PARENTERAL NUTRITION

Indications for Parenteral Nutrition (PN)

PN support has been shown to be of benefit in the some circumstances where patients cannot, should not, or will not receive nutrients adequately through the GIT to maintain their nutrient stores.

These patients are already, or have the potential of becoming, malnourished, this malnutrition is associated with increased patient complications and mortality.

Example of circumstances where PN has been shown to be of benefit include:

1- Perioperative support of patients with moderate to severe malnutrition.

2- Acute exacerbations of Crohn's disease.

3- GI fistulas 4- Extreme short bowel syndrome

5- In critically ill patients, PN is indicated if EN is not possible, and hypermetabolism is expected to last more than 4 to 5 days.

6- PN is indicated in other conditions precluding the use of the GI tract for more than 7 to 10 days.

Criteria for implementation of PN

PN is costly and may result in serious complications when used inappropriately. The costs of PN include not only the admixture but other costs, such as placing venous access, and costs to treat complications. As such, the use of PN is scrutinized. The therapy should only be used in those patients who will demonstrably benefit. Patients most likely to benefit from PN may be determined by evaluating the following criteria:

1) Nutritional Status

Severely malnourished patients are at significant nutritional risk. These include patients who experience abnormalities associated with nutrient digestion, absorption, metabolism, or excretion. Although there are many criteria that may be used to determine if a patient is severely malnourished, a few examples follow:

- More than 10% involuntary weight loss over a 2- to 3-month period.
- Less than 75% of ideal or usual body weight.
- Serum prealbumin less than 10 mg/dL or serum transferrin less than 100 mg/dL.

2) Gastrointestinal Function

Symptoms such as nausea, vomiting, diarrhea, and abdominal distention or cramps may preclude the use of the GI tract for prolonged periods. These symptoms can be associated with some medications eg. treatment toxicities in cancer patients that preclude adequate oral intake for more than a week, hence they are an indication for PN.

PN is often used when enteral tube feedings are unsuccessful as evidenced by high residuals or pulmonary aspiration.

3) Clinical Status

PN should only be initiated in patients who are hemodynamically stable and who are able to tolerate the fluid volume, protein, carbohydrate, and intravenous fat emulsions (IVFE) doses necessary to provide adequate nutrient substrate. Examples of situations where PN warrants caution are the condition that can be accompanied by blood hyperosmolarity eg:

- Hyperglycemia
- Azotemia

Parenteral Nutrition Formulations

Formulation component

Components used in formulating PN typically include protein as amino acids, energy substrates, such as carbohydrate, and fat, as well as electrolytes, vitamins, and trace elements. Sterile water for injection is added to provide necessary volume to the PN formulation. Various combinations of these components are incorporated into the regimen for intravenous (IV) administration based on the patient's individual requirements.

Energy Substrates

The most commonly used carbohydrate energy substrate is dextrose, which in its hydrated form provides 3.4 kcal/g. Dextrose is commercially available in multiple concentrations ranging from 2.5% to 70%, in partially filled containers as well as in combinations with other components of the PN formulation. Dextrose solutions are acidic, with a pH ranging from 3.5 to 6.5, and vary in osmolarity depending upon their concentration.

Higher dextrose concentrations (greater than 10%) are generally reserved for central venous administration because of the propensity to cause thrombophlebitis in peripheral veins.

Another carbohydrate energy substrate used less frequently is glycerol, a sugar alcohol which provides 4.3 kcal/g. Glycerol, or glycerin, is contained in certain pre-mixed PN formulations marketed for peripheral administration. These formulations have been shown to be protein-sparing and have been reported to induce less insulin response than dextrose-based regimens.

IVFE are used to provide energy as well as essential fatty acids for PN formulations. IVFE components include soybean oil or 50:50 mixes of soybean and safflower oils, egg yolk phospholipid as an emulsifier, glycerin to render the formulation isotonic, vitamin K, and sodium hydroxide to adjust the final pH.

IVFE are commercially available in 10% (1 kcal/mL), 20% (2 kcal/mL), and 30% (3 kcal/mL) concentrations. Of these, the IVFE 30% formulation is only approved for compounding of TNA, not for direct IV administration.

Because of enhanced microbial growth potential with infusion of IVFE separate from dextrose and amino acids formulations, the Centers for Disease Control and Prevention (CDC) recommends a 12-hour hang-time limit for IVFE (or within 12 hours of opening the original manufacturer's container) if IVFE are infused as separate preparations from dextrose and amino acids. However, an admixture containing IVFE, dextrose, and amino acids in the same container may be administered over 24 hours.

The hang time and infusion of this formulation is extended compared with infusion of IVFE alone because bacterial growth is inhibited at a reduced pH (pH approximately 5.6 to 6) and the increased total osmolarity with the combination of all three substrates in one container.

Protein

Crystalline amino acids are used in PN formulations to provide protein and yield 4 kcal/g if oxidized for energy. Nitrogen content varies depending upon concentration of the amino acid formulation and mixture of individual amino acids; however, for nitrogen balance calculations amino acid products are generally assumed to be 16% nitrogen (6.25 g of protein = 1 g of nitrogen).

Electrolytes

Maintenance or therapeutic amounts of various electrolytes are added to PN formulations depending upon the patient's requirements. Acetate and chloride do not have specific ranges for intake; rather, they are adjusted as needed to maintain acid–base balance.

Vitamins

Commercially available vitamin products for PN supplementation include single vitamin products and multivitamin products that contain both fat-soluble and water-soluble vitamins.

Trace Elements

Commonly used trace elements in PN formulations include zinc, copper, chromium, manganese, and selenium. These are commercially available as single entity products and in various multiple trace element combinations and concentrations for adults, pediatrics, and neonates. Some formulations may also contain electrolytes. Other trace elements that may be supplemented in PN iron. Three injectable iron products are available, all as single-entity products. Only iron dextran is approved for addition to PN, but this should only be considered for dextrose–amino acids formulations because IVFE are disrupted by iron

Routes of Infusion

The components of a parenteral feeding formulation will determine its osmolarity and infusion route.

PN may be prepared for peripheral venous infusion or infusion through a central venous access device. PN may also be prepared as a total nutrient admixture (TNA, 3-in-1) or a “2-in-1” solution.

2-in-1 solutions contain all necessary IV macronutrients and micronutrients in the same container except intravenous fat emulsions (IVFE), which may be infused separately.

Parenteral feeding formulations are hypertonic to body fluids and, if administered inappropriately, may result in venous thrombosis, suppurative thrombophlebitis, and extravasation.

Specifically, the osmolarity of a parenteral feeding formulation is dependent primarily on the dextrose, amino acid, and electrolyte content.

Dextrose contributes approximately 5 mOsm/g of dextrose, amino acids yield approximately 10 mOsm/g, and electrolytes provide approximately1 mOsm/mEq of individual electrolyte additive.

For example, the estimated osmolarity of a 1-L total volume parenteral feeding formulation providing 150 g of dextrose, 50 g of amino acids, and 150 mEq of electrolyte additives is 1400 mOsm/L. Central venous administration is preferred for this PN because the maximum osmolarity tolerated by a peripheral vein is 900 mOsm/L.

Central Parenteral Nutrition

Central parenteral nutrition (CPN) is often referred to as "total parenteral nutrition" because the entire nutrient needs of the patient may be delivered by this route.

A complete, balanced formulation includes dextrose, amino acids, IVFE, electrolytes such as potassium, magnesium, and phosphorus, vitamins, and multiple trace elements such as zinc, copper, manganese, chromium, and selenium.

The glucose content (usually 150-600 g/d) along with amino acids and electrolytes provides a hyperosmolar (1300–1800 mOsm/L) formulation that must be delivered into a large-diameter vein such as the superior vena cava adjacent to the right atrium.

The rate of blood flow in these large vessels rapidly dilutes the hypertonic parenteral feeding formulation to that of body fluids, minimizing risk of complications associated with IV infusion of hypertonic solutions.

CPN provides complete nutrition in a reasonable fluid volume and may be concentrated to provide adequate calories and protein for those patients requiring a fluid restriction. Because central venous access can be maintained for prolonged periods (weeks to years), CPN is preferred for use in patients who will require PN support for longer than 7 to 14 days, including those patients receiving care at home or other extended health care environments, such as assisted living or extended care facilities and nursing homes.

Peripheral Parenteral Nutrition

Peripheral Parenteral Nutrition (PPN) has a similar composition as CPN, but lower concentrations of nutrient components are necessary to allow peripheral venous administration.

It has a lower dextrose dose of 150 to 300 g/d (5%–10% final concentration) and amino acid (50–100 g/d, or 3% final concentration) content compared to CPN. Large fluid volumes must be administered to provide a comparable calorie and protein dose as CPN.

PPN is usually an undesirable option for patients with fluid restriction because concentrating the solution frequently results in a hyperosmolar solution that is not suitable for peripheral administration.

PPN is typically used for short periods (upto 2 weeks) because of limited tolerance and few suitable peripheral veins, so use in severely malnourished patients is generally not indicated.

Patients considered for PPN must meet two criteria:

(1) have good peripheral venous access, and

(2) Be able to tolerate large volumes (2.5–3 L) of fluid.

They should require at least 5 days but no more than 2 weeks of partial or total PN.

Contraindications to PPN

- Significant malnutrition.
- Severe metabolic stress.
- Large nutrient or electrolyte needs.
- Fluid restriction
- Need for prolonged parenteral nutrition (greater than 2 weeks).
- Renal compromise

Use of PPN to provide adequate doses of calories, protein, and other micronutrients in critically ill patients is difficult. PPN formulations are hyperosmolar (600–900 mOsm/L) and may cause phlebitis and require frequent peripheral IV site rotations (at least every 48–72 hours). IVFE may be used to increase the caloric density of the peripheral parenteral feeding formulation without increasing the osmolarity and has been reported to improve peripheral vein tolerance of PPN

Disease-Specific Formulations and Specific Nutrients

A) Modified Amino Acids Formulations

Specialty amino acids formulations are available for use in certain disease states or conditions.

These products are generally more expensive than standard formulations and should be reserved for patients meeting the intended indications who are expected to benefit clinically from their use.

1) Specialty formulations for use in renal failure: are composed primarily of essential amino acids based upon the theory that nonessential amino acids can be physiologically recycled from urea, while essential amino acids must be provided from the diet.

2) Modified amino acids formulations designed for use in hepatic encephalopathy:

Contain increased amounts of branched-chain amino acids (BCAA) and decreased amounts of aromatic amino acids (AAA) compared with standard parenteral amino acids formulations. Altered metabolism in patients with hepatic failure can result in a high serum ratio of AAA to BCAA. This imbalance is thought to cause increased transport of AAA into the brain, where they serve as precursors to neurotransmitters that may be responsible for altered mental status.

B) Addition of Carnitine to PN

Carnitine is necessary for proper transport and metabolism of long-chain fatty acids. Carnitine is not present in any component of PN formulations. An IV form of L-carnitine is commercially available for treatment of carnitine deficiency, and is sometimes added to PN formulations for selected patients who have a documented deficiency or are susceptible to a deficiency.

C) Modified IVFE

IVFE available in the market are currently composed mainly of long-chain triglycerides (LCT, carbon chain length greater than or equal to 14).

Formulations contain mixtures of medium-chain triglycerides (MCT, carbon chain length 6–12) and LCT, may be useful in patients intolerant to the currently available LCT products during critical illness and metabolic stress and also in patients with carnitine deficiency because transport of MCT into mitochondria is carnitine independent

National Standards for Compounded Sterile Preparations

A primary responsibility of the pharmacist is to ensure safe PN preparation. Compounding an accurate formulation free of microbial and particulate matter is an essential component of this process. A number of procedures have been developed by organizations, such as the American Society of Health-System Pharmacists (ASHP), to assist pharmacists in complying with sterile product admixture guidelines.

Three different risk levels (low, medium, and high) for each CSP based upon the potential for microbial contamination.

The low-risk level typically involves a simple, closed-system aseptic transfer.

A medium-risk level involves reconstitution of several sterile commercial products for transfer into several small-volume minibags or one large-volume parenteral preparation, such as PN.

A high-risk compounding activity involves preparation from bulk, nonsterile ingredients.

Risk level assessment is important because storage and expiration limits of CSPs are assigned based upon risk level. "Beyond-use dating" is the new terminology for what was formerly referred to as expiration dating.

The difference is that an expiration date was based on drug stability, while the beyond-use date is defined as the date established by health care professionals from the published literature or manufacturer-specific recommendations beyond which the pharmacy-prepared product should not be used because of concerns of chemical instability and product sterility.

For example, a pharmacy-prepared PN formulation stored at temperature (20–25°C) cannot be used after 30 hours, whereas a PN solution stored under refrigeration has a beyond-use date up to 9 days.