Significant Published Articles for Pharmacy Nutrition Support Practice in 2017

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Abstract

Purpose: The purpose of the article is to assist the pharmacist engaged in nutrition support therapy in staying current with pertinent literature. **Methods:** Several clinical pharmacists engaged in nutrition support therapy compiled a list of articles published in 2017 considered important to their clinical practice. The citation list was compiled into a spreadsheet where the author participants were asked to assess whether the article was considered important to nutrition support pharmacy practice. A culled list of publications was then identified whereby the majority (at least 5 out of 8 authors) considered the article to be of significance. Guideline and consensus articles from professional organizations, important to practice but not scored, were also included. **Results:** A total of 95 articles were identified; six from the primary literature were voted by the group to be of high importance. An additional 13 organizational guidelines, position, recommendation, or consensus papers were also identified. The top-ranked articles from the primary literature were reviewed. **Conclusion:** It is recommended that pharmacists engaged in nutrition support therapy be familiar with these articles as it pertains to their practice.

Keywords

consensus, enteral nutrition, guidelines, outcomes, parenteral nutrition

Staying current with the literature is an essential requirement for maintaining an evidence-based clinical practice.¹ Staying current, within a specialized field such as nutrition support, has become even more challenging as many institutions have adopted an integrated practice model whereby the clinical pharmacist provides pharmacotherapy services in addition to specialized services. Clinicians are held accountable for staying current within numerous therapeutic areas that interface with their clinical practice. Because nutrition support therapy is integrated within differing clinical practices, it is a daunting task for one individual to screen the abundance of information from numerous journals each month to seek out those clinical studies, position papers, or clinical guidelines that may enhance or change current clinical practice in pharmacy nutrition support. Over the past few years,^{2–4} as clinicians who practice full-time or part-time in pharmacy nutrition support, it has been our intent to provide a yearly source of new literature important to pharmacy nutrition support practice. This article identifies and discusses significant articles that were published in 2017.

Methods

To assist pharmacy clinicians engaged in nutrition support in staying current with the most pertinent literature, the

principal author participant of this articles (R.N.D.) invited 7 clinical pharmacists to participate in this project. The potential author participants were invited based on the principal author's perception of their active involvement in the field as supported by their educational, research, or professional committee involvement in pharmacy nutrition support, particularly in the American Society for Parenteral and Enteral Nutrition (ASPEN). All authors are board certified. Four author participants are board certified solely in pharmacy nutrition support, whereas others are certified in areas whereby nutrition support is part of their practice or

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have multiple board certifications. The duration of individual practice experience of the group members ranges from 3 years to more than 30 years post-training. Members of this authorship group have advanced practice roles with direct patient care responsibilities for prescribing parenteral nutrition (PN) and/or enteral nutrition (EN), laboratory analysis, and pharmacotherapy integrated with nutrition therapy (eg, fluid and electrolytes, vitamins, trace elements, prokinetic drugs, insulin, antidiarrheal and laxative therapy), and some have administrative or supervisory roles with respect to nutrition support therapy. This authorship group has a broad range of practice experiences. Most authors are acute care-based, but some have long-term care (home PN and EN) responsibilities. Current practices of the group range from pediatrics to geriatrics. Some members have a diverse patient population, whereas others practice within a focused patient population (e.g., pediatrics, oncology, trauma/thermal injury).

The author participants were asked to by the principal author (R.N.D.) to provide citations of articles published from January 2017 to December 2017 that they have personally accumulated which resulted in a change or affirmation of their current clinical practice or that they considered to be important for future clinical practice. Only those articles available in print format were allowed for potential inclusion. Articles available only in preprint electronic format (with intention of publication by the journal in 2018 or later) were not evaluated. The citation list was compiled into a spreadsheet where the author participants were asked to denote whether the article was considered important to pharmacy nutrition support practice. An abstract and complete citation of each article was provided along with the electronic scoring spreadsheet to assist the author participants with the evaluation process. To ensure an independent voting process without influence from the other participant members, only the principal author participant was aware of others' rankings. To prevent influence from the other author participants on the principal author, scoring of all the articles by the principal author was completed prior to review of the results from the other contributors. The votes were tallied. The article was considered important if at least 5 out of 8 participants voted for an article to be of high priority in its relevance to pharmacy nutrition support practice. From this scoring system, a culled list of the most important articles was created.

Results

A total of 95 articles were collectively collated for initial evaluation by the authorship group. Eighty-two articles were from the primary literature and scored by the authorship group. An average of 17 articles (range: 9-25) were denoted as significant by individual members of the author group. According to a majority consensus vote, 6 articles from the primary literature collective were identified as

most important for pharmacy nutrition support practice (Table 1). One additional article, that received 4 votes, was included in Table 1 but was not critically evaluated because a majority consensus was not achieved. An additional 13 articles comprising of organizational guidelines, consensus, recommendation, and position papers were not evaluated or scored but were automatically included separately as important articles to our practice. Of these 20 finalist publications, 6 were published in *Journal of Parenteral and Enteral Nutrition*, 5 were from *Clinical Nutrition*, and 3 were published in *Nutrition in Clinical Practice*. The remaining 6 articles were from 5 different journals. Individual rankings, based on relevancy to pharmacy nutrition support clinical practice according to the author participant group, are given in Table 1. The finalist articles from the primary literature are summarized in the discussion along with a narrative regarding their implications for pharmacy nutrition support practice. A narrative regarding guidelines, position, recommendation, and consensus papers was not provided but are listed in Table 2. All remaining citations from the primary literature individually received ≤ 3 votes as significant by the group and are provided in an online supplement.

Discussion

1. Compher et al: Greater protein and energy intake may be associated with improved mortality in higher risk critically ill patients: a multicenter, multinational observational study.⁵

The optimal protein and energy dose in critically ill patients remains controversial due to conflicting study results. It has been suggested that critically ill patients at higher nutrition risk are more likely to benefit from enhanced delivery of protein and energy and the NUTrition Risk in the Critically Ill (NUTRIC) score has been designed to help identify these patients. This observational study aimed to determine whether protein or energy intake interacts with high versus low NUTRIC scores to impact 60-day mortality or time to discharge alive (TDA). Data were taken from the International Nutrition Survey 2013 database, previously used to evaluate the impact of prescribed protein on mortality and TDA.²⁵ The study included patients in the intensive care unit (ICU) for at least 4 days ($n = 2853$), with subset analysis of those patients who remained in the ICU for at least 12 days ($n = 1636$). Interleukin-6 (IL-6) was unavailable and was omitted from the NUTRIC score. The NUTRIC scores ≥ 5 were considered high nutrition risk, while patients with scores < 5 were considered low risk. The majority (about two-thirds) of patients were medical ICU and the mean NUTRIC score was 4.8 in both samples.

In the 4-day sample, protein and energy intake did not significantly interact with NUTRIC category in mortality

Table 1. Rankings of Significant Articles for Pharmacy Nutrition Support Practice.

	Title	No. of authors who indicate high importance ^a
Compher ⁵	Greater protein and energy intake may be associated with improved mortality in higher risk critically ill patients: a multicenter, multinational observational study	6
Bochicchio et al ⁶	Results of a multicenter prospective pivotal trial of the first inline continuous glucose monitor in critically ill patients	5
Braunschweig et al ⁷	Role of timing and dose of energy received in patients with acute lung injury on mortality in the Intensive Nutrition in Acute Lung Injury Trial (INTACT): a post hoc analysis	5
Diamond et al ⁸	Preventing the progression of intestinal failure-associated liver disease in infants using a composite lipid emulsion: a pilot randomized controlled trial of SMOFlipid	5
Wischmeyer et al ⁹	A randomized trial of supplemental parenteral nutrition in underweight and overweight critically ill patients: the TOP-UP pilot trial	5
Zaloga et al ¹⁰	Safety and efficacy of subcutaneous parenteral nutrition in older patients: a prospective randomized multicenter clinical trial	5
Yeh et al ¹¹	Implementation of an aggressive enteral nutrition protocol and the effect on clinical outcomes	4 ^b

Note. Articles were listed in descending order by the number of author contributors who indicated that they were of high importance followed by alphabetical order of the last name of the first investigator or author.

^aOut of a total of the 8 participating authors evaluating these articles.

^bThe only article with 4 authors who indicate high importance. All remaining articles outside of this list had ≤ 3 authors who indicate high importance (see the supplemental file for a complete listing of these articles).

Table 2. Significant Guidelines, Position, Recommendations, and Consensus Papers (in Alphabetical Order by First Author).

Author(s)	Title
Arends et al ¹²	ESPEN guidelines on nutrition in cancer patients
Arends et al ¹³	ESPEN expert group recommendations for action against cancer-related malnutrition
Barazzoni et al ¹⁴	Carbohydrates and insulin resistance in clinical nutrition: recommendations from the ESPEN expert group
Boullata et al ¹⁵	ASPEN safe practices for enteral nutrition therapy
Christensen et al ¹⁶	Lipid injectable emulsion survey with gap analysis
Forbes et al ¹⁷	ESPEN guideline: clinical nutrition in inflammatory bowel disease
Guenther et al ¹⁸	Parenteral nutrition errors and potential errors reported over the past 10 years
Kumpf et al ¹⁹	ASPEN-FELANPE clinical guidelines for enterocutaneous fistula
Kwo et al ²⁰	ACG clinical guideline: evaluation of abnormal liver chemistries
Mehta et al ²¹	Guidelines for the provision and assessment of nutrition support therapy in the pediatric critically ill patient
Stoppe et al ²²	Role of nutrition support in adult cardiac surgery
Weimann et al ²³	ESPEN guideline: clinical nutrition in surgery
Worthington et al ²⁴	When is parenteral nutrition appropriate?

or TDA. In the 12-day sample, high-risk patients were found to have lower mortality for each 10% increase in protein

intake (odds ratio [OR]: 0.9; 95% confidence interval [CI]: 0.84-0.96; $P = .003$) and each 10% increase in energy intake (OR: 0.88; 95% CI: 0.83-0.94; $P < .001$) relative to goal. The TDA was shorter with greater protein intake (hazard ratio [HR]: 1.09; 95% CI: 1.03-1.16; $P = .002$) and for greater energy intake in high-risk patients (HR: 1.09; 95% CI: 1.03-1.16; $P = .002$). Protein and energy intake did not significantly affect mortality or TDA in low-risk patients.

The investigators concluded that critically ill patients with high NUTRIC scores who stay in the ICU at least 12 days may benefit from greater protein and energy provision. A similar study evaluating the “modified NUTRIC” tool (also omitting IL-6) found mortality and TDA benefits in high-risk patients who received greater protein and energy.²⁶ Previous studies have suggested receiving adequate protein may have a greater impact on outcomes than achieving energy goals,^{25,27,28} although this study also supports improved outcomes with provision of adequate energy intake in high-risk patients. Interestingly, patients in this study were prescribed 1.2 g/kg/d protein and 24 kcal/kg/d but received only about 0.7 g/kg/d protein and 16 kcal/kg/d, which is significantly less than current recommendations.²⁹ This limits the applicability of these results, as the ideal amount of protein and energy intake required for improved outcomes, particularly in high nutrition risk and nonmedical ICU patients, remains controversial. This study provides further evidence that the greatest benefit for nutrition support may be seen in patients at high nutrition risk with prolonged ICU stays, although randomized trials in more homogeneous ICU populations are warranted to determine optimal protein and energy targets for various ICU subsets with differing levels of nutrition risk.

2. Bochicchio et al: Results of a multicenter prospective pivotal trial of the first inline continuous glucose monitor in critically ill patients.⁶

Glycemic control for critically ill trauma patients improves outcomes but must be balanced with the risks of hypoglycemia and glucose variability. Glucose measurement often relies on point of care meter testing, which may be inaccurate and labor-intensive. An inline continuous glucose monitor (CGM) has been developed to address these current limitations of glucose monitoring and potentially assist nutrition support clinicians. This multicenter, prospective study evaluated the first human use of an inline near CGM (OptiScanner 5000, OptiScan Biomedical, Hayward, California) for safety and accuracy in 200 critically ill surgical and trauma patients. The inline CGM that was used connected to the patient's central venous catheter by intravenous tubing and obtained plasma sampling of 0.13 mL every 15 minutes. Glucose concentrations were measured by midinfrared spectroscopy and displayed on the monitor within 7 to 8 minutes. Patients ≥ 18 years of age with an expected minimum ICU stay of 18 hours after enrollment who required plasma glucose monitoring were included. The inline CGM occupied the most proximal port of a nontunneled central venous catheter and another access site for obtaining paired samples for comparison was required.

A total of 3735 glucose measurements obtained by inline CGM were compared with paired plasma samples analyzed by a reference standard. The study team, patients, and clinicians were blinded to the plasma glucose concentration readings by both technologies. Treatment decisions were made based on point of care meter glucose measurements. Most data points achieved the benchmark for accuracy with 95.4% of data points in zone A (ie, glucose values that deviate by no more than 20% from the reference or are in the hypoglycemic range (<70 mg/dL) when the reference is also in the hypoglycemic range) and 4.5% in zone B (ie, values outside zone A that are predicted to have no untoward effect toward the patient if considered for clinical cure) of the Clarke Error Grid. As a measure of trend accuracy, the mean absolute relative difference (MARD) was 7.6% for all paired glucose samples. No device-related adverse events were reported, but the authors indicated that nurses completed 1 device-related technical issue intervention per day. The authors concluded that inline continuous glucose monitoring is safe and accurate for use in critically ill surgical and trauma patients.

This study offers a promising solution for safe and accurate plasma glucose monitoring in critically ill surgical and trauma patients. The MARD of 7.6% for all paired glucose samples in this study is favorable because previous literature based on mathematical models of continuous glucose monitoring indicates that a MARD less than 10% is predictive of improvement in glycemic control and prevention of glucose variability.^{30,31} As midinfrared spectroscopy is not affected by hemodynamics or temperature, this technology may be

especially advantageous in the critical care setting. In fact, this technology may allow the future use of closed-loop glucose monitoring and intravenous insulin therapy for glycemic control in critically ill patients. Additional studies are warranted to investigate the use of this technology for other patient populations as well as the economic and logistic feasibility of implementation.

3. Braunschweig et al: Role of timing and dose of energy received in patients with acute lung injury on mortality in the Intensive Nutrition in Acute Lung Injury Trial (INTACT): a post hoc analysis.⁷

The INTACT was a single-center, randomized, controlled trial evaluating intensive medical nutrition therapy (IMNT) (30 kcal/kg and protein 1.5 g/kg) compared with standard physician-directed EN in patients with acute lung injury (ALI) from diagnosis to discharge. The trial was stopped early due to greater mortality (40% IMNT vs 15.8%) despite no differences in infections, ventilator days, or ICU or hospital days.³² The intent of this post hoc analysis of INTACT was to compare survivors ($n = 56$) with nonsurvivors ($n = 22$) in terms of the timing and/or dose of nutrition provided. Nonsurvivors were slightly older (64.3 vs 52.2 years), female (64% vs 43%), moderately to severely malnourished (55% vs 30%), and had higher sequential organ failure assessment (SOFA) scores (12.2 vs 8.2). Body mass index (BMI) was similar in both groups (29.5 vs 30.3 kg/m²). Mean caloric (21 vs 20.8 kcal/kg/d) and protein (0.79 vs 0.91 g/kg/d) intake were similar between nonsurvivors and survivors, respectively, as well as the amount of intravenous lipid emulsion (ILE) exposure. After adjusting for older age, female gender, and SOFA scores, nonsurvivors received significantly higher mean kcal/kg across the entire study period (OR: 1.14; 95% CI: 1.02-1.27). Multiple regression analysis showed mean kcal/kg/d had the strongest association during study days 1 to 7 and predicted subsequent death by day 3. Higher protein intake also reduced survival during days 1 to 7 (HR: 8.87; 95% CI: 2.3-34.3). Interestingly, for participants still enrolled on day 8 or after ($n = 66$), death was significantly reduced by caloric intake (HR: 0.91; 95% CI: 0.83-1). The investigators concluded that higher energy and protein intake days 1 to 7 following ALI diagnosis are associated with greater mortality, while higher energy intake after day 7 reduced mortality.

These data support other studies associating higher energy intakes with increased hospital mortality³³ and similar ventilator days or infections.³⁴ It is worth noting that the majority of patients enrolled in this trial appear to be medical ICU patients, based on the admitting diagnosis. It is possible that energy requirements may be lower during the first 7 days in the medical ICU compared with the surgical ICU patient. In addition, there appeared to be a significant number of obese patients in both groups with mean BMI of ≥ 30 kg/m². National guidelines suggest more conservative caloric dosing for hospitalized patients with obesity than what was targeted in this

study.²⁹ The benefit of reduced mortality associated with nutrition support beyond 7 days in ALI patients is worth further exploration in a larger study sample. Older age may have been a contributing factor, as another much larger study with slightly younger ALI patients did not see a difference in 60-day mortality.³⁴ Trials to determine the ideal energy and protein requirements in the first 7 days compared with after 7 days in ventilated ICU patients are warranted.

4. Diamond et al: Preventing the progression of intestinal failure-associated liver disease in infants using a composite lipid emulsion: a pilot randomized controlled trial of SMOFlipid.⁸

Pediatric patients with short bowel syndrome (SBS) or intestinal failure (IF) on long-term PN are at risk for developing intestinal failure-associated liver disease (IFALD).³⁵ Several factors influence this risk; however, ILEs, specifically soybean oil-based ILEs, have been identified as an independent risk factor when provided at standard doses (up to 3 g/kg/d) due to the presence of phytosterols and omega-6 fatty acids.^{36,37} Alternative ILE products have recently entered the US market, although not specifically Food and Drug Administration (FDA) approved for use in pediatric patients, and are receiving attention for the potential management of IFALD. This prospective, multicenter, parallel-group, blinded, randomized controlled pilot trial compared conventional ILE (Intralipid, Baxter, Deerfield, Illinois) with composite ILE (SMOFlipid, Fresenius Kabi, Lake Zurich, Illinois) in 24 PN-dependent ($\geq 40\%$ calories from PN) pediatric patients (≤ 24 months of age) with early IFALD in the absence of sepsis (serum conjugated bilirubin [CB] ≥ 1.3 mg/dL). The SMOFlipid is an alternative ILE that contains 30% medium-chain triglycerides, 30% soybean oil, 25% olive oil, and 15% fish oil. The primary outcome measure was evaluation of progression of IFALD, evidenced by change in CB. Eligible patients received Intralipid ($n = 13$) or SMOFlipid ($n = 11$) for up to 12 weeks, when full enteral tolerance was achieved, or if progressive liver disease was observed.

After adjusting for 1 statistical outlier, the mean CB, was lower at the end of the trial for those patients receiving SMOFlipid (mean: 1.3 ± 1.1 mg/dL) compared with those receiving Intralipid (4 ± 1.2 mg/dL); mean difference is -2.7 mg/dL (-4.3 to -1.2 mg/dL), $P = .001$. Study subjects in the SMOFlipid group were also more likely to achieve a CB of 0 mg/dL than those receiving Intralipid over the entire study period—HR: 10.6; 95% CI: 1.3–86.9; $P = .006$. No statistically significant differences in unconjugated bilirubin or transaminases between the 2 groups were observed; however, patients in the SMOFlipid group had significantly higher γ -glutamyl transferase at trial completion, $P = .04$. No significant differences existed in immunologic function between the 2 groups. With respect to essential fatty acid profiles, patients in the SMOFlipid group had a lower proportion of omega-6:omega-3 fatty acids compared with the

Intralipid group at trial completion, $P = .05$. No differences in safety outcomes were observed.

The authors conclude that SMOFlipid, when compared with Intralipid at the same conventional dose (up to 3 g/kg/d), reduces the risk of progressive IFALD in PN-dependent children ≤ 24 months of age. This study is the first randomized trial evaluating SMOFlipid for the prevention of progression of IFALD in children and is strengthened by the fact that similar doses were compared for up to 12 weeks. The study has several limitations including small sample size, the need to exclude 1 statistical outlier from the analysis as well as strict exclusion criteria that precluded evaluation of pre-term and low-birth weight infants who are traditionally at risk of progressive IFALD. This pilot study provides the basis of future trials to more definitively determine SMOFlipid's role for PN-dependent pediatric patients. These trials should focus on seeking answers to the several remaining questions related to the optimal provision of ILE to pediatric patients at risk of developing IFALD including, but not limited to, SMOFlipid compared with reduced soybean oil-based ILE dosing, preventative rather than treatment interventions, the role various ILEs play in the development of essential fatty acid deficiency, and the long-term growth, development, and neurodevelopmental outcomes associated with differing management approaches.

5. Wischmeyer et al: A randomized trial of supplemental parenteral nutrition in underweight and overweight critically ill patients: the TOP-UP pilot trial.⁹

This study demonstrates another attempt to evaluate optimal protein and energy delivery in critically ill patients. One aspect of this study is that it separates patients into low BMI (< 25 kg/m²) and high BMI (> 35 kg/m²) based on the hypothesis that increased energy is associated with reduced mortality in these populations. This was an open-label, randomized, control pilot study aimed to determine the feasibility of increasing calorie and protein delivery to patients by about 30% the first week of ICU stay, with the use of EN plus supplemental PN (SPN) versus EN alone. Secondary outcomes included mortality, infection complications, functional indices, and quality of life. A total of 125 adult medical or surgical ICU patients with a BMI < 25 or > 35 kg/m² were enrolled. In the control arm, patients received a standard polymeric EN formula (~ 1.2 kcal/mL), whereas in the intervention arm, patients received current EN and SPN, with daily SPN adjustment to keep caloric intake at 100% of the prescribed calories. The PN solution utilized was a commercially available 3-compartment bag supplied by the manufacturer (OLIMEL-N9, Baxter, Deerfield, Illinois), with a high protein content (14.2%) and 1.1 kcal/mL caloric density. Both EN and SPN were initiated at 20 mL/h and increased by 20 mL/h every 4 hours, either as tolerated or until the goal rate was reached. Patients were excluded if, at the time of screening, they received $\geq 60\%$ estimated caloric needs via EN with

no evidence of intolerance. Feeding regimens were continued for 7 days post-randomization or until death, whichever came first.

The patients included in the data analysis had a mean age of 55 years, Acute Physiology and Chronic Health Evaluation (APACHE) II score of 20, NUTRIC score 3.8, and were primarily Caucasians. Most demographic and clinical parameters were similar between the control and intervention group. There were more medical ICU patients (59%) than surgical ICU patients (41%). The average total calories and protein received by the patients were 26% and 22% higher, respectively, in the intervention group over the EN only group (both $P < .001$). There was no difference between the 2 groups in mortality (ICU, hospital, and 6-month), duration of mechanical ventilation, suspected infections, functional outcomes, and quality of life assessment.

This pilot study is valuable in that it paves the way to a larger clinical trial in further understanding the optimal feeding strategy for ICU patients with BMI <25 or >35 kg/m². However, it must be emphasized this is only a feasibility study, and not powered to meaningfully compare differences in survival and clinical outcomes. It is also important to point out some major irregularities and limitations. First, the definition of SPN is different from that in other published literature. The data analyzed from the intervention group included patients showing no evidence of EN intolerance or not receiving PN at all. The mean duration of PN was short at 5.9 days, and the nutrition risk appeared low, as reflected by the NUTRIC scores. In estimating caloric requirements in patients with BMI >35 kg/m², the investigators calculated adjusted body weight by using a BMI of 25 kg/m² to determine the patient's ideal body weight. This is not a validated approach, and the targeted caloric provision of 25 kcal/kg/d is clearly at odds with the current guidelines in obese ICU patients. Finally, the ILE used in the intervention arm contained 80% olive oil and 20% soybean oil. Olive oil contains a significantly higher amount of oleic acid than the more pro-inflammatory linoleic acid as present in soybean oil. If these confounders and limitations are carried over to the future clinical trial, the generalizability of the results, especially on clinical outcomes and survival, may be greatly limited.

6. Zaloga et al: Safety and efficacy of subcutaneous parenteral nutrition in older patients: a prospective randomized multicenter clinical trial.¹⁰

The objective of this prospective, randomized, open-label multicenter noninferiority study was to compare the safety and efficacy of a 12-hour daily infusion of a standardized, commercially available peripheral PN formulation (410 kcal and 28 g protein/L) via subcutaneous (SC) infusion to peripheral intravenous (PIV) infusion. One hundred twenty-one older (age: ≥ 65 years), stable hospitalized patients were included in this study. Patients were treated for 7 to 10 days and followed for 21 days or until time of discharge.

Fifty-nine patients received SC and 61 patients received PIV administration of PN. There was no significant difference in the primary composite outcome of major local side effects (27.1% SC vs 44.3% PIV, $P = .059$) which included large local edema (>10 cm), blistering (>2 cm), erythema (>10 cm diameter), unbearable pain, and switch in administration method. In the PIV group, a significantly greater number of patients had a switch in PN administration route (0% SC vs 34.4% PIV, $P < .001$) and reduced duration of treatment (7.4 ± 2.4 days SC vs 5.8 ± 2.9 days PIV, $P < .001$). As a result, the total treatment intake was significantly higher in the SC group (126.7 ± 49.7 mL/kg SC vs 101 ± 52.9 mL/kg PIV, $P = .008$). Large local edema was found to occur more in the SC group (13 patients SC vs 5 patients PIV, $P = .042$); however, it was noted to have resolved prior to the next day's infusion and did not result in patient discomfort or switch to PIV administration of nutrients. No significant differences were found in secondary outcomes related to nutritional parameters, biochemistry parameters, and clinical outcomes. The researchers concluded that SC administration of a commercially available peripheral PN formulation was not inferior to PIV administration in terms of local tolerance in older patients with malnutrition, and that this type of therapy may be useful as supplemental therapy in select patients not requiring an intravenous catheter.

This is the first study to evaluate the safety and efficacy of SC administration of a peripheral PN formulation. The results are comparable with previously published hyperdermoclisis studies using hydration and amino acid solutions.³⁸⁻⁴⁰ This study incorporated a wide range of disease states in the elderly population. One limitation is that while it was a multicenter study, all sites were within France. In addition, daily SC nutrient provision was limited to 410 kcal and 28 g of protein due to the need to limit volume (1 L/24 h) and solution osmolality (845 mOsm/L) to prevent complications. Furthermore, patients were allowed unrestricted oral intake during the study period and oral intake data were not reported; therefore, the impact of such treatment intervention is confounding, especially when looking at clinical outcomes. One potential solution to such limited nutrition administration is to use multiple sites daily which was not studied and tolerance to such is unknown. There was also potential for bias in this study as lead investigators are employed by the study sponsor. In summary, SC administration of a commercially available peripheral PN appears to hold promise; however, trials providing higher nutrient intakes are needed to provide additional guidance regarding the usefulness of such therapy in clinical practice.

Conclusion

With the large volume of publications pertinent to nutrition support therapy and their appearance in a variety of journals, it is extremely difficult for the pharmacist engaged in nutrition support practice to stay current with the literature. We

have identified what the author participants consider to be the “most important” articles from the primary literature to pharmacy nutrition support practice and provided an additional list of pertinent guidelines, consensus, and recommendation articles from various organizational groups. Although only those highest ranked articles by a majority consensus were discussed, other publications may be important depending on the patient population and the role of the pharmacist at a specific institution. However, this collection of articles has the limitation that the process for identifying significant articles lacked a structured literature search strategy. As a result, it is possible that omission of pertinent articles applicable to pharmacy nutrition support practice that were published in less common journals was not identified by the author participants. It is recommended that informed pharmacists engaged in nutrition support therapy be familiar with those articles that are applicable to their clinical practice. It is suggested that the list of other articles in the supplemental online document also be reviewed to identify those publications that might be pertinent to the reader’s practice.

Declaration of Conflicting Interests

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Supplemental Material

Supplementary material for this article is available online.

References

- Dickerson RN, Wood GC, Swanson JM, Brown RO. Redesigning journal clubs to staying current with the literature. *Pharmacy*. 2017;5:62.
- Dickerson RN, Kumpf VJ, Bingham AL, et al. Significant published articles for pharmacy nutrition support practice in 2016. *Hosp Pharm*. 2017;52:412-421.
- Dickerson RN, Kumpf VJ, Blackmer AB, et al. Significant published articles for pharmacy nutrition support practice in 2014 and 2015. *Hosp Pharm*. 2016;51:539-552.
- Dickerson RN, Kumpf VJ, Rollins CJ, et al. Significant publications for pharmacy nutrition support practice in 2013. *Hosp Pharm*. 2014;49:717-730.
- Compher C, Chittams J, Sammarco T, Nicolo M, Heyland DK. Greater protein and energy intake may be associated with improved mortality in higher risk critically ill patients: a multicenter, multinational observational study. *Crit Care Med*. 2017;45:156-163.
- Bochicchio GV, Nasraway S, Moore L, Furnary A, Nohra E, Bochicchio K. Results of a multicenter prospective pivotal trial of the first inline continuous glucose monitor in critically ill patients. *J Trauma Acute Care Surg*. 2017;82:1049-1054.
- Braunschweig CL, Freels S, Sheean PM, et al. Role of timing and dose of energy received in patients with acute lung injury on mortality in the Intensive Nutrition in Acute Lung Injury Trial (INTACT): a post hoc analysis. *Am J Clin Nutr*. 2017;105:411-416.
- Diamond IR, Grant RC, Pencharz PB, et al. Preventing the progression of intestinal failure-associated liver disease in infants using a composite lipid emulsion: a pilot randomized controlled trial of SMOFlipid. *J Parenter Enteral Nutr*. 2017;41:866-877.
- Wischmeyer PE, Hasselmann M, Kummerlen C, et al. A randomized trial of supplemental parenteral nutrition in underweight and overweight critically ill patients: the TOP-UP pilot trial. *Crit Care*. 2017;21:142.
- Zaloga GP, Pontes-Arruda A, Dardaine-Giraud V, Constans T, Clinimix Subcutaneous Study Group. Safety and efficacy of subcutaneous parenteral nutrition in older patients: a prospective randomized multicenter clinical trial. *J Parenter Enteral Nutr*. 2017;41:1222-1227.
- Yeh DD, Cropano C, Quraishi SA, et al. Implementation of an aggressive enteral nutrition protocol and the effect on clinical outcomes. *Nutr Clin Pract*. 2017;32:175-181.
- Arends J, Bachmann P, Baracos V, et al. ESPEN guidelines on nutrition in cancer patients. *Clin Nutr*. 2017;36:11-48.
- Arends J, Baracos V, Bertz H, et al. ESPEN expert group recommendations for action against cancer-related malnutrition. *Clin Nutr*. 2017;36:1187-1196.
- Barazzoni R, Deutz NEP, Biolo G, et al. Carbohydrates and insulin resistance in clinical nutrition: recommendations from the ESPEN expert group. *Clin Nutr*. 2017;36:355-363.
- Boullata JJ, Carrera AL, Harvey L, et al. ASPEN safe practices for enteral nutrition therapy. *J Parenter Enteral Nutr*. 2017;41:15-103.
- Christensen ML, Ayers P, Boullata JJ, et al. Lipid injectable emulsion survey with gap analysis. *Nutr Clin Pract*. 2017;32:694-702.
- Forbes A, Escher J, Hebutterne X, et al. ESPEN guideline: clinical nutrition in inflammatory bowel disease. *Clin Nutr*. 2017;36:321-347.
- Guenter P, Ayers P, Boullata JJ, Gura KM, Holcombe B, Sacks GS. Parenteral nutrition errors and potential errors reported over the past 10 years. *Nutr Clin Pract*. 2017;32:826-830.
- Kumpf VJ, de Aguilar-Nascimento JE, Diaz-Pizarro Graf JJ, et al. ASPEN-FELANPE clinical guidelines: nutrition support of adult patients with enterocutaneous fistula. *J Parenter Enteral Nutr*. 2017;41:104-112.
- Kwo PY, Cohen SM, Lim JK. ACG clinical guideline: evaluation of abnormal liver chemistries. *Am J Gastroenterol*. 2017;112:18-35.
- Mehta NM, Skillman HE, Irving SY, et al. Guidelines for the provision and assessment of nutrition support therapy in the pediatric critically ill patient: Society of Critical Care Medicine and American Society for Parenteral and Enteral Nutrition. *J Parenter Enteral Nutr*. 2017;41:706-742.
- Stoppe C, Goetzenich A, Whitman G, et al. Role of nutrition support in adult cardiac surgery: a consensus statement from an International Multidisciplinary Expert Group on Nutrition in Cardiac Surgery. *Crit Care*. 2017;21:131.
- Weimann A, Braga M, Carli F, et al. ESPEN guideline: clinical nutrition in surgery. *Clin Nutr*. 2017;36:623-650.
- Worthington P, Balint J, Bechtold M, et al. When is parenteral nutrition appropriate? *J Parenter Enteral Nutr*. 2017;41:324-377.

25. Nicolo M, Heyland DK, Chittams J, Sammarco T, Compher C. Clinical outcomes related to protein delivery in a critically ill population: a multicenter, multinational observation study. *J Parenter Enteral Nutr.* 2016;40:45-51.
26. Rahman A, Hasan RM, Agarwala R, Martin C, Day AG, Heyland DK. Identifying critically-ill patients who will benefit most from nutritional therapy: further validation of the "modified NUTRIC" nutritional risk assessment tool. *Clin Nutr.* 2016; 35:158-162.
27. Allingstrup MJ, Esmailzadeh N, Wilkens Knudsen A, et al. Provision of protein and energy in relation to measured requirements in intensive care patients. *Clin Nutr.* 2012;31:462-468.
28. Weijs PJ, Looijaard WG, Beishuizen A, Girbes AR, Oudemans-van Straaten HM. Early high protein intake is associated with low mortality and energy overfeeding with high mortality in non-septic mechanically ventilated critically ill patients. *Crit Care.* 2014;18:701.
29. McClave SA, Taylor BE, Martindale RG, et al. Guidelines for the provision and assessment of nutrition support therapy in the adult critically ill patient: society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.). *J Parenter Enteral Nutr.* 2016;40:159-211.
30. Van Herpe T, De Moor B, Van den Berghe G, Mesotten D. Modeling of effect of glucose sensor errors on insulin dosage and glucose bolus computed by LOGIC-Insulin. *Clin Chem.* 2014;60:1510-1518.
31. Wilinska ME, Hovorka R. Glucose control in the intensive care unit by use of continuous glucose monitoring: what level of measurement error is acceptable? *Clin Chem.* 2014;60:1500-1509.
32. Braunschweig CA, Sheean PM, Peterson SJ, et al. Intensive nutrition in acute lung injury: a clinical trial (INTACT). *J Parenter Enteral Nutr.* 2015;39:13-20.
33. Arabi YM, Haddad SH, Tamim HM, et al. Near-target caloric intake in critically ill medical-surgical patients is associated with adverse outcomes. *J Parenter Enteral Nutr.* 2010;34:280-288.
34. National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome Clinical Trials Network, Rice TW, Wheeler AP, et al. Initial trophic vs full enteral feeding in patients with acute lung injury: the EDEN randomized trial. *JAMA.* 2012; 307:795-803.
35. Duggan CP, Jaksic T. Pediatric intestinal failure. *N Engl J Med.* 2017;377:666-675.
36. Al-Shahwani NH, Sigalet DL. Pathophysiology, prevention, treatment, and outcomes of intestinal failure-associated liver disease. *Pediatr Surg Int.* 2017;33:405-411.
37. Sanchez SE, Arnold MA. Lipid management in pediatric intestinal failure. *Curr Opin Organ Transplant.* 2016;21:153-158.
38. Dasgupta M, Binns MA, Rochon PA. Subcutaneous fluid infusion in a long-term care setting. *J Am Geriatr Soc.* 2000;48:795-799.
39. Ferry M, Leverve X, Constans T. Comparison of subcutaneous and intravenous administration of a solution of amino acids in older patients. *J Am Geriatr Soc.* 1997;45:857-860.
40. Slesak G, Schnurle JW, Kinzel E, Jakob J, Dietz PK. Comparison of subcutaneous and intravenous rehydration in geriatric patients: a randomized trial. *J Am Geriatr Soc.* 2003;51:155-160.