CLINICAL INVESTIGATION

Automated Compounding of Parenteral Nutrition for Pediatric Patients: Characterization of Workload and Costs

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OBJECTIVES Parenteral nutrition (PN) compounding in large hospital centers is now largely automated using volumetric pump systems. No study has examined the pharmacy workload and costs associated with this process. This study was designed to characterize these elements at our center and to identify areas for potential improvement.

METHODS We retrospectively analyzed all PN orders compounded from May 19, 2007, to June 25, 2010. Patients were divided into groups according to the ward where PN was initiated.

RESULTS The age and weight of patients at initiation of PN were similar throughout the study, except in neonatology, where initiation now occurs earlier in life (age 1.3 ± 2.7 days in 2010 vs. 3.4 ± 9.4 in 2007; $p=0.003$). An average of 894 orders per month were compounded. A total of 59% of orders were for neonatal patients. The average cost of source solutions per PN order increased from Can\$23.27 in 2007 to Can\$37.78 in 2010. Partially used source solutions discarded at the end of the day represented between 7.7% and 9.2% of total source solution cost. Amino acids in 3-L bags were responsible for the largest waste, with Can\$953 to Can\$1048 wasted monthly.

CONCLUSIONS PN compounding at our center represents an important workload and increasing costs. A reduction in source solution waste, for example, by reducing the use of large source solution containers, would be beneficial.

INDEX TERMS drug compounding, neonatology, parenteral nutrition, pediatrics, pharmacy

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INTRODUCTION

Parenteral nutrition (PN) is a vital intervention used in pediatrics to support the nutritional needs of patients whose gastrointestinal tract is inaccessible, unusable, or not effective enough to support their metabolic demands and growth. Pediatric populations frequently receiving PN include prematurely born infants, children suffering from severe gastrointestinal conditions (especially short bowel syndrome), surgery patients, oncology and bone marrow transplant patients, and critically ill children.

Prescribing and preparing PN solutions is a complex process. Several systems have been developed, from standardized commercially available bags requiring minimal manipulation before infusion, to fully customized solutions

compounded daily on-site. PN compounding at large institutions is now largely automated using volumetric pump systems. As many as 65% of hospitals in the United States used automated compounding devices for PN in 2000,¹ and 73% used them in 2002 (this survey also included home care facilities).² A similar proportion was observed in a 2008 Canadian survey, with 62% of centers using such a system (J.F.B., unpublished data, 2008).

A compounded PN bag typically contains a mixture of more than 10 different solutions.³ Compounding these solutions requires experienced personnel (pharmacists and pharmacy technicians) and an adequate environment where microorganisms and air particles are minimized, because of a high risk of error and contamination during compounding, which can

lead to serious adverse events and even patient deaths.³ Automated compounding devices have been purported to reduce the risk of human error and improve the efficiency of compounding compared with manual preparation.^{4,5}

Guidelines have been published for the use of automated compounders in the preparation of PN.¹ However, there are no published studies examining the impact of automated compounding on pharmacy workload or on costs.

In the context of a global reassessment of our PN workflow, we designed this study with the aim of describing PN compounding at our center. Our objectives were to characterize the workload and cost profile of PN preparation using an automated compounder and identify potential targets for improvement.

MATERIALS AND METHODS

Setting

Centre Hospitalier Universitaire Sainte-Justine is a 500-bed, tertiary care mother and child hospital located in Montreal, Quebec, Canada. The pharmacy department provides PN for neonatology, gastroenterology, surgery, solid organ transplant, oncology/bone marrow transplant, general pediatrics, obstetrics/gynecology, and intensive care units. PN is fully customized for all patients and is prepared at the pharmacy using a Baxa MicroMacro 23 automated compounder (Baxa Corporation, Englewood, CO). Orders are transmitted daily by fax to the pharmacy, where a pharmacy technician enters the order into locally developed software that calculates and verifies the composition of the solution. All orders are validated by a pharmacist before being released for delivery on wards and administration. Compounding takes place in a dedicated vertical laminar airflow hood located in a clean room in conformity with USP General Chapter 797 guidelines.⁶ PN preparation is available from 8 AM to 4 PM every day, but orders must be received before 2 PM to ensure adequate time for processing and compounding. At the end of every workday, partially used solutions from opened vials and bags as well as transfer sets are discarded in accordance with manufacturer guidelines. Home PN is compounded by an external pharmacy; however, stable inpatients may have weekend passes, in which case PN is compounded at the pharmacy department. We

use 2-in-1 PN for all hospitalized patients, with the lipid emulsion connected on a Y-site to the 2-in-1 solution tubing, and 3-in-1 PN for all home PN. Operation of the PN compounder requires one full-time equivalent pharmacy technician and 0.1 to 0.2 full-time equivalent pharmacists.

Study Design

We performed a retrospective analysis of all orders entered into our PN validation software since May 19, 2007. This database includes all PN components, their quantity, and the date and time of order processing. In this study, we included all pediatric inpatients who received PN from May 19, 2007, to June 25, 2010. Inpatients for whom home PN bags were compounded were also included. Adult inpatients admitted to gynecology/obstetrics were excluded because of their rarity. These data were cross-linked using medical record numbers with the pharmacy patient database to obtain demographic information. Groups were assigned according to the ward where PN was initiated. This protocol was approved by the research ethics committee of Centre Hospitalier Universitaire Sainte-Justine.

Cost Analysis

The costs of PN source solutions per volume as well as all fluctuations of this cost during the study period were obtained from the pharmacy financial database. The volume of components in every PN order was collected, and we calculated the volume of each source solution used per day. Rounding up this total to the nearest multiple of the source container volume allowed us to determine the amount discarded at the end of the day. Yearly data for costs are presented per financial year, defined as April 1 to March 31 of the following year.

Statistical Analysis

Data are presented as mean $\pm$ SD for normally distributed variables and as median (interquartile range) for non-normally distributed variables.

RESULTS

Patient Characteristics

A total of 1948 patients received PN during the study period. Patient age and weight at initiation of PN, as well as PN duration, remained similar throughout the study period, except in neonatol-

Table 1. Age at Initiation and Duration of Parenteral Nutrition in Neonatology

	No.	Age (days) at the Beginning of PN Mean $\pm$ SD	PN Duration (days) (Interquartile Range)*
2007	588	3.4 $\pm$ 9.4	10 (6–22)
2008	665	1.6 $\pm$ 4.1	10 (6–18)
2009	692	1.3 $\pm$ 2.1	9 (5–19)
2010	154	1.3 $\pm$ 2.7	7 (4–12)
p Value		<0.001†	<0.001‡

PN, parenteral nutrition

* Median

† Post-hoc *p* with Games-Howell procedure. *p* < 0.05 is considered significant. 2007 versus 2008, *p* = 0.016; 2007 versus 2009, *p* = 0.002; 2007 versus 2010, *p* = 0.003. Other pairs non-significant‡ Post-hoc *p* with Bonferroni correction. *p* < 0.008 is considered significant. 2007 versus 2010, *p* < 0.001; 2008 versus 2010, *p* < 0.001; 2009 versus 2010, *p* = 0.001. Other pairs non-significant

ogy, where PN initiation occurred earlier in life and PN duration decreased with time (Table 1).

PN Order Profile Analysis

Composition of PN was generally consistent over the years, except in neonatology, where amino acid dose increased, and in pediatrics, where amino acid, dextrose, and phosphate doses increased (data not shown).

Workload Analysis

A total of 33,544 PN orders were compounded during the study, for an average of 894 orders per month or 29.8 orders per day. As shown in Table 2, PN orders for neonatology represented 59% of total orders. The relative workload of each patient group remained similar during the study.

Cost Analysis

The costs of source solutions used in compounding are presented in Table 3. The cost of solutions in the average PN order appeared to be increasing. Source solutions discarded at the end of the day represented between 7.7% and 9.2% of total source solution cost, averaging between

Can\$2072 and Can\$2511 monthly, but this proportion seemed to decrease slightly throughout the study period. PN components responsible for important wastage costs were primarily amino acids in a 3-L bag, with between Can\$953 and Can\$1048 wasted monthly.

DISCUSSION

In this analysis, we showed that PN compounding at our center represents an important pharmacy workload, with an average of 894 orders per month. PN compounding services were used primarily by neonatology, with 59% of activity dedicated to these patients. PN for neonates is now started earlier in life but was used for fewer days per patient in 2010 compared with 2007. These observations are consistent with clinical practice changes implemented at our center during the study period, such as an earlier start of PN in the life of premature neonates with a higher amino acid dose, and the aggressive introduction of enteral nutrition with the objective of weaning PN rapidly.⁷

Compounding customized PN represented significant costs of between Can\$20,625 and Can\$30,968 monthly for source solutions only. Solutions from partially used containers, which are to be discarded daily, amounted to Can\$2072 to Can\$2511 monthly, which is comparable with results previously reported by other centers.⁸ Amino acids in 3-L bags were responsible for the larger part of these losses. Aside from ingredient costs, an automated compounding system requires expenses for the compounder itself; transfer sets, which are changed daily; PN bags; the laminar airflow hood in which the compounder is operated; human resources dedicated to PN compounding; training and certification costs; etc. These costs are generally fixed (i.e., they do not expand with the volume of activity). In this regard, our center certainly represents a “best-case scenario” for individualized PN compounding,

Table 2. Mean $\pm$ SD Number of Parenteral Nutrition Orders per Month (% of Yearly Total)

	Neonatology	Intensive Care	Oncology	Pediatrics	Home
2007	521 $\pm$ 61 (58)	101 $\pm$ 43 (11)	132 $\pm$ 43 (15)	137 $\pm$ 31 (15)	8 $\pm$ 5 (1)
2008	564 $\pm$ 124 (64)	45 $\pm$ 15 (5)	73 $\pm$ 30 (8)	191 $\pm$ 51 (22)	7 $\pm$ 6 (1)
2009	554 $\pm$ 81 (57)	69 $\pm$ 23 (7)	88 $\pm$ 35 (9)	246 $\pm$ 47 (26)	10 $\pm$ 6 (1)
2010	430 $\pm$ 113 (56)	70 $\pm$ 31 (9)	78 $\pm$ 28 (10)	178 $\pm$ 47 (23)	18 $\pm$ 10 (2)
Overall	531 $\pm$ 107 (59)	68 $\pm$ 33 (8)	90 $\pm$ 39 (10)	196 $\pm$ 59 (22)	10 $\pm$ 7 (1)

Table 3. Cost of Source Solutions per Year Presented in Canadian Dollars

	2007 (10.5 mo)	2008 (12 mo)	2009 (12 mo)	2010 (3 mo)
Number of orders compounded	9308	11,062	11,004	2170
Average monthly cost of compounded solutions	20,625	23,551	30,968	27,325
Average cost of solutions per order	23.27	25.55	33.77	37.78
Average monthly cost of discarded solutions	2084	2072	2511	2285
Proportion of discarded solutions in total cost, %*	9.2	8.1	7.5	7.7

mo, month

* *Cost of discarded solutions / (cost of compounded solutions + cost of discarded solutions)*

with a continuously large volume of activity, allowing for important fixed-cost amortization. Smaller centers may find that operating such a system is more expensive per PN order.

A recent study evaluated the possibility of extending the use of transfer sets and opened containers by 24 hours at a center using the Automix 3+3 compounder. Although wastage costs were projected to be halved, 5 of 40 PN bags failed microbiologic control, and the proposed measure was not implemented. The authors commented on the possibility of contamination explaining these results.⁸

Standardized solutions have been advocated as a solution to the problem of the increased pharmacy workload and costs associated with customized PN, at least in adults.⁹ With increasing pharmaceutical product shortages in the United States and Canada, industry is encouraging the use of commercially available standardized PN.¹⁰ Yet, in pediatrics it is generally assumed that customized PN is preferable because of the high variability of nutritional needs across all pediatric populations, whereas commercially available standardized products are not always appropriate.

A survey conducted in the United Kingdom at the beginning of 2008 and published in 2010 indicated that 94% of neonatal intensive care units used customized PN.¹¹ In contrast, customized PN was used in only 22% of adult patients. Similar results were obtained by European and Swiss surveys conducted from the late 1990s to early 2000s.^{12,13} Nevertheless, standardized PN is gaining in popularity. Some recently published studies demonstrated the feasibility of using standardized, even commercial PN in pediatrics and neonatology, although no clear advantage has been demonstrated.¹⁴⁻¹⁹ A survey from Israel conducted in 2005 showed that 18 of 25 neonatal intensive care units used commercial PN bags,

whereas all others used standardized PN compounded on-site.²⁰

Standardized commercial PN, albeit theoretically lower in costs and workload, may be inappropriate in several clinical situations, and it forces reliance on the availability of such a product, which, as the recent drug shortage crisis has demonstrated, is not always consistent. There are currently no formulations of standardized ready-to-use PN approved in Canada and in the United States for children younger than 1 year. Furthermore, compounding standardized PN on-site may be a solution to optimize workload, but we do not believe it would affect costs substantially because all equipment and source solutions required for compounding PN would still be necessary. An interesting solution could be to outsource the production of customized or standardized PN to another, larger center, or a specialized pharmacy. Although this would definitely reduce workload, disadvantages include an increased turnaround time, which may be clinically problematic in very acute populations and an important additional markup. The 2008 United Kingdom survey showed that only 50% of neonatal intensive care units had PN compounding available on-site exclusively, and an additional 10% used a combination of outsourced and on-site compounding. However, of the 8 hospitals that could not provide a PN solution on the day it was ordered, 7 relied exclusively on outsourced compounding.¹¹

The 2007 American Society of Parenteral and Enteral Nutrition Statement on Parenteral Nutrition Standardization stated that even though standard PN had economic and clinical advantages in select populations, there was no definitive evidence of a safety advantage, and customized PN should still be available for select patients.²¹ One study in pediatric intensive care patients shows that 69% of patients were

prescribed standardized PN as opposed to fully customized PN, yet of these, 47% were modified for patients receiving total PN. The authors underlined the risk of manual modification of standardized PN, especially on wards.¹⁹

The limits of our study include the acquisition of data exclusively from centralized databases, limiting the amount of information available compared with a manual review of patient files and preventing us from analyzing clinical outcomes. Yet, this allowed us to include all PN orders during the study period, increasing the internal validity of our analysis. We also classified patients by ward rather than by age, weight, or diagnosis, which produced rather heterogeneous groups. We do not believe this affected our global analysis. Cost analysis was limited to calculating the total amount of components used per day, rather than observing the actual amount used. Finally, our observations may not be directly applicable to centers where costs are different (in the United States, for example).

In conclusion, preparing customized PN using an automated compounder at our center represents a significant workload and important expenditure. Source solution costs are considerable, and between 7.7% and 9.2% of these are wasted by discarding partially used solution containers. Amino acids in 3-L bags were responsible for the major part of these losses. These costs are also increasing with time. Although a switch to standardized PN could be interesting from this perspective, it would not eliminate the need for customized PN, or for a safe and efficient system for providing it. Switching to smaller amino acid containers may help reduce waste.

DISCLOSURE The authors declare no conflicts of financial interest in any product or service mentioned in the manuscript, including grants, equipment, medications, employment, gifts, and honoraria.

ABBREVIATION PN, parenteral nutrition

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