Intradialytic Parenteral Nutrition

Description

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.

Background

Protein calorie malnutrition occurs in an estimated 25% to 40% of those undergoing dialysis. The cause of malnutrition is multifactorial and may include under dialysis, chronic inflammation, protein loss in the dialysate solution (particularly in peritoneal dialysis), untreated metabolic acidosis, and decreased oral intake.

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 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 (ie, 3.5-3.9 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 1.3 g/kg in patients undergoing peritoneal dialysis. When malnutrition is present, a stepwise approach to treatment is generally used, beginning with dietary counseling and diet modifications, followed by oral nutritional supplements, and then by enteral nutrition supplements or parenteral nutritional supplements is needed.

IDPN, which refers to the infusion of 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 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, amino acid intraperitoneal parenteral nutrition, or intraperitoneal nutrition, parenteral nutrition is provided by using a peritoneal dialysate solution with amino acids, instead of or in addition to glucose, as the osmotic agent.

**Regulatory Status**
TPN solutions are compounded by an individual pharmacy from individual ingredients (eg, dextrose, amino acids, trace elements) into a finished medication based on a prescription and are not required to have approval from the U.S. Food and Drug Administration (FDA) through a new drug application process. Compounding pharmacies have historically been subject to regulation by state pharmacy boards, although FDA has increased its regulatory oversight with the Drug Quality and Security Act of 2013.

Peritoneal dialysis solutions are regulated as drugs by FDA. One amino acid-based peritoneal dialysate, Nutrineal™ PD4, 1.1% Amino Acid Peritoneal Dialysis Solution (Baxter Corp.) is available commercially outside of the United States, but has not been FDA approved.

**Policy**
*This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.*

Intradialytic parenteral nutrition (IDPN) may be considered medically necessary, when it is offered as an alternative to a regularly scheduled regimen of total parenteral nutrition only in hemodialysis patients who would be considered candidates for total parenteral nutrition (TPN), ie, 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 hemodialysis and peritoneal patients when added to regularly scheduled infusions of TPN and may be harmful due to the excess administration of lipids.

Intradialytic parenteral nutrition is considered not medically necessary in patients who would not otherwise be considered candidates for TPN.

**Policy Guidelines**
Patients who are considered candidates for TPN are those who have 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.

This policy is only addresses intravenous parenteral nutrition as an adjunct to hemodialysis (not peritoneal dialysis).

Also see Benefit Application on MPRM policy.
Rationale

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 three randomized controlled trials (RCTs) were identified, and one was a feasibility study only; the other 2 had methodological 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 methodological 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 recommend further clinical trials on IDPN are needed, and those trials should measure survival, quality of life, and nutritional status. In 2010, Sigrist et al reported results from a systematic review of IDPN for patients with chronic kidney disease. (4) The authors evaluated RCTs or systematic reviews of RCTs that specifically enrolled malnourished patients on hemodialysis who were randomized to either IDPN (including full IDPN or amino acids plus carbohydrates only) or any form of enteral or oral nutrition. Three studies met the authors’ inclusion criteria, only one of which reported mortality as an outcome. The data were insufficient to conduct a meta-analysis, and the authors concluded that evidence from clinical studies is insufficient to demonstrate either a net benefit or a net harm associated with the providing IDPN to malnourished hemodialysis patients.

Randomized Controlled Trials

An 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). (5) 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. (6)

Nonrandomized Comparative Studies

The largest study is a retrospective case series comparing the morbidity of 1679 IDPN-treated patients with that of 22,517 nontreated patients. (7) 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 et al performed a detailed analysis of protein metabolism in 7 patients receiving IDPN during hemodialysis. (8) 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.

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 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 was examined in a study of 196 hypoalbumineic patients receiving maintenance hemodialysis who underwent IDPN. (10) The study suggested that IDPN treatment could 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) Because of 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, ie, 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.

In 2012, results from a nonrandomized comparative study comparing changings in serum prealbumin level between hemodialysis patients treated with IDPN and controls were presented in abstract form, but no full-length published results were identified. (14) Statistical calculation was undertaken for 32 patients per study group. IDPN was reported to lead to a significant increase of prealbumin during the 16-week course of treatment (26.31 mg/L), compared with the noninterventional control group (1.84 mg/L, p=0.02). Because of the small sample size, there was a lack of statistical power to evaluate responsiveness of the secondary end points in this study (eg, albumin, transferrin, quality of life).

Section Summary: The available evidence is inadequate to allow conclusions about whether the routine use of IDPN as an adjunct to hemodialysis improves patient outcomes. Although uncontrolled
studies suggest that patients treated with IDPN may have improved biochemical markers of malnutrition and survival, controlled trials are needed to allow conclusions about whether IDPN is associated with improved outcomes. A small number of randomized controlled trials (RCTs) showed no significant improvements in health outcomes with IDPN as an adjunct to hemodialysis.

Ongoing and Unpublished Clinical Trials
Some currently unpublished trials that might influence this policy are listed in Table 1.

Table 1. Summary of Key Trials

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NCT: national clinical trial.

a Denotes industry-sponsored or cosponsored trial

Practice Guidelines and Position Statements

Clinical guidelines published by the National Kidney Foundation (NKF) have established target daily protein requirements in patients undergoing chronic dialysis. (15) NKF 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 5th percentile) receiving maintenance hemodialysis that are unable to meet their nutritional requirements through oral and tube feeding. (16)

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.” (17) 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 3 of the above-mentioned criteria are associated with the following conditions:

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

In 2010, the American Society for Parenteral and Enteral Nutrition (ASPEN) issued guidelines on nutrition support in acute and chronic renal failure. They issued a level C (supported by at least 1 level II investigation) that stated that IDPN should not be used as a nutritional supplement in malnourished chronic kidney disease-V hemodialysis patients. The rationale was that a large RCT found that mortality rates did not differ between malnourished patients receiving IDPN versus malnourished
patients who received oral supplements with no IDPN. An additional concern was that IDPN is limited by the need to complete the entire nutrient infusion during the hemodialysis treatment which may cause adverse effects because of the rapid infusion of glucose and lipids. They further recommended larger RCT’s in malnourished patients to ensure that a clinical benefit does not exist. (18)

U.S. Preventive Services Task Force Recommendations

Not applicable

Summary

Evidence demonstrating the efficacy of IDPN treatment in improving outcomes for patients undergoing hemodialysis is limited. The 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 not medically necessary in these patients.

Medicare National Coverage

Medicare Policy/Benefit:

The coverage eligibility of IDPN 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 TPN. (19, 20) 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 TPN and when the IDPN is designed to be offered in lieu of a regularly scheduled infusion of TPN.

“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.”

References


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**September 2014 Update Policy**
Policy updated with literature review. References 4 and 19 were added. The policy statement is unchanged.

**September 2015 Update Policy**
Policy updated with literature review; no references added. Policy statements edited to clarify that they are intended to apply to parenteral nutrition administered during hemodialysis; policy statements unchanged.

**Keywords**
Dialysis, Parenteral Nutrition
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*This policy was approved by the FEP® Pharmacy and Medical Policy Committee on September 18, 2015 and is effective October 15, 2015.*

*Signature on File*
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