Avoiding Patient Harm With Parenteral Nutrition During Electrolyte Shortages

Hospital Pharmacy
2018, Vol. 53(6) 403–407
© The Author(s) 2018
Article reuse guidelines:
sagepub.com/journals-permissions
DOI: 10.1177/0018578718769571
journals.sagepub.com/home/hpx

Eric W. Brown¹, Nicole H. McClellan², Gayle Minard³,
George O. Maish III³, and Roland N. Dickerson³

Abstract

Purpose: We report a case of a patient with gastrointestinal dysmotility and substantial drainage losses who required parenteral nutrition (PN) and developed a non-anion gap metabolic acidosis secondary to a shortage of concurrent potassium acetate and sodium acetate PN additives. We describe how severe PN-associated metabolic consequences were averted during this acetate shortage. **Summary:** The patient with inability to swallow and significant weight loss was admitted to the hospital and given PN after failure to tolerate either gastric or jejunal feeding due to dysmotility and severe abdominal distension and discomfort. PN was initiated and the nasogastric and jejunal tubes were left to low intermittent suction or gravity drainage (average losses of 800 mL and 1600 mL daily, respectively) to reduce abdominal distension. The patient had been stable on PN for approximately 2 months prior to when a shortage in potassium acetate and sodium acetate occurred. As a result, potassium and sodium requirements had to be met with chloride and phosphate salts. The patient developed a non-anion gap metabolic acidosis after 11 days of acetate-free PN. Progression to severe acidemia was avoided by administration of sodium bicarbonate daily for 3 days and replacement of 0.9% sodium chloride supplemental intravenous fluid with lactated ringers solution. **Conclusion:** This case report illustrates that PN component shortages require clinicians to closely monitor patients who require PN. In addition, clinicians may need to use creative therapeutic strategies to avoid potential serious patient harm during PN component shortages.

Keywords

fluid and electrolyte disorders, intravenous therapy, nutrition, nutritional support, medication safety

Introduction

The health care crisis of medication shortages continues to plague clinicians in the United States and often can have a significant detrimental impact on patient care and safety.^{1,2} These shortages have not been limited solely to drugs but also commonly occur with parenteral nutrition (PN) components including electrolytes, vitamins, trace minerals, lipid emulsion, and amino acids.^{3,4} Due to the abundance of PN component shortages, patients who receive PN may require creative therapeutic strategies to avoid patient harm under certain circumstances.⁵ We report a case of a patient with severe and voluminous gastrointestinal drainage losses who required PN and developed a mild non-anion gap metabolic acidosis secondary to a shortage of potassium and sodium acetate additives. We describe how we averted severe metabolic consequences with short-term therapy combined with a subsequent change in supplemental intravenous fluid therapy during the period of the acetate shortage.

Case Presentation

The patient, a 65-year-old, 82 kg, African American male, presented to the emergency department with complaints of inability to swallow solids for 1 to 2 months and generalized weakness. He had been having a sore throat and difficulty speaking for 4 weeks and had been complaining of symptoms associated with gastroesophageal reflux disease for 4 months. The patient had been having intermittent nausea and abdominal pain in the midepigastria region which he rated 5 out of 10 in severity. An esophagogastroduodenoscopy indicated a Los

¹UCHealth Memorial Hospital Central, Colorado Springs, CO, USA

²Regional One Health, Memphis, TN, USA

³The University of Tennessee Health Science Center, Memphis, TN, USA

Corresponding Author:

Roland N. Dickerson, College of Pharmacy, The University of Tennessee Health Science Center, 881 Madison Avenue, Suite 345, Memphis, TN 38163, USA.

Email: rdickerson@uthsc.edu

Table 1. Electrolyte Content of Gastrointestinal Fluids.⁸

Fluid	Average daily volume (mL)	Sodium (mEq/L)	Potassium (mEq/L)	Chloride (mEq/L)	Bicarbonate (mEq/L)	Magnesium (mEq/L)
Stomach	1000-2000	60-90	10-15	100-130		0.9
Duodenum	400-600	140	5-10	90-120	80	
Small intestine	2000-2500	140	5-10	90-120	30-40	6-12
Colon	<300	60	20-30	50		6-12
Pancreas	600-800	140	5-10	75	115	0.4
Bile	300-600	140	5-10	100	30	1.1

Angeles class C erosive reflux-induced esophagitis in the distal third of the esophagus. During his hospital stay, the patient experienced sepsis and required vasopressor therapy from which he recovered. However, his continued respiratory failure necessitated prolonged ventilator support. He ultimately received a tracheostomy and was transferred to a long-term acute care facility for ventilator weaning. The long-term acute care facility, legally considered a separate entity, is housed within the hospital and pharmacy services and medications are provided to the facility by the hospital. Thus, any medication shortages experienced by the hospital will also occur for the long-term acute care facility.

While at the long-term acute care facility, provision of nasogastric feeding failed due to persistent episodes of marked abdominal distension, elevated gastric residual volumes, and regurgitation despite metoclopramide and erythromycin prokinetic pharmacotherapy.⁶ A radiologic scintigraphy study revealed delayed gastric emptying: 34% of a liquid meal emptied from the stomach within 60 minutes and the calculated half-emptying time was 85 minutes. The patient underwent a laparotomy for placement of a feeding jejunostomy tube; however, subsequent attempts at jejunal feeding also failed due to severe abdominal distension and discomfort. The Nutrition Support Service was consulted to initiate PN secondary to sustained intermittent failures with enteral nutrition and severe abdominal distension and discomfort. His jejunostomy tube was changed from feeding to gravity drainage concurrently with low-intermittent gastric suction to attempt to provide some relief to the patient via abdominal decompression. Nutritional assessment revealed a significant weight loss of 20 pounds prior to admission with his current body weight at 82 kg (100% of estimated ideal body weight for a height of 74 inches), body mass index of 23.2 kg/m², calculated basal energy expenditure (BEE)⁷ of 1695 kcal/d, serum albumin concentration of 2.8 g/dL, prealbumin concentration of 5.3 mg/dL, and c-reactive protein concentration of 4.1 mg/dL.

PN was initiated. His goal regimen was comprised of 300 g of dextrose, 150 g of 15% Clinisol amino acid (Baxter Healthcare Corporation, Deerfield, Illinois), and 60 g of 30% Intralipid soybean-based lipid emulsion (Baxter Healthcare Corporation, Deerfield, Illinois) in 1.9 liters of fluid. This regimen provided 2200 kcal/d and 1.8 g/kg/d of

protein (27 kcal/kg/d or 1.3 times the BEE, 2.5 mg/kg/min of glucose, 0.7 g/kg/d of lipid) to facilitate nutritional recovery. Gastric and jejunal fluid losses averaged about 800 mL and 1600 mL per day, respectively. Additional supplemental intravenous fluids (0.9% sodium chloride and 0.45% sodium chloride) were given to compensate for excessive daily gastrointestinal fluid drainage.

The patient had been receiving a stable PN regimen without significant fluid, macronutrient, electrolyte, trace mineral, or vitamin content changes for over 2 months. Supplemental intravenous fluids were titrated accordingly to measured gastrointestinal losses to maintain euolemia and normal serum electrolyte concentrations. Chloride and acetate intakes from the PN and supplemental intravenous fluids averaged 430 mEq/d and 60 mEq/d, respectively. These intakes were estimated based on electrolyte content of gastrointestinal fluids (Table 1) and adjusted using commercially available intravenous fluids with differing electrolyte content (Table 2) based on patient's serum electrolyte concentration response. On hospital day 83, the hospital experienced an outage of both intravenous sodium acetate and potassium acetate. The patient's serum total carbon dioxide content significantly fell from 26 mEq/L to 18 mEq/L after 11 days of acetate-free PN (Figure 1). Serum chloride concentrations remained stable from an average of 107 mEq/L to 106 mEq/L. An arterial blood gas measurement was obtained which revealed a mild non-anion gap metabolic acidosis (pH of 7.28, pO₂ of 118 mm Hg, pCO₂ of 36 mm Hg, bicarbonate of 17 mEq/L, anion gap of 12 mEq/L, lactate of 0.8 mmol/L, and a serum albumin concentration of 3.6 g/dL). It was estimated that the patient had a total bicarbonate deficit of approximately 290 mEq based on an estimated volume of distribution of 0.5 L/kg and a normal arterial serum bicarbonate concentration of 24 mEq/L.⁸ The patient was given a short-term intravenous infusion of 50 mEq sodium bicarbonate daily for 3 days (a total of 150 mEq). The supplemental intravenous 0.9% sodium chloride fluid was discontinued, and the patient was then given 2 liters of lactated ringers solution daily (to provide a total of 56 mEq of lactate daily and reduced chloride intake by about 90 mEq daily compared with 0.9% sodium chloride solution) until the hospital shortage of intravenous sodium acetate and potassium acetate was resolved. Another

Table 2. Electrolyte Composition of Common Intravenous Solutions.⁸

Solutions	Sodium (mEq/L)	Potassium (mEq/L)	Chloride (mEq/L)	Bicarbonate (mEq/L)	Calcium (mEq/L)
5% dextrose in water					
0.9% sodium chloride	154		154		
0.45% sodium chloride	77		77		
5% dextrose in 0.225% sodium chloride	34		34		
Lactated ringers solution	130	4	109	28	2.7

Figure 1. Timeline of interventions and serum laboratories. Note. *ABG = day of arterial blood gas determination; CO₂ = carbon dioxide; LR = lactated ringers infusion; NaHCO₃ = sodium bicarbonate infusion; PN = parenteral nutrition.

arterial blood gas measurement obtained 9 days following completion of the bicarbonate rescue therapy and during the ringers lactate infusion which indicated resolution of the metabolic acidosis (pH of 7.36, pO₂ of 105 mm Hg, pCO₂ of 54 mm Hg, bicarbonate of 30 mEq/L). Average daily intravenous chloride and base (acetate, bicarbonate, and lactate) intakes prior to, during, and after rescue bicarbonate therapy are given in Table 3.

Discussion

This case exemplifies avoidance of significant adverse consequences due to medication shortages via a creative therapeutic strategy to substitute intravenous sodium chloride-based fluid supplementation with another commercially available solution (lactated ringers) which contains lactate in lieu of lack of potassium or sodium acetate in the PN solution (Table 2). PN component shortages have become so commonplace over the past several years that the American Society for Parenteral and Enteral Nutrition (ASPEN) has recently formed an interdisciplinary subcommittee to develop and publish recommendations for managing shortages of PN components including electrolytes,⁹ trace elements,¹⁰ vitamins,¹¹ lipids,¹² amino acids,¹³ and L-cysteine.¹⁴ It is recommended by the ASPEN subcommittee that the prescriber should consider switching to oral or enteral electrolyte products if the patient does not have malabsorption or nonfunctioning gastrointestinal tract, reserve its use for those who require PN or those with a therapeutic medical need, and to reconsider use of algorithms as “automatic” replacement therapies in otherwise asymptomatic patients.⁹ When the shortage in potassium acetate and sodium acetate occurred, we noted that the use of enteral alkalinizing agents such as sodium bicarbonate or sodium citrate could not be used due to inability to use the gastrointestinal tract, we had already reserved potassium and sodium acetate for PN solutions, and these electrolyte salts were not part of any institutional “automatic” replacement therapies. Thus, we were out of viable options as recommended by the ASPEN subcommittee.⁹

Acetate is converted to bicarbonate by the liver and is the preferred anion for providing an alkaline substrate in PN solutions due to its stability and lack of chemical binding to other cations, thus avoiding the development of precipitates. Several studies suggest comparable efficacy of sodium acetate with sodium bicarbonate in the treatment of metabolic acidosis.¹⁵ We are not the first to describe development of a non-anion gap metabolic acidosis with acetate-free PN. PN-associated hyperchloremic metabolic acidosis has been reported when patients were given chloride salts without acetate.¹⁶⁻¹⁸ The development of metabolic acidosis can be further augmented beyond that observed with a chloride-based PN solution when given to a patient with significant bicarbonate losses from intestinal drainages (Table 1) as in this case.

Table 3. Average Intravenous Acid (Chloride) and Base (Acetate, Bicarbonate, Lactate) Intakes Surrounding Rescue Bicarbonate Therapy.

Timing relative to event	Duration of observation (d)	Chloride intake (mEq/d)	Source and base intake (mEq/d)
Prior to acetate shortage	10	433	Potassium acetate, 60
During acetate shortage			
Prior to bicarbonate rescue therapy	11	286	0
During bicarbonate rescue therapy	3	324	Sodium bicarbonate, 50
After bicarbonate rescue therapy	12	313	Sodium lactate, 55

Unfortunately, the shortage of acetate PN components persisted longer than we anticipated, and the patient developed a non-anion gap metabolic acidosis with a serum chloride concentration at the higher end of normal range (Figure 1). We opted for early intervention with sodium bicarbonate therapy for 3 days followed by substitution of 2 liters of lactated ringers solution for 0.9% sodium chloride for as long as the high intestinal drainage output persisted. In this case, the patient had a bicarbonate deficit due to substantial intestinal fluid drainage and subsequent bicarbonate losses (Table 1) that were not being replaced. This intervention resulted in a similar daily base and lower chloride intake as previously given to the patient prior to the acetate shortage (Table 3). The repeated arterial blood gas measurement performed 9 days after completion of sodium bicarbonate therapy and initiation of lactated ringers infusion revealed a normal pH of 7.36 and an elevated serum bicarbonate concentration of 30 mEq/L. Although prolonged use of lactated ringers solution has been implicated in causing metabolic alkalemia,¹⁹ the elevated serum bicarbonate concentration was also attributable to the renal metabolic response to sustained hypercapnia (pCO₂ of 54 mm Hg)⁸ as the patient was undergoing ventilator weaning procedures at that time.

Sodium bicarbonate has been suggested to be a plausible intravenous source for an alkaline substrate in PN solutions.²⁰ However, addition of intravenous sodium bicarbonate injection to the PN solution in lieu of potassium acetate or sodium acetate is not recommended. This recommended avoidance is due to the theoretical potential to form calcium carbonate precipitates from the reaction between sodium bicarbonate and calcium-containing additives to the PN solution. In addition, a recent national sodium bicarbonate injection shortage provides evidence for our current reluctance to routinely use adjuvant sodium bicarbonate injection therapy except in extreme cases of acidemia. In hindsight, perhaps the need for sodium bicarbonate injection rescue therapy could have been averted altogether if lactated ringers solution was substituted for the sodium chloride-based intravenous solutions as soon as the concurrent potassium acetate and sodium acetate shortage occurred. It should be emphasized that routine use of lactated ringers solution for the management of metabolic acidosis is not recommended for all cases. It was appropriate therapy for this case in that the patient was experiencing bicarbonate loss from excessive

intestinal losses that was not being replaced, and the patient had a normal serum lactate concentration without an apparent etiology for lactic acidosis.¹⁹ If the acidemia was due to lactic acidosis or ketoacidosis, most clinicians recommend avoidance of administering lactate containing solutions. This is because during lactic acidosis and ketoacidosis, the decrease in the serum bicarbonate concentration occurs due to its conversion to another base (eg, lactate, ketones), which in given time, can be converted back to bicarbonate.¹⁵ One possible exception to this caveat is when lactated ringers solution is being used for fluid resuscitation during septic or traumatic shock.²¹

Conclusion

We describe a case of development and novel alternative treatment of a non-anion gap metabolic acidosis in a patient with large gastrointestinal volume drainages requiring PN during a potassium acetate and sodium acetate shortage. Upon evaluation of the acid-base disorder, the patient was given 50 mEq of intravenous sodium bicarbonate daily for 3 days. The 2 liters of supplemental intravenous 0.9% sodium chloride solution given to the patient daily was changed to lactated ringers solution (which provided 56 mEq of lactate daily and reduced chloride intake by about 90 mEq daily compared with 0.9% sodium chloride solution). These interventions resulted in resolution of the metabolic acid-base disorder. This case report supplements the current literature regarding techniques for avoiding severe metabolic complications during PN product shortages.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

References

1. Fox ER, Sweet BV, Jensen V. Drug shortages: a complex health care crisis. *Mayo Clin Proc.* 2014;89:361-373.
2. Kweder SL, Dill S. Drug shortages: the cycle of quantity and quality. *Clin Pharmacol Ther.* 2013;93:245-251.

3. Holcombe B. Parenteral nutrition product shortages: impact on safety. *J Parenter Enteral Nutr.* 2012;36(2) (suppl):44S-47S.
4. Mirtallo JM, Holcombe B, Kochevar M, Guenter P. Parenteral nutrition product shortages: the A.S.P.E.N. strategy. *Nutr Clin Pract.* 2012;27:385-391.
5. Guenter P, Holcombe B, Mirtallo JM, Plogsted SW, DiBaise JK. Parenteral nutrition utilization: response to drug shortages. *J Parenter Enteral Nutr.* 2014;38:11-12.
6. Dickerson RN, Mitchell JN, Morgan LM, et al. Disparate response to metoclopramide therapy for gastric feeding intolerance in trauma patients with and without traumatic brain injury. *J Parenter Enteral Nutr.* 2009;33:646-655.
7. Harris JA, Benedict FB. *A biometric study of basal metabolism in man. 1919.* Washington, DC: Carnegie Institute.
8. Dickerson RN. Fluids, electrolytes, acid-base disorders and nutrition support. In: Bass S, Bauer SR, Benken ST, et al, eds. *ACCP Updates in Therapeutics®: Critical Care Pharmacy Preparatory Review and Recertification Course.* Lenexa, KS: American College of Clinical Pharmacy; 2017:187-239.
9. Plogsted S, Adams SC, Allen K, et al. Parenteral nutrition electrolyte and mineral product shortage considerations. *Nutr Clin Pract.* 2016;31:132-134.
10. Plogsted S, Adams SC, Allen K, et al. Parenteral nutrition trace element product shortage considerations. *Nutr Clin Pract.* 2016;31:843-847.
11. Plogsted S, Adams SC, Allen K, et al. Parenteral nutrition multivitamin product shortage considerations. *Nutr Clin Pract.* 2016;31:556-559.
12. Plogsted S, Adams SC, Allen K, et al. Parenteral nutrition lipid injectable emulsion products shortage considerations. *Nutr Clin Pract.* 2017;32:427-429.
13. Plogsted S, Adams SC, Allen K, et al. Parenteral nutrition amino acids product shortage considerations. *Nutr Clin Pract.* 2016;31:560-561.
14. Plogsted S, Cober P, Gura KM, et al. Parenteral nutrition L-cysteine product shortage considerations. *Nutr Clin Pract.* 2015;30:579-580.
15. Neavyn MJ, Boyer EW, Bird SB, Babu KM. Sodium acetate as a replacement for sodium bicarbonate in medical toxicology: a review. *J Med Toxicol.* 2013;9:250-254.
16. Kushner RF. Total parenteral nutrition-associated metabolic acidosis. *J Parenter Enteral Nutr.* 1986;10:306-310.
17. Heird WC, Dell RB, Driscoll JM Jr, Grebin B, Winters RW. Metabolic acidosis resulting from intravenous alimentation mixtures containing synthetic amino acids. *N Engl J Med.* 1972;287:943-948.
18. Kato K, Sugiura S, Yano K, et al. The latent risk of acidosis in commercially available total parenteral nutrition (TPN) products: a randomized clinical trial in postoperative patients. *J Clin Biochem Nutr.* 2009;45:68-73.
19. Kraut JA, Madias NE. Lactic acidosis. *N Engl J Med.* 2014;371:2309-2319.
20. Henann NE, Jacks TT Jr. Compatibility and availability of sodium bicarbonate in total parenteral nutrient solutions. *Am J Hosp Pharm.* 1985;42:2718-2720.
21. Myburgh JA, Mythen MG. Resuscitation fluids. *N Engl J Med.* 2013;369:1243-1251.