Chapter 5

Parenteral Nutrition Compounding

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Introduction

Parenteral nutrition (PN) is a potentially life-saving therapeutic intervention for neonates, children, or adults with a dysfunctional gastrointestinal tract (e.g., chronic intestinal failure). It is used in a variety of healthcare environments from the intensive care unit (ICU) to the home care setting. Generally, PN is provided as an intravenous (IV) mixture of crystalline amino acids and dextrose, commonly referred to as a *2-in-1 solution*, while also containing electrolytes, multivitamins, trace elements, or non-nutritive medications. The addition of IV oil-in-water fat emulsion (IVFE) to PN is commonly referred to as a *total nutrient admixture* (TNA) or 3-in-1 emulsion with the same constituents mentioned above added. PN is a complex and high-alert medication with stability and compatibility issues depending on the formulation used (i.e., 2-in-1 versus 3-in-1). *Stability with PN* refers to the deterioration or degradation of an active drug changing its pharmacologic or pharmaceutical characteristic (e.g., oil-in-water IVFE coalescence to eventual emulsion cracking). *Compatibility* refers to a disruption in the coexistence of two or more components in the PN formulation (e.g., potassium phosphate and calcium gluconate forming the nearly insoluble dibasic calcium phosphate).[1] Pharmacy personnel involved in PN order review and compounding must know the complexity of these stability and compatibility concerns, along with a knowledge of PN indications, dosing, and monitoring parameters for the individual components. Pharmacist and pharmacy technician involvement in the management and compounding of PN has changed over the past several years as evidenced from the results of the ASHP surveys of hospital pharmacy practice:

- **The 2012 survey—**The 2012 survey showed pharmacists were providing PN management (e.g., initiating, modifying, and monitoring) in 4.7% (hospitals with less than 50 beds) to 44% (hospitals with 600 beds or greater) of inpatients (overall mean for all hospitals: 11.1%).[2]

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- **The 2013 survey—**The 2013 survey showed pharmacists were providing PN consults (i.e., medical record review with oral or written prescriber follow-up) in 45.1% (hospitals with less than 50 beds) to 75% (hospitals with 300–399 beds) of inpatients (overall mean for all hospitals: 43.2%).[3] It also showed pharmacists were providing PN management (e.g., standing protocol or prescriber delegation) in 32.4% (hospitals with less than 50 beds) to 59.7% (hospitals with 400–599 beds) of inpatients (overall mean for all hospitals: 55.9%).[3]
- **The 2014 survey—**The 2014 survey showed institutions were providing PN as commercially available amino acids/dextrose (2-in-1) in 7.7% (hospitals with 400–599 beds) to 64.6% (hospitals with 100–199 beds) (overall mean for all hospitals: 43%). Preparation of PN was outsourced to a compounding facility in 10.6% (hospitals with less than 50 beds) to 41.3% (hospitals with 600 beds or greater) (overall mean for all hospitals: 18.6%). Fully 70.1% of hospitals outsourced some compounded sterile preparations (CSPs) with 21.9% (hospitals with 100–199 beds) to 52.1% (hospitals 300–399 beds) partially or completely outsourcing PN. These formulations were compounded with an automated compounding device (ACD) in 1.2% of hospitals with less than 50 beds and up to 60% of hospitals with 400–599 beds (overall mean for all hospitals: 16.8%). PN formulations were compounded by gravity in no hospitals with 600 beds or greater, but in 16.7% of hospitals with 50–99 beds (overall mean for all hospitals: 10.4%). No PN formulations at all were prepared in 32.5% of hospitals with less than 99 beds because this therapy was not used (overall mean for all hospitals: 11.2%). The 2014 survey also showed cleanroom compliance with the USP Chapter <797> Pharmaceutical Compounding—Sterile Preparations in 43.5% (hospitals with less than 50 beds) to 93.5% (hospitals with 600 beds or greater) of pharmacy departments (overall mean for all hospitals: 64.7%).[4]
- **The 2015 survey—**The 2015 survey revealed an overall lower percentage (8.7%) of all hospitals with a pharmacist assigned to daily nutrition support compared to the 2011–2014 (range 11.6–13.6%) surveys. Overall, 2.4% of hospitals with 50–99 beds to 56.7% of hospitals with 600 beds or more had a pharmacist assigned to daily nutrition support.[5]

Clearly, the management and compounding of PN is different based on the size and characteristics of each institution, with most providing between 5 to 15 daily admixtures in combined populations of neonatal, pediatric, and adult patients.[6] The use of standardized, commercial PN is predominantly used in smaller facilities (i.e., less than 200 beds), while larger teaching hospitals tend to utilize ACDs more for customized PN. An American Society for Parenteral and Enteral Nutrition (ASPEN) survey revealed that only 60.2% of hospital pharmacies dedicate 0.6 full-time equivalents of a pharmacist position to review, verify, and clarify these complex, high-alert PN orders.[6] Surprisingly, 23.1% of respondents did not allocate any pharmacist time for PN order review and verification. This is especially important because ACDs, which require properly trained personnel, were used in 35.7–60% of hospitals with 200 or more beds and these ACDs rarely (16–28%) have an electronic interface with the pharmacy or hospital information system.[4,6,7]

The ASPEN survey showed either a pharmacist (54.4%) or a pharmacy technician (27.4%) manually entered the PN order into the ACD.[6] Sacks and others have previously shown that 39% of PN errors occur during the transcription process (e.g., selecting the wrong electrolyte salt or dose, wrong amino acids solution, and drug omission).[8] The extent of the adoption of ACDs has been primarily based on considerations of their cost and the risks of manual transcription errors as previously mentioned. Break-even analyses have been performed determining the volume of PN admixtures required to justify the costs comparing ACDs to manual compounding.[9,10] Besides improvements in efficiency, the value of ACDs offsetting cost also has been reported based on improvements in clinical practice including implementing a 24-hour PN admixture system, which is recommended by the ASPEN Safe Practices for PN.[11,12] A survey of compliance with USP Chapter <797> standards in hospitals found that more than half of respondents did not validate the accuracy of ACDs and more than a third of respondents had no plans to change in response to the chapter revision.[13] Errors related to ACDs occurred when actual practices bypassed the safety check system intended to verify the correct sterile product was placed in the right station on the ACD. Manipulating sterile products outside of the laminar flow hood was also a breach in ac-