Peripherally inserted central catheters optimize nutrient intake in moderately preterm infants

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BACKGROUND: While very preterm (<32 wk gestation) infants are routinely provided intensive nutritional support via central line, clinical practice varies for nutrient delivery in infants born moderately preterm (32–34 wk gestation). We sought to define the impact of nutritional support via peripherally inserted central catheter (PICC) on nutrient delivery in the first 2 wk of life and growth by discharge.

METHODS: Data were extracted from the records of 187 infants born between 32 and 34 6/7 wk gestation and admitted to the University of Iowa Children's Hospital between April 2012 and December 2013. Records of all feedings, weights, and PICC placements were collected. The growth outcomes at discharge for infants who received nutrition via PICC were compared to those who did not.

RESULTS: In the first week of life, newborns who received nutrition via PICC line received 17.6 more kilocalories (confidence interval (CI): 12.5–22.7, $P < 0.001$) and 1.2 more grams protein per kilogram body weight per day (CI: 0.9–1.4, $P < 0.001$) compared to control infants. By discharge, the PICC group had gained 302 g more body weight ($P < 0.001$).

CONCLUSION: This study demonstrates superior nutrient intake and growth in the first 2 wk of life for infants who received nutrition via PICC line.

Existing research on early nutrition has primarily focused on very preterm infants (<32 wk gestation) or very-low-birth-weight infants (<1,500 g). Given their size and immaturity, these infants are well recognized by clinicians as critical patients who require maximal nutrition support, including parenteral nutrition via central line. Utilization of peripherally inserted central catheter (PICC) lines in the neonatal intensive care unit (NICU) varies widely both between and within centers, primarily according to the training of the staff, size of the NICU, academic affiliation, and availability of radiologic services (1,2). Parenteral nutrition may not be considered in the moderate-to-late preterm infant (32 to <37 wk gestation) as their nutritional needs are often perceived as secondary to the risk of central-line associated bloodstream infections from the invasive access necessary for intravenous nutrient delivery (3,4). If sufficient parenteral nutrition support is not initiated, these patients may be at increased risk of developing early calorie and protein deficits, leading to impairment of growth (5–7). These early protein deficits are extremely difficult to overcome with higher intake later in life (8,9).

In a recent study of very-low-birth-weight infants, an optimized parenteral nutrition regimen with increased protein improved early postnatal head growth compared to a standard parenteral nutrition regimen (10), suggesting that improvement of clinical nutrition practices may be crucial in improving outcomes for premature infants. Failure to "catch up" in the first 8 mo of life is associated with lower head circumference and higher rates of poor neurologic development in very-low-birth-weight infants (11). Furthermore, impaired head growth at age 8 mo is predictive of lower performance and verbal IQ scores, increased incidence of hyperactivity, and lower scores in school topics at age 8 y (12). It is possible that optimization of growth in the first 2 wk of life would contribute to the avoidance of poor developmental outcomes in moderately preterm infants as well.

The goal of this study was to define the impact of nutrition support via PICC on nutritional intake and growth outcomes in infants born at 32–34 wk gestational age. This information could inform clinical decisions on placement of a central access line in moderately preterm infants.

RESULTS

Infants receiving nutrition support via PICC line received 17.6 (CI: 12.5–22.7, $P < 0.001$) more kilocalories per kilogram body weight per day (kcal/kg/d) and 1.2 (CI: 0.9–1.4, $P < 0.001$) more grams of protein per kilogram body weight per day (g/kg/d) on average during the first 7 d of life compared to infants who did not receive nutrition via PICC (**Table 1**). Results shown are actual intakes, not merely prescribed. This difference persisted through the first 14 d of life, with infants in the PICC group receiving 13.2 kcal/kg/d (CI: 8.4–18.4, $P < 0.001$) and 0.9 g/kg/d (CI: 0.7–1.1, $P < 0.001$) more than controls (**Figure 1**). The daily amount of energy received by route of delivery (enteral vs. parenteral) is shown in **Supplementary Figure S1** online (**Figure 1**). No differences in total daily volume intake were demonstrated. None of the infants developed sepsis during admission.

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Table 1. Mean energy and protein intakes in the first 14 d of life in neonates who received nutrition via PICC compared to those who did not (control)

	Goal	Control (n = 78)	PICC (n = 109)	Difference of means (95% CI)	P-value
Mean energy intake (kcal/kg/d)					
Total, day of life 1–7	100.0	69.2	86.8	17.6 (12.5, 22.7)	**<0.001**
Enteral		45.7	33.1	−12.6 (−17.3, −7.9)	**<0.001**
Parenteral		23.5	53.8	30.3 (25.9, 34.6)	**<0.001**
Total, day of life 8–14	100.0	97.7	106.0	7.6 (1.5, 13.7)	**0.015**
Enteral		95.9	87.8	−8.2 (−15.8, −0.5)	**0.036**
Parenteral		1.8	18.2	16.4 (12.1, 20.7)	**<0.001**
Total, day of life 1–14	100.0	83.4	96.4	13.2 (8.4, 18.4)	**<0.001**
Enteral		70.7	60.4	−10.3 (−15.8, −4.8)	**<0.001**
Parenteral		12.7	36.0	23.3 (19.9, 26.7)	**<0.001**
Mean protein intake (g/kg/d)					
Day of life 1–7	3.0	2.0	3.2	1.2 (0.9, 1.4)	**<0.001**
Day of life 8–14		3.0	3.6	0.6 (0.3, 0.8)	**<0.001**
Day of life 1–14	3.0	2.5	3.4	0.9 (0.7, 1.1)	**<0.001**

Bolded P value represents significant difference between control and PICC groups at $P < 0.05$.
PICC, peripherally inserted central catheter.

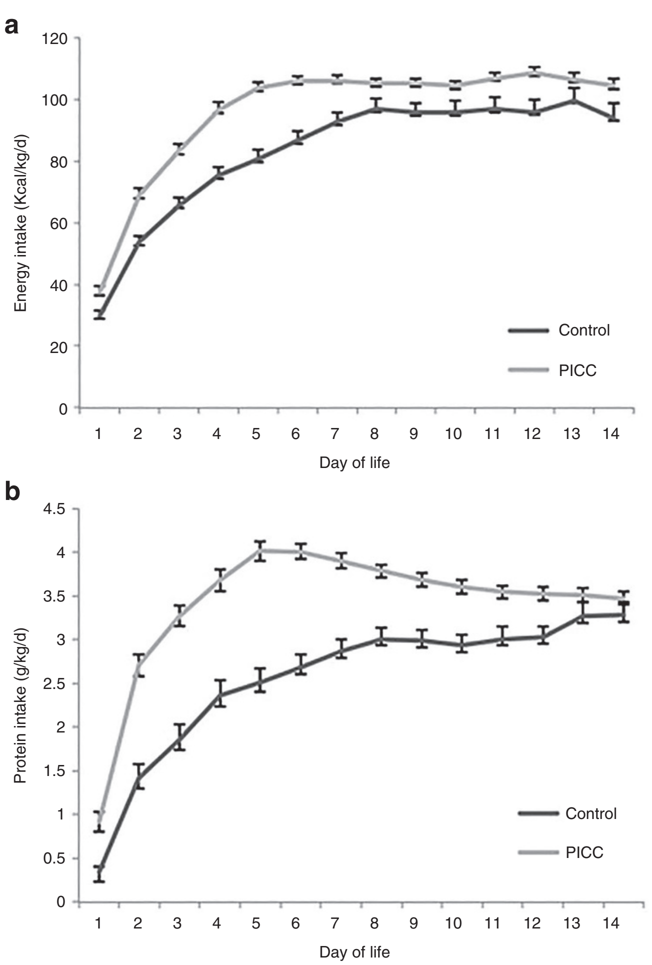

Figure 1. Energy and protein intake in the first 14 days of life. Daily intake of energy (**a**) and protein (**b**) during the first 14 d of life in neonates who received nutrition via peripherally inserted central catheter (PICC—gray line) in the first 14 d of life compared to those who did not (control—black line). Error bars represent SE.

Receiving nutritional support via PICC line improved the likelihood of receiving adequate protein (≥3 g/kg/d) (odds ratio (OR): 11.2, CI: 5.6–22.3, $P < 0.001$) averaged over the first 7 d of life. During the first 2 wk of life, infants with PICC lines received in total 47.6 g of protein, or 5.6 g more protein than the recommended minimum target of 42 g. Control infants received only 35.6 g, or 6.4 g of protein fewer than the minimum goal and 12.0 g fewer than the PICC infants. It is important to note that 100 kcal/kg/d and 3.0 g/kg/d protein is a minimum goal; many institutions aim for 120 kcal/kg/d and 3.5–4 g/kg/d. Twelve of the 109 patients with PICC lines averaged over 100 kcal/kg/d during the first 7 d of life; none of the 78 control neonates were able to meet this goal. This difference persisted through the second week of life, with PICC patients having improved odds of receiving adequate energy (OR: 4.4, CI: 2.0–9.8, $P = 0.0002$) and protein (OR: 14.1, CI: 6.8–29.1, $P < 0.0001$) as compared to control patients.

During the first week of life, control infants received 66% of kilocalories enterally, while infants in the PICC group received only 38% of kilocalories enterally. Additionally, infants in the PICC group were supplied with 212 more kilocalories per kilogram body weight via parenteral administration, and 124 more kilocalories in total than the control group during the first 7 d of life (Table 1).

As anticipated, improved nutritional intake was associated with increased weight gain throughout admission. Although infants in the PICC group were, on average, born earlier and at lower weights, they were discharged at similar postmenstrual age to the control infants and at higher weights (Tables 2 and 3). Infants in the PICC group gained an average of 6.7 g more per day compared to control infants when calculating this figure as the weight gained from birth to discharge standardized by the length of stay in days. Infants in the PICC group also

Table 2. Demographic and clinical characteristics of neonates who received nutrition via PICC in the first 14 d of life compared to those who did not (control)

	All (N = 187)	Control (n = 78)	PICC (n = 109)	P value
Male, *n* (%)	94 (50)	35 (45)	59 (54)	0.23
Gestational age (weeks), mean (SD)	33.7 (0.8)	34.1 (0.6)	33.3 (0.8)	**<0.001**
Mean birth weight (g), n (SD)	2,054.0 (28.9)	2,154.3 (38.8)	1,982.2 (39.8)	**<0.01**
Completed weeks gestation, *n* (%)				
32	43 (23)	4 (5)	39 (36)	**<0.01**
33	54 (29)	17 (22)	37 (34)	0.24
34	90 (48)	57 (73)	33 (30)	**0.03**
Size for gestational age				
Appropriate	163 (87)	72 (92)	91 (83)	0.49
Small	18 (10)	5 (6)	13 (12)	0.16
Large	7 (4)	1 (1)	6 (6)	0.15
Maternal race/ethnicity				
White, non-Hispanic	149 (80)	57 (73)	92 (84)	0.30
Black	19 (10)	11 (14)	8 (7)	0.86
White, Hispanic	13 (7)	7 (9)	6 (6)	0.56
Asian	6 (3)	3 (4)	3 (3)	0.74
Known maternal risk factors, *n* (%)				
Pre-eclampsia	50 (28)	21 (27)	29 (27)	0.90
Diabetes	27 (14)	10 (13)	17 (16)	0.68
Smoking	34 (18)	19 (24)	15 (14)	0.08
2+ factors	15 (8)	6 (8)	9 (8)	0.72
Average length of stay (days), *n* (SD)	26.2 (10.6)	22.2 (6.5)	29.1 (11.9)	**<0.001**
Mean postmenstrual age at discharge (wk), *n* (SD)	37.4 (1.4)	37.3 (1.0)	37.5 (1.6)	0.23
Primary cause of prematurity, *n* (%)				
Pre-eclampsia	37 (20)	15 (19)	22 (20)	0.51
Fetal distress	31 (17)	13 (17)	18 (17)	0.96
Spontaneous labor	22 (12)	10 (13)	12 (11)	0.70
Chorioamnionitis	21 (12)	9 (12)	12 (11)	0.89
PPROM	2 (1)	0 (0)	2 (2)	0.23

Bolded P value represents significant difference between control and PICC groups at $P < 0.05$.
PICC, peripherally inserted central catheter; PPROM, preterm prolonged rupture of membranes.

demonstrated significantly increased weight gain at 7 and 14 d of life (**Table 3**). While both groups had decreased Z scores for weight at discharge, infants with PICC lines only decreased 0.54 from their birth score while control infants decreased 0.70 (P = 0.011). Improvements in occipital-frontal circumference were not significant at discharge. The mean PICC dwell time was 8.8 d (median 8 d, mode 6 d).

DISCUSSION

As the focus of neonatal research shifts from achieving survival to optimizing quality of life outcomes, the importance of adequate nutrition to promote growth cannot be overestimated. Numerous studies have shown the advantages of early nutrition and avoidance of protein deficits (10,13–15). However, provision of adequate nutrition in the early postnatal period remains a challenge, and current clinical practices for the delivery of adequate nutrition may be insufficient (8,9,16,17).

In this study, neonates who were given supplemental nutrition via PICC line received more kilocalories and protein than those who did not. Additionally, neonates in the PICC line group gained more weight at discharge and were better able to maintain their birth weight Z scores at discharge. These results provide the first demonstration of the efficacy of nutritional support via central line for infants born moderately preterm. We would like to emphasize that while we refer to use of PICC lines for central venous nutrition, similar results could be obtained with use of umbilical venous catheters. Our clinical practice is to use PICCs in this population, but any appropriately placed central catheter that allows for adequate dextrose concentration to be delivered would be efficacious. It has been

Table 3. Weight and head circumference at birth and at discharge in neonates who received nutrition via PICC in the first 14 d of life compared to those who did not (control)

	Control (n = 78)	PICC (n = 109)	*P* value
Weight, Z			
At birth	−0.14	−0.11	0.89
At discharge	−0.84	−0.65	0.13
Change	−0.70	−0.54	**0.01**
Weight, g			
At birth	2,154.3	1,982.2	**0.003**
Day 7	2,099.9	2,019.0	0.13
Day 14	2,285.5	2,189.0	0.06
Discharge	2,561.3	2,691.0	**0.04**
Weight change, g			
Day 7	−47.0	37.9	**0.001**
Day 14	138.6	207.9	**0.004**
Discharge	407.0	708.8	**<0.001**
Head circumference, Z			
At birth	0.21	0.21	0.98
At discharge	−0.37	−0.20	0.19
Change	−0.59	−0.43	0.12
Head circumference, cm			
At birth	31.3	30.60	**0.004**
At discharge	32.9	33.07	0.60
Change	1.26	2.15	0.12

Bolded *P* value represents significant difference between control and PICC groups at $P < 0.05$.
PICC, peripherally inserted central catheter.

previously demonstrated that optimized early nutrition can improve growth for infants born very preterm or at very low birth weights, and this study suggests that moderately preterm infants benefit similarly. Aggressive parenteral nutrition also appears to prevent retinopathy of prematurity (15,18). Optimized early nutrition has been shown to improve neurodevelopment outcomes throughout childhood for infants born very preterm or at very low birth weights, with increased head circumference predicting later school performance and positive behavioral outcomes (11). Body weight is a strong early predictor of development in the areas of the brain controlling attention, language, and executive function (19,20).

Currently, the risk of central line-associated bloodstream infection (CLABSI) is a deterrent to the placement of PICC lines in moderately preterm infants. Incidence rates vary widely by center and standard placement practices. A recent multicenter study reported a CLABSI incidence in neonates due to PICC lines of 1.66 per 1,000 catheter days, with greater risk associated with increased catheter dwell time (3). It should be noted that the mean dwell time in their study was 14 d, compared to a mean dwell time in our group of infants of 8.8 d, with a median of 8 d and mode 6 d. None of the infants involved in our study developed CLABSI. Several centers have successfully implemented strategies for the reduction of CLABSIs with PICC line placement (21–23). While it is important to consider the risks of central line placement, the necessity of optimal nutrient delivery should also be considered.

The strengths of this study include the comparison of actual nutrient intakes, not prescribed, as well as the analysis of the protein composition of each feeding. Use of weight-for-age Z scores allowed for relative comparison of growth outcomes in infants born at different gestational ages. We have also stated the growth outcomes after the first and second weeks of life to demonstrate improved growth irrespective of the duration of hospitalization. The limitations of this study include the short-term focus, which precludes the ability to evaluate if later neurodevelopmental outcomes would be comparably improved in infants born moderately preterm. This study was also limited by the inability to accurately record breastfeeding intakes, leading to an unknown underestimation of exact nutrient intake in both groups. The limitations of observational study design also include the potential for bias; control group infants may have been deemed unlikely to need aggressive parenteral nutrition support based on birth weight or gestational age without equal consideration of overall clinical status.

It is essential that clinicians deliver adequate nutrition for optimal growth while a preterm infant is admitted to the NICU. Our data show that using PICC lines for nutritional support provides an excellent supplementation for enteral feeds. As expected, greater nutrient intake was associated with improved growth outcomes at discharge, suggesting that moderately preterm infants may receive similar benefits from nutrition delivery via central access as their very preterm peers. Utilization of PICC lines for optimal nutrient delivery is an excellent strategy to improve outcomes for infants born moderately preterm.

Conclusion

Administration of nutritional support via PICC was associated with greatly improved energy and protein delivery in this study of moderately preterm infants. This indicates moderately preterm infants may substantially benefit from central line nutrient delivery in ways similar to very preterm or very-low-birth-weight infants. Recognition of this opportunity to improve growth outcomes should be an important consideration in the clinical decision of central line placement.

METHODS

Information on nutrient intake and growth from day of life 1–14 was collected from the medical records of 187 infants born at 32 0/7 to 34 6/7 wk gestation who were admitted to the University of Iowa Children's Hospital NICU between 1 April 2012 and 31 December 2013 and survived to discharge home. This group excluded infants born with major congenital abnormalities, those who required major surgery during admission, and those who were transferred to other facilities. The nutrition information included route of administration, type of feeding, and daily intake (actual, not prescribed) of fluid, kilocalories and protein from formula, breast milk, fortifiers, total parenteral nutrition, lipids, and dextrose solutions. All daily intakes were standardized by the neonate's body weight on the day of intake.

At our institution, infants are generally provided breast milk or donor breast milk on day of life 0–1, with trophic feeds advanced slowly. Our typical practice for provision of intravenous fluids is placement of a peripheral venous catheter on admission, with PICC placement taking place within the first 24 h of age. PICC lines are preferred for parenteral nutrition support, while umbilical venous catheter lines are generally reserved for critically ill infants requiring immediate central access for medications such as prostaglandin or inotropes. When in place due to critical illness, we do use these catheters for parenteral nutrition administration as well.

While the reported energy requirements of moderate to late preterm infants vary, the World Health Organization recommends 70–135 kilocalories per kilogram per day during the first 2 wk of life (24). In addition, moderate to late preterm infants are estimated to require 3.0–4.0 g protein per kilogram body weight per day to maintain growth in the early postnatal period (25–27). Therefore, minimum intake goals of 100 kcal/kg/d and 3 g/kg/d protein were chosen for evaluation of adequate nutrient delivery in this study.

Measurements of each patient's body mass and head circumference at birth and at discharge were also collected and converted to Z-scores according to the 2013 Fenton growth charts, allowing for standardization by postmenstrual age and sex (28). Because length measurements were not consistently recorded at discharge, length was not collected. Intake and body measurements from patients who received nutrition via PICC during the first 14 d of life were compared to infants who did not receive nutrition via PICC (control). The control group also included neonates who received nutrition via umbilical or peripheral lines. Data were analyzed using independent sample t-test, Chi-square test, or logistic regression with significance set at $P < 0.05$ using IBM SPSS version 23 (Armonk, NY). All analyses were bivariate and unadjusted, no multivariable modeling was performed. Informed consent was waived due to the retrospective nature of this study. All methods were approved by the University of Iowa Institutional Review Board (Approval #201403744).

AUTHOR CONTRIBUTIONS

A.L.S. conceptualized and designed the study, performed data collection and analysis, drafted the initial manuscript, and approved the final manuscript as submitted. A.B.K. and S.J.C. conceptualized the study, coordinated data collection, and approved the final manuscript as submitted. T.T.C. designed the data collection instruments, coordinated data analysis, and approved the final manuscript as submitted. J.M.D. conceptualized the study, coordinated IRB approval, reviewed and revised the manuscript, and approved the final manuscript as submitted.

SUPPLEMENTARY MATERIAL

Supplementary material is linked to the online version of the paper at http://www.nature.com/pr

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