Parenteral Nutrition

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Introduction

Protein–calorie malnutrition (PCM), which encompasses major loss of lean body mass and body fat stores, with or without concomitant depletion of essential micronutrients (vitamins, minerals, trace elements) remains common in hospitalized surgical (and medical) patients in developed countries [1–8]. The prevalence of various degree of malnutrition among total hospital admissions and in intensive care unit (ICU) settings have reported to occur in 20 % to as high as 60 % of surgical and medical patients [1–4]. Generally, the majority of surgical patients will advance to oral diet shortly after operation and require minimal nutritional intervention; however, major surgery or postoperative complications can delay advancement to a full oral diet. Eventually, the degree of PCM worsens in those patients secondary to the stress of operation, increased nutritional needs for wound healing, and increased metabolic rate related to postoperative recovery, insufficient food intake and repeated catabolic insults [4, 9–11]. PCM prior to and during hospitalization are each associated with increased morbidity and mortality, length of hospital stay, and added cost of care [9, 12–17].

As early as 1936, Studley showed that preoperative weight loss significantly increased postoperative morbidity and mortality in patients undergoing gastric surgery, independent of age, impaired cardiovascular and respiratory function, and type of operation [18]. Giner et al. later confirmed that PCM is a major determinant for developing postoperative complications [3]. In highly catabolic surgical ICU patients, PCM has been associated with increased risk for infectious complications, impaired wound healing and muscle strength, and requirements for postsurgical intubation [6, 8, 12–17, 19, 20]. Various pathophysiologic factors contribute to nutritional deficiencies among patients undergoing elective or major surgery (Table 12.1) [20]. Identifying malnourished surgical patients and provision of proper nutritional support has long been a key focus of surgical patients. Research has emphasized methods of delivery to minimize surgery-associated metabolic changes. Nutrition support can be delivered safely with specialized enteral and/or parenteral nutrition [21]. This chapter will focus on parenteral nutrition (PN), which provides fluid, calories, carbohydrate, essential and nonessential amino acids, essential fats, vitamins, trace elements, and minerals.

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Table 12.1 Pathophysiologic factors that contribute to malnutrition in surgical patients

• Diminished dietary intake prior to or after surgery (e.g., anorexia, pain, altered gastrointestinal function awaiting for bowel function to return, NPO status)
• Increased catabolic hormones and cytokines concentrations (e.g., catecholamines, cortisol, interleukins, tumor necrosis factor-α)
• Decline in anabolic hormones levels (e.g., insulin-like growth factor-I, testosterone)
• Resistance to anabolic hormones with subsequent underutilization of substrate(e.g., resistance to insulin)
• Abnormal nutritional losses (e.g., diarrhea, surgical drainage, emesis, polyuria, renal replacement therapy, wounds)
• Decreased protein synthesis secondary to decreased physical activity (e.g., bed rest, deceased ambulation, chemically-induced paralysis)
• Medication–nutrient interactions (e.g., corticosteroids, diuretics, vasopressors)
• Increased requirements for calories, protein, and/or specific micronutrient (e.g., with infection, oxidative stress, trauma, large wounds)
• Iatrogenic factors (e.g., prolonged suboptimal enteral or parenteral nutrition provision in relation to metabolic requirements)

NPO nil per os

Current Clinical Practice Guideline Overview

There is limited published data from well-designed, adequately powered intent-to-treat randomized control trials (RCTs) on PN efficacy in hospital settings [5, 6, 22, 23]. Therefore, current PN utilization in hospital patients is largely based on international guidelines by major professional societies [6, 8, 9, 24–29]. A caveat regarding efficacy of current PN practices is that no rigorous RCT has featured an unfed or minimally fed control group; thus the safe duration for minimal to no feeding in surgical patients is unknown [29]. In addition, many of the earlier studies were conducted with excessive PN caloric doses and liberal blood glucose control strategies compared to current practice today, in which lower caloric doses (20–25 kcal/kg/day) and stricter blood glucose control (140–180 mg/dL) is the standard of care. Nonetheless, current research suggests that patients with moderate to severe generalized malnutrition benefit from PN in terms of overall morbidity and possibly mortality if enteral nutrition (EN) is not possible [20, 28].

Major professional societies have outlined clinical practice guidelines for calorie and protein (as amino acids in PN) intake in hospitalized adult medical and surgical patients [6, 8, 24, 25, 28]. Guidelines for pediatric patients have been published, but are beyond the scope of this chapter [26, 27]. It is important to recognize that caloric needs in hospitalized surgical patients, especially those with critical illness, can vary significantly secondary to serial changes in clinical conditions [6, 8]. Optimal caloric and protein intake in surgical patients are not well defined due to a lack of current rigorous, randomized, controlled clinical trials [6, 8, 29, 30].

Nutritional Assessment

Complete nutritional status assessment requires incorporation of medical and surgical history, current clinical and fluid status and tempo of illness, dietary intake history, body weight history, gastrointestinal and functional status, physical examination and selected biochemical tests (Table 12.2) [20]. There is no "gold standard" for nutritional assessment in surgical patients. Commonly, serum levels of albumin and prealbumin were obtained, which can be helpful in outpatient or epidemiologic settings; however, they are neither reliable nor practical postoperation because inflammation, infection, lowered hepatic synthesis, and/or increased clearance can markedly decrease blood concentrations. Plasma levels of albumin and prealbumin are also subject to fluid status (increased with hypovolemia or decreased with hypervolemia). On the other hand, serum albumin level can be an excellent prognostic indicator, with an inverse correlation between postoperative morbidity and mortality compared with preoperative serum albumin level [31, 32]. Concentrations of specific vitamin and trace elements are useful to follow in certain at-risk patients, however their levels can fluctuate secondary to volume status, inflammation, and inter-organ shifts that require serial levels to

Table 12.2 Important steps in nutritional assessment of hospitalized surgical patients

• Assess past medical and surgical history, tempo of current illness and expected hospital/perioperative course
• Evaluate dietary intake history and previous specialized nutrition support utilization
• Review body weight changes (e.g., % weight loss from usual body weight, rate of loss)
• Complete physical examination with attention to fluid status, organ functions and evidence of protein–calorie malnutrition and skin/conjunctival/tongue lesions consistent with vitamin–mineral deficiency
• Evaluate gastrointestinal tract status to assess feasibility and tolerance for enteral feeding
• Determine ambulatory capacity, mental status
• Serial evaluation of standard blood tests (organ function indices, electrolytes, pH, triglycerides, and selected vitamins and minerals if at risk for deficiency)
• Assess calorie and protein needs
• Determine enteral and parenteral access for nutrient delivery

Patients weighing less than 90 % of their ideal body weight, those with involuntary body weight loss of >5–10 % of usual body weight in the previous several weeks or months, patients, or those with a body mass index (BMI) less than 18.5 kg/m^2 should be carefully evaluated for malnutrition

guide repletion strategies. In addition, body weight often changes markedly in relation to volume status [32].

A simple and practical bedside method known as subjective global assessment (SGA) has been validated for nutritional assessment and use as prognostic indicator of clinical outcomes in stable patients without significant fluctuation in fluid status [33, 34]. The SGA integrates various components, such as history of weight loss and food intake, functional capacity, gastrointestinal symptoms that continued >2 weeks (e.g., diarrhea, nausea, and vomiting), and physical examination (e.g., muscle or fat mass wasting, edema/ascites, wounds, hair loss, skin breakdown), to categorize the degree of malnutrition (e.g., well nourished, mildly malnourished, moderately malnourished, or severely malnourished) [33, 34]. Another method commonly used in European hospitals for evaluation of nutritional risk calculates a nutritional risk score accordingly to body mass index (BMI), percent reduction in usual food intake, body weight history, age, and severity of illness [35]. New clinical practice guidelines for the identification and documentation of adult malnutrition have recently been published by the Academy of Nutrition and Dietetics and American Society for Parenteral and Enteral Nutrition that consider key elements such as percent weight loss history, dietary energy intake history, loss of skeletal muscle and fat mass, functional status, and presence of inflammation—and which disregard circulating proteins such as albumin (given their non-specificity) or BMI [36]. A detailed comprehensive nutritional assessment outline is available as an online supplement to a recent review of PN in the critically ill patient [20].

Nutrition Support Goals

Indirect calorimetry accurately measures resting energy expenditure (REE) for hospitalized patients, but its utilization is restricted by cost, availability, and inaccuracies due to technical issues [6, 37]. REE is most commonly calculated using traditional predictive equations, such as the Harris-Benedict equation, that incorporates the patient's age, gender, height, and weight [6, 20]. Unfortunately, predictive equations may over- or underestimate REE in surgical patients secondary to changes in clinical conditions and/or fluid status [20, 37]. Current American and European clinical practice guidelines suggest an approximate caloric goal of 25 kcal/kg/day for most surgical patients, which is approximately 1–1.2 times of the measured or estimated REE. For severely stressed patients, estimated caloric needs may range higher, from 25 to 30 kcal/kg/day. Ongoing RCTs are designed to better define caloric dosing guidelines in ICU patients, as data are particularly conflicting in these settings. Prehospital and preoperative body weight should be used for calculating caloric needs because measured body weight in the hospital (especially in the ICU) may be influenced by fluid status and can be much higher than recent "dry" weight. Ideal body weight (IBW) derived from routine tables or equations can be used as an alternative when recent dry weight is not available.

For the obese patient (body weight is 20–25 % above IBW), adjusted body weight should be used to estimate energy requirements [20].

Providing adequate amino acids (protein equivalents) in PN is crucial for cell and tissue function, wound healing, and to improve net protein balance, especially after major operation. In the 1980s, studies in ICU patients showed that amino acid/protein provision at a dose greater than 2.0 g/kg/day was inefficiently utilized for protein synthesis; the excess amino acids were oxidized and contributed to azotemia [38, 39]. The commonly recommended protein dose is between 1.2 and 1.5 g/kg/day for most surgical patients with normal renal and hepatic function (i.e., 50–100 % above the recommended daily allowance (RDA) of 0.8 g/kg/day); however, a dose range of 2.0–2.5 g/kg/day is currently recommended in patients with certain severely catabolic conditions such as burns, presence of large wounds, and those receiving continuous renal replacement therapy (CRRT) [6, 8, 20, 30]. Administered doses of amino acids may need to be adjusted downward to 0.6–0.8 g/kg/day in relation to the extent and progression of renal dysfunction in the absence of dialysis treatment. In the event of acute hepatic dysfunction and hyperbilirubinemia, patients are at risk for developing amino acid-induced hyperammonia and it may be prudent to administer lower doses of amino acids (0.6–1.2 g/kg/day) in relation to the degree of acute hepatic dysfunction [6, 8, 20, 30]. Protein restriction is generally not necessary in patients with stable chronic hepatic dysfunction, but clinical judgment is required.

Timing of Parenteral Nutrition Support

Although there is limited evidence to support preoperative PN overall, some data suggest that adequate feeding of severely malnourished patients for at least 7–10 days prior to surgery and continued after surgery may decrease postsurgical morbidity [32, 40]. Delaying elective surgery for preoperative nutritional support is recommended for patients with one or more of the following conditions: lost more than 10–15 % of actual body weight within 3–6 months, BMI < 18.5 kg/m^2, SGA score grade C (severe malnutrition), serum albumin <30 g/L without hepatic or renal dysfunction, or an ideal body weight <90 % [6, 9, 25].

Although most patients, in general, can tolerate advancement of oral diet within 6–9 days after surgery, this is dependent on the type of operation (e.g., gastrointestinal), minimal or no feeding for 10–14 days after major surgery can significantly increase morbidity and mortality [9, 16]. Even a short duration of starvation or insufficient oral intake was strongly correlated with worsened surgical outcome in one study [41]. Current guidelines recommend starting nutrition support immediately after operation if patients are not expected to meet their caloric need within 7–10 days (independent of their preoperative nutritional status), have developed complications impairing the resumption of dietary intake, or under conditions that affect metabolic homeostasis or increase nutrient needs such as infectious complications [9, 25].

While it may seem intuitive that early nutritional intervention is warranted for most patients, the American Society of Parenteral and Enteral Nutrition (ASPEN) ASPEN-NIH review and others consistently suggested that early postoperative PN does not improve clinical outcomes in surgical patients, except for the severely malnourished patients [42–45]. However, a major caveat is that these conclusions were developed evaluating data from studies before the current tight control of blood glucose and when overfeeding, especially of calories, was common in surgical patients. In patients with severe malnutrition requiring parenteral feeding, administration of PN for a minimum of 7–10 days has resulted in a clinically significant decrease in both infectious and non-infectious complications [42, 45–47].

Based on existing (and still limited) data, PN, either alone or as a supplement to inadequate EN, probably should not be initiated immediately during the postoperative period in well-nourished patients, but may be delayed for 3–7 days if oral dietary intake and/or enteral nutrition (i.e., tube

feeds) are not feasible or not tolerated (especially in the ICU setting) [29, 48–50]. In a recent large unblinded multicenter study of critically ill adults in Belgium (4,640 patients, largely on surgical services), supplemental PN given to achieve caloric/amino acid goals in ICU patients unable to meet needs with EN alone was associated with modestly increased infectious morbidity and renal or pulmonary dysfunction when started 2–3 days after ICU admission compared to results when supplemental PN was delayed to day 8 after admission [48]. Length of hospital and ICU stay was also shorter in those randomized to delayed PN versus early PN but mortality indices were similar [48]. Caveats of this study, however, were that differences between the two groups were small, most patients were not significantly malnourished at entry, a large proportion of patients were studied after cardiac surgery, exclusion criteria included those who had prior to the ICU admission been receiving specialized nutrition support or were ICU readmissions, and both study groups received daily intravenous mineral, vitamins, and trace elements [29]. In a subsequent smaller study of adult ICU patients from two Swiss institutions ($n = 305$; ≈25 % from surgical services), patients who achieved <60 % of their energy intake goal via early EN (day 1 of ICU admission) were randomized to supplemental PN on day 4 and continued until day 9 of ICU stay versus administration of EN alone [49]. Supplemental PN resulted in significantly lower rates of nosocomial infection compared to the EN-alone group, without a change in mortality or length of hospital or ICU stay [49].

In a more recent multicenter trial from Australia and New Zealand, 1,372 adult ICU patients were randomized to pragmatic standard nutritional care (time to begin EN and/or PN ≈3 days after admission) versus early PN initiated immediately after ICU admission, with EN advanced and PN weaned as tolerated [50]. Early PN resulted in significantly fewer days of mechanical ventilation and less muscle and fat loss, but otherwise there were no differences between groups in mortality, infections, organ function, or length of ICU or hospital stay [50]. Of note, current practice guidelines (CPGs) of ASPEN recommend delaying initiation of PN until day 8 in well-nourished ICU patients, but not to delay attempts to meet nutritional goals in patients with PN in ICU patients with preexisting significant malnutrition [6].

ASPEN CPGs recommend the following: (1) patients with moderate to severe malnutrition scheduled for major GI surgery should receive 7–14 days of preoperative nutritional support (as PN if EN not possible) if surgery can be safely delayed and (2) PN should routinely be prescribed in the "immediate" postoperative period for patients undergoing major GI surgery unable to tolerate EN and inadequate oral nutrition is anticipated for 7–10 days [9].

Indications

Perioperative PN is generally indicated only for patients who are severely malnourished and cannot be adequately fed by mouth or EN [25]. In settings when EN either not feasible or tolerated, PN is probably indicated for the following patients: (1) after major upper GI surgery when the GI tract is not accessible or not functioning (e.g., mechanical obstruction, paralytic ileus); (2) after extensive small bowel resection with or without colonic resection; (3) with perforated small bowel; (4) with high-output (>600 mL) and/or proximal fistulas that necessitate bowel rest; and (5) other conditions leading to prolonged EN intolerance (e.g., severe diarrhea, persistent emesis, significant abdominal distention, acute GI bleeding, hemodynamic instability, impaired gastric emptying, or paralytic ileus) preventing sufficient EN provision for >3–7 days [6, 8, 20]. No data to date to support withholding PN in patients with preexisting PCM who cannot tolerate EN. However, starting supplemental PN before this 7–10 day period in the patient already on EN does not improve outcome and may be detrimental if not carefully administered in light of potential metabolic and infectious complications [47]. PN is contraindicated (not evidence based) for the following patients: (1) those with functional GI tract and accessibility for EN; (2) fluid restricted patients who cannot tolerate the

intravenous fluid load provided for PN; (3) those with severe hyperglycemia or electrolyte abnormalities at the planned day of PN initiation; (4) PN therapy is unlikely to be given for >5–7 days; and (5) if new access line placement solely for PN causes unnecessary risks [6, 8, 20].

Administration

Complete PN solutions, can be administered through a peripheral or central vein. The choice of venous access and catheter type for PN mainly depends on the anticipated duration of therapy. For short-term PN needs (<14 days), peripheral intravenous IV lines can be used for 10–14 days if the patient can tolerate the required fluid load to meet amino acid and energy needs. In our service, a central vein PN is required and is deemed to be needs for 30 days or less, a percutaneous non-tunneled central venous catheter (PICC) can be used [9, 32]. When long-term PN is required, a tunneled, cuffed, silicone catheter is preferred (not evidence based). Table 12.3 outlines a comparison of peripheral and central vein PN, as well as fluid, macronutrient and micronutrient content. Due to risk of phlebitis with hypertonic central vein-type PN formulations, peripheral vein PN (PPN) provides low amount of dextrose (5 %; dextrose = 3.4 kcal/g) and amino acids (≤3 %; 4 kcal/g) and a larger proportion of calories as lipid emulsion (≤5 %; 10 kcal/g; 50–60 % of total calories) [9, 32]. PPN usually requires a 2–3 L/day fluid volume to provide adequate protein and calorie needs (based on patient body size), which limits its use for ICU patients and those require fluid restriction due to cardiac, hepatic, and/or renal dysfunction. In contrast, central venous PN (CPN) is delivered through the superior vena cava, which permits hypertonic CPN infusions. Thus, CPN can be the concentrated complete solutions (1–1.5 L/day), while meeting caloric and protein need for vast majority of patients. Non-PN hydration fluid rate should be proportionally adjusted in accordance of fluid status when PN is initiated [48–50].

Table 12.3 Parenteral nutrition (PN) indications in relation to the feasibility of enteral nutrition (EN)

Absolute contraindications for EN:
– Intestinal obstruction
– Ischemic bowel
– Acute peritonitis
Relative contraindications for EN: (use PN if EN deemed to be not feasible)
– High output fistulas
– Severe malabsorption
– Septic shock with impaired splanchnic perfusion
– Fulminant sepsis

PN electrolyte dosing is adjusted as needed to maintain normal serially measured serum levels. With high and/or low blood levels of specific electrolytes, daily dose adjustment may be required until serum levels are within the normal range. Higher dextrose concentrations in CPN may result in increased requirements for potassium, magnesium, and phosphorus. The relative percentage of sodium and potassium salts as chloride and acetate is increased to correct metabolic alkalosis and metabolic acidosis, respectively [6, 9, 32]. The most recent clinical practice guidelines recommend a glycemic goal range in hospitalized adult patients receiving nutrition support to be 140–180 mg/dL (7.8–10 mmol/L) [51]. Glycemic goals can be achieved by addition of regular insulin in PN and/or reduction of dextrose load in CPN as needed. Separate intravenous insulin drips are commonly utilized to prevent hyperglycemia in ICU settings [20, 32, 51].

Commercially available amino acid formulation used in PN provides all nine essential and several non-essential amino acids [20]. Although now controversial, European, but no American, guidelines recommend routine addition of glutamine in critically ill patients given the evidence that glutamine may become conditionally essential in certain catabolic patients [6, 8]. Although numerous small, randomized controlled trials (RCTs) suggest clinical benefits of PN supplemented with glutamine [52–54], several larger RCTs have recently shown that glutamine-containing PN does not improve clinical outcomes [55–57]. Amino acid concentration in PN may need to be adjusted downward or upward in relation to requirements as a function of the

severity of azotemia or hyperbilirubinemia in patients with renal and hepatic dysfunction, respectively. PN also contains intravenous lipid emulsions (LE) as a source of both energy and essential linoleic and α-linolenic fatty acids [32]. Soybean oil-based LE is the long-standing commercially available formulation in the USA, although a mixed lipid emulsion containing 80 % olive oil and 20 % soybean oil was recently approved for adults requiring PN. In Europe and other countries, intravenous soybean oil/medium-chain triglyceride mixtures, fish oil, olive oil/soybean oil mixtures, and combinations of oils are available for use in PN. Recent systemic reviews of alternative oil-based lipid emulsion may be associated with clinically important (but not statistically significant) reductions in mortality, ventilation days, and ICU length of stay when compared to PN containing soybean oil-based lipid emulsion in critically ill patients [58]. However, a recent double blind, randomized, controlled study in 100 mixed medical and surgical ICU patients found no differences in clinical outcomes in patients receiving PN containing soybean oil-based lipid emulsion versus the group receiving PN containing the recently approved olive/soybean oil product [59].

Lipid is typically mixed with dextrose and amino acids in the same PN infusion bag ("all-in-one" solution) and given with PN over 16–24 h [32]. Lipid emulsions may also be use as a separate infusion over 10–12 h. The maximal recommended dose of lipid emulsions infusion is 1.0–1.3 g/kg/day, with monitoring of blood triglyceride levels at baseline and then approximately weekly and as indicated to assess clearance of intravenous fat [9, 20, 28]. Triglyceride levels should be maintained below 400–500 mg/dL by lowering lipid emulsion concentration in PN to decrease risk of pancreatitis and diminished pulmonary diffusion capacity in patients with severe chronic obstructive lung disease. A typical central venous PN provides 60–70 % of non-protein calories as dextrose and 30–40 % of non-protein calories as LE [6, 8, 20, 28, 29, 32].

Specific needs for intravenous vitamins and minerals have not been rigorously defined for hospitalized patients [5, 8, 20, 28, 32]. Therefore, standardized intravenous preparations of combined vitamins and minerals have been added in PN to maintain normal blood levels in most stable patients (Table 12.3). However, several studies show that a significant proportion of critically ill patients receiving standard nutrition support may variously experience zinc, copper, selenium, vitamin C, vitamin E, and vitamin D deficiencies [5, 32]. Low micronutrient levels can be related to pre-ICU depletion; increased requirements possibly secondary to oxidative stress associated with critical illness, and increased excretion and/or tissue redistribution [5, 32]. Depletion of these essential nutrients may impair antioxidant capacity, immunity, wound healing, and other important body functions. Thus, as with electrolytes, therapy is directed at maintaining normal blood levels, with serial measurements in blood as clinically and biochemically indicated.

PN formulations can be individually compounded under a sterile hood in an IV pharmacy by trained pharmacy technicians and/or pharmacists; however, PN is available commercially as a "premixed" of the standardized solutions. An infusion pump to regulate delivery rates administers PN and the infusion catheters incorporate in-line filter to prevent microbial contamination [32].

Complications and Monitoring

Administration of PN has been associated with infectious, mechanical, and metabolic complications [20, 25, 28, 32]. Catheter-related bloodstream infections can occur. Mechanical complications are mainly related to insertion and use of central venous catheters, such as pneumothorax, hemothorax, thrombosis, and bleeding. Proper and safe administration of both peripheral and central vein PN requires strict catheter care protocols, including use of designated catheter ports for PN administration and subclavian vein insertion sites for central venous PN [9, 20, 25, 28, 32].

Potential metabolic and clinical consequences of overfeeding and refeeding syndrome during PN in critically ill patients are shown in Table 12.4 [20, 32]. High caloric, dextrose, amino acid, and fat loads ("hyperalimentation") are readily

Table 12.4 Sample formulations of typical peripheral and central parenteral nutrition

Component	Peripheral vein PN	Central vein PN
Volume (L/day)	2–3	1–1.5
Dextrose (%)	5	10–25
Amino acids (%)	2.5–3.0	3–8
Lipid (%)	2.5–5.0	2.5–5.0
Sodium (mEq/L)	50–150	50–150
Potassium (mEq/L)	20–35	30–50
Phosphorus (mMol/L)	5–10	10–30
Magnesium (mEq/L)	8–10	10–20
Calcium (mEq/L)	2.5–5	2.5–5
Multivitamins (mL/day)[a]	10	10
Trace elements/minerals (mL/day)[b]		

[a]Multivitamins are consisted of vitamins A, B_1 (thiamine), B_2 (riboflavin), B_3 (niacin), B_5 (pantothenic acid), B_6 (pyridoxine), B_9 (folate), B_{12} (cobalamin), C, D, and E, biotin, and with or without vitamin K. Specific vitamins such as vitamin B_1, B_6, B_9, B_{12}, C, and K, are available as individual supplement

[b]Trace elements/minerals consisted of chromium, copper, manganese, selenium, and zinc in various concentrations. Only copper, selenium, and zinc are available as individual supplement

Table 12.5 Potential complications of overfeeding and refeeding syndromes in patients receiving parenteral nutrition

- Intracellular shift of magnesium, phosphorus, and/or potassium (due to: excess dextrose; refeeding hyperinsulinemia)
- Immune cell dysfunction and infection (due to: hyperglycemia)
- Cardiac dysfunction or arrhythmias (due to: excess fluid, sodium and other electrolytes; intracellular/extracellular shift of electrolytes related to refeeding)
- Neuromuscular dysfunction (due to: thiamine deficiency; electrolytes shifts due to refeeding)
- Renal dysfunction or azotemia (due to: excess amino acid; inadequate caloric provision relative to amino acid dose)
- Edema or fluid retention (due to: excess fluid and/or sodium; refeeding hyperinsulinemia)
- Elevated liver function tests and/or hepatic steatosis (due to: excessive calorie, dextrose or fat content)
- Increased blood ammonia levels (due to: excessive amino acids provision with hepatic dysfunction)
- Hypercapnia (due to: excessive total caloric provision)
- Respiratory insufficiency (due to: refeeding-associated hypophosphatemia; excess fluid, calorie, carbohydrate or fat content)
- Hypertriglyceridemia (due to: excessive carbohydrate or fat provision; carnitine deficiency)

administered via central vein. While not the standard of care per current guidelines, excess dextrose, fat, and overall calorie administration remains a common practice in some centers [9, 20, 25, 28, 32]. Risk factors for PN-associated hyperglycemia include: (1) use in obese, diabetic, and/or septic patients; (2) poorly controlled blood glucose at PN initiation; (3) initial use of high dextrose concentrations (>10 %) or dextrose load (>150 g/day); (4) insufficient insulin administration and/or inadequate monitoring of blood glucose; and (5) concomitant administration of corticosteroids and vasopressor agents.

Electrolyte administration requires careful monitoring and generally day-to-day adjustment in PN to maintain normal blood levels. Overfeeding can induce several metabolic complications of varying degrees of severity affecting several organ systems (Table 12.5) [20, 32]. A recent large study found that PN use per se; overfeeding and sepsis were the major risk factors for liver dysfunction in critically ill patients [60]. Thus, PN should be advanced carefully to goal rates and the composition adjusted as appropriate based on the results of close metabolic and clinical monitoring performed daily. The calories provided by dextrose present in non-PN intravenous fluids, the soybean oil lipid emulsion carrier of propofol, a commonly used ICU sedative, and the nutrients provided in any administered EN must be taken into account in the PN prescription to avoid overfeeding [32].

Refeeding syndrome is well recognized and relatively common in at-risk patients (preexisting malnutrition or electrolyte depletion; prolonged periods of intravenous hydration therapy alone) [20, 61, 62]. Refeeding syndrome is mediated by administration of excessive intravenous dextrose (>150–250 g or 1 L of PN with 15–25 % dextrose). This markedly stimulates insulin release, which may rapidly decrease blood potassium, magnesium, and especially phosphorus concentrations due to intracellular shift and utilization in metabolic pathways. High doses of carbohydrate increase thiamine utilization and can precipitate symptoms of thiamine deficiency. Hyperinsulinemia may cause sodium and fluid

retention by the kidney. This, together with decreased blood electrolytes (which can cause cardiac arrhythmias) can result in heart failure, especially in patients with preexisting heart disease [61, 62]. Prevention of refeeding syndrome requires identification of at-risk patients, use of initially low PN dextrose concentrations (e.g., 1 L of PN with 10 % dextrose), provision of higher PN doses of potassium, magnesium, and phosphorus, based on initial and adjusted on serial blood levels within the first several days of PN administration, and renal function, and supplemental PN thiamine (e.g., 100 mg/day for 3–5 days) [20, 61, 62].

Consultation with an experienced multidisciplinary nutrition support team for recommendations regarding the PN prescription is ideal when such personnel are available. Nutrition support team daily monitoring has been shown to reduce complications, costs and to decrease inappropriate use of PN [63, 64]. Research shows that patients in need of nutritional support attain more energy, are more closely monitored and have fewer complications when treated by a multidisciplinary nutrition support team compared to non-team approach. Team approach results in improved patient care, and therapeutic and economic benefits.

Monitoring of PN therapy in the hospital setting requires daily assessment of the multiple factors outlined in Tables 12.1 and 12.2. Blood glucose should be monitored several times daily and blood electrolytes and renal function tests should be determined generally daily [20, 32]. Blood triglyceride levels should be measured at baseline and then weekly until stabile. Although guidelines are few, some centers routinely monitor periodic blood levels of copper, selenium, zinc, thiamine, vitamin B6, vitamin C, and 25-hydroxyvitamin D [20]. Liver function tests should be measured at least a few times weekly. pH should be monitored generally daily in ventilated patients when arterial blood gas pH measurements are available [20, 32].

Home Parenteral Nutrition

Home parenteral nutrition (HPN) was introduced as treatment option in 1967 primarily for patients with long-term intestinal failure [65]. HPN can be a life-saving or life-extending therapy. The goal of HPN is to prevent and/or correct malnutrition for a period of months or the rest of one's life. The HPN is commonly indicated for patients with Crohn's disease, mesenteric vascular disease, cancer, intestinal failure, and radiation enteritis who cannot meet their nutritional needs by EN, and who can be treated outside the acute care setting [66, 67]. Intestinal failure in surgical patients can be caused by obstruction, dysmotility, and surgical resection. Current practice guidelines recommend clinicians to identify a minimal expected duration of therapy before initiating HPN, and are not recommended for patients with a short life expectancy for at least 40–60 days [66]. HPN is delivered via subcutaneously tunneled catheters or implanted ports. HPN is usually given overnight (cyclic) to maintain the patients' freedom of movement during the day.

HPN therapy is not without risks. Thrombosis and catheter occlusion for occur while patients receiving HPN, but catheter-related infections are most problematic. Liver dysfunction and metabolic bone disease are also common complications related to long-term PN. The prevalence of catheter-related bloodstream infections ranges between 0.16 and 1.09 episodes per catheter years, as much as 13.2 episodes per 1,000 catheter days [56]. A PICC can be used for short-term PN, however, it has been associated with an almost twofold increased risk of infection when compared to subcutaneously tunneled catheters or implanted ports [67]. Currently there is no evidence to recommend the use of PICC for HPN [68]. To minimize these complications, several factors (e.g., medical, emotional, financial, and functional capabilities of the patients and caregivers) are considered before deciding that HPN is the appropriate treatment for patients and require careful monitoring. Recent data strongly suggest that ethanol locks, which must be administered via a silicone catheter (i.e., not via a plastic PICC), may markedly reduce PN-associated bloodstream infections, presumably by clearing microbe-containing biofilm on the catheter [69]. All available guidelines recommend routine monitoring by a multidisciplinary nutrition support team to minimize complications [66].

Conclusion

The optimal timing for EN and PN intervention in surgical patients remain major areas of uncertainty. Little prospective data is available on the clinical effects of minimal or no feeding over time (e.g., >7 days), and such data are unlikely to be forthcoming given difficulty in recruiting for such studies and in blinding [20, 29]. Rigorous RCTs are needed to define optimal caloric and protein dose regimens in subgroups of ICU patients [20, 48–50]. Some studies show that larger doses of standard soybean oil-based intravenous fat emulsions induce pro-inflammatory and pro-oxidative effects and possibly immune suppression [70]. However, conflicting results of small RCTs comparing soybean oil-based lipid emulsion with other types of lipid emulsion have not clarified optimal use. Available data suggests that the glutamine may become a conditionally essential amino acid in subsets of ICU patients, although conflicting data have been published recently [52–57]. Phase III level double-blind, intent-to-treat RCTs are needed in specific ICU patient subgroups to define clinically optimal calorie, protein/amino acid, and specific vitamin and mineral requirements, as well as efficacy of supplemental PN combined with EN to achieve caloric and protein/amino acid goals [6, 8, 20, 29, 71]. Large, multicenter RCTs are in progress and will help to define optimal use of PN in both medical and surgical over the next several years.

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