Abstract

- **Objective:** To discuss the role of parenteral nutrition (PN) support in the care of critically ill patients.
- **Methods:** Review of the literature.
- **Results:** Malnutrition is highly prevalent among hospitalized patients, with critically ill patients being at higher risk. To attenuate the complications experienced in this patient population, enteral nutrition (EN) and PN are used as nonvolitional nutrition support. Meta-analyses that compare EN with PN in critically ill patients show reduced infectious complications with EN. However, some evidence points to a mortality benefit for PN. Findings indicate that PN can be used as an adjunct to EN for improving nutritional delivery.
- **Conclusion:** Future studies are warranted to define the emerging role of PN in nutrition support.

Malnutrition is highly prevalent among hospitalized patients, with reported rates approaching 50% among general medicine patients [1,2] and 43% among intensive care unit (ICU) patients [3]. The risk of malnutrition is heightened in patients who are critically ill. Studies show an association between poor nutritional status and morbidity and mortality. In a prospective observational study of 50 ICU patients, Dvir et al [4] showed that patients receiving mechanical ventilation for over 96 hours accrued a mean cumulative negative energy balance of 4767 kcal during their ICU stay, with 22% of these patients having a negative caloric balance exceeding 10,000 kcal. The degree of negative energy balance was significantly correlated with the incidence of complications, including adult respiratory distress syndrome, sepsis, and renal failure. A prospective study of 57 selected surgical patients at risk for multiple organ failure showed that cumulative caloric deficit measured by indirect calorimetry at the time of hospital discharge was associated with increased mortality risk [5]. Nonvolitional nutrition support (ie, enteral [EN] and parenteral nutrition [PN]), has traditionally been used in the critically ill population to provide exogenous fuels to support the patient during the stress response [6]. It is now also seen as a proactive therapeutic strategy to improve patient outcomes [7].

Nonvolitional nutrition support is generally indicated for critically ill medical or surgical patients who will be unable to tolerate oral nutrition for 5 days. EN is the mainstay of nonvolitional nutritional support and is primarily indicated for patients who have a functional gastrointestinal (GI) tract but for whom oral intake is impossible, inadequate, or unsafe. EN is provided by tube feedings, described according to the anatomic feeding site: nasogastric, nasoduodenal, nasojejunual, gastrostomy, or jejunostomy. EN is conventionally viewed as preferable to PN as it is less expensive, more physiologic, and less likely to be associated with biliary stasis and hyperglycemia [8]. While few studies have shown differences in mortality between the 2 modalities, EN is associated with reduced infectious morbidity.

PN is indicated for patients with a nonfunctioning or inaccessible gastrointestinal tract and for patients who have failed an EN trial. PN is given as either central parenteral nutrition when the central venous catheter access lies at the junction of the superior vena cava and right atrium or peripheral parenteral nutrition. The Table lists the general contraindications for EN and PN in adults.

Clinical Evidence

Two meta-analyses comparing PN with standard care (oral diet plus intravenous dextrose) in critically ill and surgical patients have shown that PN does not influence overall mortality rate, although it may reduce the complication rate among malnourished patients [9,10]. The 2009 guidelines of the Society of Critical Care Medicine and American Society for Parenteral and Enteral Nutrition (ASPEN) on nutrition support therapy in the critically ill adult recommend PN over standard care in patients who are malnourished on admission and EN is not feasible [6].

A number of meta-analyses are available that compare EN with PN in critically ill patients [10–14]. They all show...
reduced infectious complications with EN. However, some evidence points to a mortality benefit for PN. Simpson et al [14] included trials with complete follow-up data, allowing the authors to conduct an intention-to-treat analysis. The authors compared PN with both early EN (defined as feeding within 24 hours of ICU admission or injury, 6 studies) or late EN (3 studies). While the authors found no difference in mortality between PN and early EN recipients, they found a statistically significant mortality benefit in favor of PN versus late EN (odds ratio, 0.29 [95% confidence interval, 0.12–0.70]; P = 0.006). The findings suggest that PN should be used in patients for whom EN cannot be initiated within 24 hours of ICU admission.

In addition to the systematic reviews, a study by Woodcock et al [15] compared PN and EN. A total of 562 patients were assigned to 1 of 4 groups. Group 1 patients (n = 267) had inadequate GI function and were given PN. Group 2 patients (n = 231) had adequate GI function and were given EN. In 64 patients, there was clinical uncertainty of GI function; these patients were randomized to either PN (group 3) or EN (group 4; both, n = 32). The rate of adequate nutritional intake was higher in group 3 compared with group 4 (75% vs. 21.9%), and patients in this group had fewer complications related to nutritional delivery. Mortality was greater in both EN groups than in the PN groups, and no difference in rates of septic morbidity was seen.

There are limitations to the evidence comparing EN and PN. Thompson [16] suggests the findings are methodologically limited for clinical interpretation because they artificially combine heterogenous patient populations, limiting generalizability. In addition, these studies provide fixed intervention “menus” rather than individualized approaches to nutritional support as would occur in the setting of patient management. Another methodological limitation involves the ascertainment of clinical infections, as some studies report the total number of positive blood cultures rather than the number of patients with a positive blood culture. In addition, as the specific infections acquired may not be reported, the clinical importance of the differences in infections rates is open to interpretation.

**PN as Adjunctive Therapy**

Published reports describe difficulty in achieving adequate nutrient delivery with EN [17–19], with an average reported caloric intake as low as 50% of target. In a prospective observational study of 59 ICU patients, O’Meara et al [19] found that EN feedings were interrupted 27.3% of the time. Reasons for interruption included problems with small-bore feeding tubes, residual volumes and weaning, radiological procedures, preparation for surgery, shock, and bathing.

PN has been shown to increase nutritional delivery when used as an adjunct to EN. In a randomized controlled study of 120 ICU patients receiving EN, the 2 arms were assigned to either EN plus PN or EN plus placebo for 4 to 7 days, with a goal of achieving 25 kcal/kg/day [20]. Ninety-eight percent of patients receiving EN plus PN met this goal compared with 57% receiving EN with placebo. However, there were no differences in infection rate, ICU length of stay, or mortality. The use of EN with PN was also associated with a decreased length of hospital stay (31.2 vs. 33.7 days, P = 0.002).

A randomized clinical trial with 50 ICU patients by Anbar et al [21] assessed the effect of EN vs. EN plus PN to achieve measured energy needs balance. During this study, the PN intervention group had a positive 1888 kcal balance while the control group had a negative 2904 kcal balance. Although no difference was noted in ICU outcomes, the intervention group had a shorter length of hospital stay and lower mortality rate (26 vs. 52 deaths, P < 0.02).

**Improvements in PN Safety**

PN poses a risk for infections, which can result from colonization of the device (ie, catheter-related) or contamination of the infusate [22]. A prospective study of 1098 patients with central venous catheters (although not specifically receiving PN) showed bloodstream infections occurred in 2.7% of patients, of which 45% were extraluminal, 26% were intraluminal, and 29% were of unknown source. Catheter care has been shown to effectively reduce PN catheter-related infections [23].

Another concern with the use of PN is the risk of adverse events related to compounding—the process of customized

---

**Table. General Contraindications for Enteral and Parenteral Nutrition in Adults**

<table>
<thead>
<tr>
<th>Enteral</th>
<th>Parenteral (central)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonoperative gastrointestinal mechanical obstruction</td>
<td>Functional gastrointestinal tract</td>
</tr>
<tr>
<td>Intractable vomiting/diarrhea</td>
<td></td>
</tr>
<tr>
<td>Short-bowel syndrome*</td>
<td></td>
</tr>
<tr>
<td>Paralytic ileus</td>
<td></td>
</tr>
<tr>
<td>High-output fistulas</td>
<td></td>
</tr>
<tr>
<td>Severe gastrointestinal bleed</td>
<td></td>
</tr>
<tr>
<td>Severe gastrointestinal malabsorption†</td>
<td></td>
</tr>
<tr>
<td>Mesenteric ischemia</td>
<td></td>
</tr>
<tr>
<td>Inability to gain access to gastrointestinal tract</td>
<td></td>
</tr>
<tr>
<td>When need is expected &lt; 5 to 7 days for malnourished patients</td>
<td></td>
</tr>
</tbody>
</table>

Adapted from reference 6.

*May be an indication if intent is to enhance intestinal adaptation.

†Depends on the nature of the malabsorption.
combining, mixing, or altering ingredients adhering to the U.S. Pharmacopeia (USP) 797 compounding guidelines. Findings from an ASPEN survey on PN ordering and compounding showed significant variation in the manner in which PN is ordered and labeled [24]. Forty-six percent of respondents reported adverse events related to PN, with 25% resulting in harm. 

A study by Flynn et al [25] found a mean compounding error rate of 9% with PN compounding errors noted to be the highest (26%) of all products. Data submitted to USP’s 2 medication error reporting programs indicate compounding errors involving PN appear to be more frequent and of greater severity than for other products. A 2004 MEDMARX report showed a total of 2519 PN errors, of which 4.4% showed patient harm compared with a 2.5% overall harm rate for all MEDMARX error reports [26]. Similarly, the Medication Errors Reporting (MERS) program showed the PN harm rate was 18%, compared with 14% in cases overall. A 2008 MEDMARX report shows 60% of injection compounding errors involved PN [27]. Based on these findings, suggestions for improved PN safety include standardized order forms, validation of hospital compounding, policies for outsourcing, visual inspection of PN bags, and improved catheter care policy [6].

Findings suggest that PN errors could be potentially reduced by decreasing the number of preparation steps and dose calculations available in ready-to-use products [25]. Banchik et al [28] conducted a retrospective study in 100 patients to assess PN formula substitution with a multichamber bag consisting of dextrose and amino acids with a 20% lipid solution added if needed. Formulas were matched by nutrition content and volume. Nutrient delivery was similar for the compounded versus multichamber bag (total calories/day, 1784 vs. 1803; g protein/day, 83 vs. 83; g carbohydrate/day, 290 vs. 316; P < 0.001; g lipids/day, 228 vs. 194; P = 0.0075). Increased volume may preclude multichamber bag use in fluid-restricted patients (1665 vs. 1920 mL/day). Similarly, a study comparing standardized PN formulas with customized formulas found a higher percentage of laboratory electrolyte tests were within normal limits among standardized PN versus customized PN recipients (73% vs. 67%) [29]. The use of multichamber-bag PN formulas appears to be widely accepted in Europe, with more than 80% of standard PN formulas provided by multichamber bags in Switzerland and France [30].

Conclusion
PN is an important modality for delivery of nonvolitional nutrition support therapy in the critically ill. Current findings from randomized trials and meta-analyses suggest PN may have a niche role as an adjunct to EN for improving nutritional delivery, providing it is administered judiciously and with due care. Future studies are warranted to define the emerging role of PN in nutritional support.

Corresponding author: David Alexander Leaf, MD, MPH, Div. of GIM, 111G Greater Los Angeles VA Healthcare System, Wilshire & Sawtelle Blvds. Los Angeles, CA 90073, david.leaf@med.va.gov.

References


