Published in final edited form as:

Nutr Clin Pract. 2017 December ; 32(6): 820–825. doi:10.1177/0884533617722759.

Home Parenteral Nutrition and Intravenous Fluid Errors Discovered through Novel Clinical Practice of Reconciling Compounding Records: A Case series

Margaret K. Murphy, PharmD¹, Kathleen M. Gura, PharmD^{1,2}, Christina Tascione, BS², Alexandra N. Carey, MD², Christopher P. Duggan, MD, MPH², Bram P. Raphael, MD²

¹Department of Pharmacy, Boston Children's Hospital, Boston, Massachusetts, USA

²Division of Gastroenterology, Hepatology and Nutrition, Boston Children's Hospital, Boston, Massachusetts, USA.

Abstract

Home parenteral nutrition (HPN) and home intravenous (IV) hydration are complex, high-risk life-sustaining therapies for children and adults with severe digestive disorders. HPN compounding errors have the potential to cause serious patient harm. Here we present a retrospective case series at an interdisciplinary pediatric HPN program that includes specialized pharmacists reconciling prescriptions against commercial compounding records. Seven HPN or IV hydration patients were affected by significant errors in anion balance, copper, potassium, sodium, and infusion volume. Outpatient pharmacists' review of compounding records as part of routine quality assurance process may be critical for identifying and preventing errors.

Keywords

parenteral nutrition; medication reconciliation; home nutrition support; medication errors; compounding; short bowel syndrome

Introduction

Parenteral nutrition (PN) is a complex intravenous nutrition admixture that contains 15 or more individual components including dextrose, amino acids, electrolytes, trace elements and vitamins that are combined using sterile technique. This high-risk, life-sustaining therapy may be prescribed for use by patients in the home setting. Use of home parenteral nutrition (HPN) has increased among children, as medical advances have improved survival of children with primary digestive disorders that result in intestinal failure.¹ Although premixed PN solutions are available commercially, these solutions are often not ideal for pediatric use, especially for those patients with chronic gastrointestinal conditions, because of the high variability of their nutrition and hydration needs.² Over 1,500 commercial home infusion pharmacies exist in the United States to compound customized HPN.³ Due to

Corresponding author and request of author for reprints: Bram P. Raphael, M.D., Division of Gastroenterology, Hepatology and Nutrition, Boston Children's Hospital, 300 Longwood Avenue, Boston, MA 02115, 617-355-6439, bram.raaphael@childrens.harvard.edu.

consolidation within the industry, many large commercial home infusion pharmacy companies now operate local branches nationwide. While there are published guidelines available, there are currently no standardized methods for prescribing or compounding HPN.^{4–7} Errors in PN compounding have the potential to cause serious patient harm.^{8,9} While PN compounding errors in the inpatient setting have been well documented, there is limited data regarding HPN errors compounded by home infusion pharmacies.^{8,10} In our previous 4-month pilot study, we reported a 46% rate of discrepancies between HPN prescriptions and composition among pediatric outpatients during a 4-month pilot period.¹¹

We aim to describe our experience with pediatric HPN patients in the outpatient setting affected by compounding errors in order to better appreciate underlying causes of common errors which may inform future safety initiatives.

Methods

The Home Parenteral Nutrition Program at Boston Children's Hospital (BCH) is an interdisciplinary program with HPN specialists including pediatric gastroenterology, nutrition, nursing and pharmacy. At routine ambulatory encounters, pharmacists specialized in nutrition support review HPN compounding records (provided by the home infusion pharmacy) and compare these records within the current HPN prescription to assess for accuracy. Currently this occurs with solutions that have been already compounded and are in use by the patients. Similarly, the pharmacists also review compounding records for any intravenous (IV) hydration solutions prescribed for patients who have been weaned from PN support. IV hydration solutions may contain only dextrose and electrolytes, not amino acids. The HPN pharmacists report any discrepancies found to the team and to the home infusion pharmacy. The team discusses any clinically significant discrepancies with the family and plans interventions based on the nature of the discrepancy and the patient's clinical status. The HPN pharmacists also collaborate with the team during inpatient admissions to ensure continuity of care. Here we report our experience with seven pediatric patients affected by significant compounding errors in their HPN or IV hydration. The errors occurred over a time period from April 2011 until November 2015. During this time period, greater than 216 distinct patients were followed in by the BCH HPN clinic (database began October 2011). The findings are summarized in Table 1. This work did not require institutional review board approval, since it was consistent with our institution's definition of quality improvement.

Case 1

A 2-year-old female with short bowel syndrome secondary to neonatal midgut volvulus and malrotation developed acute agitation, headaches and vomiting after starting infusion of newly delivered IV hydration. In the emergency department the following morning, her laboratory studies were notable for glucose 370 mg/dL (61–100mg/dL) and sodium 176 mmol/L (135–148 mEq/L). A head CT showed two intraparenchymal hemorrhages, a new finding in this patient, which were attributed to hypernatremic dehydration. The national home infusion pharmacy was contacted who then referred the team to a different local pharmacy that had been subcontracted to prepare the first doses of this hydration solution. At the time of the event, the HPN team was not aware that a secondary pharmacy was being

used. The HPN pharmacist then contacted this pharmacy where IV hydration had been prepared and uncovered a ten-fold increase in the sodium content (770 mEq/L compounded vs. 77mEq/L as prescribed). Inpatient laboratory testing of the home IV hydration provided by the family confirmed the compounding error. Unfortunately, a root cause analysis was not available for review. Over the first 36 hours of hospitalization, the patient's sodium was gradually normalized. The patient was discharged home after three days at near baseline neurologic status, with no lasting effects. The national homecare company no longer utilizes a secondary pharmacy and established their own local branch, thereby overseeing all compounding.

Case 2

A 6 month-old female with history of intra-uterine meconium pseudo-cyst leading to short bowel syndrome was discharged on HPN following a prolonged hospitalization. The patient's home infusion pharmacy contacted her mother to report that the PN bags they had delivered to the patient's home the day prior were made incorrectly with sodium 10% higher and potassium 5% lower than prescribed. The home infusion pharmacy also told the mother that they would be compounding a new, corrected shipment of HPN for same-day delivery. The patient's mother alerted the BCH HPN team about the error. The patient was asymptomatic, and PN therapy continued without interruption once the new delivery was made. A root cause analysis of the compounding error revealed that the home infusion pharmacist had been doing calculations using a spreadsheet and had not been using a proprietary software program available for their PN automated compounding device (ACD). The spreadsheet was known to have limitations when balancing electrolyte salt amounts in the solution, so some calculations were still being done by hand. Although the company had double-checks of calculations in place, the error was not recognized prior to dispensing of the HPN bags. The specific company branch that compounded this solution also reported having a high pharmacist turnover rate with many pharmacists still in various phases of training.

Case 3

A 10 year-old male with short bowel syndrome secondary to abdominal wall blast injury presented for routine outpatient visit. Upon review of compounding records, the HPN pharmacist discovered that the solution contained copper 700 mcg/day (23.3mcg/kg/day) instead of the prescribed amount of 400 mcg/day (13.3mcg/kg/day). The HPN prescription specified a trace element combination product providing copper 300 mcg/day with instructions to add additional 100 mcg/day of copper for a total of 400 mcg/day. Instead, the home infusion pharmacy provided the correct amount of trace element combination product but added an additional 400 mcg/day of copper for a total of 700 mcg/day. This error had been occurring for approximately one week. The patient's exam was at baseline. The team deferred additional laboratory studies since the total copper dose provided was still within a normal range for the patient's weight and the duration of exposure was only 7 days. The HPN team contacted the home infusion pharmacy, and a correctly compounded shipment of HPN was delivered shortly thereafter.

Case 4

A 9 month-old former 24-week gestation infant female with short bowel syndrome secondary to necrotizing enterocolitis presented for a routine clinic visit. The HPN pharmacist reviewing her compounding records noted the solution contained sodium 108 mEq/L (7.5 mEq/kg/day) as opposed to the prescribed 65 mEq/L (4.5 mEq/kg/day). The patient had received the incorrect solution for 10 days. At the outpatient appointment, the patient was well-appearing but weight gain was greater than expected. Her serum sodium concentration was normal at 137 mEq/L (normal reference range 135–148 mEq/L). Clinicians attributed the excess weight gain to sodium-related fluid retention as opposed to excess calorie provision. The team did not make any adjustments to the HPN prescription until the patient could be reassessed once receiving the solution with the correct amount of sodium. The home infusion pharmacy was contacted regarding the error and new, corrected HPN bags were compounded. The pharmacy attributed the sodium discrepancy to human error and planned to follow-up with a root cause analysis. However, no further follow up has been documented to date.

Case 5

A 12 month-old, former 35-week gestation male infant with short bowel syndrome secondary to gastroschisis presented for a routine clinic visit. The HPN pharmacist reviewing his records found that her HPN contained copper 500 mcg/day (56 mcg/kg/day) versus the prescribed 140 mcg/day (16 mcg/kg/day). The typical dose range is 15–30 mcg/kg/day. The patient had been receiving this greater than 3-fold copper overdose for approximately 2 months until the HPN pharmacist uncovered the discrepancy. Physical exam was at baseline. Hepatic laboratory values, coagulation studies, serum copper, and ceruloplasmin were all within normal limits. The team decided to remove all copper supplementation from prescribed HPN for the next few months with careful laboratory monitoring in order to allow time for attenuation of total body copper stores. The homecare company's root cause analysis revealed a chain of errors. One pharmacist made a ten-fold mathematical error when adding copper to the HPN solution. Although the amount of copper added was outside of the typical dose range, the compounding software did not make use of dose range checking with automatic dose range alerts. When a second pharmacist performed a double-check, the original prescription was not used as the source document and thus the error was missed again. Though the HPN was dispensed several times in subsequent weeks, only the adjusted ingredients were reviewed each time. Because copper was never adjusted, it was never re-checked and thus the copper dose remained incorrect in the HPN solution for two months.

Case 6

A 2 year-old male with short bowel syndrome secondary to a history of malrotation and midgut volvulus was seen for routine outpatient visit. The pharmacist reviewing the patient's HPN compounding records discovered that the HPN volume and electrolyte concentrations were not compounded as prescribed. The prescription specified a total nutrient admixture (TNA), containing lipids in the same bag as the dextrose/amino acid solution, with a total

volume of 690 ml (600 ml amino acid and dextrose solution with 90 ml lipid solution). However, the TNA was compounded with a total volume of only 600 ml (510 ml amino acid and dextrose solution with 90 ml lipid solution). Because the TNA was compounded based on a smaller volume, the final concentration of all electrolytes in the solution was also incorrect. The patient had recently transferred to a new home infusion pharmacy. This new pharmacy was contacted to discuss the error and the pharmacist at that company reported that the HPN prescription was misinterpreted upon formulation.

Case 7

A 5 year-old male with short bowel syndrome secondary to a history of necrotizing enterocolitis presented for a routine clinic visit. Upon review of compounding records, the HPN pharmacist discovered that the potassium content and anion balance did not match the prescription. The patient had been receiving HPN compounded with potassium 27 mEq/L (2.4 mEq/kg/day) instead of 20mEq/L (1.8 meq/kg/day) as prescribed. Additionally the solution was compounded with anion amounts of 89.9 mEq acetate and 113.4 mEq chloride instead of 94.7 mEq acetate and 94.7 mEq chloride as prescribed. At clinic visit, serum chemistries revealed potassium 4.11 mMol/L (3.2–4.5 mMol/L) and CO₂ 21mMol/L (22–30mMol/L). It was discovered that the home infusion pharmacist had not accounted for the amount of potassium contributed by the potassium phosphate during HPN formulation. This error resulted in the higher total HPN potassium concentration. The anion balance had also been calculated incorrectly upon formulation. Both calculations were done by hand without using compounding software and no double-check was performed. The home infusion pharmacy subsequently prepared a corrected shipment of HPN.

Discussion

For children with severe digestive disorders, HPN and IV hydration are life-saving therapies that many families and caregivers can safely administer at home.¹² They are also complex, high-risk medications associated with errors that can lead to serious patient harm. Errors can occur at any point along the medication¹³ use process: prescribing, transcribing, dispensing¹⁴, administering, and monitoring.¹⁵ The errors reported here occurred in the dispensing phase at the home infusion pharmacy and highlight important points for clinicians involved in the HPN process to be aware of to help identify and prevent errors.

Open communication can help HPN teams to identify knowledge gaps with home infusion pharmacy staff and to avoid errors. In Case 1, the IV hydration solution was compounded by a subcontracted pharmacy which had previously demonstrated knowledge gaps and was no longer receiving referrals by this HPN program. Similarly, HPN pharmacists communicating with the home infusion pharmacy involved in Case 2 identified that the pharmacy involved was not utilizing the software available for their ACD. Such software programs have been shown to improve compounding accuracy.^{5, 16} Prescribers should communicate uncommon compounding requests clearly and directly to the home infusion pharmacy to prevent confusion. In Case 3, the home infusion pharmacy misinterpreted the copper amount ordered on the HPN prescription, resulting in an overdose. It is well-known that backorders of nutritional products needed for PN compounding are frequent¹⁷ and may necessitate

substitution of one product for another, often on short notice. Home infusion pharmacists should clearly communicate any substitutions or omissions back to the prescriber so that HPN teams can put in place any additional clinical monitoring necessary. These opportunities for communication allow clinicians to foster ongoing professional relationships with their colleagues, facilitating exchange of knowledge and enhancing patient care.

After submitting HPN prescription changes, the clinical team should review the compounding records as soon as possible. Reconciliation of each compounded HPN or IV hydration solution prior to infusion would be ideal, such that errors could be detected before they reach the patient. In Cases 4 and 5, the errors had been occurring for 10 days and 2 months respectively without being noticed. Several obstacles may prevent HPN teams from performing such reconciliation in a timely fashion. It is currently not common practice for the home infusion pharmacy to send compounding records to the prescribers to review for accuracy. Based upon our experience, HPN teams may benefit from proactively requesting compounding records. There are challenges, however, to incorporating a pharmacist into workflow.

Pharmacists are in an ideal position to review and interpret HPN compounding records due to their specialized knowledge of different drug products and the effects they may have on the physical and chemical profile of an HPN solution. One challenge is that few programs have the resources to support a clinical pharmacist for non-billable activities such as prescription reconciliation. Furthermore, an HPN pharmacist may not always be available to do an immediate review since home infusion compounding may happen on evenings, weekends or holidays. While reconciliation by a pharmacist may be ideal, other clinicians specialized in nutrition support (e.g. dietitians, nurses, nurse practitioners, physicians) could be trained to perform HPN reconciliation. Though it may require a good deal of extra effort on the part of both HPN teams and home infusion pharmacies, timely HPN reconciliation can enhance patient safety and improve outcomes.

Standardized prescribing and compounding guidelines would be helpful for both the prescribers and the pharmacies in reducing errors.⁶ There is currently no legally mandated standard for prescribing or compounding HPN or IV hydration. As a result, HPN and IV hydration prescriptions are written in widely varying formats and home infusion pharmacies differ in compounding practices. The lack of standardization can lead to confusion, especially when patients change healthcare settings.¹⁸ Case 6 demonstrated confusion that occurred when a patient transitioned to a new home infusion pharmacy which misinterpreted the volume of the prescribed TNA. The American Society of Parenteral and Enteral Nutrition (ASPEN), American Society of Health-System Pharmacists (ASHP) and Institute for Safe Medication Practices (ISMP) have all published clinical guidelines and safe practice recommendations regarding PN prescribing and compounding^{5-7,19,20} but adherence is voluntary and not all pharmacists may be aware of these guidelines. Home infusion pharmacies vary widely in their approaches to compounding, depending on that company's software, equipment, staffing and other variables. We observed compounding errors resulting from failure to follow two specific safety recommendations: utilization of dose-limit warnings (Case 5) and independent double-checks (Case 7). ACD software may

include dose-limit warnings that alert clinicians when a PN ingredient is ordered in an amount outside of the usual dose range and can help to prevent catastrophic dosing errors. However, it should be noted that not all ACD software programs utilize dose range checking as part of their safety alerts.²¹ Independent double-checks of high risk medications such as PN are recommended in order to identify and prevent errors.²² Such errors demonstrate the need for standardization of HPN prescribing and compounding practices. Limiting variation of these practices can minimize opportunities for misinterpretation and errors, and may be especially important during transitions of care.

Although this report focuses on errors made by home infusion pharmacies, HPN teams can also be culpable. Prescriptions may not be able to be compounded as ordered by the home infusion pharmacy for a variety of reasons, including product backorders and formulary preferences. Additionally, PN stability limitations are quite different between the inpatient setting, in which solutions are compounded and immediately infused, and the homecare setting, in which the solution may not be infused for days after compounding. Home infusion pharmacists should alert prescribers to potential product backorders or solution instabilities and should feel comfortable suggesting prescription changes that improve safety. Regardless of whether or not a pharmacist is involved in the prescription review process, HPN staff should never assume the inpatient prescription is appropriate for home use and should critically review and clarify. Timely communications between pharmacies and HPN teams can be challenging, especially because compounding and delivery of HPN to the patient's home are often time sensitive.

Conclusion

HPN compounding errors with potential for patient harm can and do occur, though the literature documenting such instances is limited. Open communication between HPN teams and home infusion pharmacies is vital. In addition, timely review of HPN and IV hydration compounding records may be critical for identifying and preventing errors before clinical signs or symptoms develop. Pharmacists specialized in nutrition support are uniquely able to interpret and analyze compounding records and are integral HPN team members. Standardized prescribing and compounding processes, though not mandated, should be encouraged. Despite the many challenges, HPN teams and home infusion pharmacies should promote collaboration to improve patient and medication safety. Further study and documentation of HPN and IV hydration compounding errors are warranted.

Conflict of Interest –

Alexandra N. Carey receives funding from Fresenius Kabi as part of an FDA-approved pilot study. A license agreement for the use of Omegaven has been signed by Boston Children's Hospital and Fresenius Kabi, and a patent has been submitted by Boston Children's Hospital on behalf of Kathleen M. Gura, who also serves on the Scientific Advisory Boards for Pronova-BASF and Sancilio and Company. Kathleen M. Gura also serves on the Pharmaceutical Advisory Board for B. Braun USA.

We thank all the past and present members of the Home Parenteral Nutrition Team (Mary Gallotto, Melissa Takvorian-Bene, Jennifer McClelland, Carolyn Rosa, Glendalis Grullon, Megan Dalton, Casey Wall, Brittany Depaula, Megan Gray, Sharon Collier, Carlotta Hayes, Clifford Lo and Denise Richardson), as well as Center for Advanced Intestinal Rehabilitation teams for their expert care of these patients.

Abbreviations:

PN	parenteral nutrition
HPN	home parenteral nutrition
BCH	Boston Children's Hospital
IV	intravenous
TNA	total nutrient admixture
ACD	automated compounding device

References

- Colomb V, Dabbas-Tyan M, Taupin P, et al. Long-term outcome of children receiving home parenteral and enteral nutrition: a 20-year single center experience in 302 patients. *J Pediatr Gastroenterol Nutr.* 2007;44:347–53. [PubMed: 17325556]
- Singh A, Rauch D. Commercial Premixed parenteral nutrition and its potential role in pediatrics. *Hosp Pediatr.* 2016 1;6(1):34–6. Epub 2015 Jan 1. [PubMed: 26644046]
- National Home Infusion Association. Infusion FAQs. <http://www.nhia.org/faqs.cfm#faq13>. Accessed October 31, 2016.
- Mirtallo J, Canada T, Johnson D, et al. Safe practices for parenteral nutrition. *JPEN J Parenter Enteral Nutr.* 2004;28:S39–S70. [PubMed: 15568296]
- Ayers P, Adams S, Boullata J, et al. American Society for Parenteral and Enteral Nutrition. A.S.P.E.N. parenteral nutrition safety consensus recommendations. *JPEN J Parenter Enteral Nutr.* 2014;38(3): 296–333. [PubMed: 24280129]
- Boullata JI, Gilbert K, Sacks G, et al. American Society for Parenteral and Enteral Nutrition. 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. [PubMed: 24531708]
- American Society of Health-System Pharmacists. ASHP guidelines on the safe use of automated compounding devices for the preparation of parenteral nutrition admixtures. *Am J Health-Sys Pharm.* 2000;57:1343–1348.
- 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): 966–974. [PubMed: 19637950]
- Cohen MR. Safe practices for compounding of parenteral nutrition. *JPEN J Parenter Enteral Nutr.* 2012 Mar;36(2 Suppl):14S–19S. [PubMed: 22383681]
- Flynn EA, Pearson RE, Barker KN. Observational study of accuracy in compounding iv admixtures at five hospitals. *Am J Health Syst Pharm* 1997;54:904–912. [PubMed: 9114922]
- Raphael BP, Murphy M, Gura KM, et al. Discrepancies between prescribed and actual pediatric home parenteral nutrition solutions. *Nutr Clin Pract.* 0884533616639410, first published on 4 18, 2016 doi:10.1177/0884533616639410.
- Forchielli ML, Richardson D, Folkman J, Gura K, Lo CW. Better living through chemistry, constant monitoring, and prompt interventions: 26 years on home parenteral nutrition without major complications. *Nutrition.* 2008;24:103–107. [PubMed: 17996420]
- Diamanti A, Basso MS, Castro M, Calce A, Pietrobattista A, Gambarara M. Prevalence of life-threatening complications in pediatric patients affected by intestinal failure. *Transplant Proc.* 2007 6;39(5):1632–3. [PubMed: 17580205]
- Dibb M, Teubner A, Theis V, Shaffer J, Lal S. Review article: the management of long-term parenteral nutrition. *Aliment Pharmacol Ther.* 2013 3;37(6):587–603. [PubMed: 23331163]
- Institute of Medicine. Preventing medication errors. Washington, DC: National Academy Press; 2007.

16. Flynn EA, Pearson RE, Barker K. Observational study of accuracy in compounding IV admixtures in five hospitals. *Am J Health-Syst Pharm*. 1997; 54(8):904–912. [PubMed: 9114922]
17. Storey MA, Weber RJ, Besco K, Beatty S, Aizawa K, Mirtallo JM. Evaluation of Parenteral Nutrition Errors in an Era of Drug Shortages. *Nutr Clin Pract* 4 2016 31: 211–217. [PubMed: 26507187]
18. Carey LC, Haffey M. Incident: home TPN formula order misinterpreted after hospital admission. *Home Care Highlights*. Spring 1995:7.
19. Institute for Safe Medication Practices. Medication Safety Alert, April 21, 2011. Safety Brief: Parenteral Nutrition deaths tied to drug shortage. <http://www.ismp.org/newsletters/acutecare/articles/20110421.asp>. Accessed October 2016.
20. Institute for Safe Medication Practices. Medication Safety Alert, September 6, 2007. Fatal 1,000-fold overdoses can occur, particularly in neonates, by transposing mcg and mg. <http://www.ismp.org/newsletters/acutecare/articles/20070906.asp>. Accessed October 2016.
21. Boullata JI, Guenter P, Mirtallo JM. A parenteral nutrition use survey with gap analysis. *JPEN J Parenter Enteral Nutr*. 2013; 37:212–222. [PubMed: 23112276]
22. ISMP. Santa checks his list twice. Shouldn't we? ISMP Medication Safety Alert! 2009;14(25):1–2.

Table 1:

Summary of errors in compounded home parenteral nutrition and intravenous hydration solutions

Case	Component	Error type	Error cause	Amount prescribed	Amount compounded	Issue at play	Possible prevention strategy
1	sodium	incorrect dose	miscalculation	77 mEq/L	770 mEq/L	unknown	open communication
2	sodium potassium	incorrect dose incorrect dose	Miscalculation miscalculation	35 mEq/L 15mEq/L	38.5 mEq/L 14 mEq/L	technical limitations, human error	utilization of ACD software
3	copper	incorrect dose	misinterpretation	400 meg/day	700 meg/day	human error	open communication
4	sodium	incorrect dose	unknown	65 mEq/L	108 mEq/L	human error	double-checks
5	copper	incorrect dose	miscalculation	140 meg/day	500mcg/day	human error	utilization of dose-range checking alerts
6	volume	incorrect volume	misinterpretation	690 mL/day	600 mL/day	human error	open communication
7	potassium anion amounts	incorrect dose incorrect dose	Miscalculation miscalculation	20 mEq/L 94.7 mEq acetate 94.7 mEq chloride	27 mEq/L 89.9 mEq acetate 113.4 mEq chloride	technical limitations, human error	double checks, utilization of ACD software