

Michael D. Kraft, PharmD, BCNSP¹; Anne M. Tucker, PharmD²; Sharon M. Durfee, RPh³; Todd Jones, MSN⁴; Peggi Guenter, PhD, RN, FAAN⁵, David E. Banko, CPA⁶; Phil Ayers, PharmD, BCNSP, FMSHP, FASHP⁷, Joseph Boullata, PharmD, RPh, CNS-S, FASPEN, FACN⁸, Erica Raymond, MS, RD⁹; and Gordon S. Sacks, PharmD, BCNSP, FASPEN, FCCP¹⁰



Nutrition in Clinical Practice Volume 36 Number 2 April 2021 480–488 © 2020 American Society for Parenteral and Enteral Nutrition DOI: 10.1002/ncp.10600 wileyonlinelibrary.com

WILEY

Abstract

Introduction: Errors have been reported in the literature to occur at each step of the parenteral nutrition (PN) use process, necessitating standardized processes, clinician competence, and open communication for those involved. This study was performed at Central Admixture Pharmacy Services (CAPS®) in collaboration with the American Society for Parenteral and Enteral Nutrition (ASPEN) with the purpose to study the need for and success of PN pharmacist interventions. *Methods:* A survey was developed and sent to all CAPS customers for study enrollment and to identify their demographic and practice characteristics. For those enrolled, CAPS pharmacists reviewed every PN order in a 1-month period using an error/intervention tool to capture data on prescription elements requiring intervention, along with acceptance of that intervention. *Results:* Two hundred thirty-two unique CAPS customers (23% response rate) participated in the study, representing 37,634 unique PN prescriptions. Two hundred forty-eight PN prescriptions (0.66%) from 59 customers required ≥ 1 intervention. A greater number and percentage of interventions were required for neonatal prescriptions, as compared with adult and pediatric prescriptions. No significant difference was found in many of the other customer characteristics. *Conclusion:* This study supports the need for institutions to develop systems to comply with published PN safety recommendations, including knowledgeable and skilled pharmacists to complete the order review and verification steps for this high-alert medication. (*Nutr Clin Pract.* 2021;36:480–488)

Keywords

parenteral nutrition; pharmacists; surveys; safety; prescriptions; electrolytes

From the ¹Department of Pharmacy Services Ann Arbor, University of Michigan College of Pharmacy, Michigan, USA; ²Critical Care/Nutrition Support The University of Texas M D Anderson Cancer Center, Houston, Texas, USA; ³Central Admixture Pharmacy Services, Inc, Denver, Colorado, USA; ⁴Marketing Central Admixture Pharmacy Services, Inc, Denver, Colorado, USA; ⁵Clinical Practice, Quality, and Advocacy American Society for Parenteral and Enteral Nutrition, Silver Spring, Maryland, USA; ⁶Health Economics & Outcomes, Research B Braun Medical Inc, Bethlehem, Pennsylvania, USA; ⁷Clinical Pharmacy Services, Mississippi Baptist Medical Center, Jackson, Mississippi, USA; ⁸Clinical Nutrition Support Services, Hospital of the University of Pennsylvania, Philadelphia, Pennsylvania, USA; ⁹Patient Food and Nutrition Services, Michigan Medicine, Ann Arbor, Michigan, USA; and the ¹⁰Fresenius Kabi USA, LLC, Lake Zurich, Illinois, USA.

Financial disclosure: None declared. Employee of CAPS.

Conflict of interest: S. M. Durfee and T. Jones are employed by Central Admixture Pharmacy Services, Inc. D. E. Banko is employed by B Braun Medical Inc. P. Ayers is a speaker for Fresenius Kabi and consultant for American Regent. J. Boullata is a consultant for American Regent and B Braun and a speaker for B Braun and Fresenius Kabi, North America. G. S. Sacks is employed by Fresenius Kabi, North America. All other authors report they have no conflicts of interest to disclose.

Received for publication February 6, 2020; accepted for publication October 14, 2020.

This article originally appeared online on December 4, 2020.

Corresponding Author:

Peggi Guenter, FASPEN, Senior Director, Clinical Practice, Quality, and Advocacy American Society for Parenteral and Enteral Nutrition, Silver Spring, MD, USA.

Email: peggig@nutritioncare.org

Introduction

Parenteral nutrition (PN) is a high-alert medication prescribed for >250,000 hospitalized patients and \sim 25,000 home patients each year.^{1,2} The complex PN use process requires standardized processes, with good communication among competent professionals from the disciplines involved (see Figure 1).³ Errors in the PN prescribing and order review steps have been reported in individual institutions, surveys, and case reports.⁴⁻⁶ Larger data sets are required to analyze where the errors are occurring in the PN use process and where potential errors could occur and be prevented with systems improvements. There is additional value in identifying which patient populations are commonly affected. The American Society for Parenteral and Enteral Nutrition (ASPEN) PN Safety Committee developed a partnership with the University of Michigan and CAPS to review CAPS multicenter prescriptions, pharmacist order review practices, and clarification interventions to meet the aims listed below:

- 1. Describe the types of PN prescriptions requiring interventions in this large data set.
- 2. Correlate the pharmacist interventions with characteristics of the prescribing facilities.
- 3. Analyze these data to identify any site-of-care or population differences.

Background

The PN use process encompasses many steps, each with numerous tasks at which errors may occur and interventions are required. These steps and assigned tasks involve several different disciplines. See Figure 1. This study specifically ex-

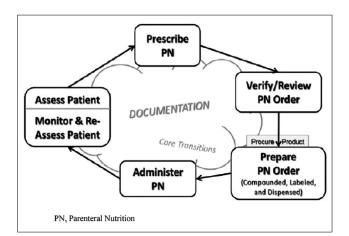


Figure 1. Parenteral nutrition (PN) use process. Reprinted with permission from Ayers P, Boullata J, Sacks GS. Parenteral Nutrition Safety: The Story Continues. *Nutr Clin Pract*. 2018;33(1):46-52.³

amined interventions related to the PN ordering/prescribing step and the PN order review and verification step.

In 2009, Sacks and colleagues published a paper on frequency and severity of harm of medication errors related to the PN process in a large university teaching hospital. These authors found that of the >4000 PN prescriptions, 1.6% were associated with medication error (or 15.6 errors per 1000 PN prescriptions). Of the 74 errors found, 1% were related to prescribing, 39% were related to order transcription, 24% during preparation, and 35% during administration. Although the PN review step was not singled out, it is presumed to have been incorporated within the transcription and preparation steps at an institution where the nutrition support service/team (NSS) prescribed the PN. Eight percent of the errors contributed to or resulted in temporary harm to the patient. These findings demonstrated that PN-related errors occur and can cause harm to patients.⁴

In 2012, Boullata and colleagues performed a survey of nutrition support clinicians on the PN use process.7 Participants reported that PN was most frequently prescribed by the primary medical or surgical service, and the PN ordered was most often communicated by using a handwritten, standardized order form. At the time of this survey in 2011, <33% of organizations used electronic order entry for PN. Participants cited a series of measures that reduced the risk of order entry errors when electronic order entry was used. Pharmacists reported only 7.1% of electronic PN orders had an interface with the automated compounding device; thus, 92.8% required a manual transcription process, an avoidable step that introduces potential errors. Twentythree percent of pharmacists reported that their PN order process did not include time for order review, verification, and clarification of the order, resulting in an increased risk for errors. Less than 40% of organizations reported a recognized clinical effectiveness or quality improvement program for PN. Fifty-three percent of respondents reported an estimated monthly PN-related medication error frequency of 0-10 errors; however, 44% reported not knowing the frequency or that their institution did not track PN error rates.7 Just recently, a review of 10 years of Institute for Safe Medication Practices (ISMP) Medication Errors Reporting Program reports on PN errors was published.⁶ This paper reviewed and categorized types of errors using the PN use process and found errors in each step, including prescribing.

In 2015, Durfee and CAPS conducted a PN orderprescribing pilot study of 2 CAPS pharmacies over a 31day period of observation. Each CAPS pharmacist reviewed customer (institution/agency will be called customer) PN orders, noted any orders that required interventions, and documented any intervention made by that pharmacist reviewing the orders. They noted the type of institution or agency, the type of patient population, the type of error, and if the order was changed based on the pharmacist

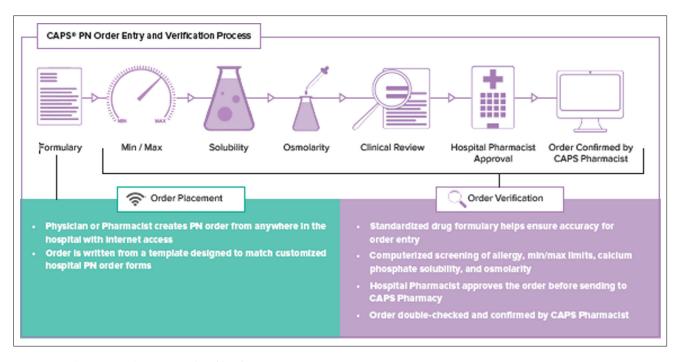


Figure 2. CAPS PN order entry and verification process.

intervention. Their results found that of the 8055 orders reviewed, 65 specific interventions were necessary (0.8% of the total orders). Of the orders that required interventions, 35% or 70% were changed in collaboration with the customer pharmacist. The types of PN prescribing errors varied greatly.⁸

The CAPS order placement and verification process can be seen in Figure 2. It includes a template and agreed upon minimum/maximum limits, clinical review, hospital pharmacy review, and then a final review by the CAPS pharmacist prior to compounding.

Even with this system, and keeping this cited error literature in mind, the need for PN prescribing and order review data was evident, with the goal that education and quality improvement programs could be instituted. The CAPS pilot study led to the need for a larger multisite trial to capture intervention rates and types and whether interventions led to prescription change.

Methods

In 2016, an ASPEN workgroup composed of PN Safety Committee members was created to conduct this study in partnership with CAPS. The study proposal was reviewed by the University of Michigan Institutional Review Board and was determined to be a project not regulated as human subjects research. The inclusion criteria were CAPS customers that had PN prescriptions and enrolled in the study. The exclusion criterion was any customer that did not agree to participate.

The workgroup developed data collection tools for 2 parts of the study. First, to collect data about the characteristics of a facility, CAPS asked each customer for permission to participate in the study and provided them a 1-time survey to complete of general questions about their institution/agency/care setting. Customer identification data were kept confidential with CAPS and not entered onto the data collection tool shared with the workgroup. Each CAPS customer was assigned a study number known only to CAPS and not to ASPEN or the other investigators. Second, the assigned CAPS pharmacists for each of the study customers reviewed every PN order received for a 1-month period during October 2016 using a potential for error/intervention paper tool designed to capture data on prescription elements requiring intervention. The CAPS pharmacists were trained to review the prescription and check any of the prescription elements listed on that data collection tool and flag those for intervention. The high- and low-ordered elements on the data collection sheet were based on ASPEN documents (see Appropriate Dosing for Parenteral Nutrition: ASPEN Recommendations). It was assumed by the CAPS pharmacist that the prescriber had assessed the patient for altered organ function and integrated that into the ordering process. The data collection sheet was compiled for each order, and these forms were communicated to the central CAPS office by the CAPS site Director of Pharmacy. The CAPS Clinical Nutrition Support Pharmacist coordinated entry of data into a secure electronic database, and the data were aggregated and deidentified by CAPS. The deidentified data for both sections of the survey and the customer- and prescription-

Table 1. Customer Description.

Customer characteristics	Number (%)
Facility type $(n = 232)$	
Hospital only	177 (76.3)
Home care only	7 (3)
Both hospital and home	9 (3.9)
care	
LTAC only	33 (14.2)
LTC only	6 (2.6)
Institutional bed size $(n =$	
225)	
1–100 beds	72 (32)
101–200 beds	42 (18.7)
201–500 beds	87 (38.7)
\geq 501 beds	24 (10.6)
Region $(n = 232)$	
Northeast	54 (23.3)
Midwest	56 (24.1)
South	72 (31)
West	50 (21.6)

LTC, long-term care; LTAC, long-term acute care.

level interventions were shared with an ASPEN staff member assigned to manage the statistical analyses. χ^2 was used to conduct descriptive and statistical analyses.

Results

Customer Survey

CAPS issued a survey asking their customers permission to participate in the deidentified ASPEN-CAPS study. There was a 23% customer response rate, and 80% of those responding customers gave permission to participate in the study. This equated into 232 participating customers that represented many types of institutions and agencies (see Table 1).

Tables 2 and 3 provide customer demographic and practice characteristics related to the PN process. Nearly two-thirds of customers use CAPS-only compounded PN formulations, with 28% using a combination of CAPS compounded formulations and multichamber bag (MCB) PN products. CAPS did not provide MCB PN products, and information related to MCB PN products was not included in this study. Physicians were the primary ordering provider for all predefined age groups. There was an equal distribution of electronic computerized provider order entry and standardized handwritten PN orders, with an average number of PN orders per day of 0-5. Order review of PN orders by a dedicated clinical person prior to transfer of the PN prescription to CAPS occurred in 96.6% of customers, and 62% had a formal NSS. Fifty percent of customers used CAPS-specific minimum/maximum limits, with deviation due to institution-specific limits predominantly in pediatric Table 2. Customer PN Processes.

Customer characteristics	Number (%)
CAPS PN and/or other	
(n = 232)	
CAPS only	149 (64.2)
CAPS + MCB	65 (28)
CAPS +	3 (1.3)
self-compounding	
All 3 types	8 (3.4)
Other	7 (3.1)
Dedicated clinical	
person review order	
(n = 232)	
Yes	224 (96.6)
No	8 (3.4)
Formal nutrition	
support service/team	
(n = 232)	
Yes	144 (62.1)
No	88 (37.9)
Nutrition support	
service/team manages	
home PN ($n = 232$)	
Yes	28 (12.1)
No	133 (57.3)
Some patients	9 (3.9)
Don't know	62 (26.7)
Use CAPS min/max	
limits $(n = 232)$	
Yes	117 (50.4)
Combo or depends	75 (32.3)
No	40 (17.2)

MCB, multichamber bag; PN, parenteral nutrition.

and neonate populations. Minimum/maximum limits are defined as the high and low amounts of a specific nutrient (or nutrients) set in the automated PN-compounding device that will alarm if the PN prescription falls outside of these limits.

Interventions

CAPS received 163,324 PN prescriptions during the study period, of which 37,634 (23%) were eligible for inclusion, as they agreed to participate in this study (see Table 4). These data are presented to set the scenario for the remainder of the results. Two hundred forty-eight prescriptions from 59 customers required intervention from CAPS prior to compounding, with 97.2% of those PN prescriptions from hospitals, 1.2% from long-term acute care (LTAC), 0.4% from long-term care (LTC), and 1.2% from homecare. From those prescriptions, 252 individual interventions were identified because some prescriptions required >1 intervention. Those customers that needed interventions were

Customer characteristic	Number (%)				
Average number of PN	Adults (n=224)	Pediatrics (n=68)	Neonates (n=120)		
orders per day					
0–5	182 (81.3)	61 (89.7)	96 (80)		
6–10	28 (12.5)	2 (2.9)	16 (13.3)		
11–15	3 (1.3)	0 (0)	3 (2.5)		
≥16	5 (4.9)	5 (7.4)	5 (4.2)		
PN order format	Adults $(n = 224)$	Pediatrics $(n = 68)$	Neonates $(n = 120)$		
Electronic CPOE	94 (42)	31 (45.6)	54 (45)		
Electronic outside CPOE	25 (11.1)	7 (10.3)	14 (11.7)		
Standardized handwritten	94 (42)	25 (36.8)	48 (40)		
Nonstandardized	11 (4.9)	5 (7.3)	4 (3.3)		
handwritten					
Primary prescribers	Adults $(n = 223)$	Pediatrics $(n = 70)$	Neonates $(n = 124)$		
NP/PA/CNS	6 (2.7)	3 (4.3)	28 (22.5)		
PharmD/RPh	41 (18.4)	7 (10)	3 (2.4)		
Physician	97 (43.5)	46 (65.7)	70 (56.5)		
RĎ	10 (4.5)	2 (2.9)	2 (1.6)		
Nutrition support service	10 (4.5)	1 (1.4)	1 (0.8)		
Combination of above	59 (26.5)	11 (15.7)	20 (16.1)		

Table 3. Customer PN Processes Based on Patient Type.

PN, parenteral nutrition, CPOE, Computerized Provider Order Entry, NP, Nurse Practitioner, PA, Physician Assistant, CNS, Clinical Nurse Specialist, RD, Registered Dietitian, RPh, Registered Pharmacist, PharmD, Doctor of Pharmacy.

Table 4. Total Number of PN Prescriptions.

	Number of PN prescriptions for all customers that agreed to be in the study (n = 232) (%)	Number of PN prescriptions from customers that needed interventions ($n = 59$) (%)
Total	37,634	19,797
Adult patients	24,952 (66.3)	10,678 (53.9)
Pediatric patients	2906 (7.7)	2296 (11.6)
Neonatal patients	9776 (26)	6823 (34.5)

PN, parenteral nutrition.

 $\sim 25\%$ of the total customers, showing a representative sample. The top 3 intervention types included electrolyte dose clarification (31.7%), calcium/phosphate incompatibility (25.4%), and amino acid dose clarification (10.3%). Of the calcium/phosphate incompatibility interventions, 60 (94%) orders were not changed primarily because of institution-specific limits that differed from default limits set by CAPS for all customers. Customers have the option of setting their own limits in the order entry system; CAPS intervened only when the order exceeded the customer's specific limits. Forty-seven (19%) orders consisting of 53 interventions led to changes in the PN prescription. Interventions included dose clarifications of nutrients and insulin (33), osmolality issues related to peripheral PN (9), calcium/phosphate incompatibility (4), and amino acid omission (1). A greater overall number and percentage of interventions were required for neonatal prescriptions (47.2%) compared with both adult (30.2%) and pediatric (22.6%) prescriptions.

With respect to customer characteristics, only the number of institutional beds and average number of PN prescriptions per day were significantly different between those that required an intervention compared with those that did not (see Table 5). The significant differences were for the entire variable using the χ^2 method—that is, the proportions within the variable between those that required interventions and those that did not. Other characteristics, such as facility type, geographical region, use of CAPS products, use of a dedicated clinical person to review the order at the facility prior to submission to CAPS, presence of a formal NSS, management of home PN, use of CAPS-suggested minimum/maximum limits, ordering format, number of manual order entry steps, or type of prescriber were not significantly different between those customers that had required an intervention and those that did not. Of note, out of the 59 customers requiring interventions, 37 (62.7%) have an NSS. The intervention rate for customers with an NSS was 1.8% vs 0.53% in those that did not have an NSS.

Table 5.	Significant	Customer	Characteristics	Based on	Need for	or Intervention.
----------	-------------	----------	-----------------	----------	----------	------------------

Customer Characteristic ($N = 232$)	No Intervention $(N = 173)$	Intervention $N = 59$	<i>P</i> -value
Bed size (N = 225)	N = 167	N = 58	P < .05
1–100 beds	62 (37.13%)	10 (17.24%)	
101–200 beds	29 (17.37%)	13 (22.41%)	
201–500 beds	60 (35.93%)	27 (46.55%)	
>501 beds	16 (9.58%)	8 (13.79%)	
Average number of PN orders per day:	N = 167	N = 57	P < .05
adult (N = 224)			
0–5	144 (86.2%)	38 (66.7%)	
6–10	14 (8.4%)	14 (24.6%)	
11–15	2 (1.2%)	1 (1.8%)	
<u>≥16</u>	7 (4.2%)	4 (7%)	
Average number of PN orders per day:	N = 48	N = 20	P < .05
Pediatric $(N = 68)$			
0–5	46 (95.8%)	15 (75%)	
6–10	1 (2.1%)	1 (5%)	
11–15	0(0)	0(0)	
>16	1 (2.1%)	4 (20%)	
Average number of PN orders per day:	N = 77	N = 43	P < .05
Neonate ($N = 120$)			
0–5	68 (88.3%)	28 (65.1%)	
6–10	5 (6.5%)	11 (25.6%)	
11–15	2 (2.6%)	1 (2.3%)	
≥16	2 (2.6%)	3 (7%)	

PN, parenteral nutrition.

The rate of change in the PN order upon CAPS pharmacist intervention was 14.3% in customers with an NSS team and 42.2% for customers without an NSS.

Discussion

In a large national data set of patients receiving PN from CAPS, <1% of prescriptions required a clinical intervention on secondary review. This study was completed through a unique collaboration between academia, a clinical professional association, and an industry service company and represents an important contribution to the literature on PN interventions and PN safety. This also represents one of the largest samples on PN interventions (Table 1), given that the results included data and evaluation of 37,634 PN prescriptions from 232 institutions across multiple care settings in the US. Although most respondents reported being in a hospital setting, the data also included home care and LTAC and LTC facilities. In addition, the institutional customers represented a wide range of facility sizes, based on bed capacity, and were evenly distributed across the country. These characteristics suggest the data represent a wide cross-section of practice settings. Furthermore, facility type and geographical region were not significantly different between those customers that required an intervention and those that did not, suggesting that a focus on PN safety and the possible need for PN interventions is warranted, regardless of the setting. As a matter of everyday practice, the customer has to validate the prescription prior to the order being sent to CAPS. The degree or intensity of initial customer review and interventions performed prior to submitting the PN order to CAPS was beyond the scope of the study. See Figure 2 for an illustration of the process.

Approximately 62% of respondents indicated they had a formal NSS; however, almost 97% indicated they had a dedicated clinical person to review the PN order prior to transmission to CAPS, resulting in ~3% of respondents that do not have a dedicated clinical person review the PN order prior to submission. The customer determined the definition of what constituted a formal NSS or the qualifications of the clinician reviewing the PN order. A previous national survey of nutrition support clinicians suggested that just >76% dedicated a pharmacist to review PN orders.⁷ Although there was no significant difference between PN orders requiring intervention compared to those that did not, a review of the PN order by a knowledgeable and skilled pharmacist could be an area of opportunity to further improve PN safety.^{9,10}

A higher intervention rate was identified when an NSS was present in PN management vs no NSS; however, the rate of PN order adjustments was lower when the NSS was involved in the patient's PN management. Although this study was not designed to assess specifics as to why this may have occurred, 1 plausible explanation is that the presence of an NSS may translate into an interdisciplinary group of clinicians with higher-level training and expertise, leading to more aggressive and "out of the box" PN management. It may also indicate the presence of higher-acuity/more complex patients. These factors likely necessitate a higher number of interventions by the pharmacist conducting order review to clarify and assess appropriateness, especially if practice falls outside the predefined system limits. This further supports PN order review by a knowledgeable and skilled pharmacist to ensure PN safety.

An encouraging finding from this investigation was that the order format was not significantly different between those institutions that required a PN intervention and those that did not. Standardized electronic PN orders have been recommended for use in all patients⁹⁻¹¹, and other studies have demonstrated a significant reduction in PN errors when converting to a standardized electronic PN order.^{9,10,12} A PN prescribing error rate of >20% was reduced to 3.2% with a transition to electronic prescribing with format standardization.¹³ Building decision support into electronic prescribing has been well received to reduce error risk.¹⁴ A recent study evaluating pharmacist review of >3000 PN orders identified an error rate of 3.9%, of which 12% had potentially harmful consequences if not for the intervention.¹⁵ In this study, the overall percentage of PN interventions was consistent with the previous CAPS intervention study⁸ and low (248 of 37,634 PN orders [$\sim 0.7\%$]), as compared with the total prescriptions, even when respondents reported using a nonstandard handwritten PN order format (3.3%-7.3%), depending on the patient population. See Table 3. Despite these low percentages, the need for intervention was fairly widespread over the customer bases, as 60 of 232 customers required >1 intervention (25.9%). The size of the institution (based on number of beds) and the number of PN orders per day were significantly different between those institutions that required PN interventions and those that did not (Table 5). Although it is not possible to assess where the specific differences exist with the statistical tests used, the percentage of customers requiring a PN intervention was higher than the percentage of those that did not require a PN intervention in all bed categories except for the 1-100 beds category. A similar result was observed, based on the number of PN orders per day, in which the proportion of customers requiring a PN intervention was higher than that of those that did not require an intervention in all ranges of daily PN order volume except the 0-5 orders category.

There are several possibilities to explain these observations. Larger institutions may care for higher-acuity/more complex patients and may have more patients receiving PN per day. It is also possible that increasing bed size is associated with more complex workflows as well. This could be supported by the fact that there was a higher overall number and percentage of interventions required for neonatal PN prescriptions (47.2%) compared with adult or pediatric PN prescriptions. These factors could contribute to a greater need for PN interventions, but further study is needed to accurately determine the reason(s) for these observed differences.

Although PN orders were reviewed by 2 or more independent reviewers at 224 of the 232 (\sim 97%) customer institutions, and electronic order entry or a standard handwritten PN order was used in >90% of the customer institutions, 248 prescriptions required interventions, confirming the need for a knowledgeable pharmacist in the PN process.

The most common interventions were electrolyte dose clarification, calcium/phosphate incompatibility, and amino acid dose clarification. In the absence of these interventions, the inappropriate PN formulations could have been infused and led to harm. Pharmacists play an essential role in the PN use process and are particularly critical in PN order review and verification. This was again highlighted in a recent ISMP report in which a pharmacist at CAPS identified and prevented a potential 1000-fold overdose of zinc from being compounded in a PN order and administered to a pediatric patient.¹⁶ A prescriber inadvertently prescribed zinc in mg instead of mcg when ordering PN for a 2year-old child. The error was not identified during a 2pharmacist review at the institution prior to transmission, and an alert was not triggered in the institution's electronic health record system. An alert was triggered in the electronic system at CAPS during a pharmacist order review. There were several other warnings that also fired, most of which were not clinically significant, so it is possible that alert fatigue played a role in the error not being identified. The pharmacist identified the error at the time of compounding, when the large dose of zinc and the volume that would have been required to prepare the PN order became apparent. The pharmacist contacted the prescriber, and the order was changed. During the current study, a similar error occurred in which a CAPS pharmacist identified a 10fold dosing error for zinc, copper, and selenium during order review and verification of a pediatric PN order, avoiding a potential adverse event. These data and examples further support that pharmacists' review and verification of PN orders is essential. In addition, following ASPEN and other safety recommendations is important, including using standardized electronic PN orders; avoiding manual transcription of PN orders; standardizing the PN order process; building, testing, and responding to warnings; and using double-checks; but these steps alone are not adequate to eliminate the need for an independent review and verification by a knowledgeable and skilled pharmacist.9,10,16 Errors viewed in context can enhance learning, and the subsequent remedies and systems improvements help create a safer environment for patients receiving PN.17 Conducting methodical (ie, systematic) systems review of medication errors has been well described.¹⁸ This study contributes to the PN-specific literature. Out of the presented data come opportunities for education, further standardization (policies, procedures, and practices), automation, and forcing functions. A persistent recommendation remains that clinicians with expertise in nutrition support need to be involved in the PN process.

Conclusion

PN order review and verification is a crucial step in the PN process to reduce the potential for patient harm. This study supports the need for institutions to not only develop systems to comply with published PN safety recommendations but to also include knowledgeable and skilled pharmacists to complete the order review and verification step for this high-alert medication. Larger multisite trials are essential to capture and further define intervention rates, types, and success.

Statement of Authorship

M. D. Kraft, A. M. Tucker, S. M. Durfee, T. Jones, P. Guenter, D. E. Banko, P. Ayers, J. Boullata, E. Raymond, and G. S. Sacks equally contributed to the conception and design of the research; M. D. Kraft, A. M. Tucker, S. M. Durfee, T. Jones, P. Guenter, D. E. Banko, and P. Ayers contributed to the design of the research; M. D. Kraft, A. M. Tucker, S. M. Durfee, T. Jones, P. Guenter, D. E. Banko, and P. Ayers contributed to the design of the research; M. D. Kraft, A. M. Tucker, S. M. Durfee, T. Jones, P. Guenter, and D. E. Banko contributed to the acquisition and analysis of the data; M. D. Kraft, A. M. Tucker, S. M. Durfee, T. Jones, P. Guenter, and D. E. Banko contributed to the interpretation of the data and drafted the manuscript. All authors critically revised the manuscript, agree to be fully accountable for ensuring the integrity and accuracy of the work, and read and approved the final manuscript.

References

- HCUP National Inpatient Sample (NIS), 2016, Agency for Healthcare Research and Quality (AHRQ). www.HCUPnet.ahrq.gov Accessed February 26, 2019.
- Mundi MS, Pattinson A, McMahon MT, Davidson J, Hurt RT. prevalence of home parenteral and enteral nutrition in the United States. *Nutr Clin Pract*. 2017;32(6):799-805.
- Ayers P, Boullata J, Sacks G. Parenteral nutrition safety: The story continues. *Nutr Clin Pract*. 2018;33(1):46-52.
- Sacks GS, Rough S, Kudsk KA. Frequency and severity of harm of medication errors related to the parenteral nutrition process in a large university teaching hospital. *Pharmacotherapy*. 2009;29(8):966-74.
- Grissinger M. Mismatched prescribing and pharmacy templates for parenteral nutrition lead to data-entry errors. *Pharmacy and Therapeutics*. 2015;40(6):349-350.
- Guenter P, Ayers P, Boullata JI, Gura KM, Holcombe B, Sacks GS Parenteral nutrition errors and potential errors reported over the past 10 years. *Nutr Clin Pract*. 2017;32(6):826-830.
- Boullata J, Guenter P, Mirtallo J. A parenteral nutrition use survey with a gap analysis. JPEN J Parenter Enteral Nutr. 2013;37:2, 212-222.

- Durfee S, Jones TN, RN, Wormington D, Banko D. Assessing order entry errors and interventions in 2 CAPS pharmacies. A.S.P.E.N. Clinical Nutrition Week Research Poster M92. Austin, TX 2016. https: //onlinelibrary.wiley.com/doi/10.1177/0148607115621052
- Ayers P, Adams S, Boullata J, et. al. A.S.P.E.N. Parenteral Nutrition Safety Consensus Recommendations. *JPEN J Parenter Enteral Nutr.* 2014; 38:3, 296-333.
- Boullata J, Gilbert K, Sacks G, et al. A.S.P.E.N. clinical guidelines: parenteral nutrition ordering, order review, compounding, labeling, and dispensing. *JPEN J Parenter Enteral Nutr.* 2014;38:3, 334-377.
- Brown CL, Garrison NA, Hutchinson AA. Error reduction when prescribing neonatal parenteral nutrition. *Am J Perinatol.* 2007;24:7, 417-427.
- MacKay M, Anderson C, Boehme S, Cash J, Zobell J. Frequency and severity of parenteral nutrition medication errors at a large children's hospital after implementation of electronic ordering and compounding. *Nutr Clin Pract*. 2016;31:2, 195-206.
- Crews J, Rueda-de-Leon E, Remus D, et al. Total parenteral nutrition standardization and electronic ordering to reduce errors: a quality improvement initiative. *Pediatr Qual Safety*. 2018;3:4, 093.
- Papandreou P, Ntountaniotis D, Skouroliakou M, Massara P, Siahanidou T. Does a parenteral nutrition decision support system for total nutrients improve prescription procedure and neonatal growth? J Matern Fetal Med. Published online May 23, 2019. https://doi.org/10. 1080/14767058.2019.1615432
- Hermanspann T, Schoberer M, Robel-Tillig E, et al. Incidence and severity of of prescribing errors in parenteral nutrition for pediatric inpatients at a neonatal and pediatric intensive care unit. *Front Pediatr.* 2017;5:149-158.
- Institute for Safe Medication Practices. Too close for comfort: Fatal zinc overdose narrowly avoided. July 4, 2019. https://www.ismp.org/ resources/too-close-comfort-fatal-zinc-overdose-narrowly-avoided.
- Boullata JI. Safe practices for enteral and parenteral nutrition. In: Seres DS, Van Way CW (eds). *Nutrition Support for the Critically Ill.* New York, NY: Springer, 2016:229-241.
- Duchscherer C, Davies JM. Systematic systems analysis: a practical approach to patient safety reviews. *Calgary: Health Quality Council of Alberta*. 2012.

APPENDIX

CAPS Study Appendix Study Instruments

One-time Customer Survey. General questions and customer to be identified by random number (survey completed upon agreement to be in the study.)

- Customer type: Hospital, LTAC, LTC, Homecare, Other
- Number of beds in facility
- Home care- # of PN patients/ how many active patients
- Geographic region of US (use federal regions- HCUP data)
- Is a customer pharmacist or someone else entering and reviewing each order (they all need to be verified by a customer pharmacist)
- Does the customer use CAPS only PN or other products-(such as multi-chamber or standardized

commercially available PN products or self-compound)

- Do they have a formal inpatient nutrition support service?
- Does a nutrition support service have oversight for home care patient orders? (Yes No, don't know, some patients
- Do they use CAPs Min max or customized?
- Number of average PN orders per day
 - Neonates____
 - Pediatrics
 - Adults____
- For your Parenteral Nutrition orders, do you use? (check the primary one)

Adult patients.

- A. a standardized template within your CPOE
- B. standardized electronic template outside of your CPOE
- C. standardized handwritten order form
- D. nonstandard handwritten order form
- E. Don't have adult patients

Pediatric patients.

- A. a standardized template within your CPOE
- B. standardized electronic template outside of your CPOE
- C. standardized handwritten order
- D. nonstandard handwritten order
- E. Don't have pediatric patients

Neonatal patients.

- A. a standardized template within your CPOE
- B. standardized electronic template outside of your CPOE
- C. standardized handwritten order
- D. nonstandard handwritten order
- E. Don't have neonatal patients
- F. List number of manual order entry processes or transcription steps needed to complete communication of the PN order (0, 1, or > 1) (example- unit clerk to a CPOE, then Pharmacist into a Pharmacy system, then into the CAPS e-system.)
 - Neonates_____
 - Pediatrics _____
 - Adults_____
- G. Who are the primary prescribers for each of your PN patient populations? Choose from PA, NP, MD/DO, RD, Nutrition Support Service (NSS), pharmacist/PharmD (write in)

- Neonates____
- Pediatrics _____
- Adults_____

Per Order Data Collection Sheet

- Institution study number
- Customer type (hospital, home care, LTACH, LTC pharmacy, etc)
- CAPS Pharmacy site
- Pharmacist initials
- RX number
- Date
- Patient age group: Neonate, Pediatric, Adult
- 2 in 1 or 3 in 1
- Weight verified daily Yes/No

Type of Error

- Calcium phosphate incompatibility
- Negative QS water
- Osmolarity issue in PPN
- Amino Acid dose: High or low
- Amino Acid omission
- Dextrose dose: High or low
- Dextrose omission
- IV fat emulsion dose: High or low
- Electrolyte dose: High or low
- \circ $\;$ Trace element dose: High or low
- Trace element omission
- Drug additive dose: High or low (other drugs such as insulin)
- Multivitamin omission
- Multivitamin dose: High or low (usually omitted, less or greater than, or per L).
- Other vitamin dose: High or low
- Other meds that shouldn't be added
- Meds that were omitted from day before
- Insulin issues
- Latex allergy
- Other meds allergy
- Other reason (Please specify)
- Infusion rate omitted
- Nutrients ordered per liter
- Electrolytes and minerals ordered as ions
- Formulation unstable

Intervention- CAPS pharmacist identified error on the tool and then made a phone call to customer pharmacist. Was the order changed after the intervention: Yes or No

Note what the change was:_____