Intradialytic parenteral nutrition (IDPN) is the infusion of an intravenous nutritional formula of hyperalimentation, such as amino acids, glucose, and lipids, during dialysis, to treat protein calorie malnutrition in an effort to decrease the associated morbidity and mortality experienced in patients with renal failure.

Protein calorie malnutrition occurs in an estimated 25–40% of those undergoing dialysis. The clinical evaluation of malnutrition is multifactorial but typically includes measurement of serum albumin. Serum albumin levels correlate with nutritional status but are imperfect measures of nutrition because they can be affected by multiple other disease states. Protein calorie malnutrition is an important clinical consideration since it is associated with increased morbidity and mortality. For example, the risk of death is increased more than 10-fold in those whose serum albumin levels are less than 2.5 g/dL, and those with a serum albumin near the normal range (i.e., from 3.5 to 3.9 g/dL) have a mortality rate twice as high as those with albumin greater than 4.0 g/dL.

In patients receiving chronic dialysis, the National Kidney Foundation currently recommends a daily protein intake of equal to or greater than 1.2 g/kg in patients undergoing hemodialysis and equal to or greater than 1.3 g/kg in patients undergoing peritoneal dialysis. Intradialytic parenteral nutrition, i.e., infusing hyperalimentation fluids at the time of either hemodialysis or peritoneal dialysis, has been investigated as a technique to treat protein calorie malnutrition in an effort to decrease the associated morbidity and mortality. In hemodialysis, the intradialytic parenteral nutrition (IDPN) infusion is administered through the venous port of the dialysis tubing, typically, 30 minutes after dialysis has begun, and continued throughout the remainder of a dialysis session. In peritoneal dialysis, sometimes referred to as intraperitoneal parenteral nutrition (IPPN) or intraperitoneal nutrition (IP), parenteral nutrition is infused into the peritoneal cavity during peritoneal dialysis.
Policy

Intradialytic parenteral nutrition may be considered **medically necessary** when it is offered as an alternative to a regularly scheduled regimen of total parenteral nutrition only in those patients who would be considered candidates for total parenteral nutrition (TPN), i.e., a severe pathology of the alimentary tract that does not allow absorption of sufficient nutrients to maintain weight and strength commensurate with the patient’s general condition.

Intradialytic parenteral nutrition is considered **not medically necessary** in those patients who would be considered a candidate for TPN, but for whom the intradialytic parenteral nutrition is not offered as an alternative to TPN, but in addition to regularly scheduled infusions to TPN.

Intradialytic parenteral nutrition is considered **investigational** in those patients who would not otherwise be considered candidates for TPN.

Policy Guidelines

None

Rationale

This policy was originally created in 2003 and was regularly updated with searches of the MEDLINE database. The most recent literature search was performed for the period of March 2011 through April 2012. The following is a summary of the key findings to date.

Systematic Reviews

While intradialytic parenteral nutrition (IDPN) has been available for many years, there has never been a consensus regarding either its efficacy or patient selection criteria. In 1993, the Office of Health Technology Assessment, the technology assessment arm of Medicare, published a review concluding that studies of IDPN reported equivocal results and the data did not validate its efficacy. (1) Subsequently, in 1999, Foulks reported on an evidenced-based evaluation of IDPN. (2) The analysis concluded that the overall quality of the literature was poor; only 3 randomized studies were identified, and 1 was a feasibility study only; the other 2 had methodologic flaws or used types of IDPN that were not routinely used or were not available in the United States. The remaining literature consists of case series, which obviously cannot control for the many variables in the renal dialysis population that may contribute to increased morbidity and mortality. According to Foulks’ analysis, the majority of case series had methodologic flaws including heterogeneity in study design, patient selection criteria, types of IDPN used, and adequacy of dialysis. Dukkipati and colleagues conducted a systematic review of IDPN for the treatment of malnutrition in hemodialysis patients in 2010. (3) The authors identified only 3 RCTs and found the data were insufficient to conduct a meta-analysis and to demonstrate net benefits in health outcomes with the use of IDPN. The authors concluded
further clinical trials on IDPN are needed, and those trials should measure survival, quality of life, and nutritional status.

**Randomized Controlled Trials**

A randomized controlled trial (RCT) of 186 malnourished hemodialysis patients from 38 treatment centers in France studied the effects of adding IDPN to oral supplementation compared to oral supplementation alone (1 year of treatment with 2-year follow up). (4) Based on intention-to-treat analysis, no differences were found in 2-year survival, hospitalizations, Karnofsky score, body mass index (BMI), or serum albumin and prealbumin levels between treatment groups. The study was powered to detect a 10% reduction in mortality with 78% power (5% α error). Meeting the stated nutritional goals (orally or parenterally) may have improved outcomes; an editorialist suggests that both groups had approximately 15% improved survival compared to historical controls. (5)

**Nonrandomized Comparative Studies**

The largest study is a retrospective case series comparing the morbidity of 1,679 IDPN-treated patients with that of 22,517 nontreated patients. (6) This study found that dialysis patients with a serum albumin level of less than 3.4 g/dL who were treated with IDPN had significant increases in albumin and creatinine over time. In addition, these patients experienced a significant decrease in the odds ratio for death at 1 year compared to those who were not treated with IDPN. Interestingly, the odds ratio for death increased for IDPN-treated patients who had an albumin level of greater than 3.4 mg/dL. Pupim and colleagues performed a detailed analysis of protein metabolism in 7 patients receiving IDPN during hemodialysis. (7) These patients would not have been considered candidates for IDPN on the basis of their nutritional status. While the administration of IDPN was associated with a sharp increase in protein anabolism, the effect was only transient. An accompanying editorial points out that in patients with renal disease, malnutrition is a multifaceted problem that is not related to insufficient or improper food or diet and probably cannot be corrected by simply supplying more or a different balance of nutrition. (8)

A case series was published of 22 hemodialysis patients with acute illnesses (major surgery, infection) treated with IDPN for 1.5 to 48 months as nutritional supplementation (not support). (9) IDPN was discontinued when the following were met: weight ceased to decline, stabilized, or increased; protein catabolic rate was greater than 1.0 g/kg/d; and serum albumin levels were greater than 3.8 g/dL. IDPN was well-tolerated and associated with improvements from baseline of several nutritional parameters. Without a comparison group, it is impossible to conclude that the effects were due to IDPN, and therefore this study does not affect the policy statement regarding patients who would otherwise not be candidates for TPN.

Predictors of IDPN response on hypoalbuminemia were examined in a study of 196 hypoalbuminemic patients receiving maintenance hemodialysis who underwent IDPN. (10) The study suggested that IDPN treatment can improve hypoalbuminemia in patients receiving maintenance hemodialysis and that the likelihood and magnitude of response to IDPN in these patients is associated with the baseline severity of hypoalbuminemia. The authors suggest that this association may be useful in risk stratification of malnourished dialysis patients and recommend that their findings be confirmed through further controlled trials. Also of potential future interest, Pupim et al. reported that in a small series (n=8) of chronic hemodialysis...
patients, intradialytic oral nutrition or IDPN both led to highly positive whole-body net balance during hemodialysis. (11)

Two other uncontrolled studies also suggest an improved outcome associated with IDPN. (12, 13) Due to the numerous biases inherent in any uncontrolled trial, these studies cannot validate whether IDPN is associated with an improved mortality. The observed treatment effect could be related to a selection bias in which very ill patients, i.e., those expected to die, were not offered IDPN. In addition, IDPN administration may be associated with an increased attentiveness to dialysis parameters, counseling, and nutritional advice, etc. These studies suggest that being selected for IDPN may be associated with an improved mortality rate, but analysis of the direct contribution of IDPN will require controlled trials.

No studies were identified addressing IDPN in peritoneal dialysis patients.

Ongoing Clinical Trials

A May 7, 2012 search of online site ClinicalTrials.gov identified only one multicenter German study on IDPN, NCT00501956, which has been completed. In this study, 130 malnourished hemodialysis patients were randomized to receive hemodialysis without IDPN or hemodialysis with 16 weeks of IDPN during each dialysis session followed by 12 weeks without IDPN.

Summary

Intradialytic parenteral nutrition is the infusion of an intravenous nutritional formula of hyperalimentation, such as amino acids, glucose, and lipids, during dialysis, to treat protein calorie malnutrition in an effort to decrease the associated morbidity and mortality experienced in patients with renal failure.

Evidence of efficacy of IDPN treatment is limited. Available evidence demonstrates improvements in intermediate outcomes such as increases in serum albumin and catabolic rate. However, long-term data on survival, quality of life, and other nutritional status outcomes are unavailable. Therefore, IDPN may only be considered medically necessary when it is offered as an alternative to a regularly scheduled regimen of total parenteral nutrition (TPN) in patients who would be considered candidates for TPN. IDPN is considered not medically necessary when added to regularly scheduled infusions of TPN and may be harmful due to the excess administration of lipids. Finally, due to the limited availability of data on IDPN in patients who would not otherwise be considered TPN candidates, the impact on net health outcome is not known and therefore, is considered investigational in these patients.

Practice Guidelines and Position Statements

As noted in the Description section, clinical guidelines published by the National Kidney Foundation have established target daily protein requirements in patients undergoing chronic dialysis. (14) The National Kidney Foundation updated their pediatric nutrition guideline to recommend a trial of IDPN to augment inadequate nutritional intake for malnourished children (BMI for height and age below the fifth percentile) receiving maintenance hemodialysis who are unable to meet their nutritional requirements through oral and tube feeding. (15) It has been suggested that intradialytic nutrition may be reasonable in patients who cannot meet these requirements. However, this patient population is already addressed by the published medical literature, and thus scientific evidence is inadequate to determine whether intradialytic nutrition in these patients leads to improved outcomes.
The German Association for Nutritional Medicine guidelines indicate “IDPN should only be carried out when modifiable causes of malnutrition are excluded and enhanced oral or enteral supply is unsuccessful or cannot be carried out.” (16) These guidelines note the “following international criteria for malnutrition have been suggested, even though they are not based on firm evidence:

- Middle predialysis serum albumin <3.4 g/l for >3 months
- Middle predialysis serum creatinine <8.0 mg/l for >3 months
- Weight loss >10% of ideal body weight or >20% of normal body weight (no time limit)
- Clinical examination indicates moderate to severe malnutrition
- Dietary history indicating protein intake <0.8 g/kg, reduced calorie intake <25 kcal/kg
- Subjective Global Assessment (SGA) “C”= severe malnutrition

IDPN should be considered when three of the above-mentioned criteria are associated with the following conditions:

- Aborted attempts to increase oral/enteral food intake
- Refusal of enteral gavage

**Medicare National Coverage**

**Medicare Policy/Benefit**

The coverage eligibility of intradialytic parenteral nutrition for Medicare beneficiaries is summarized in a Health Care Financing Administration (HCFA) ruling from December 1996, which established that intradialytic nutrition would be considered eligible for coverage only if the patient would otherwise be a candidate for total parenteral nutrition. (17, 18) This ruling reads in part:

“Medicare coverage policies which apply to parenteral and enteral nutrition therapy items and services apply identically to intradialytic parenteral nutrition therapy items and services, because intradialytic parenteral nutrition therapy is a subset of parenteral and enteral nutrition therapy. Coverage of parenteral and enteral nutrition therapy is amplified in Medicare Coverage Issues manual section 65-10. Daily parenteral therapy is ‘considered reasonable and necessary for a patient with severe pathology of the alimentary tract which does not allow absorption of sufficient nutrients to maintain weight and strength commensurate with the patient’s general condition.’ Intradialytic parenteral nutrition therapy is administered to end stage renal disease (ESRD) patients while they are receiving dialysis. ESRD patients sometimes undergo parenteral therapy to replace fluids and nutrients lost during dialysis. ESRD patients must meet all of the parenteral nutrition therapy coverage requirements to receive intradialytic parenteral nutrition therapy. Those patients who do not meet all of the parenteral nutrition therapy coverage requirements are ineligible to receive Medicare coverage of intradialytic parenteral nutrition therapy under the prosthetic device benefit….”

The HCFA ruling goes on to clarify the benefits for patients who would be considered candidates for total parenteral nutrition and when the intradialytic parenteral nutrition is designed to be offered in lieu of a regularly scheduled infusion of total parenteral nutrition.
“However, parenteral and enteral nutrition, including intradialytic parenteral nutrition therapy, services and items which are otherwise covered under section 1861(s)(8) can be denied under section 1862(a)(1) for lack of medical necessity: … Example, if a Medicare beneficiary with ESRD, a dialysis patient who meets all of the requirements for coverage of parenteral nutrition therapy, receives intradialytic parenteral nutrition therapy during dialysis and also receives parenteral nutrition therapy on the other days of the week when the patient is not on dialysis, it may be determined that the patient is receiving an excessive number of lipids. A claim for Medicare payment that is denied because the patient, who qualifies for parenteral nutrition therapy coverage, is receiving an excessive number of lipids would be denied as not reasonable and necessary under section 1862(a)(1)(A) of the Act… Therefore the precise statutory basis for the coverage or denial of parenteral and enteral nutrition therapy, including intradialytic parenteral nutrition therapy, services and items is crucial and determinative as to whether or not limitation on liability protections can be applied.”

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