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ORIGINAL ARTICLE

A standardized nutrition approach for very low birth weight neonates improves outcomes, reduces cost and is not associated with increased rates of necrotizing enterocolitis, sepsis or mortality

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OBJECTIVE: To assess how a standard practice for nutrition support in very low birth weight (VLBW) neonates would impact on their hospital course.

STUDY DESIGN: This was a prospective, single center, before vs after comparison of a non-standardized approach to nutrition in VLBW neonates to a standardized approach. Standardization of feeding initiation, feeding volume and caloric advancement, management of feeding aspirates (residuals), use of starter parenteral nutrition (PN), use of breast milk and donor breast milk, initiation and discontinuation of intravenous (IV) intralipids, documentation of protein use, and utilization of percutaneously inserted central venous catheters were performed. Multiple outcome measures were evaluated. Fisher's exact, Mann–Whitney *U*-tests and χ^2 tests were used for statistical analysis.

RESULT: Sixty-nine infants in the pre-standardization (non-standardized) group were compared with 154 infants in the standardized approach group. Analysis was performed for each group as a whole. Statistically significant improvements were seen in multiple areas for the standardized group including the day of life birth weight was regained ($P<0.0005$), use of breast milk as the initial feeding ($P<0.0001$), use of starter PN on admission ($P<0.0001$), earlier time for initiation of PN ($P<0.0001$), decreased use of PN overall ($P<0.0001$), enteral protein use ($P<0.0001$), earlier time for initiation of IV intralipids ($P<0.002$), day of life for full enteral feeds ($P<0.0005$) and first day for initiation of enteral feeds ($P<0.0001$). Fewer infants born microcephalic at birth remained so at discharge in the standardized group as compared with the pre-standardized group ($P<0.02$). Similarly, less infants born small for gestational age at birth remained so at discharge in the standardized group as compared with the pre-standardized group ($P<0.05$). Two cases of necrotizing enterocolitis (NEC) occurred in the pre-standardization group and one in the standardized group. No coagulase-negative *Staphlococcal* infections or line infections occurred during the entire study period. Two cases of sepsis occurred in the pre-standardization group, both in infants <750 g. No cases of sepsis occurred in the standardized group. Cost savings were remarkable from decreased PN usage in the standard group.

CONCLUSION: Implementation of a standardized approach to nutrition in VLBW infants reduces the use of PN thereby reducing cost, causes a more rapid regain of birth weight, decreases the number of babies that are small for gestational age and microcephalic at discharge, and decreases the time to full enteral feeds. No adverse increases in mortality, sepsis, NEC, coagulase-negative *Staphlococcal* infections or line infections occurred.

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INTRODUCTION

Necrotizing enterocolitis (NEC) causes a significant number of deaths in neonatal intensive care units.[1] Prevention strategies to reduce the occurrence of NEC such as the promotion of human breast milk for feeding, early human milk enteral feeding and slower vs faster rates of feeding advancement have been recommended with varying results.[2–7] Management of residuals (gastric aspirates) varies widely and has been considered an indicator for the presence of NEC but this association is not confirmed[8–10] and has even been considered erroneous.[11,12] What is known, is that the delay in the initiation and advancement of enteral feeds is usually attributed to a fear of residuals.[11,12] Fear of NEC leads to a widely varied, cautious, delayed approach to feeding very low birth weight (VLBW) infants but this may cause postnatal growth restriction.[12] In fact, low protein intake was considered the main cause of postnatal growth restriction in one article.[12] Postnatal growth restriction has been shown to cause deleterious effects on neurodevelopmental outcome.[12–16] Consequently, neonatologists are presented with the dilemma of trying to avoid NEC while simultaneously avoiding postnatal growth restriction and neurodevelopmental problems. This ambiguity results in a wide variation in feeding practice. Such issues include how physicians initiate feeds, advance feeds, increase calories for enteral feeds, manage residuals, use initial (starter) parenteral nutrition (PN), advance PN protein and intralipids, discontinue intralipids and decide when to discontinue central lines. In addition, how these nutrition issues may affect cost, age for attaining full enteral feeds, age for regaining birth weight, growth parameters, NEC, sepsis and line infection rates is not well studied.

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Decreasing variation has been shown to improve health care.[17,18] To our knowledge, no comprehensive, prospective, standardized (reduced variation) method describing such an approach has been published. In this article, we describe how a standard practice for early enteral nutrition support in VLBW neonates would impact on their hospital course and outcomes.

METHODS

This study was performed at the 59 bed level 3C (extracorporeal membrane oxygenation and cardiothoracic surgery capable) neonatal intensive care unit (NICU) at Akron Children's Hospital and the 17 bed, level 2, special care nursery leased by Akron Children's Hospital from Akron General Medical Center in Akron, OH, USA. Deliveries occur at Akron General Medical Center but not at Akron Children's Hospital. Eight neonatologists staffed both units on a rotating schedule every 2 weeks.

Before initiation of this project we achieved a low rate of line related sepsis by implementing a line practice bundle for percutaneously inserted central venous catheters. We routinely used a base solution (also called starter PN or starter hyperalimentation) of D10W, with 2% amino acids and 10 mEq of calcium per liter after birth. Fortification of caloric content was achieved with a non-Prolacta, powder-based human milk fortifier throughout the study.

Data were collected prospectively from 1 December 2008 until 31 August 2009 comprising the pre-standardization group. At this time, we had no standardized feeding protocols and feeding practices were entirely at the discretion of the attending neonatologist, except for the routine use of base solution and method for fortification of calories as described in the preceding paragraph. However, the timing of these interventions was up to the neonatologist and was also not standardized. This group was compared with a similar group of babies whose data was collected prospectively from 1 September 2009 until 1 November 2010 using the standardized approach. Before initiation of this standard approach, we developed an evidence-based protocol for feeding practices, aspirate management, feeding advancement and percutaneously inserted catheter usage. These documents were discussed among all the neonatologists, nursing leadership and nutritionist groups. Once they were approved, a multidisciplinary educational process was implemented before their introduction.

Infants were eligible for the study if they were $\leqslant$1500 g at birth, had no surgical abdominal condition such as a gastroschisis or bowel obstruction, were $<$24-h old on admission, had no genetic abnormality and who survived to discharge. Eight infants were excluded from the pre-standardization group resulting in 69 infants for analysis and 11 infants were excluded from the standardized group resulting in 154 infants for analysis.

Multiple outcome measures were evaluated. Fisher's exact, Mann–Whitney *U*-tests and χ^2 tests were used for statistical analysis where appropriate. A *P*-value of <0.05 was considered significant. Graphpad Instat version 3 statistical software, Graphpad Software, San Diego, CA, USA (www.graphpad.com) was used.

This process was discussed with the institutional review board but did not require approval as it was felt to be an alteration of existing medical practice and was therefore deemed a quality improvement project not necessitating approval.

The standardized approach

The neonatologists agreed on the following standardized approach to nutrition in VLBW infants:

The following guidelines were named the Nutrition Group Guidelines and were attached to the accompanying documents referenced in this article as Figures 1 and 2. All of these documents were available every day on rounds and accompanied the rounding teams for easy referral and to prevent lapses in memory.

1. Base solution (starter PN) was started as soon as possible in all infants $<$1501 g at birth.

2. Mother's milk was the preferred substrate for all infants $<$1501 g at birth. If no maternal breast milk was available by 48 h of age then donor breast milk was used unless a parental objection occurred.

3. Intravenous (IV) lipids were started on day of life two (for infants requiring PN) at 1 g kg^{-1} day^{-1} and advanced to 2 g kg^{-1} day^{-1} the next day. We recommended a maximum of 3 g kg^{-1} day^{-1}. The daily progress note template was changed to document lipid use in g kg^{-1} day^{-1} as a daily reminder. Lipids were discontinued once the infant was taking one-half the total desired daily volume enterally.

4. Enteral feeding was initiated by 24 h of age and advanced by following our Feeding Guideline for Infants $\leqslant$1500 g at birth (Figure 1). Full feeds were defined as $\geqslant$150 cc kg^{-1} day^{-1}.

5. Percutaneously inserted central venous catheters were discontinued (for nutrition purposes) when the infant was taking 3 g kg^{-1} day^{-1} of enteral protein and 100 kcal kg^{-1} day^{-1} of nutrition. Percutaneously inserted central venous catheter lines could be left in patients if they were used for other reasons such as antibiotics.

6. We strived to achieve a total of 3 to 4 g kg^{-1} day^{-1} of protein; enterally, by IV or by a combination of both.

7. Protein use was documented in the daily progress note. The progress note template was changed to document protein as enteral protein in g kg^{-1} day^{-1}, IV protein in g kg^{-1} day^{-1} and total protein in g kg^{-1} day^{-1}. This allowed the desired protein use to be reviewed daily and adjusted according to the guidelines.

8. Amino acids in the base solution were increased to 3% with the intention of giving 70 cc kg^{-1} day^{-1} immediately after birth thereby achieving 2 g kg^{-1} day^{-1} of protein initially. After 24-h, protein was advanced to 3 g kg^{-1} day^{-1}.

9. Enteral calories were increased to 24 kcal per ounce once the infant took one-half of their total desired daily volume enterally (approximately 80 cc kg^{-1} day^{-1}). PN vitamins were reduced at this point to one-half. IV protein was reduced to achieve our desired total daily protein amount (as explained above in number 6).

10. Residuals (aspirates) were managed by using the aspirate (residual) algorithm (Figure 2).

The first paragraph in the Feeding Guideline for Infants $\leqslant$1500 g at birth reminded the rounding team of our purpose; why early enteral nutrition was so important. It also detailed our approach for feeding method—gravity vs feeds over a specified pump time vs continuous nasogastric feeds. We initially tried gravity feeds and if this was not tolerated because of aspirate issues then changing to feeds over a pump time of 1 to 2 h was recommended. If issues still arose with pump feeds then continuous feeds were recommended. In addition, it gave feeding advancement guidelines based on birth weight.

The aspirate (residual) algorithm clearly stated it was not an emesis or NEC guideline. It also reiterated the importance of early enteral feeds and our agreed on principles concerning residuals (which we determined from our literature review, which was partially quoted in the introduction). It reminded the rounding team about the importance of aspirate management in achieving full enteral feeds.

RESULTS

Demographic characteristics are listed in Table 1. There were no significant differences in birth weight, gender, race, completion of antenatal steroids, gestational age or mortality among the two groups.

Outcome measures are listed in Table 2. They will be discussed in groups.

Nutrition intake outcomes

The use of protein fortification increased significantly. Intralipids were initiated earlier by 1 day on average and at greater levels and both of these factors were significant. Enteral feeds were started $>$2 days earlier on average and the day of life for achieving full enteral feeds was decreased by 3 days on average—both significant. PN use was decreased by an average of 5 days in the standard approach group, was initiated by 24 h of age in 100% of patients, and was used in 100% of the standard group on admission, a significant increase from pre-standardization. Enteral calories and volume were higher when PN was discontinued and enteral protein was greater when full feeds were achieved in the standardized group. IV amino-acid levels were greater on admission and were maintained at higher levels during use of PN in the standardized group. While breast milk was used more frequently as the initial feeding in the standardized group, there was no difference in the use of breast milk at full feeds or at discharge. There was no difference in the day of life that intralipids were discontinued.

Purpose: The purpose of this guideline is to promote early enteral nutrition. Starting enteral nutrition as early as possible prevents gut atrophy, generates intestinal trophic effects, enhances hormonal and peptide responses, and induces rapid maturation of gastrointestinal tract motor function. Advantages to early feeding include a shorter time to full enteral feeds, less use of phototherapy, a lower incidence of direct hyperbilirubinemia, smaller gastric residuals, less feeding intolerance, faster weight gain, better head growth, potentially shorter hospital stays, lower sepsis rates, and a lower incidence of necrotizing enterocolitis.

Initiation: Feeds should be started by 24 hours of age on infants ≤ 1500 grams. Special consideration will be given to infants in the following categories or felt to be at risk of compromise by the rounding team.

- infants in ≥ 60% FiO2
- infants receiving pressors for blood pressure support > 10 mcg/kg/min
- infants with a known structural GI abnormality
- infants with a patent ductus arteriosus requiring therapy *

* Infants receiving pharmacotherapy for a PDA should not be made NPO if feeds are tolerated. We recommend not advancing feeds but continuing the feeds as ordered before treatment was initiated.

Guideline:

1. Colostrum for oral care may be started as soon as possible after birth. An order for use after the initial oral care is required.
2. Colostrum is the preferred initial substrate.
3. We recommend following the Nutrition Group Guidelines (attached).
4. The aspirate/ residual algorithm should be used for aspirates (attached).
5. For babies < 1000 grams we recommend trying gravity feeds initially when nutritional feeding is begun (not just trophic feeds). If feeding intolerance occurs with gravity feeds we recommend trying feeds given over a specified pump time (usually 1 or 2 hours). If feeding intolerance still occurs with pump time feeds then continuous feeding may be considered. Babies ≥ 1000 grams may be started on gravity feeds from the start.
6. Based on feeding tolerance this guideline may need to be altered on an individual basis at MD discretion.
7. This Guideline is based on birth weight but daily fluid calculations are based on current weight.

Birth weight	Initial trophic feeding (by 24 hrs of age)	1st trophic advance (24-48 hrs after initial trophic feed)	2nd trophic advance (24 hrs after 1st trophic advance)	Nutritional feeding advancement (24 hrs after 2nd trophic advance and increase daily until desired feeding goal is reached)
≤ 699 grams	0.5 ml q 3 hrs	1 ml q 3 hrs	1.5 mls q 3 hrs	20 ml/kg/day, given q 3 hrs
700-999 grams	1 ml q 3 hrs	2 mls q 3 hrs	3 mls q 3 hrs	20 ml/kg/day, given q 3 hrs
1000-1500 grams	20 ml/kg/day, given q 3 hrs	20 ml/kg/day, given q 3 hrs	20 ml/kg/day, given q 3 hrs	20 ml/kg/day, given q 3 hrs

Figure 1. Feeding guideline for infants <1500 g at birth.

Growth outcomes

Birth weight was regained on average 4 days earlier in the standard group when compared with the pre-standard approach. After implementation of the standard approach, we observed a significant reduction in the number of infants who were born microcephalic that remained so at discharge. This was also true for infants whose birth weight was <10th percentile small for gestational age (SGA) at birth as determined by the Fenton Growth Chart. Fewer of these infants remained SGA at discharge in the standard group. Of note, in the pre-standard group three babies born normocephalic became microcephalic at discharge and four babies born appropriate for gestational age (birth

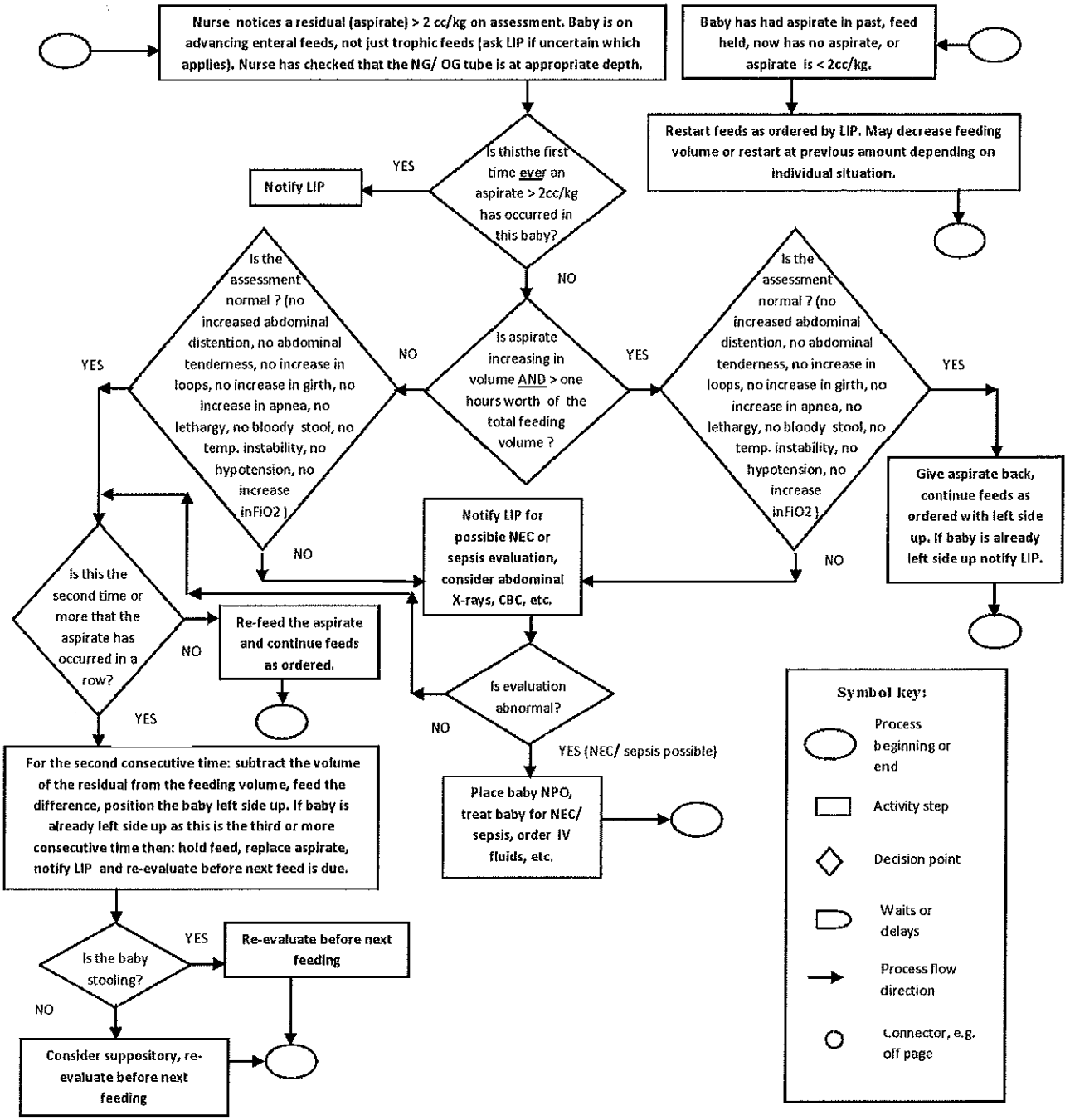

Figure 2. Aspirate (residual) algorithm. (Note: Does NOT apply to emesis. A bilious emesis needs an evaluation.) This is NOT an necrotizing enterocolitis (NEC) algorithm. If NEC is suspected notify the licensed independent practioner (LIP). Agreed on principles: (1) withholding food for >48 h causes villous atrophy. (2) Residuals ALONE only indicates gut immaturity, and NOT NEC. (3) The key to reaching full enteral feeds as early as possible is the mgt. of residuals. (4) The color of residuals does NOT indicate anything significant. (5) Residuals should never be discarded unless NEC exists. CBC, complete blood count; FiO_2, fraction of inspired oxygen; NPO, nothing per os.

weights 10–90%) were SGA at discharge. This did not occur in the standard approach group.

Other outcomes

There were no differences in the number of cases of NEC or sepsis. There was a significant reduction in the number of days that percutaneously inserted central venous catheter lines were used but no difference in the rate of line infections between groups.

Cost savings are listed in Table 2. These figures are based on a daily patient cost (or charge) of PN of $500.00, while the cost to the hospital is $45.00 per day. The daily patient cost of intralipids is $50.00 and the hospital cost is $4.00 per day. The lipid cost savings are listed as potential savings from 4 less days of lipid use on average, although statistically there was no difference between groups.

DISCUSSION

Implementation of these feeding practices reduced variation and resulted in improved outcomes for our patients with no increase in adverse outcomes from NEC, sepsis, mortality or line infections.

Table 1. Demographics

	Pre-standard approach	*Standard approach*	P-*value*
Total	N = *77*	N = *165*	
After exclusions number for analysis	N = *69*	N = *154*	
	N *(%)*	N *(%)*	
Birth weight (g)			
<750	15 (22)	16 (10)	NS
751–1000	16 (23)	55 (36)	NS
1001–1250	17 (25)	35 (23)	NS
1251–1500	21 (30)	48 (31)	NS
Male gender	40 (58)	88 (57)	NS
Race			
White	34 (49.3)	76 (49.4)	NS
Black	33 (47.8)	74 (48.0)	NS
Other	2 (2.9)	4 (2.6)	NS
Completed antenatal steroids			
Yes	69 (100)	154 (100)	NS
No	0	0	
Gestational age (weeks), median (range)	27 (24–31)	27 (24–32)	NS
Mortality	5 (6.5)	9 (5.5)	NS
Exclusion reasons: died (sepsis)	2	0	
Died (NEC)	2	0	
Gastroschisis	2	1	
Bowel obstruction	1	3 (2 died)	
Died (genetic abnormality)	1	1	
Referred >24 h of age	0	6 (all died)	
Exclusion total	8	11	

Abbreviations: NEC, necrotizing enterocolitis; NS, not significant.

In addition to achieving full enteral feeds in a significantly shorter time, we also regained birth weight sooner and most importantly, improved growth in both body weight and head circumference as evidenced from improved parameters at discharge. In the pre-standard group, these parameters actually worsened with more babies discharged microcephalic and SGA than were present on admission. There is evidence that earlier initiation and achievement of full enteral feeding has been associated with better neurologic outcomes.[13] In addition, earlier administration of adequate IV protein improves the protein deficit described in VLBW patients.[16,19,20] We achieved a significantly earlier introduction of protein IV in the standard group. Although IV protein was discontinued earlier in the study group, it was maintained at higher levels until discontinuation and was supplemented with higher amounts of enteral protein and volume. This practice of earlier introduction of IV protein, and increased levels of IV protein for shorter periods when coupled with earlier initiation and maintenance of enteral protein at higher amounts, achieving full enteral nutrition sooner, and earlier and increased levels of intralipids led to an overall result of improving growth in these babies. Other investigators have reported that improvements in NEC rates, first day for enteral feeding initiation, decreased number of days of PN use and achievement of desired feeding volumes was improved by initiating standard feeding guidelines.[21,22] These practices also impacted on our infection risk.

Indwelling central line use was significantly reduced, which decreases the risk from line infections, although our NICU had a low rate of line/coagulase-negative *Staphlococcal* (CONS) infections throughout the study. We feel our results may not have been achievable unless we first had adopted a line practice bundle that reduced our line infection rate to an extremely low level. For example, our unit had a consecutive 815-day period without a CONS line infection.

The reduction in use of PN was significant, and any reduction in exposure to PN further reduces the risk for infections, as well as PN-associated liver disease.[23] The use of intralipids decreased by 4 days on average and while this was not significant, on an individual case-by-case basis undoubtedly had benefit as prolonged lipid use is associated with an increased infection risk as well.

This study did not use Prolacta, which has been associated with a reduction in NEC.[24] However, we did not observe any detrimental effect by doing so. We used powder protein fortification during this study. Now there is a sterile liquid protein fortifier but this was not available to us during this study.

The use of breast milk initially may be protective against NEC[25] and we showed an improvement in the initiation of feedings with breast milk. However, we could not sustain the exclusive use of breast milk later in the hospitalization or at discharge. We did use maternal breast milk or donor breast milk exclusively until the infant reached 1500 g and was on full feeding volume then we introduced formula. This was due to the high cost of donor breast milk to our hospital. We also would not use donor breast milk if the mother had an objection to its' use but during this study only one mother declined donor breast milk and that was in the pre-standard group. That baby did not develop NEC or sepsis and survived till discharge.

Cost savings to patients were impressive primarily because of decreased use of PN. The key to using less IV nutrition and more rapid achievement of enteral nutrition is the management of residuals. Our aspirate algorithm accomplished our goal of standardizing our unit's approach to residuals enabling us to reach full enteral feeds faster. This significantly reduced delays in enteral feeding advancement at no adverse medical consequence to the patient. One can only wonder how much money could be saved annually in this country if every NICU used less PN.

One reason we achieved our goals of increased protein, lipid and calories was that we changed our daily progress note template. This initially was done on paper then converted to an electronic medical record template when our hospital went paperless. It reminded the rounding team to calculate daily enteral, IV and total amounts of these nutrients thereby ensuring an adequacy of caloric intake. So for example, when enteral levels of protein were increasing the IV protein could be reduced but still maintenance of the goal of 3 to 4 g kg^{-1} day^{-1} of total protein could be achieved. Before changing the note, protein levels in the pre-standardized group were significantly lower in PN when it was discontinued, as well as enterally at full feeds when compared with the standardized group. Also, enteral calories and volume were significantly lower when PN was stopped. Having the Feeding Guideline for Infants ⩽1500 g at birth, Nutrition Group Guidelines and aspirate (residual) algorithm present on rounds daily allowed the team to easily access our agreed on practices and refer to them when their memory lapsed. This non-reliance on memory was instrumental to the success of this project.

Assessing compliance is important to any new initiative. By tracking whether or not you are actually doing what you said you would do clearly demonstrates lapses in practice and provides opportunities for improvement. This helps maintain the gains you have seen. Random safety audits are an easy to use tool to assess compliance and have been used in the medical field.[26,27] Since the conclusion of this project we have performed random safety audits of each element of our guidelines several times a year. To date, we have maintained an overall compliance rate of 94% with

Table 2. Outcomes

	Pre-standard approach	*Standard approach*	*P-value*
	N = *69*	N = *154*	
Use of protein fortification (*N*, %)	15, 22%	100, 65%	<0.0001
DOL intralipids begun (mean)	3	2	<0.002
DOL enteral feeds initiated (mean)	4.6	2	<0.0001
DOL for full enteral feeds (mean)	14	11	0.0005
Time PN initiated <24 h of age (%)	71	100	<0.0001
DOL PN discontinued (mean)	13	8	<0.0001
DOL birth weight regained (mean)	13	9	0.0004
Enteral protein (mean g kg^{-1} day^{-1}) when at full feeds	2.1	3	<0.0001
Enteral volume (mean cc kg^{-1} day^{-1}) when PN dc'd	95	110	0.0006
Enteral calories (mean kcal kg^{-1} day^{-1}) when PN dc'd	95	105	0.0002
Enteral protein (mean g kg^{-1} day^{-1}) when PN dc'd	1.7	2.6	<0.0001
IV AA when PN dc'd (mean g kg^{-1} day^{-1})	1.1	2.3	<0.0001
IV AA on admission (mean g kg^{-1} day^{-1})	0.75	2	<0.0001
Intralipids on initiation (mean g kg^{-1} day^{-1})	0.5	1	<0.002
Use of base solution on admission (%)	75	100	<0.0001
HC < 10% (*N* birth, *N* DC, DC %)	15, 18, 100%*	28, 16, 57%	0.011 for DC %
Weight < 10% (*N* birth, *N* DC, DC %)	15, 19, 100%#	24, 16, 67%	0.042 for DC %
Use of breast milk as initial feed (%)	87	97	<0.0001
Use of breast milk only at full feeds (*N*, %)	48, 70	118, 77	NS
Use of any breast milk at DC (*N*, %)	21, 30	71, 46	NS
Any breast feeding at DC (*N*, %)	5, 7	21, 14	NS
Cases of NEC (*N*)	2	1	NS
Cases of sepsis (*N*)	2	0	NS
Cases of line/CONS infections (*N*)	0	0	NS
DOL intralipids discontinued (mean)	10	6.1	NS
DOL PICC line discontinued (mean)	14.9	8	0.002
Cost savings to the patient (charges):			
From less PN use (mean)	NA	$385 000.00	
Potential from less lipid use (mean)	NA	$30 800.00	
Cost savings to the hospital:			
From less PN use (mean)	NA	$34 650.00	
Potential from less lipid use (mean)	NA	$2464.00	

Abbreviations: AA, amino acids; CONS, coagulase-negative *Staphlococcus*; DC, discharge; dc'd, discontinued; DOL, day of life; HC, head circumference; IV, intravenous; NA, not applicable; NEC, necrotizing enterocolitis; NS, not significant; PICC, percutaneously inserted central venous catheter; PN, parenteral nutrition. *Three babies born normocephalic became microcephalic at DC. #Four babies born AGA were SGA at DC. AGA, appropriate for gestational age; SGA, small for gestational age.

our processes. This is reported back to the neonatologists at our weekly division meeting.

In addition to random safety audits, we compare our growth outcomes to other similar NICUs by using the Child Health Corporation of Americas data base for babies 22 to 29 weeks gestation. For example, since 2010 our NICU's average rate of weight accretion is better than other centers by 0.8 g kg^{-1} day^{-1}. Although our mean head circumference at birth is similar to other centers (24.1 vs 24.4 cm), at discharge we have a greater mean head circumference (33 vs 31.5 cm), less microcephalic babies <10th percentile (12.5% vs 27.6%), less microcephalic babies <3rd percentile (2.5% vs 13.1%) and our average head growth is 0.1 cm per week greater for all infants including SGA babies. These data have remained consistent through the end of 2012.

Naturally, the results from a single center study may not be applicable to all centers. Every NICU should develop their own local consensus on what practices they feel they can support given their individual context. When clear scientific evidence is lacking, however, we feel just following the status quo will not cause improvement so the best evidence available should be used in an attempt to improve outcomes. This is the foundation of our NICUs culture and led us to change our nutrition practices. Hopefully, this study will be used by other centers as a reasonable approach to build on.

Reducing variation in nutrition practices can significantly improve outcomes for VLBW infants without adverse effects. By implementing these changes and tracking compliance with the protocols, these benefits may be sustained and lead to impressive cost reductions.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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ORIGINAL ARTICLE

Randomized controlled trial of prophylactic rectal stimulation and enemas on stooling patterns in extremely low birth weight infants

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OBJECTIVE: We hypothesized that rectal stimulation and small volume enemas would accelerate normalization of stooling patterns in extremely low birth weight infants.

STUDY DESIGN: In a randomized controlled trial, infants with a gestational age ⩽28 weeks received one of the following: twice daily rectal stimulation and/or enemas until two stools were passed daily, without enemas or stimulation, for three consecutive days. Intervention only occurred when symptoms, abdominal distension and no defecation, occurred in the previous 24 h. Enema administration occurred if abdominal distension persisted without defecation occurring after rectal stimulation. Multivariable linear regression was used to determine the contribution of a patent ductus arteriosus (PDA) on normalization of stooling patterns and feeding tolerance.

RESULT: Rectal stimulation and/or small volume enemas did not accelerate the median (quartile range) time normalization of stooling patterns, 13 (11–20) days in control group and 16 (12–25.5) days in intervention group. A higher frequency of PDA occurred in the intervention than the non-intervention group. Infants with a persistent PDA had a longer duration of parenteral nutrition, worse feeding tolerance and more days to achieve normal stooling patterns. In multivariable regression analysis, a PDA, not repeated rectal stimulation and/or enemas, was significantly related to stooling and feeding tolerance.

CONCLUSION: Twice daily administration of rectal stimulation and/or enemas did not normalize stooling patterns (fecal frequency). A PDA is an important determinant of acquisition of normal stooling patterns and feeding tolerance of very immature newborns.

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Keywords: ELBW; gastrointestinal tract; enteral feeding; feeding intolerance

INTRODUCTION

Despite advances in neonatal intensive care, extrauterine growth restriction remains high in extremely low gestational age neonates.[1] Establishing enteral feeding is an important goal in the care of very low birth weight infants. Earlier full enteral feeding is associated with less postnatal growth failure.

In preterm infants, immature intestinal motility may lead to feeding intolerance.[2] Rapid meconium evacuation appears to be a key factor associated with feeding tolerance of extremely low birth weight (ELBW) infants during the first 14 days of life.[3] Daily administration of small volume enemas had no effect on total meconium evacuation defined by the time of last meconium passage.[4] Normalization of stooling patterns may be an important determinant of full enteral feeding of very immature infants.[5] To improve the timing of normalization of stooling patterns, ELBW infants may be frequently administered enemas. We hypothesized that rectal stimulation and small volume enemas would: (1) accelerate normalization of stooling patterns and (2) improve feeding tolerance in ELBW infants.

METHODS

Study design

The study design was an open randomized parallel controlled trial conducted within a level 3 neonatal unit in La Paz University Hospital in Madrid, Spain. Premature infants with a gestational age ⩽28 weeks were eligible for inclusion in the study. Exclusion criteria were major congenital malformations and severe asphyxia. The study was approved by the La Paz University Hospital Research Ethics Committee. Written informed consent was obtained from the parents after full explanation of the procedure. Infants were randomly assigned to the intervention or control group. Randomization was carried out by a list of random numbers. Masking was unfeasible. An exploratory approach of 30 infants per group was planned.

Study groups

The intervention group was treated as follows: defecation was stimulated by twice daily enemas (10 ml kg^{-1} saline) until the complete evacuation of meconium, and with rectal stimulation every 12 h twice daily thereafter. If the infant had not passed stools during the 8 h following the stimulation, an enema was administered. Rectal stimulation was applied via a single use catheter,[4] coated with vaseline as a lubricant before insertion into the rectum 1.5–2 cm. The enema was placed in a syringe, heated at 37 °C and applied via a catheter into the rectum in 2–3 ml aliquots. Control group: intervention was only administered when symptoms, abdominal distension and no defecation occurred in the previous 24 h; enema administration was performed if abdominal distension persisted and no defecation occurred after rectal stimulation. Standard departmental guidelines were followed with regard to ventilation, invasive monitoring and use of inotropes for both the intervention and the control groups.

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