Enteral Nutrition Practices in Critically Ill Children Requiring Noninvasive Positive Pressure Ventilation*

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Objectives: Evaluate the practice of providing enteral nutrition in critically ill children requiring noninvasive positive pressure ventilation.

Design: Retrospective cohort study.

Setting: PICU within a quaternary care children's hospital.

Patients: PICU patients older than 30 days requiring noninvasive positive pressure ventilation for greater than or equal to 24 hours from August 2014 to June 2015. Invasive mechanical ventilation prior to noninvasive positive pressure ventilation and inability to receive enteral nutrition at baseline were additional exclusionary criteria.

Interventions: None.

Measurements and Main Results: The primary outcome was enteral nutrition initiation within 24 hours of admission. Secondary outcomes included time to goal enteral nutrition rate, adequacy of nutrition, adverse events (pneumonia not present at admission, intubation after enteral nutrition initiation, feeding tube misplacement), and lengths of noninvasive positive pressure ventilation and PICU stay. Among those included ($n = 562$), the median age was 2 years (interquartile range, 39 d to 6.8 yr), 54% had at least one chronic condition, and 43% had malnutrition at baseline. The most common primary diagnosis was bronchiolitis/viral pneumonia. The median length of time on noninvasive positive pressure ventilation was 2 days (interquartile range, 2.0–4.0). Most (83%) required continuous positive airway pressure or bi-level support during their PICU course. Sixty-four percent started enteral nutrition within 24 hours, with 72% achieving goal enteral nutrition rate within 72 hours. Forty-nine percent and 44% received an adequate cumulative calorie and protein intake, respectively, during their PICU admission. Oral feeding was the most common delivery method. On multivariable analysis, use of bi-level noninvasive positive pressure ventilation (odds ratio, 0.40; 95% CI, 0.25–0.63) and continuous dexmedetomidine (odds ratio, 0.59; 95% CI, 0.35–0.97) were independently associated with decreased likelihood of early enteral nutrition. Twelve percent of patients had at least one adverse event.

Conclusions: A majority of patients requiring noninvasive positive pressure ventilation received enteral nutrition within 24 hours. However, less than half achieved caloric and protein goals during their PICU admission. Further investigation is warranted to determine the safety and effectiveness of early enteral nutrition in this population. (*Pediatr Crit Care Med* 2017; 18:1093–1098)

Key Words: critical care; enteral nutrition; noninvasive ventilation; pediatrics; positive pressure ventilation

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Providing adequate nutritional support is a cornerstone of high-quality pediatric critical care with well-documented benefits (1). Early initiation of enteral nutrition (EN) has been associated with decreased mortality and lengths of stay among critically ill infants and children (2, 3). However, delays in EN initiation and frequent interruptions are commonly seen in this population, resulting in inadequate

nutrition with uncertain impact on clinical outcomes (4, 5). The use of noninvasive positive pressure ventilation (NIPPV), a technique of providing respiratory support without use of an endotracheal tube, has dramatically increased in the PICU over the last 10–15 years (6). Although NIPPV use has been associated with a decreased need for intubation, it has also been independently associated with delayed provision of EN in critically ill children (7).

When using NIPPV, positive pressure is delivered at the mouth and nares, allowing air to enter both the respiratory and gastrointestinal tract contributing to the potential complications of feeding intolerance, aspiration, and pneumonia (8). Concern for these complications may lead to reluctance to initiate EN in children who require NIPPV despite the potential benefits of early EN. Currently, there is a paucity of data on the practice of providing EN to patients on NIPPV, including feasibility, safety, and impact on patient outcomes. The goal of this study was to describe our institutional practice of providing EN to critically ill patients on NIPPV and to determine the factors associated with the initiation of early EN (2, 9).

METHODS

The study protocol was approved by the Colorado Multiple Institutional Review Board at the University of Colorado, with waiver of consent granted.

Data Sources

Data for this study were obtained from two sources: the Virtual PICU Systems (VPS) LLC database and the Children's Hospital Colorado (CHCO) electronic health records (EHRs). VPS (www.myvps.org) is a multi-institutional registry of PICUs, developed to support benchmarking and quality improvement efforts within pediatric critical care. Trained local data collectors abstract certain data elements, which are then submitted to the VPS database. Regular quality checks are performed to ensure data integrity and quality. Local VPS data were initially queried to identify the cohort of interest. Additional clinical and nutrition data for the identified cohort were subsequently abstracted from the EHR. Such data included demographics, baseline nutritional status, acute and chronic diagnoses, level of NIPPV support, provision and mode of EN, and clinical and nutritional outcomes. Oral intake was estimated and calculated using hospital food and beverage nutrient analyses, and tube feeding intake was obtained from an internal EHR-based nutrition flowsheet designed for quality improvement. Achievement of cumulative calorie (kcal) and protein intake goals were assessed according to American Society for Parenteral and Enteral Nutrition guidelines (1).

Abstracted data were collected and managed using the Research Electronic Data Capture (REDCap) electronic data tools hosted at University of Colorado (10). REDCap is a secure, web-based application designed to support data capture for research studies, providing 1) an intuitive interface for validated data entry, 2) audit trails for tracking data manipulation and export procedures, 3) automated export procedures for seamless data downloads to common statistical packages, and 4) procedures for importing data from external sources.

Study Design and Cohort Development

This study was a retrospective cohort study of children admitted to the CHCO PICU between August 2014 and June 2015. CHCO is a quaternary, free-standing children's hospital with a maximum 40-bed capacity PICU, which is a mixed medical-surgical unit, excluding cardiac surgery patients. Generally, only children more than 1 month old are admitted to the PICU. Dietitian support is available 7 days a week, with a PICU-dedicated dietitian participating in multidisciplinary rounds 5 days a week. Our PICU guideline for patients unable to start oral nutrition recommends initiation of gastric or transpyloric nutrition within 24–48 hours, although the decision to start EN is left up to clinician discretion. Our institution uses anesthesia guidelines to determine appropriate nothing by mouth time for planned intubations including 8 hours for solid foods, 6 hours for formula or fortified human milk, 4 hours for breast milk, and 2 hours for clear liquids.

All patients older than 30 days and requiring NIPPV during their PICU admission were first identified through the local VPS database. Consistent with prior studies, NIPPV was defined as heated high-flow nasal cannula (HHFNC), continuous positive airway pressure (CPAP), bi-level positive airway pressure (BiPAP), or average volume assured pressure support (AVAPS) (6–8, 11). Children who required NIPPV for less than 24 hours, required intubation and invasive mechanical ventilation prior to initiation of NIPPV, or had parenteral nutrition dependence and could not receive EN at baseline were excluded. For patients meeting inclusion criteria on multiple PICU admissions during the study period, only the first chronologic admission was included in the final analyses to ensure independent observations.

The primary outcome of interest was early EN, defined as initiation within 24 hours of admission. The definition of early EN varies from 24 to 48 hours, though there is no consensus on which is more appropriate (2, 9). Secondary nutritional outcomes included time to goal EN rate, the adequacy of EN (based on cumulative goal caloric and protein intake achieved), and frequency of EN interruptions greater than 6 hours. We selected the greater than 6-hour interruption time point based on our institutional NPO guidelines described above. Additionally, EN interruption of 6 hours is 25% of the day, and 75% of kcal and protein goals can theoretically still be achieved. Longer interruptions increased the likelihood of failure to achieve an adequate intake (> 67% kcal and protein goals) for the day. Goal EN rate was defined as 100% of estimated kcal and protein requirements met via the hourly rate or bolus volume of tube feedings or through oral intake at a meal. Adequate EN was defined as achieving greater than 67% of kcal and protein goals as an averaged, cumulative intake over the course of the PICU stay (12, 13). Malnutrition was defined as body mass index (BMI), *z* score of less than –1 or greater than 1. For children less than 2 years old, weight-for-length *z* score was used instead of BMI (14). Other outcomes

of interest included need for multiple x-rays to confirm feeding tube placement, length of NIPPV use during PICU admission, weight change during PICU stay, and PICU length of stay. Adverse events (development of pneumonia not present at admission, intubation after EN initiation, feeding tube misplacement) were identified in the EHR. The diagnosis of pneumonia was based on clinical diagnosis by the medical team, as documented within the EHR.

Statistical Analyses

Descriptive statistics were used to characterize the cohort, the level of NIPPV support, and outcomes of interest. Logistic regression was used to measure the unadjusted association between candidate factors and early initiation of EN (primary outcome). Factors meeting statistical significance were then included in a multiple logistic regression model to estimate the independent association with early EN. Statistical significance was considered at an alpha of less than 0.05.

Because children requiring only HHFNC may represent a different population than those requiring higher levels of support, we also performed subgroup analyses comparing nutritional outcomes by level of NIPPV support required using chi-square analyses. The two mutually exclusive groups are as follows 1) initial and maximum levels of support were HHFNC (HHFNC only), and 2) initial support was HHFNC, CPAP, or BiPAP/AVAPS, but the maximum level of support required was CPAP or BiPAP/AVAPS. Finally, as a sensitivity analysis, regression analyses were performed excluding those children only requiring HHFNC during their PICU admission.

All analyses were performed using Stata SE, version 14.0 (StataCorp LP, College Station, TX).

RESULTS

Over the study period, 562 patients met inclusion criteria for this study. A majority of patients were less than 5 years old, had at least one chronic condition, and had a primary diagnosis of bronchiolitis or viral pneumonia (**Table 1**). Forty-three percent of the cohort had malnutrition at admission. Most patients were initiated on either CPAP (26%) or bi-level support (33%), with a median length of time on NIPPV of 2 days (interquartile range [IQR], 2.0–4.0). Among those initiated on HHFNC or CPAP ($n = 379$), over half (57%) required escalation of support during their PICU admission. Eighteen percent of the cohort ($n = 99$) only required HHFNC support.

EN was initiated in less than 24 hours in 64% of patients, with 54% provided nutrition orally and the remainder using a newly placed or preexisting feeding tube. Among those using a feeding tube, most were transpyloric in location. At the time of EN initiation, 42% of patients were on HHFNC, 13% on CPAP, and 32% on bi-level support. Thirteen percent of patients had been weaned off of NIPPV prior to EN initiation. Among children requiring bi-level support at the time of EN initiation, the median peak inspiratory pressure was 16 cm H_2O (IQR, 14–18 cm H_2O). For those on either CPAP or bi-level support at EN initiation, the median positive end-expiratory pressure was 7 cm H_2O (IQR, 6–8 cm H_2O). A majority of patients (72%) achieved goal EN rate within 72 hours. However, only 49% and 44% of the cohort received adequate caloric and protein goals during their PICU stay, respectively (**Table 2**). Early initiation of EN was associated with a greater likelihood of reaching goal EN rate within 72 hours (odds ratio [OR], 1.86; 95% CI, 1.28–2.71) and receiving greater than 67% of cumulative kcal (OR, 2.11; 95% CI, 1.48–3.00) and protein goals (OR, 2.12; 95% CI, 1.48–3.05) during the PICU stay. A majority of patients (87%) did not have a second weight documented prior to PICU discharge.

Univariate analyses demonstrated a decreased likelihood of early EN initiation associated with age greater than 5 years, higher initial NIPPV support (CPAP and bi-level support), malnutrition at admission, presence of at least one chronic condition, and the use of continuous sedation with dexmedetomidine. However, with multivariable analyses, only bi-level support (OR, 0.40; 95% CI, 0.25–0.63) and the use of dexmedetomidine (OR, 0.59; 95% CI, 0.35–0.97) were independently

TABLE 1. Cohort Characteristics ($n = 562$)

Characteristics	*n* (%) or Median (IQR)
Age category (yr), *n* (%)	
< 1	131 (23)
1–5	260 (46)
5–10	72 (13)
> 10	99 (18)
Sex, *n* (%)	
Male	312 (56)
Primary service, *n* (%)	
Medical	551 (98)
Surgical	11 (2)
Primary diagnosis, *n* (%)	
Bronchiolitis	269 (48)
Viral pneumonia	92 (16)
Status asthmaticus	103 (18)
Bacterial pneumonia	37 (7)
Septic Shock	9 (2)
Other	52 (9)
Presence of at least one chronic health condition, *n* (%)	305 (54)
Malnutrition at admission, *n* (%)	243 (43)
Pediatric Risk of Mortality III probability of death (%), median (IQR)	0.51 (0.3–0.6)
Length of time on noninvasive positive pressure ventilation, d, median (IQR)	2.0 (2.0–4.0)
ICU length of stay, days, median (IQR)	2.8 (2.0–4.3)

IQR = interquartile range.

TABLE 2. Nutritional Outcomes

Outcomes	*n* (%) or Median (IQR)
Time from PICU admission to initiation of EN (hr), *n* (%)	
< 24	361 (64)
24–48	168 (30)
49–72	24 (4)
> 72	7 (< 1)
Mode of EN delivery, *n* (%)	
Transpyloric	167 (30)
Nasogastric	41 (7)
Oral	305 (54)
Existing J tube	8 (1)
Existing G tube	41 (7)
Time to goal EN rate, *n* (%) (hr)	
< 24	111 (20)
24–48	202 (36)
49–72	89 (16)
> 72	37 (7)
Did not reach goal EN rate, *n* (%)	123 (22)
%kcal goals achieved during PICU stay, median (IQR)	67 (48–89)
Achieved > 67% kcal goals, *n* (%)	276 (49)
%protein goals achieved during PICU stay, median (IQR)	63 (37–92)
Achieved > 67% protein goals, *n* (%)	250 (44)
Any periods of feeding cessation > 6 hr, *n* (%)	88 (16)

IQR = interquartile range, EN = enteral nutrition.

associated with decreased likelihood of initiating EN within 24 hours (**Table 3**). Sixteen percent of the cohort had at least one feeding interruption of more than 6 hours, with a median of one interruption per patient (range, 1–8). Twelve percent had at least one adverse event of interest. Fifty-four patients subsequently developed pneumonia (occurrence rate 2.2/1,000 NIPPV d in PICU). Sixteen patients were intubated after the initiation of EN, four for elective procedures and 12 for progressive respiratory failure. All patients who received a feeding tube required radiologic confirmation, per institutional policy. Ninety-four patients (17%) required multiple x-rays to confirm feeding tube placement, with a median of two x-rays per patient (range, 2–7). In three patients, the feeding tube was misplaced into the lungs.

In the subgroup analyses, patients who remained on HHFNC throughout their stay were younger, less likely to have a chronic condition, and slightly less likely to have malnutrition at baseline (**Supplemental Table 1**, Supplemental Digital Content 1, http://links.lww.com/PCC/A514). They were more likely to start EN within 24 hours of admission compared with those who required higher levels of respiratory NIPPV support (84% vs 60%; $p < 0.001$). However, they were less likely to achieve greater than 67% kcal (41% vs 51%; $p = 0.09$) and protein (35% vs 46%, $p = 0.04$) goals during their PICU stay. When the subgroup requiring only HHFNC was excluded from analysis, initial bi-level NIPPV support and need for continuous dexmedetomidine remained independently associated with decreased likelihood of early EN initiation.

DISCUSSION

In this retrospective cohort study, a majority of patients on NIPPV started EN within 24 hours of admission to the PICU and nearly all initiated EN within 48 hours. Although fewer than half met recommended kcal and protein goals during their PICU stay, earlier EN initiation was associated with a greater likelihood of achieving an adequate intake. Multiple patient factors were associated with decreased likelihood of early EN initiation, but only bi-level NIPPV and use of continuous dexmedetomidine with NIPPV were independently associated with decreased likelihood for initiating feeds within 24 hours on multivariable analyses. Only a minority of patients had feeding interruptions or had one of the identified adverse events during their PICU course. Although there is a body of literature describing the nutritional practices for critically ill children in general, there is more limited research on EN for patients requiring NIPPV, and these studies have been restricted to preterm infants and adults (15–17). To the best of our knowledge, this is the first study to focus on the specific population requiring NIPPV.

Use of NIPPV, as compared to no respiratory support, has been associated with delayed EN (after 48 hr) in critically ill children (7). Yet, within our institution, almost two thirds initiated EN within 24 hours and almost all (94%) within 48 hours despite the potential complications associated with NIPPV. This finding likely reflects both the widespread belief among providers that early EN is important and the active presence of PICU dietitians advocating for early feeding. However, decreased likelihood of EN initiation within 24 hours of admission was independently associated with initial bi-level support and the use of continuous dexmedetomidine for tolerance of NIPPV. The need for bi-level support indicates a more severe respiratory illness, with greater risk of intubation. The time delay in initiating EN allows the practitioner to determine the likely clinical course of the patient and minimize the complications associated with intubation with a full stomach (e.g., aspiration). Additionally, the delivery of higher pressures can also lead to abdominal distention and risk of feeding intolerance. The use of continuous dexmedetomidine to assist with tolerance of NIPPV would only occur with CPAP or bi-level support and so may also reflect a greater severity of illness. Additionally, continuous dexmedetomidine can also lead to altered sensorium which may impair the patient's ability to protect their airway during an aspiration event (18).

TABLE 3. Unadjusted and Adjusted Association Between Patient and Noninvasive Positive Pressure Ventilation Characteristics and the Initiation of Enteral Nutrition Within 24 Hours

Characteristics	Unadjusted Risk Estimates, OR (95% CI)	Adjusted Risk Estimates, OR (95% CI)[a]
Age category (yr)		
< 1	Reference	Reference
1–5	0.63 (0.39–1.00)	0.69 (0.43–1.12)
> 5	0.42 (0.23–0.77)	0.63 (0.35–1.12)
Initial mode of noninvasive positive pressure ventilation		
Heated high-flow nasal cannula	Reference	Reference
Continuous positive airway pressure	0.60 (0.38–0.94)	0.68 (0.42–1.11)
Bi-level support (bi-level positive airway pressure, average volume assured pressure support)	0.35 (0.23–0.52)	0.40 (0.25–0.63)
Admission body mass index *z* score		
>−1 to <1	Reference	
< −1	0.78 (0.49–1.25)	
> 1	0.95 (0.73–1.43)	
Malnutrition at admission	0.76 (0.64–0.90)	1.00 (0.69–1.45)
Presence of at least one chronic condition	0.69 (0.48–0.98)	0.93 (0.62–1.39)
Pediatric Risk of Mortality III probability of death	0.86 (0.76–0.98)	0.89 (0.79–1.01)
Type of feeding tube at initiation of enteral nutrition		
Existing G or J tube	Reference	
Transpyloric tube placed	1.32 (0.68–2.57)	
Nasogastric tube placed	0.67 (0.29–1.56)	
Required continuous sedation	0.58 (0.36–0.94)	0.59 (0.35–0.97)

OR = odds ratio.

[a]All variables within column were included in regression model.

These concerns may have led providers to withhold EN early in their clinical course. Although EN has demonstrated benefits in the intubated population, evidence is lacking in patients on NIPPV (3, 12, 13). Therefore, the initial delay in EN may be appropriate for this population given uncertain risk-benefit balance.

Patients who started EN within 24 hours of admission to the PICU had an increased likelihood of meeting goal EN rate and an adequate cumulative kcal and protein intake. However, more than 50% of patients never achieved kcal and protein goals while in the PICU. When we stratified our cohort by level of NIPPV required, we found the HHFNC only group was less likely to achieve caloric and protein goals as compared to those who required higher levels of NIPPV support. These seemingly disparate findings have several potential explanations. First, the predominant modality of feeding for the children only requiring HHFNC was oral. Oral intake may have been of limited nutritional value explaining the failure to meet kcal and protein goals. Those receiving nutrition via feeding tube have consistent delivery, and quantification, of EN and thus are more likely to achieve their targeted nutritional goals. Indeed, those initiated on EN via feeding tube were more likely to achieve their nutritional goals, irrespective of initial NIPPV mode, or level of support at the time of EN. Additionally, the children requiring only HHFNC may have received minimal EN prior to transfer from the PICU to the general pediatric wards, and our study was not designed to assess nutrition outcomes after PICU discharge. These findings are in line with recent publications that evaluated feeding of patients less than 2 years old with bronchiolitis on HHFNC and found that oral feeding was the most common mode of nutrition delivery and that 42% achieved nutrition goals prior to PICU discharge (19, 20).

The overall rate of adverse events was 12% in this cohort which is considerably lower than an adult study that found complications in 53% of patients receiving EN on NIPPV (15). Ten percent of patients developed pneumonia that was not present at admission. It is difficult to discern whether pneumonia was a complication of feeding or the natural progression of disease. Only 16 patients, 3%, required intubation after the initiation of EN while on NIPPV, with three quarters due

to progressive respiratory failure. Of those with nonelective intubations, a majority did not initiate feeds within 24 hours. Importantly, 17% of patients required multiple abdominal x-rays to confirm feeding tube position, likely related to the high rate of transpyloric tube utilization and a policy that requires x-ray confirmation of feeding tube placement at our institution. Although not defined as an adverse event associated with EN in our study, repeated x-rays expose patients on NIPPV to unnecessary radiation and cost. Furthermore, repeated attempts may be psychologically stressful for both patient and families. This finding raises the question of the risk-benefit balance associated with transpyloric feeding in these patients.

Our study has several limitations to consider when interpreting these results. Although our institution keeps detailed records of enteral and parenteral kcal and protein intake for quality improvement, the ability to accurately assess oral intakes retrospectively is limited, and therefore, it could have over- or under-estimated these nutritional measures in these patients. Furthermore, we lacked information about the clinical decision-making regarding use of NIPPV and EN, making any definitive conclusion about willingness to initiate feeding based on individual patient clinical status difficult. Furthermore, given our team-based approach to decision-making, we were unable to link, retrospectively, the decision to initiate enteral feeds to a single provider. Therefore, we could not examine the association between provider-specific factors and the decision to initiate EN. Additionally, assessing for the potential complications of EN such as clinical aspiration, the development of pneumonia and factors leading to intubation was limited, which diminishes our ability to understand the overall safety of this practice. Finally, although this was a relatively large cohort, it represents a single institution's experience and generalizability to others is unknown.

CONCLUSION

EN is considered a desirable intervention in the critically ill population. Our institutional experience suggests that EN can be provided to children on NIPPV, and in certain subsets, goal EN can be achieved while in the PICU. However, these results generate additional areas for future study about the safety and effectiveness of this practice. For instance, the limited duration of NIPPV and PICU lengths of stay raises the question about need for aggressive early feeding practices, as desired in children requiring invasive mechanical ventilation. We demonstrated limited ability to achieve nutritional goals with oral feeding, but this may be acceptable in the less ill population. Furthermore, although use of a feeding tube was associated with improved delivery of nutrition, limited data exist to determine whether gastric or transpyloric EN is preferable for patients on NIPPV. Given the widespread and growing use of NIPPV within pediatric critical care, additional research on the need for early EN, the optimal mode of delivery, and the impact on clinical outcomes, including adverse, remains essential.

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