a single administration of IDPN.\[^{80}\] The patients were stable and adequately nourished. In all patients, whole-body protein and forearm muscle protein synthesis were increased, and whole-body proteolysis was significantly decreased. A change from an essentially catabolic to an anabolic state was observed. However, the anabolic effects observed were evident only during the IDPN infusion and did not carry over to the post-hemodialysis phase. This suggests that long-term administration of IDPN for several weeks to months may be necessary to produce a sustained improvement in nutrition.

**Effects on Nutritional Status**

No benefit in nutritional status was observed in a randomized, double-blind study involving seven apparently well-nourished patients undergoing hemodialysis and treated with intravenous and oral essential amino acids for 6 months.\[^{69}\]

Another study involved 72 patients who met well-defined criteria for malnutrition (weight loss > 10% of usual body weight over 30 days or serum albumin concentration < 3.5 g/dl).\[^{6}\] The patients' dietary protein intake was less than 0.75 g/kg/day. Intradialytic parenteral nutrition was not started until a 2-week course of dietary counseling and a trial with commercial oral nutritional supplements were completed. Patients were classified as responders if they had a weight gain of 10% or more, or an increase in serum albumin or total protein concentration of more than 0.5 g/dl. In this group of responders, significant differences in weight gain, serum albumin concentration, and total protein concentration were observed.

In an evaluation of long-term administration of IDPN in 24 patients with malnutrition, 26 courses of IDPN were given over a mean treatment duration of 4.3 months.\[^{79}\] This study found a significant increase in dry body weight and serum albumin concentrations in
Based on studies currently available, the response to IDPN was dependent on baseline nutritional status of the patients and duration of treatment. Patients who were malnourished to begin with seemed to benefit more, with demonstrable improvement in nutritional parameters compared with those who were adequately nourished at baseline. This observation mirrors the findings of the Veterans Association total parenteral nutrition trial.\(^6\)!

**Effects on Morbidity and Mortality**

The effects of IDPN on odds of death were examined in a retrospective, randomized, open-label study.\(^4\) This study involved 1679 patients who received at least one IDPN infusion and 22,517 control patients who did not receive IDPN. In the IDPN-treated patients with low concentrations of serum albumin (≤ 3.0 g/dl) and creatinine (≤ 8.0 mg/dl) before IDPN administration, these values were increased and odds of death were reduced. Conversely, odds of death were greater in IDPN-treated patients whose concentrations of serum albumin (≥ 3.5 g/dl) and creatinine (> 8.0 mg/dl) were near normal before treatment. In addition, their serum albumin and creatinine concentrations continued to decline.

These results suggest a treatment advantage with IDPN in patients with malnutrition and low baseline serum albumin and creatinine concentrations. However, this was an nonblinded study that could have yielded biased results. In addition, the baseline hypoalbuminemia might have been transient; thus, risk of adverse outcome would have been small.

In an evaluation of the effects of IDPN on mortality, IDPN was administered to 81 malnourished patients for 9 months during hemodialysis.\(^5\) Dietary counseling and/or supplements were tried for 2 months before IDPN was started. The results showed significant weight gain and decreased mortality in patients who received IDPN. The treated survivors also lived significantly longer.

A nonrandomized study found a significant decrease in hospitalization rate and mortality in malnourished patients undergoing hemodialysis who responded to IDPN therapy.\(^6\) However, it is not known whether responders and nonresponders to IDPN had the same risk of death or hospitalization based on their medical condition before hospital admission. In addition, all patients might not have received equal amounts of nutritional supplementation, and their dialysis adequacy was not determined.

A retrospective, uncontrolled study involving 43 patients who received IDPN demonstrated decreased hospitalization rates, length of stay, and costs.\(^7\) Similarly, a retrospective evaluation of 45 patients with malnutrition and ESRD showed a significant decrease in number of hospitalizations, length of stay, and morbidity in patients treated with IDPN.\(^8\)

Based on these available studies, it appears that IDPN use in malnourished patients who are undergoing hemodialysis may result in decreased morbidity and mortality. However, further large-scale, randomized, controlled trials are needed to confirm these findings.

**Evidence-Based Review of Studies**

An evidence-based review and evaluation of 24 studies related to IDPN yielded only one randomized, double-blind, controlled trial.\(^8\) Three other studies were randomized; one of these was a feasibility study, and the other two were randomized, controlled trials with heterogeneous results. The rest were either observational studies or case reports. In general, the study design, patient selection, types of IDPN regimen used, and outcome assessment criteria of most of the studies were inconsistent and not homogeneous. The results of this evaluation indicated that data supporting the use of IDPN were weak, and clear recommendations cannot be made. Regardless, the author concluded that IDPN seems to be associated with decreased mortality and should be available to patients who have hypoalbuminemia and meet the published criteria for malnutrition.

**Limitations of the Studies**

Considerable heterogeneity and inconsistency in study design were observed in most of the studies evaluating IDPN. Many were nonrandomized or retrospective. Patient selection, IDPN regimens, and outcome measures differed among studies, making comparison difficult. The samples in most of the studies were small, thus statistical power was insufficient. In addition, many studies evaluated only the short-term effects of IDPN, and the potential longer-term beneficial effects might not have been apparent in such limited study periods. Also, most studies did not indicate a measure of dialysis adequacy.

Many studies used nutritional parameters such as body weight, appetite, serum albumin concentration, blood urea nitrogen level, and

anthropometric measurements as their outcome measures. Few reported the effects of IDPN on clinical outcome markers such as quality of life, morbidity, and mortality. Further, some studies involved patients who did not have malnutrition before treatment, and many did not indicate whether previous attempts had been made to reverse malnutrition by means other than IDPN. In fact, no trial has compared IDPN with placebo or other methods of managing malnutrition, such as dietary counseling, or oral or enteral supplementation.

Due to these deficiencies in study design, the improved outcomes reported in some of the studies could have been affected by factors such as improved nutritional counseling; physician attention or diagnosis; treatment of concomitant medical conditions such as infection, depression, or anorexia; and variations in dialysis adequacy.

So far, no pharmacoeconomic analysis has compared the cost of IDPN with that of other available treatment options. The results of such a study would help in determining the financial benefits of IDPN, if any, and clarify the role of IDPN in the management of malnutrition in patients undergoing hemodialysis. It would also help with establishing reimbursement criteria to direct prudent use of limited resources for the best possible patient outcome.

Characteristics of a Well-Designed Clinical Trial

Considering the limitations in the studies conducted to date, a well-designed, large-scale, randomized, controlled trial is needed. With respect to design, it should be prospective, randomized, and controlled; the effects of IDPN should be compared with those of other methods of nutritional support, such as dietary counseling, oral feeding, enteral feeding, and total parenteral nutrition. Selection of study patients should be based on proper, well-defined inclusion and exclusion criteria. In particular, patients with well-defined malnutrition should be included. The sample should be large enough for the study to attain statistical power. The study period should be long enough to assess outcomes (at least 4-6 mo). Finally, outcome measures such as changes in nutritional, biochemical, and anthropometric parameters; quality of life; morbidity (frequency and length of hospitalization); mortality; and cost-effectiveness should be examined to determine the benefits of IDPN therapy.

Conclusion

The impact of IDPN on nutritional status and clinical outcomes such as morbidity and mortality in patients with ESRD is potentially promising. However, well-defined recommendations and quality data to support its use are lacking. The current restrictive reimbursement criteria limit the use of enteral nutrition and IDPN in patients undergoing hemodialysis and thereby limit the opportunities to conduct large-scale evaluative studies.

No well-designed, randomized trial using clinically valid or meaningful outcome criteria has compared IDPN with other modes of nutritional therapy in well-defined malnourished patients undergoing hemodialysis. Large-scale, prospective studies therefore are needed to identify the clinical significance, cost-effectiveness, and benefits of IDPN therapy.

Tables

Table 1. Criteria That Must Be Met to Be Eligible for Medicare Coverage.[37]

Medicare Criteria for Coverage of Intradialytic Parenteral Nutrition

- Massive surgical removal of the small bowel within the past 3 months
- Severe short bowel syndrome
- Bowel rest for at least 3 months for treatment of symptomatic pancreatitis, severe exacerbation of regional enteritis, or a proximal enterocutaneous fistula precluding tube feeding distal to the fistula
- Complete mechanical small bowel obstruction precluding surgery
- Malnutrition (10% weight loss over <= 3 months or serum albumin concentration <= 3.4 g/dl) and severe

- Malnutrition (as above) and severe motility disturbance of the small intestine and/or stomach unresponsive to prokinetic drug therapy

- Other gastrointestinal conditions: malnutrition; severe disease of small intestine, exocrine glands, or stomach that interferes with nutrient absorption; failed trial of enteral nutrition product; and drug therapy through tube feeding

### Table 2. Main Characteristics of Studies Evaluating Intradialytic Parenteral Nutrition

<table>
<thead>
<tr>
<th>Year of Study</th>
<th>Study Design</th>
<th>No. of Patients</th>
<th>IDPN Composition</th>
<th>Duration and Method of IDPN Administration</th>
<th>Parameters for Efficacy Evaluation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1975</td>
<td>Nonrandomized</td>
<td>18</td>
<td>100 kcal, 2 g NEAA + histidine, 100 g oral protein</td>
<td>60 wks during last 90 min of hemodialysis</td>
<td>Transferrin, serum albumin, total protein, and complement levels</td>
</tr>
<tr>
<td>1977</td>
<td>Randomized, double-blind</td>
<td>7</td>
<td>17.25 g EAA IDPN</td>
<td>6 mo during last 90 min of hemodialysis</td>
<td>Several amino acids</td>
</tr>
<tr>
<td>1980</td>
<td>Randomized</td>
<td>6</td>
<td>14.1 g EAA</td>
<td>8 wks during last 90 min of hemodialysis</td>
<td>Body weight, MAMC, serum albumin level, nitrogen balance</td>
</tr>
<tr>
<td>1980</td>
<td>Nonrandomized</td>
<td>4</td>
<td>Modified to patient: 10–50% dextrose, 5.5–8.5% amino acids, 10% lipids</td>
<td>6 mo</td>
<td>Serum albumin level, nitrogen balance</td>
</tr>
<tr>
<td>1981</td>
<td>Nonrandomized</td>
<td>16</td>
<td>16.5 g EAA + 1 NEAA, 200 g glucose</td>
<td>20 wks through dialysis venous return line at 200 ml/hr rate</td>
<td>Body weight, NEAA</td>
</tr>
<tr>
<td>1982</td>
<td>Randomized</td>
<td>8</td>
<td>Group 1: 800 ml 0.9% NaCl, Group 2: 400 ml 8.5% dextrose, 400 ml 8.5% EAA + NEAA</td>
<td>2 treatments during 4-hr dialysis</td>
<td>Positive amino acid balance for group 2</td>
</tr>
<tr>
<td>1987</td>
<td>Nonrandomized, prospective</td>
<td>10</td>
<td>250 ml 50–70% dextrose, 250 ml 20% lipid, 500 ml 8.5% EAA + NEAA</td>
<td>2 mo during each dialysis session</td>
<td>Body weight, serum albumin level, appetite</td>
</tr>
<tr>
<td>1987</td>
<td>Nonrandomized</td>
<td>8</td>
<td>500 ml 50% dextrose, 500 ml 8.5% EAA + NEAA, Ensure Plus HN (given orally)</td>
<td>3 mo during dialysis through venous line</td>
<td>Serum albumin level</td>
</tr>
<tr>
<td>1989</td>
<td>Randomized</td>
<td>11</td>
<td>26.5 g modified EAA</td>
<td>6 mo during the last 3 hrs of hemodialysis</td>
<td>Nerve conduction velocity</td>
</tr>
<tr>
<td>1989</td>
<td>Nonrandomized</td>
<td>18</td>
<td>250 ml 50% dextrose, 250 ml RenAmin</td>
<td>45–165 infusions</td>
<td>Weight gain</td>
</tr>
<tr>
<td>Year</td>
<td>Study Type</td>
<td>Participants</td>
<td>Diet Description</td>
<td>Duration</td>
<td>Outcomes</td>
</tr>
<tr>
<td>------</td>
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</tr>
<tr>
<td>1989</td>
<td>Nonrandomized, retrospective</td>
<td>20</td>
<td>50 g EAA + NEAA, 50 g lipids, 125 g glucose</td>
<td>Minimum 90 days</td>
<td>Body weight, MAMC</td>
</tr>
<tr>
<td>1990</td>
<td>Randomized</td>
<td>12</td>
<td>32 g EAA + NEAA, 100 g lipids</td>
<td>3 mo during dialysis</td>
<td>Body weight, appetite, MAMC, visceral proteins</td>
</tr>
<tr>
<td>1990</td>
<td>Nonrandomized</td>
<td>9</td>
<td>42.5 g EAA + NEAA, 50 g lipids, 125 g glucose</td>
<td>2 mo during dialysis</td>
<td>Body weight, appetite, serum albumin level</td>
</tr>
<tr>
<td>1991</td>
<td>Nonrandomized</td>
<td>10</td>
<td>16.75 g EAA</td>
<td>3 mo</td>
<td>Body weight, hematocrit, quality of life</td>
</tr>
<tr>
<td>1991</td>
<td>Nonrandomized, prospective</td>
<td>6</td>
<td>42.5 g EAA + NEAA, 50 g lipids, 125 g glucose</td>
<td>3 mo during dialysis</td>
<td>Dietary protein and energy intake</td>
</tr>
<tr>
<td>1993</td>
<td>Nonrandomized</td>
<td>9</td>
<td>40 g EAA + NEAA, 50 g lipids, 75 g glucose</td>
<td>4 mo during hemodialysis</td>
<td>Serum albumin level, BUN</td>
</tr>
<tr>
<td>1993</td>
<td>Nonrandomized (patients as own controls)</td>
<td>7</td>
<td>250 ml 8.5% amino acids, 250 ml 50% dextrose, rhGH 5 mg with dialysis</td>
<td>6 wks IDPN, 6 wks IDPN + rhGH</td>
<td>Transferrin level (IDPN), serum albumin level, IGF-1 (IDPN + rhGH)</td>
</tr>
<tr>
<td>1993</td>
<td>Nonrandomized, retrospective</td>
<td>47</td>
<td>400 ml 15% amino acids, 150 ml 70% dextrose, 250 ml 20% lipids</td>
<td>Minimum 3 mo during dialysis</td>
<td>Serum albumin level, transferrin level</td>
</tr>
<tr>
<td>1994</td>
<td>Nonrandomized</td>
<td>72</td>
<td>0.64 g nitrogen/kg, 3.78 kcal/kg as dextrose and lipids</td>
<td>Mean of 159 days in responders, 222 days in nonresponders</td>
<td>Decreased mortality and hospitalization rate in responders</td>
</tr>
<tr>
<td>1994</td>
<td>Nonrandomized, retrospective</td>
<td>81</td>
<td>50 g EAA + NEAA, 50 g lipids, 125 g glucose</td>
<td>9 mo during dialysis</td>
<td>Serum albumin level, decreased mortality rate in those receiving IDPN</td>
</tr>
<tr>
<td>1994</td>
<td>Randomized, retrospective, open-label</td>
<td>1679</td>
<td>1.2 g/kg protein, 15 kcal/kg at each dialysis session</td>
<td>1 yr during hemodialysis or until death</td>
<td>Odds of death, serum albumin level, URR</td>
</tr>
<tr>
<td>1995</td>
<td>Nonrandomized, prospective</td>
<td>16</td>
<td>0.8 g/kg EAA + NEAA</td>
<td>16 wks during dialysis</td>
<td>Serum albumin level, skin test reactivity, serum creatinine level, white blood cell count</td>
</tr>
<tr>
<td>1998</td>
<td>Nonrandomized, retrospective, uncontrolled</td>
<td>43</td>
<td>63 g EAA + NEAA, 18.4 g lipids, 92.5 g carbohydrates</td>
<td>6 mo during dialysis</td>
<td>Serum albumin level, BUN, hospitalizations (cost, length of stay, no.)</td>
</tr>
<tr>
<td>1998</td>
<td>Nonrandomized, prospective</td>
<td>10</td>
<td>200 ml 50% dextrose, 200 ml 7% EAA, 200 ml 20% lipids</td>
<td>1 yr during hemodialysis</td>
<td>Body weight, BMI, MAMC, serum EAA, food intake</td>
</tr>
<tr>
<td>1999</td>
<td>Nonrandomized, retrospective</td>
<td>18</td>
<td>Intensive dietary advice</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1999</td>
<td>Nonrandomized, prospective</td>
<td>16</td>
<td>250 ml 50% glucose, 250 ml 20% lipids, 250 ml 7% amino acids</td>
<td>9 mo during dialysis</td>
<td>Body weight, lean body mass, MAMC, serum prealbumin and transferrin levels</td>
</tr>
<tr>
<td>1999</td>
<td>Nonrandomized, retrospective</td>
<td>45</td>
<td>Not specified</td>
<td>6 mo during dialysis</td>
<td>BUN, serum albumin level, decreased no. of hospitalizations, length of</td>
</tr>
</tbody>
</table>
IDPN = intradialytic parenteral nutrition; NEAA = nonessential amino acids; EAA = essential amino acids; MAMC = midarm muscle circumference; NaCl = sodium chloride; HN = high nitrogen; BUN = blood urea nitrogen; rhGH = recombinant human growth hormone; IGF = insulin-like growth factor; URR = urea reduction ratio; BMI = body mass index; Kt/V = measure of urea removal, represented by the amount of plasma cleared of urea divided by the urea distribution volume.

References


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