Early Human Development 90 (2014) 227–230

Contents lists available at ScienceDirect

Early Human Development

journal homepage: www.elsevier.com/locate/earlhumdev

Early enteral feeding in very low birth weight infants

Emily Hamilton *, Cynthia Massey, Julie Ross, Sarah Taylor

Division of Neonatology, Department of Pediatrics, Medical University of South Carolina, Charleston, SC, United States

ARTICLE INFO

Article history:
Received 8 June 2013
Received in revised form 7 February 2014
Accepted 11 February 2014

Keywords:
Early enteral feeding
Very low birth weight infants
Necrotizing enterocolitis
Parenteral nutrition
Prematurity

ABSTRACT

Background/aim: Debate exists about when to initiate enteral feeding (EF) in very low birth weight (VLBW) preterm infants. This retrospective study compared the effectiveness of an education-based quality improvement project and the relationship of time of the first EF to necrotizing enterocolitis (NEC) or death incidence and parenteral nutrition (PN) days in VLBW infants.
Study design/subjects: VLBW infants born in 2 epochs were compared for hour of the first feed, PN days, NEC or death incidence, and feeding type. The 2 epochs were temporally divided by a quality improvement initiative to standardize initiation of EF in postnatal hours 6–24.
Results: 603 VLBW infants were included. Median time of feed initiation decreased from 33 (Epoch 1) to 14 h (Epoch 2) ($p < 0.0001$). Median PN days were 14 vs. 12, respectively ($p = 0.07$). The incidence of NEC or death was 13.4% vs. 9.5%, respectively ($p = 0.14$). When controlling for birth weight, gestational age, race, gender, and time period, earlier feed initiation was associated with decreased NEC or death ($p = 0.003$). Evaluation of the relationship of early EF (defined as within the first 24 h) in Epoch 2 alone showed that early EF was significantly associated with decreased NEC or death (6.3 vs 15.1%) (RR, 95% CI = 0.28, 0.13–0.58) and less PN days ($p < 0.0001$).
Conclusions: In a VLBW infant cohort, an education-based process improvement initiative decreased time of EF initiation to a median of 14 h with no associated increase in NEC or death. In fact, results suggest that earlier feeding is associated with decreased NEC or death.

1. Introduction

Debate continues regarding early postnatal readiness for enteral feeding in very low birth weight (VLBW) (<1500 g) infants [1]. Much has been published about the potential benefits of early feeds. Early enteral nutrition is known to decrease gut atrophy and intestinal permeability [2] and has been associated with improved postnatal growth and decreased incidence of sepsis [3]. However, concern for an association with necrotizing enterocolitis (NEC) has propagated delaying enteral nutrition in this population [4]. Recent data suggest that implementation of a feeding protocol not only is safe but also may decrease the incidence of NEC [5,6].

At our institution, despite a feeding order to initiate minimal enteral nutrition at 6–24 postnatal hours, this clinical plan was not widely accepted by the nursing staff and required an education-based quality improvement initiative to improve the process. This education consisted of a presentation on the purpose of the feeding plan and the evidence supporting early enteral feeding. We hypothesized that there would be a significant decrease in time to the first enteral feed following the educational initiative and that this would result in fewer total parenteral nutrition days, as infants would reach full feeds faster. With the long-standing concern that early feeding increases the risk for NEC, we also followed this outcome as a safety measure.

2. Patients and methods

After IRB approval, this retrospective study was performed at a single university-based tertiary care neonatal intensive care unit (Medical University of South Carolina). In 2005, neonatal service admission orders were revised to have the default feeding plan include initiation of feeds between 6 and 24 postnatal hours. In July 2008, general clinician subjective experience concluded that this feed initiation order was not consistently followed by nursing staff. At that time, a process improvement plan was initiated to educate staff in regard to this order and the scientific evidence supporting the importance and safety of early enteral nutrition. Additionally, staff received education and instructions to initiate maternal breast pumping within 6 h of infant delivery and to request maternal assent for donor human milk at infant delivery. This education occurred over a 6-month period.

The university hospital perinatal information database was queried to identify and collect demographics for VLBW infants admitted January 1, 2007–June 30, 2008 (Epoch 1) and January 1, 2009–June 30, 2010

* Corresponding author at: Division of Neonatology, MUSC Children's Hospital, 165 Ashley Avenue, MSC 917, Charleston, SC 29425, United States. Tel.: +1 843 792 2112; fax: +1 843 792 8801.
E-mail address: Emily8680@gmail.com (E. Hamilton).

http://dx.doi.org/10.1016/j.earlhumdev.2014.02.005
0378-3782/

(Epoch 2). Infants were excluded if they had congenital gastrointestinal or cardiac anomalies, were transferred in after 24 postnatal hours, or died in the first 24 postnatal hours prior to initiation of feeding protocol. Infant demographics including the incidence of small-for-gestational-age (SGA) status defined by Fenton growth chart [7], the hour of the first feed, age at initiation and total days of parenteral nutrition, NEC or death incidence, and type of feed given during the first 24 postnatal hours were obtained. Additionally, central line days, central line associated blood stream infections, feeding intolerance (defined as documentation of diagnosis by clinical provider), bronchopulmonary dysplasia (defined as requiring oxygen at 36 weeks gestation), retinopathy of prematurity (Stages 3–4), weight gain velocity from birth to hospital discharge, and length of stay was compared between the two groups. In further evaluation of growth, the infants in each epoch who were discharged at 35–37 weeks post-menstrual age (PMA) and had weight, length, and head circumference measurements at hospital discharge had comparison of these growth parameters.

During both time periods, infants were fed by the same feed advancement protocol. This protocol standardizes both duration of trophic feeds and feed volume advancement until 160 ml/kg/day volume is reached. The protocol includes a statement to not initiate feeds for infants with a surgical abdomen, hypotension requiring inotropic or vasopressor support, or $FiO_2 \geq 0.6$. Upon initiation of feeds, infants were preferentially fed mother's milk unless contraindicated. When mother's milk was not available, donor human milk was substituted for infants born <30 weeks gestation, and 24 kcal/oz preterm infant formula was substituted for more mature infants. Once feeds were initiated, feed advancement was performed by standardized orders stratified by birth weight, and details are as follows: (1) trophic feeds (12 ml/kg/day) for 1–5 days; (2) feed volume advancement by 15–30 ml/kg/day; (3) human milk fortification to 24 kcal/oz at 100 ml/kg/day; (4) goal feed volume of 160 ml/kg/day; and (5) human milk fortification with whey protein to 26 kcal/oz at 160 ml/kg/day. Additionally, parenteral nutrition was initiated on postnatal day 1 and discontinued when the infant was receiving at least 120 ml/kg/day enteral feeds.

3. Statistical analyses

The patient sample was defined by date of birth based on the time of the quality improvement initiative. Therefore, no power analysis was performed. The first outcome measurement was to determine whether the process improvement plan was associated with feed initiation per protocol (6–24 postnatal hours) and whether feed initiation was significantly earlier in Epoch 2 than in Epoch 1. Following these assessments, if a significant clinical difference was observed, then evaluation of factors associated with this change was to be investigated. The studied factors were days of parenteral nutrition, incidence of NEC or death, and type of enteral nutrition received in the first 24 postnatal hours, central line days, central line associated blood stream infections, feeding intolerance, hospital weight growth velocity, retinopathy of prematurity, bronchopulmonary dysplasia, and length of hospital stay. Outcomes for days of parenteral nutrition, incidence of NEC or death, and type of enteral nutrition in the first 24 postnatal hours were also compared by postnatal hour of the first feed. To further evaluate growth between the two epochs, for infants with hospital discharge at 35–37 weeks PMA, hospital discharge weight, length, and head circumference were compared. Results were tested for normality followed by the appropriate test (Student's *t*-test or Wilcoxon Rank Sum) for comparison. Chi-square, Fisher's exact, linear regression, and logistic regression were also performed. Significance was defined a priori as $p < 0.05$.

In the secondary analysis, the outcome factors were evaluated in relationship to early feeding, defined as feeding before 24 postnatal hours, and postnatal hour of the first feed in Epoch 2 only. This epoch was chosen due to standardization of feed initiation practice. In Epoch 1, the practitioner choice to delay feeds may have biased the association of feed initiation and outcome.

4. Results

A total of 603 VLBW infants (Epoch 1 = 277, Epoch 2 = 326) met the inclusion criteria. Their characteristics are shown in Table 1. The groups were comparable for race, gender, and incidence of SGA status but statistically different for median gestational age and birth weight, with infants in Epoch 1 having lower gestational age at birth and smaller size than infants in Epoch 2.

As shown in Fig. 1, compared to Epoch 1, a significantly larger proportion of infants in Epoch 2 was receiving enteral nutrition by postnatal hour 24 (75.5 vs. 36.5%, $p < 0.0001$). The hour of enteral feed initiation significantly decreased from Epoch 1 to Epoch 2 (median of 33 vs. 14 h, $p < 0.0001$) (Table 2).

As shown in Table 2, no significant difference in median total parenteral nutrition days was observed ($p = 0.07$), but the decrease in median days may be considered clinically important. Also of note, due to a concomitant improvement initiative, compared to Epoch 1, significantly more infants in Epoch 2 had initiation of parenteral nutrition on the first day (85.9% versus 96% respectively, $p < 0.001$). Additionally, the percent of infants diagnosed by a clinician as having feeding intolerance was significantly higher in Epoch 1, and hospital growth velocity was significantly higher in Epoch 2 without a significant difference in length of hospital stay.

In evaluation of NEC and NEC or death, no significant difference existed between epochs. However, death alone was significantly higher in Epoch 1, and the associated morbidity of central line associated blood stream infections was also significantly higher in Epoch 1. Since the lower gestational age and birth weight observed in Epoch 1 are risk factors for NEC and death, a logistic regression was performed to account for these factors. When controlling for birth weight, gestational age, race, gender, and time period, the postnatal hour of feed initiation was associated with NEC or death ($p = 0.003$). Meaning the earlier feeding was initiated, the less likely NEC or death were to occur.

In further appraisal of growth between epochs, infants with hospital discharge at 35–37 weeks PMA had comparison of growth parameters (Table 3). For these infants, weight at discharge was significantly higher in Epoch 2, but no difference was found for length or head circumference at discharge. The higher weight at discharge was congruent with the significantly higher growth velocity also observed during Epoch 2.

Table 1
Patient characteristics.

	Epoch 1 (n = 277)	Epoch 2 (n = 326)	p-Value
Birth weight median (grams) (range)	1030 (385–1496)	1135 (385–1495)	0.002
Gestational age (PMA) median (weeks) (range)	28 (22–35)	29 (23–35)	0.04
Male (%)	44.4	46.6	NS
Black (%)	57.8	52.5	NS
White (%)	32.9	39.6	NS
Hispanic (%)	8.3	6.8	NS
Asian (%)	1.1	1.2	NS
SGA (%)	16.3	12.3	NS