Artificial Nutrition Support in Intestinal Failure: Principles and Practice of Parenteral Feeding

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ABSTRACT

Patients with intestinal failure are at risk for malnutrition and its associated adverse consequences. In many of these patients it is not possible to feed via the gastrointestinal tract, and nutrients must be provided directly into the bloodstream. For some patients with irreversible intestinal failure, this is a lifelong requirement. Parenteral nutrient solutions may be tailored specifically to individual requirements and are usually administered directly into a central vein using an indwelling catheter. Serious complications related to both the indwelling catheter and metabolic consequences of the nutritional support may occur. A team approach to the provision and monitoring of parenteral nutrition in intestinal failure produces the best results.

KEYWORDS: Intestinal failure, parenteral nutrition, nutrient solutions, complications

Objectives: Upon completion of this article, the reader should be able to summarize the indications for, provision of, and complications associated with parenteral nutrition in patients with intestinal failure.

Most patients with intestinal failure (IF) have reduced absorption of nutrients and are at risk for becoming undernourished unless adequate nutritional support is implemented. In some cases insufficient net absorption of water and electrolytes is the predominant problem, and such patients are susceptible to dehydration and electrolyte imbalance unless corrective measures are taken.

The parenteral route is one option for the provision of nutrients and/or water and electrolytes to patients suffering from IF, and in some groups of patients this is the only route that it is appropriate. The successful provision of what we recognize today as total parenteral nutrition (TPN) was first reported in 1968,[1] and since then the practice has developed considerably. In more recent years there have been unfounded concerns regarding the safety and benefits of parenteral nutrition (PN) compared with enteral feeding.[2] In the setting of IF, PN remains a life-preserving treatment for many patients.[3]

In this article a practical approach to the provision of PN for IF patients is presented. Indications for PN, routes of parenteral access, formulation of parenteral feeding regimens, and important complications of the process are considered.

INDICATIONS FOR PARENTERAL FEEDING IN INTESTINAL FAILURE

PN should be used to prevent or treat undernutrition in IF patients in whom the intestinal tract is likely to be

Intestinal Failure; Editor in Chief, David E. Beck, M.D.; Guest Editor, Alastair C. J. Windsor, M.B.B.S., M.D., F.R.C.S., F.R.C.S. (Ed). *Clinics in Colon and Rectal Surgery*, volume 17, number 2, 2004. Address for correspondence and reprint requests: Dr. Timothy E. Bowling, Clinical Nutrition Unit, Queen's Medical Centre, Nottingham NG7 2UH, United Kingdom. E-mail: tim.bowling@mail.qmcuh-tr.trent.nhs.uk. [1]Clinical Nutrition Unit and Wolfson Digestive Diseases Centre, University Hospital, Nottingham, United Kingdom. 1531-0043,p;2004,17,02,099,105,ftx,en;ccrs00169x.

Table 1 Causes of Intestinal Failure Where Prolonged Parenteral Nutrition Is Often Required

Severe intestinal inflammation:
Crohn's disease
Radiation enteritis
Chemotherapy enteritis/mucositis
Short bowel following extensive resection
Intestinal pseudo-obstruction
High-output gastrointestinal fistula
Disseminated abdominal malignancy with inoperable intestinal obstruction

nonfunctioning or inadequately functioning for a prolonged period of time. Typical indications for PN are shown in Table 1. These generally comprise failure of intestinal absorptive function related to disease, such as severe mucosal inflammation, inadequate bowel length, or failure of intestinal motility. PN may also be indicated when enteral feeding has been unsuccessful (for whatever reason) or fails to meet nutritional requirements fully. PN may also be used in situations in which a period of bowel "rest" is required (e.g., to allow a high-output intestinal fistula to heal). Some patients have an irreversible cause of IF (e.g., short bowel syndrome or intestinal pseudo-obstruction) and require long-term PN with enrolment in a home PN program.

PARENTERAL FEEDING CATHETERS

Routes of venous access for administration of PN are shown in Table 2. For the majority of patients, PN is optimally administered into the subclavian vein using a silicone rubber catheter with subcutaneous tunneling proximal to an exit site on the anterior chest wall. Delivery of hyperosmolar nutrient solutions into a large-bore, high-flow vein avoids development of thrombophlebitis. Subclavian catheters have lower rates of catheter-related sepsis than jugular or femoral catheters and are more comfortable and convenient for the patient, especially when ambulant. The tip of the catheter should be sited at the junction of the superior vena cava and right atrium, as demonstrated by a chest radiograph.[4] Ideally, parenteral feeding catheters should be inserted and subsequently managed by experienced members of a multidisciplinary team, to reduce catheter-associated complications. Patients who require long-term PN and/or their carers may also be trained in catheter care by the team.

Table 2 Common Sites of Venous Access for Administering Parenteral Nutrition

Type of Parenteral Nutrition	Venous Access Site
Central	Subclavian
	Internal jugular
	Femoral
	Antecubital fossa (PICC line)
Peripheral	Antecubital fossa (PIC line)
	Vein on back of hand

PIC, peripherally inserted catheter; PICC, peripherally inserted central catheter.

Peripherally inserted central catheters (PICC lines) are suitable for short- to medium-term use. Their insertion requires good size veins in the antecubital fossa. PICC lines are usually $\sim$60 cm in length and therefore the tip is centrally sited. The advantages of PICC lines therefore are that they avoid both the complications of central venous cannulation and the problems associated with peripheral line feeding. For many, a PICC line is the route of choice in patients requiring PN for less than 28 days (or thereabouts). However, PICC lines are harder to site correctly and are associated with more thrombophlebitis than subclavian catheters.[5] Their exit site position in the antecubital fossa makes PICC lines vulnerable to dislodgement and can limit activity, especially in ambulant patients. Peripherally inserted catheters (PICs) are usually $\sim$20 cm in length and therefore the tip often sits in the axillary vein. They are frequently complicated by thrombophlebitis, which considerably limits their longevity. Overall there is little, if anything, to recommend them over a PICC line.

PN can be administered directly into a peripheral vein using a standard cannula for short-term use ($<$2 weeks).[6] This may occasionally be suitable for some IF patients, mainly as a bridge between a failed old central line and the insertion of a new one, and has the advantage that feeding may be (re)started promptly. To avoid thrombophlebitis, only hypo-osmolar (and therefore hypocaloric) nutrient solutions should be administered. Peripheral feeding, whether by cannulae or PIC, is therefore not suitable for patients with high nutritional requirements or for those requiring long-term nutritional support. On the whole, peripheral feeding is not the route of choice, and although it has been popular in the past, its limitations outweigh its benefits.

For IF patients requiring long-term PN (months to years, including home PN), a feeding catheter with a Dacron anchoring cuff (e.g., Hickman line; Fig. 1) or an implantable venous access port that has no external catheter (e.g., portacath) is preferable. Such devices may remain usable for several years with proper care.

FORMULATION OF PARENTERAL NUTRIENT SOLUTIONS

The aim of nutritional support is to maintain and/or improve nutritional status, both in the short term during illness and in the long term in cases of irreversible IF. Parenteral nutrient solutions should meet all requirements in the form of energy, protein, carbohydrate, fat,

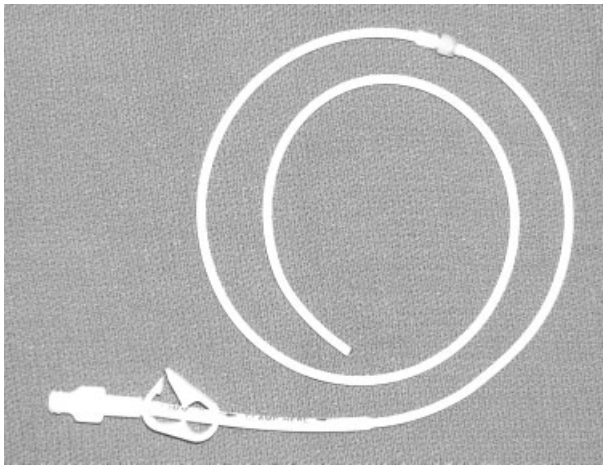

Figure 1 Single-lumen left subclavian Hickman line, suitable for the provision of parenteral nutrition.

electrolytes, trace elements, vitamins, and water. In theory, the formulation of the solution should be individualized to each patient's needs, but in practice standard commercially prepared solutions suit most patients. These generally contain macronutrients (protein, carbohydrate, and fat) in variable quantities and volumes. To these electrolytes, trace elements, vitamins, and sometimes drugs can be added by the formulating pharmacy. Similar solutions with lower osmolalities are also available for peripheral PN. The components of a typical parenteral feeding solution are shown in Table 3. A dietitian and pharmacist should be involved in the formulation of parenteral nutrient solutions for IF patients.

Energy

Calories derived from the nutrient solution come from carbohydrate, lipid, and protein. The energy requirement of a patient can be determined using formulae such as the Harris-Benedict[7] or Schofield[8] equations, which estimate the basal energy expenditure. Alternatively, a simple estimate of energy requirements is 25 to 35 kcal/kg/day. Patients who are catabolic (e.g., postoperative, sepsis) require 30 to 35 kcal/kg/day, whereas patients who are clinically and metabolically stable need only 25 to 30 kcal/kg/day. Overfeeding can be dangerous and is associated with metabolic and infectious complications. It is therefore better to supply too few calories than too many, particularly when initiating PN in severely malnourished or critically ill patients.[4,9–11]

Protein

Nitrogen is supplied in PN solutions in the form of amino acids. The amount of nitrogen provided should be increased with metabolic stress to promote protein synthesis and preserve lean body mass.

Carbohydrate

Hyperosmolar glucose solution is usually used as the carbohydrate energy source, to provide 50 to 60% of the nonprotein energy. Excess glucose energy (compared with lipid) can cause acidosis, hyperglycemia, and liver dysfunction.

Lipid

Lipid emulsions used in most PN solutions are isosmolar and consist of triglycerides and essential fatty acids and should provide 40 to 50% of the nonprotein energy. Because of the risk of pancreatitis, lipid emulsions should be used with caution in patients with hypertriglyceridemia.

Water and Electrolyte

From 2.5 to 3 L of water per day is required by most patients. Patients with IF may suffer large electrolyte losses through vomiting, diarrhea, stoma outputs, and fistulae and thus may require additional supplementation. In some patients with IF, for example, due to a high-output jejunostomy, loss of water and electrolytes

Table 3 Daily Components of a Typical Parenteral Nutrition Nutrient Solution

Total energy	~ 2000 kcal (25 kcal/kg/day + allowance for metabolic stress and activity *or* use Harris-Benedict equation)
Protein	0.15–0.3 g N/kg/day (i.e., 1–2 g protein/kg/day) as amino acid solution
	27 kcal/g N (4 kcal/g protein)
Carbohydrate	Glucose solution; 50–60% nonprotein energy
	3.8 kcal/g glucose
Fat	Lipid emulsion; 40–50% of nonprotein energy
	9.4 kcal/g lipid
Electrolytes	Including sodium (90 mmol), potassium (60 mmol), calcium (8 mmol), phosphorus (30 mmol), magnesium (9 mmol)
Trace elements	Standard commercial preparation such as Additrace®
Vitamins	Standard commercial preparation such as Vitlipid®, Solvay®

may be the main problem. Such patients may just require parenteral replacement of saline (and often magnesium), being able to meet their energy requirement enterally.[12]

Immunonutrition

A variety of nutrients, including glutamine, arginine, and omega-3 fatty acids, act as immunomodulators and may be beneficial as supplements to feeding solutions in some illnesses. This is an area of considerable current interest particularly in critically ill patients, but at present the role of immunonutrients in the management and nutritional support of IF patients is yet to be established.[13]

ASSESSING RESPONSE TO AND MONITORING PARENTERAL NUTRITION

For patients receiving PN, careful monitoring is required both to confirm the efficacy of the treatment and to recognize the development of complications. Before PN is initiated, baseline height and weight, vital signs, and laboratory values should be recorded. During the first few days of treatment, vital signs should be checked 8 hourly. Bedside blood glucose should be checked 4 to 6 hourly to monitor for hyperglycemia and for hypoglycemia where insulin therapy is also being used. Fluid balance and body weight should be recorded daily and assist in clinical estimations of fluid overload or dehydration. Serum electrolytes including magnesium and phosphate and liver function should be checked daily until stable and then once or twice weekly. Magnesium deficiency may be associated with refractory hypokalemia and hypocalcemia. Triglyceride levels should also be measured in a similar fashion to ensure that hypertriglyceridemia does not occur. For stable patients receiving long-term home PN, blood tests are probably required only three or four times a year.[4,9,14]

A satisfactory clinical response to PN in IF patients is a demonstration of maintenance and/or gain of body weight and improved well-being of the patient. Muscle function is regained before body mass increases. As patients respond to PN, the nutrient solution formulation should be reviewed and it may be possible to increase the amounts of protein and energy supplied, with a view to weight gain. It is essential that an appropriately experienced dietitian is involved in follow-up of the patient.

Discontinuing Parenteral Nutrition

Where the cause of IF is reversible, it should be possible to introduce enteral nutrition progressively as intestinal function is restored or adapts during recovery. PN is continued concurrently and then progressively reduced if enteral feeding is tolerated and provides significant and increasing portions of the daily nutritional requirement. When daily requirements are reliably met by the enteral route, PN can be discontinued.

Table 4 Parenteral Nutrition Catheter-Related Complications

Problems of central vein cannulation:
Pneumothorax, arterial puncture, thoracic duct damage, nerve injury, malposition of catheter
Catheter-related sepsis
Central vein thrombosis and thrombophlebitis
Catheter occlusion
Mechanical problems:
Catheter fracture, distal embolization

COMPLICATIONS OF PARENTERAL NUTRITION

Catheter-Related Complications

Catheter-related complications are the main cause of morbidity and mortality associated with PN. Common catheter-related complications are shown in Table 4.

Complications Related to Central Venous Cannulation

Pneumothorax, arterial puncture, and catheter malposition (e.g., passage of subclavian catheter intracranially) are the most common problems encountered during subclavian and jugular vein cannulation. Reported frequencies are up to 3.5%, even in experienced hands.[15] A chest radiograph a few hours after the procedure usually demonstrates pneumothorax and catheter malposition and may also show apical hematoma or hemothorax caused by arterial puncture.

Other rare but recognized complications of catheter placement are thoracic duct damage causing chylothorax, hydrothorax due to infusion of fluid through a catheter lying outside the vein, brachial plexus injury, air embolism, pneumo- and hemopericardium, and arrhythmias.[15]

Catheter-Related Infection

Catheter-related sepsis caused by internal infection of the catheter lumen occurs in 5 to 8 per 1000 patient-days and is an important cause of mortality and morbidity among patients receiving PN.[4] Catheter-related sepsis may be categorized as primary, when the catheter is the sole source of sepsis, or secondary, when bacteria from another infection have migrated to and colonized the catheter. Catheter-related sepsis usually arises with fever and rigors shortly after a new infusion is commenced. The catheter may also become infected externally, at the exit site or inside the subcutaneous tunnel. Exit site

infections usually arise with local pain and erythema and discharge from the exit site. Tunnel infections arise similarly but with erythema spreading along the track of the catheter proximal to the exit site. Exit site swabs and peripheral venous and catheter blood cultures should be taken to confirm the diagnosis and identify the infecting organism.[15] If the catheter is removed because of suspected infection, the tip should also be sent for culture. Common catheter-infecting organisms are *Staphylococcus epidermidis*, *Staphylococcus aureus*, enterococci, *Klebsiella pneumoniae*, and *Candida albicans*.

Catheter-related infection is reduced by simple hygienic measures, tunneled catheters, and high standards of catheter care achieved using a nutrition team approach.[16,17] Single-lumen catheters dedicated solely for PN are less likely to become infected than multiple-lumen catheters used for other purposes, even if one of the lumens is used only for PN.[18]

Exit site infections can often be resolved by frequent dressing changes and appropriate systemic antibiotics. Infection of the subcutaneous tunnel requires removal of the catheter, treatment with appropriate systemic antibiotics, and placement of another catheter in an alternative site. If catheter-related sepsis is suspected, prompt action should be taken and a general approach is as follows. In some cases the catheter may be salvaged,[19] and this may be particularly desirable if alternative venous access is scarce. PN should be stopped and the catheter locked with heparin while the results of peripheral and central catheter blood cultures are awaited. If cultures are negative, the catheter can be reused, but with caution, while an alternative source of sepsis is sought if the patient is still unwell. If blood cultures are positive, systemic appropriate antibiotics should be commenced for at least 7 to 10 days. The catheter may also be locked with an appropriate antibiotic, such as vancomycin. If the patient improves clinically with this treatment and subsequent blood cultures from the catheter are negative, parenteral feeding can be recommenced cautiously. If, however, there is no clinical improvement after 48 hours of systemic antibiotics or if the infection is due to *S. aureus* or *Candida*, the catheter should be removed and antibiotic treatment continued. A replacement catheter may be placed at an alternative site when the patient has been asymptomatic for 48 hours.

Central Vein Thrombosis

Central vein thrombosis in PN is also associated with serious morbidity and mortality, mainly due to thromboembolism, secondary infection, and loss of vascular access. Reported frequency ranges from 5 to 28%, but subclinical thrombosis is probably more common.[15,20] Catheter infection, dehydration, hyperosmolar feeds, malposition of the catheter tip, and procoagulant states are all risk factors for thrombosis. In high-risk patients receiving long-term PN, low-dose warfarin may reduce the incidence of thrombosis.[21]

Painful swelling of the arm and neck with the appearance of prominent collateral veins on the chest wall suggests thrombosis. Venography or Doppler ultrasonography is used to confirm the diagnosis. Anticoagulation with heparin and then warfarin for 6 months should be instituted to reduce the risk of thromboembolism. Ideally, the catheter should be removed and a new one inserted at a different site, particularly if there is any suspicion of secondary infection.[15] Alternatively, thrombolytic agents have been used to dissolve the clot, leaving the catheter in situ.[22]

Thrombophlebitis

Thrombophlebitis necessitating catheter replacement is a major problem of peripheral vein PN using standard cannulae or PIC lines. Mechanical trauma during insertion, infected catheters, and high-osmolality feeding solutions are the main predisposing factors.[23] Topical nitrate patches applied over the vein distal to the cannula increase local blood flow and may prolong the catheter life. Heparin and corticosteroid within the nutrient solution may also help.[6]

Catheter Occlusion

Complete occlusion is a frequent complication of long-term PN. Incomplete occlusion manifests as resistance to flushing or a failure to aspirate. Occlusion is usually due to backflow of blood into the catheter (fibrin) or components of the nutrient solution (lipid or mineral precipitate) within the catheter lumen. Some catheters (e.g., Groshong) have a valve at their tip that prevents blood entering the lumen, thus preventing occlusion related to fibrin deposition. Good catheter care with flushing after each use helps prevent the problem. Irrigation of the catheter with thrombolytic agents, ethanol, or hydrochloric acid may dissolve the deposit and restore patency.[15,24]

Mechanical Catheter Problems

Catheter fracture is rare but potentially dangerous with the risk of air embolism or migration of catheter segments distally into the heart or pulmonary circulation. External fractures should be treated by immediate proximal clamping followed by catheter repair or replacement. Embolized fragments need to be removed by interventional radiology, or sometimes surgically.[15]

Long-Term Vascular Access Problems

Maintaining vascular access after repeated episodes of central vein thrombosis and/or catheter-related sepsis

can be a major problem in some IF patients receiving long-term PN. A variety of solutions may be available.[25] If central vein thrombosis is recognized early, thrombolytic therapy may restore patency, allowing recannulation. When the superior vena cava and its tributaries are thrombosed, feeding catheters may be introduced into the inferior vena cava through the femoral vein or by a translumbar or transhepatic approach with the help of vascular radiologists. In some cases patency can be restored to thrombosed major veins by balloon angioplasty and stenting, to allow further catheter placement. Finally, forearm arteriovenous fistulas, similar to those used for renal hemodialysis patients, have been used for administration of PN, but these too may be prone to thrombosis.

Metabolic Complications of Parenteral Nutrition

A variety of metabolic complications may be encountered in patients receiving PN (Table 5). Common complications are problems with glucose homeostasis in the short term and hepatobiliary abnormalities in the longer term. Particular problems for patients receiving long-term PN are micronutrient deficiencies, liver disease, and bone disease.

Glucose

Hyperglycemia is most common in diabetics or critically ill patients. It is associated with impaired immune function and infections and to counter this should be controlled with insulin.[26] Hypoglycemia can occur if PN is stopped suddenly, particularly if lipid has been omitted from the nutrient solution.

Hepatobiliary Abnormalities

Mild transient elevations in serum liver enzymes may be seen during the first month in up to two thirds of patients receiving PN. More serious chronic liver disease is reported in up to 40% of patients after several years of PN, and mortality related to liver failure does occur. Liver biopsy in patients with PN-associated liver disease shows changes including steatohepatitis, cholestasis, fibrosis, and cirrhosis. The cause of PN-related liver disease is unknown and is probably multifactorial. In some cases the underlying condition causing IF (e.g., Crohn's disease) and sepsis may be responsible. Other theories include bacterial translocation from an atrophic gut with portal endotoxemia, excess glucose and lipid energy, and specific nutrient deficiencies such as choline and carnitine. Gallbladder sludge and cholelithiasis may contribute to cholestasis. Management options include reducing glucose and lipid energy, cycling the infusion (i.e., stopping for 10 hours each day), metronidazole for bacterial overgrowth, ursodeoxycholic acid, and attempting to promote biliary flow by some enteral intake if possible. Hepatobiliary complications need to be taken seriously because if progression is allowed to occur there is a risk of liver failure, and organ transplantation may then be the only option.[27]

Table 5 Common Metabolic Complications of Parenteral Nutrition

Hyperglycemia
Hepatobiliary dysfunction
Metabolic bone disease
Refeeding syndrome

Bone Disease

Osteopenia, osteoporosis, and osteomalacia are quite common in patients receiving PN but rarely cause clinical problems in the form of fragility fracture. PN can cause a calcium wasting state through a variety of proposed mechanisms, but much of the metabolic bone disease seen is probably due to the underlying condition causing IF (e.g., short bowel, Crohn's disease, and corticosteroid therapy) and predates the use of PN. Bone density should be assessed in patients receiving long-term PN by dual-energy x-ray absorptiometry (DEXA) scanning. An adequate calcium balance should be achieved using calcium, magnesium, and phosphate supplements, and parenteral bisphosphonates can be considered in some cases.[28]

Micronutrient Deficiency

Vitamin and trace element deficiencies can result in a variety of clinical manifestations, such as night blindness in vitamin A deficiency and cardiomyopathy in selenium deficiency.[29] These were seen in the early days of PN but are now rare with the use of commercial supplement preparations and adequate monitoring.

Refeeding Syndrome

Administration of nutritional support to severely malnourished patients can result in life-threatening complications if care is not taken.[30] Sudden provision of a high glucose energy load causes an intracellular shift of electrolytes with profound hypophosphatemia, hypokalemia, hypomagnesemia, and hypocalcemia. Cardiac arrhythmias, congestive heart failure, seizures, and coma can occur as a result. To avoid these complications, attempts should be made to correct electrolyte abnormalities before initiating feeding. For the first few days the amount of fluid and energy provided should be limited (1 L, 15 kcal/kg) and electrolytes checked daily, with supplementation as needed.

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