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Shortages of clinical nutritional components and management strategies

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ABSTRACT

Parenteral nutrition (PN) solution is a medication of high concern due to its intricate drug utilization procedure. It has been reported that since 2010, nearly every component involved in the preparation of PN admixtures has experienced a shortage at least once. Shortages may lead to therapy delays in hospitals, clinics and other health-related facilities or reductions in quality, prompting healthcare providers to recommend alternative treatments, potentially leading to medication errors, negatively influencing patient outcomes, and consume healthcare assets. The causes of medication shortages are diverse and encompass unidentified factors (44%), manufacturing complications (36%), supply and demand imbalances (8%), discontinued product lines (8%), insufficient access to raw materials (4%), and natural disasters. The duration for the resolution of these shortages was inconsistent, with certain product shortages that were resolved experiencing a recurrence, while others persisted for several months to years. The pharmacy department can take the lead in efficiently managing drug shortages by guaranteeing that its institution possesses the essential infrastructure and a clearly outlined management strategy well in advance of any shortages arising. During periods of shortages, it is extremely important to limit the use of nutritional products to patients with valid indications and those with nonfunctional gastrointestinal systems. Effective management of drug shortages, including PN components, necessitates a comprehensive plan and the involvement of an interprofessional team. This team should contribute to the development of the plan and be ready to implement it swiftly in case of a shortage or outage. Once the shortage of PN components is deemed resolved, all rationing and conservation strategies should be halted, as these measures are meant to be employed exclusively during shortages. Once the PN component shortage has been resolved, it is crucial to resume providing the full dosage of PN components to all patients in need of PN therapy.

Keywords: Component, drug shortage, management, parenteral nutrition

INTRODUCTION

Parenteral nutrition (PN) solution is a medication of high concern due to its intricate drug utilization procedure. The measures and precautions, encompassing guidelines, protocols, and support mechanisms, associated with this procedure, play a crucial role in upholding patient safety.[1] Automated compounding devices are employed for the creation of PN in approximately 64% of institutions, particularly those of a larger scale and standardized commercially accessible PN products are utilized in 21% to 43% of institutions.[1]

It has been reported that since 2010, nearly every component involved in the preparation of PN admixtures has experienced a shortage at least once.[2,3] Drug shortages, characterized by an inadequate drug supply, lead to adjustments in the drug preparation processes by the pharmacy and sometimes require the selection of alternative therapeutic options.[4]

In general healthcare providers are contending with a substantial risk to patient well-being and are actively addressing issues related to the availability of PN

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components and product limitations, and are exploring alternative treatment options constantly.[4] However, shortages in medications, such as components for PN, pose a substantial risk to public health and safety while also impacting the healthcare system.[2]

Shortages may lead to therapy delays in hospitals, clinics and other health-related facilities or reductions in quality, prompting healthcare providers to recommend alternative treatments, potentially leading to medication errors, negatively influencing patient outcomes, and consume healthcare assets.[2,4]

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Administering PN therapy is a notable challenge for healthcare professionals due to the intricate nature of PN as a medication, which could consist of 40 or more distinct components. Among these components, several may face concurrent shortages, further complicating the situation. At every stage of utilizing PN, from prescribing the therapy to a patient to its actual administration, one must take into account the availability of PN components. Unlike antibiotics, there are no substitute treatments available in the absence of PN components, which play a life-sustaining role for many adults, neonates, and pediatric patients.[2] Especially during and after the Covid-19 pandemic period, hospitals experienced a lot of problems due to drug shortages. In this review, our objective is to offer an updated set of fundamental principles to help healthcare experts address the issue of nutrient shortages in patients undergoing PN.

Main Points

- It has been reported that since 2010, nearly every component involved in the preparation of PN admixtures has experienced a shortage at least once.
- Shortages may lead to therapy delays in hospitals, clinics, and other health-related facilities or reductions in quality, prompting healthcare providers to recommend alternative treatments, potentially leading to medication errors, negatively influencing patient outcomes, and consume healthcare assets.
- Staying proactive and prepared for shortages is essential for maintaining patient care standards.
- Effectively managing drug shortages, including PN components, necessitates a comprehensive plan and the involvement of an interprofessional team.

The Importance of Parenteral Nutrition Component Shortages

Medication shortages raise significant patient safety concerns. The likelihood of medication errors increases when a pharmacy modifies the process of ordering, preparing, or dispensing a product or when prescribing practices shift to less familiar alternative agents. This risk is especially pronounced with agents that are less effective, have more adverse effects, or necessitate an uncommon or complicated dosing regimen. When establishing best practices for managing drug shortages, the primary consideration should be the potential effects on patient safety.[5]

Shortages in PN and the limited availability of alternative therapies have compelled certain institutions to take measures such as delaying treatment, adjusting dosages or treatment plans, deferring surgeries, and relocating patients to other facilities.[4]

Besides macronutrients, the absence of other essential components such as electrolytes, micronutrients (vitamins and trace elements) present a significant risk to the patient's nutritional well-being, potentially leading to deficiencies, metabolic abnormalities, and death in severe cases.[3,6]

What to Do in Parenteral Nutrition Component Shortages

The pharmacy department can take the lead in efficiently managing drug shortages by guaranteeing that its institution possesses the essential infrastructure and a clearly outlined management strategy well in advance of any shortages arising. In order to respond efficiently to medication shortages, certain crucial infrastructure components should be established proactively. These include a drug shortage team, a committee for resource allocation, and established protocols for approving substitute therapies and handling ethical concerns.[5]

During periods of shortages, it is extremely important to limit the use of nutritional products to patients with valid indications and those with nonfunctional gastrointestinal systems. Whenever feasible, alternative or accessible products should be utilized to prevent the occurrence of deficiencies. In such shortages, it may be necessary to obtain alternative products like pre-mixed PN solutions and electrolyte solutions. While it's extremely challenging to foresee when a nutritional product might go on shortage, it's crucial to have established formal procedures ready that can be swiftly and effectively put into action in the event of a drug shortage.[4]

Certain international societies, such as the American Society for Parenteral and Enteral Nutrition (ASPEN), the British Association for Parenteral and Enteral Nutrition (BAPEN), and the French Society for Clinical Nutrition and Metabolism (SFNCM), have developed guidelines to prioritize the provision of micronutrients when shortages occur. These societies have determined that enhanced monitoring of vitamins and trace elements is necessary in such circumstances.[6] In response to the recurring shortages of intravenous micronutrient preparations for PN, ASPEN published shortage considerations in 2016 to help clinicians manage these situations. The authors of the publication suggested that clinicians should continuously assess each patient to determine if PN is still necessary and if there is a possibility to provide nutrition orally or enterally. They also advised switching to oral or enteral products whenever feasible. The British Society put forth similar recommendations, including the suggestion to monitor micronutrient levels more frequently than before, particularly if there are any clinical suspicions or concerns regarding micronutrient deficiency. Regardless of the chosen approach, it will be crucial to closely monitor micronutrient levels to prevent complications.[3] During a period of electrolyte and mineral product shortages, clinicians should consider implementing one or more of the following measures:[3,7]

1. Evaluate each patient to determine the necessity for PN and consider providing nutrition through the oral or enteral route if feasible.
2. Consider switching to oral or enteral electrolyte or mineral supplement products if oral or enteral intake is possible (except for patients with malabsorption syndromes or nonfunctioning gastrointestinal tracts). Seek advice from a pharmacist for product details.
3. Acquire an electrolyte and mineral injection supply only in the required quantities. To ensure fair distribution to all patients nationwide, avoid hoarding or stockpiling.
4. Set aside intravenous (IV) electrolyte and mineral products specifically for patients who are receiving PN or those with a documented therapeutic medical requirement for intravenous electrolytes and minerals.
5. Avoid utilizing parenteral electrolyte and mineral injections as supplemental additives in enteral nutrition products.
6. Restrict the use of electrolyte and mineral additives in IV fluids to patients with specific disease states and clinical conditions for which they are medically appropriate.
7. Reevaluate the use of serum electrolyte algorithms or protocols as "automatic" IV electrolyte replacement therapies in patients who are otherwise asymptomatic.
8. Utilize commercially available IV multi-electrolyte and mineral products for replacement therapy whenever feasible.
9. Examine the complete range of PN electrolyte and mineral products available nationwide. While there may be a shortage in one concentration or salt form, there may be availability in another form.
10. Evaluate your PN patient population to ascertain whether a standardized, commercially available PN product with standard electrolytes may be suitable for a subset of your patients. Typically, supplementary components can be incorporated into these products as needed.
11. Analyze your PN patient population to ascertain if a standardized, commercially available multi-electrolyte product may be suitable for a subset of these patients.
12. In the event of extended shortages of IV electrolytes and mineral products, country-specific healthcare authorities such as the Turkish Medicines and Medical Devices Agency may grant temporary approval for the importation of alternative products. These imported products may have varying salts, concentrations, packaging, and labeling compared to products approved in the country. It's important to carefully read the product information of the imported products.
13. Consider reducing or even eliminating the daily quantity of electrolytes added to the PN regimen.
14. Monitoring serum electrolyte concentrations closely.
15. Be vigilant for a potential rise in deficiencies during the ongoing shortages. Enhance your awareness and assessment of signs and symptoms indicative of electrolyte and mineral deficiencies.
16. Consider the possibility of preparing PN at a single, central location, either within a centralized pharmacy or through outsourced preparation, to minimize inventory waste.
17. Facilities and healthcare practitioners must maintain their diligence in adhering to product labeling (e.g., package insert), USP General Chapter <797> Pharmaceutical Compounding—Sterile Preparations guidelines, and federal rules and regulations.
18. Incorporate PN component shortages and outages into your healthcare organization's strategies and protocols for managing medication shortages and outages.
19. Ensure that information regarding severe drug product shortages is reported to the country-specific authorities, such as the Turkish Medicines and Medical Devices Agency.

20. Report any patient-related issues arising from shortages to the Medication Errors Reporting Program.

There are also ASPEN recommendations for electrolyte and mineral shortages which are shown in Table 1.

Besides the electrolyte and mineral, multivitamin and trace element shortages should also be considered for patients with PN. Clinicians should be careful when transitioning from one trace element or multivitamin preparation to another, as the dosages and individual components in each formulation are not standardized. Specific strategies for addressing these shortages include shifting supplementation from IV to enteral administration when possible, limiting the supply to critically ill pediatric or adult patients or those with pre-existing deficiencies, and exploring alternative dosing regimens, such as administering every other day or three times a week. Another option is to reduce the daily dosage by 50%.[4] If supplies of multi-trace and multivitamin preparations are depleted, institutions may consider supplementing individual parenteral vitamin and trace element components as an alternative.[4] Information on the shortage and deficiency symptoms of multi-trace elements and multivitamins are shown in Table 2 and the ASPEN recommendations are shown in Table 3.

When we focus on macronutrients many clinicians view protein as the cornerstone of nutrition therapy because of its crucial role in promoting wound healing, bolstering immune function, and preserving lean body mass. When the supply of amino acids reached critically low levels, the Nutrition Therapy and Pharmacy and Therapeutics Committees endorsed guidelines to limit the use of PN to patients who met the ASPEN criteria. This helped ensure the availability of adequate supplies.[4]

Lipids play a crucial role in PN therapy as they provide essential fatty acids and help reduce the required dose of glucose in the parenteral formulation. Essential fatty acid deficiency (EFAD) is linked to symptoms such as rash and alopecia, which typically manifest after several weeks of lipid-free PN therapy. During the shortage, the administration of lipid therapy in patients on long-term PN can be limited to twice-weekly sessions, typically on Mondays and Fridays, with a maximum daily dose of 50 grams, if they were undergoing therapy for over 14 days or were receiving home PN.[4] In response to the challenges posed by shortages of PN products, practitioners have undertaken a reevaluation of the criteria for PN usage and the timing of administering specific macronutrients such as lipids.[2]

Table 1. ASPEN recommendations for electrolyte and mineral shortages

Component	What to Do	Signs and Symptoms of Deficiency
Calcium	• If inorganic calcium salts are available administer separately from PN.	Irritability, hyperventilation, tetany, other neuromuscular, central nervous system, and cardiovascular symptoms.
Magnesium	• Minimize the use of IV magnesium additives in IV fluids.	Electrocardiogram (ECG) changes, arrhythmias, muscle spasms/tetany, nausea, lethargy, confusion, seizures, coma, and death.
Phosphate	• Consider using the alternate salt IV phosphate as available and balance the sodium and potassium accordingly. • Consider provision of daily IV fat emulsion to all PN patients as clinically appropriate. Note: IV fat emulsions contain 15 mmol/L of phosphate as egg phospholipids. • Reserve phosphates for pediatric and neonatal patients requiring PN.	Impaired diaphragmatic contractility, tachycardia, hypocapnia, respiratory failure, tissue hypoxia, decreased myocardial contractility, paralysis, weakness, paresthesias, neurologic dysfunction, seizures, and death.
Potassium	• Consider using alternate IV potassium salts as available and balance the chloride, acetate, and phosphate accordingly.	Nausea, vomiting, weakness, muscle cramping, constipation, ECG changes, cardiac arrhythmias, sudden death, paralysis, respiratory compromise, and rhabdomyolysis.
Sodium	• Consider using alternate IV sodium salts and concentrations as available and balance the chloride, acetate, and phosphate accordingly. • Consider administering IV medications in 0.9% sodium chloride (normal saline) instead of 5% dextrose in water (D5W) when compatible. • Consider using 0.9% sodium chloride (normal saline) for irrigation with enteral nutrition when patients are on both enteral and parenteral therapy.	Headache, lethargy, disorientation, restlessness, nausea, vomiting, muscle cramps or weakness, depressed reflexes, seizures, coma, and death.

Table 2. Management of some trace elements and vitamins shortage		
Component	**What to Do**	**Signs and symptoms of deficiency**
Vitamin C	• Restrictions may be needed. Patients who may warrant preferred access are those with a nonfunctioning gastrointestinal tract or patients who need high-dose supplementation.	Fatigue, poor wound healing, gingivitis, conjunctival hemorrhages, and ecchymosis
Vitamin B12	• Restrict its use to those patients with malabsorption and severe neurologic manifestations.	Macrocytic anemia, cognitive decline, and neuropathy
Vitamin K	• Oral and enteral administration strongly encouraged whenever feasible. Intravenous use should be reserved for patients with severe or life-threatening bleeding during product disruptions according to the current guidelines.	Problems in the hemostasis that stimulates synthesis of clotting factors II, VII, IX, and X. Problems in bone development and remodeling.
Vitamin A	• Oral and enteral administration encouraged in those patients who require it for wound healing, xerophthalmia, or who are high risk for deficiency.	Detrimental effects on mucosal integrity, immune function, wound healing, and vision.
Chromium	• An administration schedule of three times weekly is likely sufficient to prevent severe deficiency in high-risk patients.	Hyperlipidemia, peripheral neuropathy, encephalopathy, and glucose intolerance
Copper	• Enteral administration is strongly encouraged in patients with functional gastrointestinal tracts. If restrictions are necessary due to future supply disruptions, use in patients with severe deficiencies with clinical manifestations is appropriate.	Anemia, leukopenia, myelopathy, and osteoporosis.
Selenium	• Enteral supplementation is highly encouraged in cases of deficiencies with clinically significant signs or symptoms. Intravenous formulation should be restricted to those symptomatic patients with severe malabsorption syndromes.	Cardiomyopathy, myositis, and muscle cramps
Zinc	• Restrictions of the individual IV formulations should be established for patients with supraphysiologic losses and malabsorption. Oral or enteral administration should be optimized in other clinical scenarios.	Alterations in sight and taste perception, growth and development, immune defense, and wound healing.

Table 3. ASPEN recommendations for vitamins and trace elements shortage
Vitamins
• Use a 13-vitamin product • Use a 12-vitamin product (without vitamin K) if 13-vitamin product is unavailable • In patient on warfarin: • Use a 12-vitamin product (without vitamin K) • Use a 13-vitamin product (with vitamin K) if the 12-vitamin product is unavailable: monitor and adjust anticoagulation • When all options to obtain IV multivitamins have been exhausted, ration IV multivitamins in PN, such as reducing the daily dose by 50% or giving 1 multivitamin infusion dose 3 times a week • If IV multi-vitamins are no longer available, administer individual IV vitamin entities: Thiamine 6 mg, ascorbic acid 200 mg, pyridoxine 6 mg, folic acid 0.6 mg daily, and B12 100e1000 mcg, vitamin K 150 mcg may be given weekly • The use of pediatric IV multivitamins for adults is not recommended
Trace Elements
• When all options to obtain IV adult multi-trace element (MTE) products have been exhausted, ration IV adult MTE products in PN, such as reducing the daily dose by 50% or giving 1 MTE product infusion 3 times a week • Withhold IV adult MTE products from adult patients receiving partial enteral/parenteral nutrition or who can tolerate oral/enteral supplements. • Consider withholding IV adult MTE products for the first month of therapy to newly initiated adolescent and adult PN patients who are not critically ill or have pre-existing deficits • The use of Pediatric and Neonatal IV multi-trace element products for adults is strongly discouraged.

Teams and institutions can adhere to a specific process for managing drug shortages, as illustrated in Figure 1. If this process is functioning as intended, institutions should receive a minimum of 2 weeks' notice before the product is completely depleted.[4]

The operational assessment evaluates both the severity and the expected duration of the shortage. The therapeutic assessment aims to identify the patient populations that will be affected by the shortage and to pinpoint potential therapeutic alternatives for them. The therapeutic assessment should be carried out by a multidisciplinary team comprising physicians, dietitians, pharmacists, nurses, and other relevant clinicians as needed. A comprehensive plan should encompass several key components, including the identification of nutritional alternatives, allocation criteria for the remaining product, revised distribution and administration processes, a cost analysis for the institution, and an evaluation of potential secondary shortages. It's important to note that the management of shortages should not involve stockpiling the product, as this practice is discouraged by professional societies such as the European Society for Clinical Nutrition and Metabolism (ESPEN) and the American Society of Hospital Pharmacists (ASHP).[4]

The concluding phases of the plan encompass communication, education, and implementation. It is

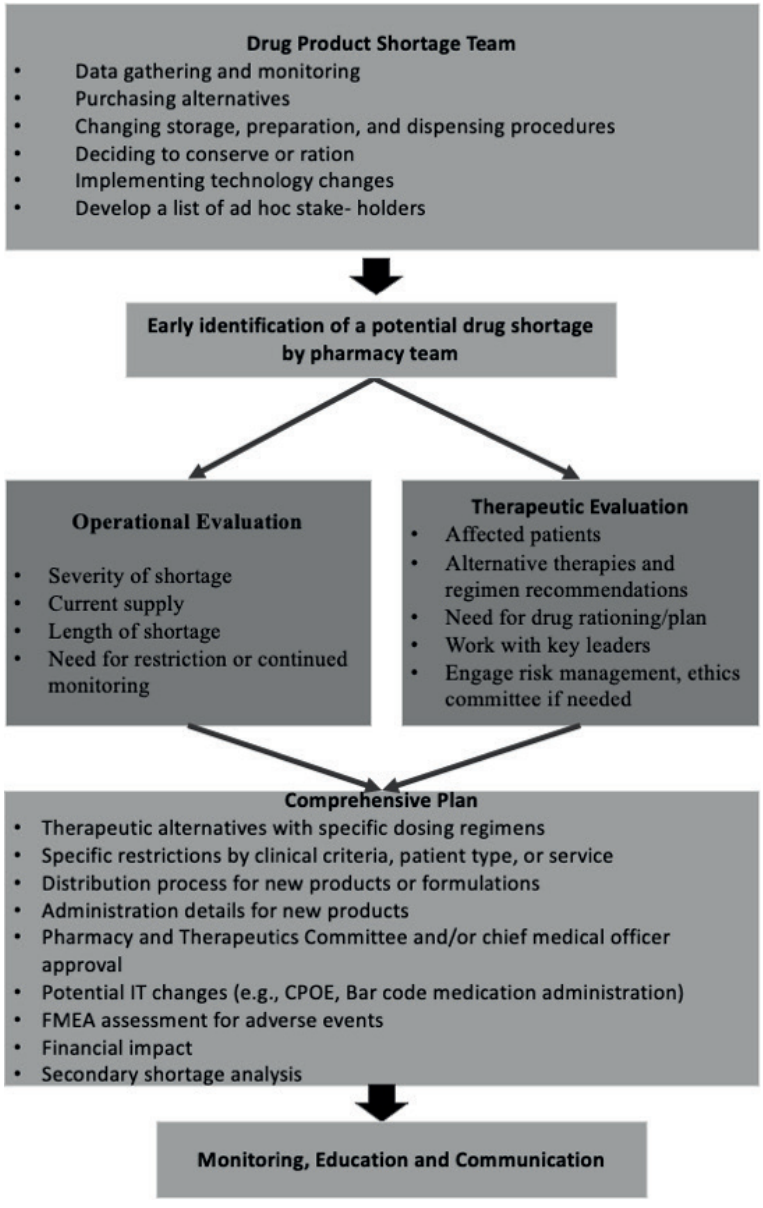

Figure 1. Process for managing drug shortages

crucial to provide education to all disciplines involved before implementing the plan, as shortages can lead to nutritional errors. Errors have been documented as a consequence of alterations in electrolyte or macronutrient concentrations stemming from product shortages. Education is paramount to preventing errors and should be disseminated through various channels, including emails, staff meetings, bulletin boards, websites, dashboards, and in-service training.[4]

Once the shortage of PN components is deemed resolved, all rationing and conservation strategies should be halted, as these measures are meant to be employed exclusively during shortages. Upon the resolution of the PN component shortage, it is crucial to resume providing the full dosage of PN components, and sufficient quantities should be procured to supply these full daily components to all patients in need of PN therapy. The absence of observed adverse events or deficiencies during the rationing of a PN component and the potential cost savings linked to "partial" dosing should not serve as a justification to continue with less than optimal dosing. The focus should always be on providing the best possible care and meeting patients' nutritional needs.[2]

CONCLUSION

Shortages of nutritional products continue to exert a significant impact on patient care. Clinicians should remain informed about both current and past shortages while also preparing for potential shortages of critical nutritional supplements. Staying proactive and prepared is essential for maintaining patient care standards. Institutions should be well-prepared with the knowledge and resources to implement a protocol for managing shortages and identifying therapeutic alternatives when necessary. Effective management of drug shortages, including PN components, necessitates a comprehensive plan and the involvement of an interprofessional team. This team should contribute to the development of the plan and be ready to implement it swiftly in case of a shortage or outage. Collaboration and planning are key to mitigating the impact of shortages on patient care.

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REFERENCES

1. Boullata JI, Holcombe B, Sacks G, et al. Standardized Competencies for Parenteral Nutrition Order Review and Parenteral Nutrition Preparation, Including Compounding: The ASPEN Model. *Nutr Clin Pract*. 2016;31:548-555. [Crossref]
2. Holcombe B, Mattox TW, Plogsted S. Drug Shortages: Effect on Parenteral Nutrition Therapy. *Nutr Clin Pract*. 2018;33:53-61. [Crossref]
3. Joly F, Mundi M, Barazzoni R, et al. How to deal with micronutrient product shortage - Editorial. *Clin Nutr*. 2023;42:143-147. [Crossref]
4. 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. [Crossref]
5. Fox ER, McLaughlin MM. ASHP guidelines on managing drug product shortages. *Am J Health Syst Pharm*. 2018;75:1742-1750. [Crossref]
6. Berger MM, Shenkin A, Schweinlin A, et al. ESPEN micronutrient guideline. *Clin Nutr*. 2022;41:1357-1424. [Crossref]
7. 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. [Crossref]