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Use of Premixed Parenteral Nutrition during a Phosphate Shortage in a Non-Critically Ill Population

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Abstract

Background—Drug shortages pose prescribing problems to clinicians. During fiscal year (FY) 2014, an acute shortage of intravenous potassium phosphate (K-Phos IV), a common supplement in parenteral nutrition (PN), prompted the use of premixed instead of individualized PN to conserve K-Phos IV. Here we quantify the K-Phos IV conserved by using premixed PN and the associated cost differences.

Materials and Methods—Costs of preparing premixed PN vs individualized PN of equivalent composition were calculated for FY 2014 at a single center tertiary care facility. Quantity and cost of K-Phos IV saved was calculated based on the number of premixed PN prescriptions. Costs for FY 2015 were projected based on drug costs from July 2014.

Results—During FY 2014, prescribing premixed in lieu of individualized PN conserved 16,440 mmol K-Phos IV but increased cost of PN by \$4,080.45. However, increases in K-Phos IV cost at the end of FY 2014 resulted in premixed PN as a relatively less expensive therapy than individualized PN for our institution. Cost savings of \$7,092.20 due to use of premixed PN is projected for FY 2015.

Conclusions—Prescribing premixed PN conserves K-Phos IV during shortages, but it increased direct drug spending in non-critically ill patients at our institution during FY 2014. Persistent

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shortages can drive market costs of K-Phos IV however, necessitating frequent reconsideration of resource utilization.

Background

Medication shortages pose significant and ongoing challenges to modern health system pharmacies. According to the American Society of Health-System Pharmacists (ASHP), 302 active national shortages occurred in the final quarter of 2013, up 50% from three years prior.¹ Generic injectable products account for greater than 80% of all medication shortages, with intravenous electrolytes making up 7% of overall drug shortages. As such, parenteral nutrition (PN) admixtures are disproportionately affected by these shortages despite lack of publicity. As of January 2014, ASHP listed 19 PN additives on national shortage.¹ These specific drug shortages create significant challenges for nutrition support prescribers and, while some national guidelines have been proposed to cope with PN additive shortages, few data exist showing the effects of these guidelines on resource utilization, cost, and patient outcomes.

In response to ongoing national shortages of intravenous potassium phosphate (K-Phos IV) since 2010, our institution progressively restricted K-Phos IV supplementation. Prior to 2011, prescribers could order K-Phos IV for any patient with a serum phosphate level less than 3.0 mg/dL. In 2011, the prescription threshold for K-Phos IV was restricted to a serum phosphate < 2.5 mg/dL and in March 2013 to a serum phosphate < 2.0 mg/dL in non-critically ill patients. Providers were further encouraged to prescribe oral electrolyte supplementation whenever possible.

An acute shortage of K-Phos IV during fiscal year (FY) 2014 prompted a significant change in our hospital's PN prescribing algorithms. This shortage incited a strategic move toward prescribing premixed PN, Clinimix E (Baxter, Deerfield, IL), instead of individually compounded PN whenever possible to conserve K-Phos IV. Clinimix E is a commercially available premixed PN product distributed as a ready-to-use PN admixture complete with amino acids, dextrose, and electrolytes. It contains 15 mmol of K-Phos IV per liter so further addition of K-Phos IV to PN may not be necessary. Individually compounded PN typically contains 15–30 mmol of K-Phos IV per liter in its preparation.

The American Society of Parenteral and Enteral Nutrition (ASPEN) recommends the use of “premixed PN” products when clinically appropriate during drug shortages.² This report describes our experience using premixed PN for adult PN in a non-critically ill population in the setting of a national K-Phos IV shortage. Primary outcomes evaluated include the quantity of K-Phos IV conserved through the use of premixed PN in lieu of individually compounded PN as well as institutional product costs accrued using this method. Additionally, the study evaluates the projected cost of premixed PN during FY 2015.

Methods

Pharmacy management quantified the number of bags of premixed PN and their cost per prescription used in the treatment of adult patients in FY 2014 (July 1, 2013 to June 30, 2014) at a 566-bed academic tertiary referral hospital. All PN (premixed or individualized)

was prescribed by the Nutrition Support Team (NST). Patients receiving premixed PN largely consisted of previously well-nourished, stable post-operative patients with delayed return of bowel function beyond one week following abdominal surgery. As a result of our previous experience with premixed PN in critically ill patients³, this formula was not used in patients with renal or hepatic failure, hyponatremia, metabolic acidosis or alkalosis, or patients at high risk for refeeding syndrome. The study was certified as not human subjects research by the Institutional Review Board of the University of Wisconsin-Madison (Protocol 2014-1513).

Pharmacy management also retrospectively queried product costs during this time period to determine the cost of producing both individualized and premixed PN. The costs evaluated in our analysis are listed in Table 1. They include: 1) the daily line set necessary for compounding, 2) the lease on the automated compounder (ExactaMix 2400 Automated Compounding Device, Baxter, Deerfield, IL), 3) the non-PVC (non-polyvinyl chloride) bag used during compounding, and 4) the raw macronutrients, electrolytes, and sterile water necessary to compound an individualized PN admixture with the same composition as Clinimix E 4.25/10 (Baxter, Deerfield, IL) (4.25% protein, 10% dextrose) and Clinimix E 5/15 (Baxter, Deerfield, IL) (5% protein, 15% dextrose), (Table 2). Costs of the line set and compounder lease were divided by the average number of bags of PN compounded daily. Cost data for all PN components except for K-Phos IV were averaged over the course of the 12-month study period. Cost data for K-Phos IV were averaged monthly due to anticipated cost changes associated with K-Phos IV shortage throughout FY 2014. These data were used to determine the cost of individualized PN identically formulated to corresponding premixed PN including monthly variation in cost of K-Phos IV.

The quantity of K-Phos IV conserved by prescribing premixed PN instead of individualized PN was determined based on the number of premixed PN prescriptions and quantity of K-Phos IV in each of those prescriptions (30 mmol in each 2 liter bag). Cost savings associated with K-Phos IV conservation as a result of prescribing premixed PN were determined based on the monthly cost of K-Phos IV and aggregated over the study period.

The maximal potential cost to our institution if individualized PN had been prescribed for all patients during FY 2014 was calculated. The actual product cost of premixed PN dispensed was analyzed independently for both Clinimix E products. Cost savings represents the difference between actual cost of premixed PN prescribed and the potential maximal cost if individualized PN with equivalent composition to the premixed PN had been prescribed. Costs were determined monthly and aggregated over the study period.

To determine projected costs of K-Phos IV for FY 2015, we evaluated the cost of K-Phos IV to our institution in the month following FY 2014. Since the cost of K-Phos IV only fluctuated during the final month of FY 2014, we determined the cost of K-Phos IV for FY 2015 based on its cost during July 2014 with the assumption that it was unlikely to decrease in price.

Results

During FY 2014 our NST prescribed an average of 18 2-liter bags of either individualized or premixed PN daily, and the hospital dispensed a total of 259 2-liter bags of Clinimix E 4.25/10 and 289 2-liter bags of Clinimix E 5/15 (average of 22 and 24 bags per month, respectively). Given the 30 mmol of K-Phos IV included in each 2-liter bag, prescribing premixed PN instead of individualized PN conserved a maximum of 16,440 mmol of K-Phos IV during FY 2014 (Figure 1). This K-Phos IV was available for other uses at our institution, (i.e. support of critically ill or pediatric patients, electrolyte repletion, etc.).

Prescribing premixed PN incurred additional costs, however. Use of premixed PN increased direct drug spending by \$4,080.45 during the study period based on pricing of supplies and raw ingredients at our institution. Based on materials alone, premixed PN remains more expensive than individualized PN at our institution. During the first 11 months of FY 2014, Clinimix E 4.25/10 and 5/15 cost \$7.10 and \$8.07 more per 2-liter bag of PN than comparable individualized PN, respectively. During the final month of our study, June 2014, the excess cost per bag of premixed PN decreased on average to \$5.05 and \$6.02, respectively, as a direct result of increased cost of K-Phos IV due to its national shortage. In fact, the bulk cost of 3750 mmol K-Phos IV increased 14-fold during the final days of the fiscal year (Figure 2). Despite the very small portion of our study period affected by this cost increase (3 of 365 days), it resulted in a relative price decrease for the cost of Clinimix E 4.25/10 and 5/15 of 29 % and 25 % per 2-liter bag, respectively. Projecting the new cost of K-Phos IV over FY 2015, preferential prescription of premixed PN over individualized PN results in an extrapolated savings of \$7,092.20, counterbalancing losses from FY 2014 provided the cost of K-Phos IV remains stable or increases (Figure 3), for a net savings of \$3,011.75.

Discussion

Drug shortages are expensive with estimated labor increases costing the U.S. healthcare system \$216 million annually in addition to a \$200 million increase in drug spending.⁴ Associated indirect costs include increased medication errors and altered clinical course, particularly in patients receiving PN.^{5,6} In fact, following laparotomy for small bowel obstruction, patients receiving PN during an extensive period of drug shortage sustained significant increases in length of hospital stay and average hospital cost compared to a period of limited drug shortage.⁷ Data demonstrating the impact of PN component shortages is scarce and our current coping strategies remain inadequate despite persistent shortages. As a nutrition support community we have been challenged to evaluate and share policies implemented in the face of drug shortages and to assess their effects on “resource utilization, hospital length of stay, readmission rate, and other related clinical events.”⁸

Our institution relies on pharmacy to manage available resources during drug shortages. Over the last three years, shortages of amino acids³, lipids, multivitamins, trace elements, and electrolytes have disproportionately affected PN mandating changes in practice by our NST. Most recently, unavailability of K-Phos IV lead to preferentially using premixed PN rather than individualized PN in clinically appropriate patients. Changing our practice

during this critical shortage successfully conserved 16,440 mmol of K-Phos IV making it available for other uses, such as electrolyte supplementation in the setting of moderate-to-severe deficiency.

Prescribing premixed PN rather than individualized PN modestly increased direct drug spending for our hospital by \$4,080.45 (\$340.04 per month) during the study period. However, this number fluctuates with the cost of individual ingredients and is dependent on institutional contracts and PN production. If costs of K-Phos IV continue to escalate, preferentially prescribing a premixed PN formula will generate a cost savings of \$7,092.20 (\$591.02 per month) in the subsequent fiscal year with a net cost savings of \$3,011.75 over the two year period at our institution.

A large confounding factor in this study is the price of labor. Our study does not account for the labor of the prescribing pharmacist, in our case the NST member, the technician labor required for PN preparation/compounding, and the dispensing pharmacist's labor. Undoubtedly individualized PN is more labor intensive than premixed PN across these three areas. Our retrospective study was not designed to capture these costs. A recent report suggests that approximately 60 minutes of combined technician and pharmacist labor is saved per bag of PN when premixed PN is used instead of individualized PN, with the bulk of this time attributable to technician labor of compounding.⁹ This study does not account for the PN prescriber's labor though. While dollar amounts can be ascribed to the time saved, more likely the time is reallocated within the pharmacy. Previously our group reported on the effect of prescribing premixed versus individualized PN on piggyback electrolyte use during an amino acid shortage in 2010.³ We concluded that using premixed PN significantly increased intravenous electrolyte supplementation and cost at our institution. While the studies differ in several aspects (reason for using premixed PN, acuity of the patient population, supplemental phosphate availability, etc.), it highlights that labor saved by using premixed PN may be reallocated preparation and dispensing of supplemental electrolyte prescriptions. Studies incorporating the cost associated with prescribing, compounding, and dispensing labor are needed in addition to studies determining how "saved time" is reallocated.

There are several other limitations to our study. First, this retrospective study cannot absolutely conclude that the cost of K-Phos IV increased solely due to the drug shortage or that increased PN costs were dependent only on the cost of that single additive. For instance, a concurrent calcium shortage developed during FY 2014 which ultimately affected our prescribing practices. However the cost of calcium chloride was held constant in our calculations to focus on the K-Phos IV shortage which we viewed as more acute as it is what prompted this study. Additionally, in our projection of cost savings over the two year period, we assume K-Phos IV expenses will remain constant or increase during FY 2015; this may or may not prove to be true. Thirdly, to calculate the costs for K-Phos IV during the period of study, we applied the costs of a standard size vial using the concentrations needed for PN preparation. Acute drug shortages may necessitate purchasing larger or smaller vial sizes or negotiating with compounding pharmacies to obtain adequate quantities of electrolyte solutions. These changes may result in higher or lower unit costs which were not captured by our analysis although we expect that the purchase price would rarely be lower than

purchase directly from the manufacturer. Furthermore, we captured neither quantity nor cost of piggyback electrolytes administered to this patient population. Lastly, these data reflect costs to our institution, a tertiary-care center with a formal NST and capabilities for individually compounding PN with an average daily PN census of 18 preparations during FY 2014. Comparable prescribing changes at other hospitals likely generate different results based on volume of PN prescribed daily and vendor contracts.

In conclusion, medication shortages increase healthcare costs and disrupt patient care. By preferentially prescribing premixed PN in non-critically ill patients, our NST helped conserve K-Phos IV over FY 2014. While this intervention resulted in increased direct drug spending at our institution, enough K-Phos IV was conserved by this means to meet our clinical needs and limit outsourcing. If the current K-Phos IV shortage persists and product costs continue to rise, premixed PN may become a feasible alternative for our population of non-critically ill adults. Frequent assessment and reevaluation of product availability and cost is necessary to optimize resource utilization in the face of persistent drug shortages.

References

1. Hassig TB, McKinzie BP, Fortier CR, Taber D. Clinical management strategies and implications for parenteral nutrition drug shortages in adult patients. *Pharmacotherapy*. 2014; 34:72–84. [PubMed: 24399661]
2. Holcombe B, Andris DA, Brooks G, Houston DR, Plogsted SW. Parenteral nutrition electrolyte/mineral product shortage considerations. *JPEN J Parenter Enteral Nutr*. 2011; 35:434–436. [PubMed: 21700963]
3. Busch RA, Curtis CS, Levenson GE, Kudsk KA. Use of Piggyback Electrolytes for Patients Receiving Individually Prescribed vs Premixed Parenteral Nutrition. *JPEN J Parenter Enteral Nutr*. 2014 Epub ahead of print.
4. Kaakeh R, Sweet BV, Reilly C, et al. Impact of drug shortages on U.S. health systems. *Am J Health Syst Pharm*. 2011; 68:1811–1819. [PubMed: 21930639]
5. Holcombe B. Parenteral nutrition product shortages: impact on safety. *JPEN J Parenter Enteral Nutr*. 2012; 36:44S–47S. [PubMed: 22282871]
6. Drug shortages: national survey reveals high level of frustration, low level of safety. ISMP Medication Safety Alert!. 2014; 15:1–4. <http://www.ismp.org/newsletters/acutecare/articles/20100923.asp>.
7. Bible JR, Evans DC, Payne B, Mostafavifar L. Impact of drug shortages on patients receiving parenteral nutrition after laparotomy. *JPEN J Parenter Enteral Nutr*. 2014; 38:65S–71S. [PubMed: 25239113]
8. Chan LN. Iatrogenic malnutrition: a serious public health issue caused by drug shortages. *JPEN J Parenter Enteral Nutr*. 2013; 37:702–704. [PubMed: 24186877]
9. Blanchette LM, Huiras P, Papadopoulos S. Standardized versus custom parenteral nutrition: impact on clinical and cost-related outcomes. *Am J Health Syst Pharm*. 2014; 71:114–121. [PubMed: 24375603]

Figure 1.
Injectable potassium phosphate (K-Phos IV) conserved from Clinimix E 4.25/10 and Clinimix E 5/15 prescription instead of individualized parenteral nutrition prescription

Cost of K-Phos IV During Fiscal Year 2014

Figure 2.

Cost of injectable potassium phosphate (K-Phos IV) during fiscal year 2014. Costs represent average monthly price for bulk K-Phos IV.

Projected Cost Savings of Prescribing Premixed PN Instead
of Individualized PN During Fiscal Years 2014 and 2015 with
K-Phos IV Shortage

Figure 3.

Pooled cost savings from Clinimix E 4.25/10 and Clinimix E 5/15 prescription instead of individualized PN prescription extrapolated through fiscal year 2015. PN: parenteral nutrition; K-Phos IV = injectable potassium phosphate.

Table 1

Costs considered in analysis of preparing individualized versus premixed parenteral nutrition. PN: parenteral nutrition; PVC: polyvinyl chloride.

Costs	Individualized PN	Premixed PN
Daily Line Set	(cost of line set)/(average number of bags compounded daily)	-
Compounder Lease	(cost of monthly compounder lease)/(30 days)/(average number of bags compounded daily)	-
Non-PVC Bag	Non-PVC bag for compounding	-
PN Ingredients	Raw ingredients at concentrations equivalent to Clinimix E	Clinimix E cost to our institution

Table 2

Composition of Clinimix E 4.25/10 and Clinimix E 5/15. Note both Clinimix E products are dispensed as 2-liter bags at our institution.

Component	Clinimix E 4.25/10	Clinimix E 5/15
Dextrose, g/L	100	150
Amino Acids, g/L	42.5	50
Sodium, mEq/L	35	
Potassium, mEq/L	30	
Magnesium, mEq/L	5	
Calcium, mEq/L	4.5	
Chloride, mEq/L	39	
Acetate, mEq/L	70	80
Phosphate, mmol/L	15	