

Oral Nutrition in Children With Bronchiolitis on High-Flow Nasal Cannula Is Well Tolerated

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ABSTRACT

OBJECTIVES: To determine the incidence of aspiration-related respiratory failure and nutrition interruptions in children with bronchiolitis on high-flow nasal cannula (HFNC) receiving enteral nutrition.

METHODS: We performed a single-center, prospective, observational cohort study within a 313-bed tertiary medical center from January through December 2015. We included term children 1 month to 2 years of age without comorbid bacterial pneumonia or chronic medical conditions who were diagnosed with bronchiolitis while receiving HFNC and enteral nutrition. Primary outcomes were incidence of aspiration-related respiratory failure and nutrition interruptions. Secondary outcomes were duration of HFNC therapy, length of stay, and nutrition characteristics.

RESULTS: Of the 344 children admitted with bronchiolitis, 132 met the inclusion criteria. Ninety-seven percent received enteral nutrition by mouth and 3% by nasogastric tube. HFNC flow rates at the time of nutrition initiation ranged between 4 and 13 L per minute (0.3–1.9 L/kg per minute) and respiratory rates from 18 to 69 breaths per minute. One (0.8%) subject had aspiration-related respiratory failure and 12 (9.1%) experienced nutrition interruptions. Children with interruptions in nutrition had a longer length of stay by 2.5 days ($P < .01$) and received an additional day of HFNC therapy ($P < .01$). By discharge, 55 (42%) children achieved all nutritional goals: caloric, volume, and protein. Children admitted overnight had an increased incidence of delay to nutrition initiation (30% vs 11%; $P < .01$).

CONCLUSIONS: We observed a low incidence of aspiration-related respiratory failure in term children with bronchiolitis on HFNC receiving enteral nutrition. Oral nutrition was tolerated across a range of HFNC flow and respiratory rates, suggesting the practice of withholding nutrition in this population is unsupported.

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Acute viral bronchiolitis is the most common lower respiratory tract infection in infants and children. In the United States, it accounts for ~172 000 admissions, nearly 100 deaths, and health care costs in excess of \$1.7 billion annually.^{1–6} Acute care management is largely supportive, including the use of noninvasive ventilation.

Heated, humidified high-flow nasal cannula (HFNC) is an efficacious mode of noninvasive ventilatory support for bronchiolitis, resulting in decreased work of breathing, oxygen requirements, and incidence of intubation.^{7–11} These benefits are attributed to a combination of washout of nasopharyngeal dead space, attenuation of inspiratory resistance, improvement in lung conductance and compliance, generation of mild distending pressure, and a reduction in energy expenditure for gas conditioning.¹² Although the incidence of noninvasive ventilation in bronchiolitis is increasing, the practices with regard to enteral nutrition, including initiation timing, route, and type of nutrition, are widely variable. Although there is an association between adequacy of nutrition with mortality and length of stay in critical illness,^{13–15} the use of noninvasive ventilation such as HFNC has been strongly associated with delayed enteral nutrition.¹⁶ There exists an anecdotal reluctance among pediatric providers to initiate enteral nutrition during HFNC therapy due to the perceived risk of aspiration and subsequent respiratory failure.¹⁷

There are no epidemiologic data on aspiration-related respiratory failure to guide clinicians in their enteral nutrition practice during HFNC therapy in children with bronchiolitis. The primary aim of this study was to measure the incidence of aspiration-related respiratory failure and nutrition interruptions in otherwise healthy children admitted with bronchiolitis on HFNC. The secondary aim was to evaluate the impact of these events on outcomes such as achievement of goal nutritional intake, length of stay, and duration of HFNC therapy.

METHODS

Study Design and Setting

We performed a single-center, prospective, observational cohort study. Enrollment

occurred from January through December of 2015 and included children admitted to the PICU at a 313-bed, university-affiliated, tertiary pediatric medical center. In our institution there is no intermediate care unit, and all patients with respiratory failure requiring HFNC are cared for in the PICU. This 44-bed PICU admits ~3300 patients per year. This study was reviewed and approved by our institutional review board, which permitted a waiver of consent. All participants and families were provided verbal and/or written documentation regarding research activities, with an opportunity for study exclusion upon request.

Inclusion Criteria

Inclusion criteria were age 1 month to 2 years, with a clinical diagnosis of acute viral bronchiolitis, receiving HFNC therapy on admission to the PICU, and with concurrent administration of enteral nutrition. Both Fisher-Paykel (Auckland, New Zealand) and Vapotherm (Exeter, New Hampshire) HFNC systems are used in our institution. The clinical diagnosis of bronchiolitis was made via 2015 American Academy of Pediatrics guidelines.¹⁸ Study subjects were prospectively identified for enrollment by review of daily census data.

Exclusion Criteria

We aimed to evaluate otherwise healthy children with acute viral bronchiolitis; therefore, subjects were excluded for diagnoses of prematurity (gestational age <37 weeks), chronic lung disease, congenital heart disease, neuromuscular disease, metabolic disease, craniofacial or laryngeal anomalies, coexisting bacterial pneumonia, or gastroesophageal reflux disease (GERD). Diagnoses of bacterial pneumonia required a clinical or radiographic diagnosis and a completed or planned completion of an antibiotic course ≥ 7 days. Those receiving proton pump inhibitors or histamine-2 blockers before admission were presumed to have GERD. Patients receiving other noninvasive ventilation modalities, such as bilevel positive airway pressure, nasal continuous positive airway pressure, and Ramanathan cannula, were excluded.

Variable Definitions

The primary outcome was the incidence of aspiration-related respiratory failure. Respiratory failure was identified as aspiration-related when there was clinical or radiographic evidence of aspiration¹⁹ and if invasive ventilation occurred temporally after nutrition initiation, bolus nutrition, or clinician-observed emesis. In addition, children were divided into cohorts on the basis of the presence or absence of interruptions in enteral nutrition, defined as continuous pauses >8 hours in nutrition. We assessed the impact of nutrition interruptions on achievement of goal nutritional intake, length of stay, and duration of HFNC therapy. We noted the etiology of interruption and the time delay to nutrition initiation from admission. Nutrition goals were determined by using patient anthropometric measurements, the Institute of Medicine's Dietary Reference Intakes,²⁰ and the Holliday-Segar equation.²¹ Additional independent variables included the following: HFNC flow rate (L per minute), weight-adjusted HFNC flow rate (L/kg per minute), and patient respiratory rate on admission and nutrition initiation. The decision to initiate enteral nutrition was at the discretion of fellow and attending PICU providers. All clinical data were obtained via electronic health record, except for Pediatric Index of Mortality–III Risk of Mortality percentages, which were queried from the Virtual PICU System database (Virtual PICU Systems, LLC, Los Angeles, CA).

Statistical Analysis

Descriptive data are reported as means \pm SDs or as medians (interquartile range [IQR]). After assessing data variance, we used Student's *t* test or Wilcoxon rank-sum test for continuous variables and Fisher's exact test for categorical variables. Paired statistics were performed, where appropriate. A multiple regression analysis was anticipated to test the association between HFNC flow rates and the development of aspiration-related respiratory failure adjusting for age, weight, day of illness, and route of nutrition delivery. For all tests, the level of significance was set at $P < .05$. All statistical analyses were performed by

using Stata version 13.1 software (StataCorp, College Station, TX).

RESULTS

Between January and December of 2015, 344 children were hospitalized with bronchiolitis, of whom 323 (94%) received enteral nutrition. One hundred ninety-one of the 323 who received enteral nutrition were excluded (see Fig 1), leaving 132 children eligible for enrollment. Table 1 shows general demographic and clinical characteristics of the study sample. The median age was 8 (IQR: 4.5–15) months, median weight was 8.8 (IQR: 7.1–10.8) kg, there was a male predominance of 62.1%, and the median duration of HFNC use was 1.7 (IQR: 1.1–2.4) days. Ninety-eight children had viral testing by polymerase chain reaction, with 51% found positive for respiratory syncytial virus and 34% for rhinovirus. No deaths were observed during the study period.

The primary outcome, development of aspiration-related respiratory failure, occurred in 1 subject (0.8%). This patient was 3 months of age and receiving 5 L per minute of HFNC flow (weight-adjusted: 0.6 L/kg per minute) and had a respiratory rate of 22 breaths per minute immediately before initiation of enteral nutrition via

nasogastric tube. The aspiration event was witnessed by physician providers, occurred within 30 minutes of starting continuous nasogastric nutrition, and showed radiographic evidence of aspiration pneumonitis.¹⁸

Interruptions in enteral nutrition occurred in 12 (9.1%) children at a median of 10.5 (IQR: 4.5–105) hours after the initiation of nutrition. The etiology of interruption in 10 of the 12 children was tachypnea (63 ± 22.3 breaths per minute). One patient experienced nutritional interruption as a result of increased work of breathing, and the last due to aspiration-related respiratory failure described above. Interruptions in nutrition were associated with longer median length of stay by 2.5 days ($P < .01$) and longer use of HFNC therapy by 1 day ($P < .01$), as noted in Table 1. There were no differences in age, weight, sex, Pediatric Index of Mortality–III Risk of Mortality, day of illness on admission, or viral pathogen between those with and without nutrition interruptions. We did not detect a difference in clinical characteristics between those with and without interruptions in terms of respiratory rate, HFNC flow rate, or weight-adjusted HFNC flow rate on admission or at nutrition initiation (Table 2). The median

HFNC flow rate at the time of nutrition interruption was 6 (IQR: 5–8.5) L per minute and was no different than flow rates at the time of nutrition initiation (7 [IQR: 5.5–9] L per minute; $P = .46$).

Nutrition data, including route, time delay to nutrition initiation, and percentage of goal achievement, are shown in Table 3. Four (3%) children received continuous nutrition via nasogastric tube and 128 (97%) by mouth. None were given parenteral or post-pyloric tube nutrition. Twenty-nine (22%) children began enteral nutrition on admission. The remainder had a median delay in nutrition initiation of 10.5 (IQR: 6.9–16.3) hours. Compared with children in whom enteral nutrition was initially withheld, those permitted nutrition at the time of PICU hospitalization had marginally lower mean HFNC flow rates (7.3 ± 2.1 vs 8.5 ± 2.2 L per minute; $P = .01$), equivalent mean respiratory rates (50.8 ± 12.5 vs 51.3 ± 14.5 breaths per minute; $P > .99$), and were of similar age (8 [IQR: 5–13] vs 8 [IQR: 4–15] months; $P = .83$).

By discharge, 55 (42%) children achieved all nutritional goals (caloric, volume, and protein goals). During HFNC therapy, only 34 (26%) achieved all nutritional goals. The difference in median time to goal nutrition was 0.9 days ($P = .03$) between those with

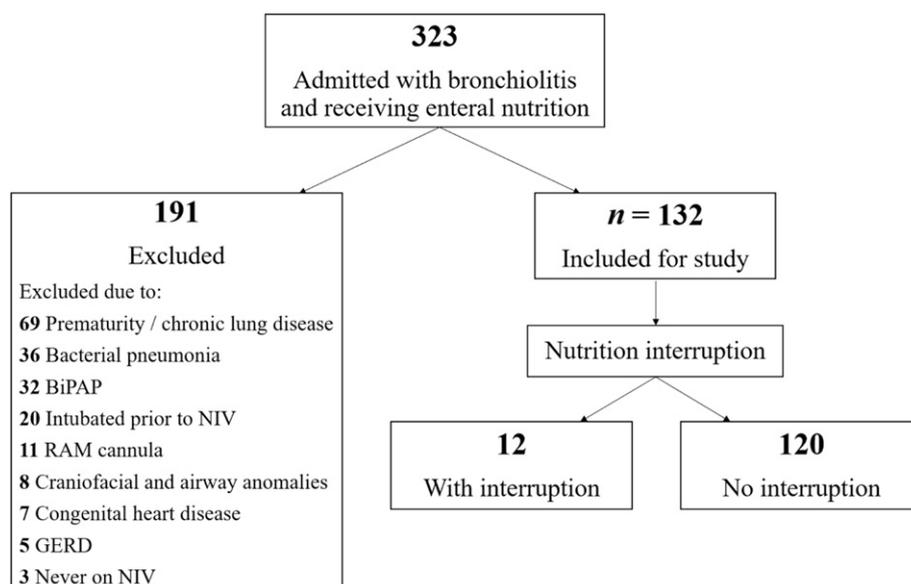


FIGURE 1 Study enrollment and cohorts from January to December 2015. BiPAP, bilevel positive airway pressure; NIV, noninvasive ventilation; RAM, Ramanathan.

TABLE 1 Demographic and Clinical Data for Children With Acute Viral Bronchiolitis on HFNC Receiving Enteral Nutrition With and Without Nutrition Interruptions

Characteristics	All Subjects (N = 132)	No Interruptions (n = 120)	Interruption Cohort (n = 12)	P
Age, mo (median)	8 (4.5–11.5)	8 (4.5–15)	7 (4.5–14.5)	.8
Weight, kg (median)	8.8 (7.1–10.8)	8.7 (7–10.9)	9.1 (7.3–10.3)	.88
Male, n (%)	82 (62)	72 (60)	10 (83)	.13
PIM-III ROM, % (IQR)	0.18 (0.17–0.21)	0.18 (0.17–0.21)	0.19 (0.17–0.22)	.74
Day of illness, d (IQR)	3 (2–4)	3 (2–4)	3 (2–5)	.44
Positive viral testing, n	98	88	10	
Respiratory syncytial virus, n (%)	50 (51)	43 (49)	7 (70)	.32
Rhinovirus, n (%)	33 (34)	30 (34)	3 (30)	>.99
Human metapneumovirus, n (%)	9 (9.2)	8 (9.1)	1 (10)	>.99
Adenovirus, n (%)	6 (6.1)	5 (5.7)	1 (10)	.45
Influenza, n (%)	3 (3.1)	2 (2.3)	1 (10)	.26
Parainfluenza, n (%)	2 (2)	1 (1.1)	1 (10)	.18
Length of PICU stay, d (IQR)	2.4 (1.7–3.2)	2.3 (1.7–3.1)	4.8 (2.7–6.1)	<.01*
Duration of HFNC, d (IQR)	1.7 (1.1–2.4)	1.6 (1.1–2.2)	2.6 (1.9–4.6)	<.01*
Intubation, n (%)	1 (0.8)	0	1 (8.3)	.09
Mortality, n	0	0	0	

PIM-III ROM, Pediatric Index of Mortality–III Risk of Mortality.

* Significant, $P < .05$.

and without interruptions. Just before nutrition initiation, there was a slight reduction in median HFNC flow rate of 8 (IQR: 6–10) to 8 (IQR: 6–8.5) L per minute ($P < .01$) and mean respiratory rate of 51 ± 14 to 40 ± 11 breaths per minute ($P < .01$) compared with rates at admission. Fifty-five (41.7%) children were admitted between

10 PM and 7 AM and had an increased incidence of delay in initiation of enteral nutrition compared with daytime admissions (30% vs 11%; $P < .01$).

DISCUSSION

In this prospective, observational cohort study, 131 of 132 (99.2%) children with acute

viral bronchiolitis tolerated enteral nutrition during noninvasive support with HFNC without incidence of aspiration-related respiratory failure or respiratory embarrassment. The incidence of interruptions in nutrition in our sample was 9.1% and interruptions were nearly all a result of tachypnea (63 ± 22.3 breaths per minute) rather than emesis, aspiration, or perceived feeding intolerance. A majority of children initiated enteral nutrition by mouth, with only 4 receiving nasogastric tube nutrition and none receiving post-pyloric tube or parenteral nutrition during the hospital stay; however, only 42% achieved their nutrition goal by PICU discharge.

To our knowledge, this study is the first to prospectively evaluate the incidence of aspiration-related respiratory failure and interruptions in enteral nutrition in children with acute viral bronchiolitis receiving HFNC. Traditional barriers to providing enteral nutrition in hospitalized children receiving noninvasive ventilatory support include concern for fluid overload, frequent interruptions for procedural safety, and perceived feeding intolerance.^{14,17} In our experience, the hesitancy for permitting enteral nutrition in bronchiolitis originates from perceived ventilation-swallowing dysfunction at higher HFNC flow rates or patient respiratory rates in the setting of infection-related upper airway edema, increased secretions, iatrogenic nasal airway obstruction from the nasal prongs, and potentially increased nasopharyngeal airway pressures. Anecdotally, HFNC flow rates and patient respiratory rates are commonly used as a metric for bedside determination of nutritional safety by pediatric providers. Yet, no published data exist to support these practices. Interestingly, 65% of children in our sample were receiving equal or higher HFNC flow rates and 25.8% had equal or greater respiratory rates at the time of enteral nutrition initiation compared with values on admission and HFNC initiation. This finding suggests that the use of HFNC flow and patient respiratory rates alone to determine nutrition safety is insufficient and requires further evaluation.

TABLE 2 Respiratory and HFNC Flow Rates for Children With Acute Viral Bronchiolitis on HFNC With and Without Nutrition Interruptions

Variables	All Subjects (N = 132)	No Interruptions (n = 120)	Interruption Cohort (n = 12)	P
Mean respiratory rate, breaths/min \pm SD				
Admission	51.2 ± 14.1	51 ± 13.8	53.2 ± 16.9	.61
Nutrition initiation	39.8 ± 11.1	40 ± 11.3	37.8 ± 8	.54
Nutrition interruption	N/A	N/A	63 ± 22.3	N/A
Median HFNC flow rate, L/min (IQR)				
Admission	8 (6–10)	8 (6–10)	8 (7–8)	.72
Nutrition initiation	8 (6–8.5)	8 (6–8.5)	7 (5.5–9)	.64
Nutrition interruption	N/A	N/A	6 (5–8.5)	N/A
Median weight-adjusted HFNC flow rate, L/kg per minute (IQR)				
Admission	0.9 (0.7–1.2)	0.9 (0.7–1.2)	0.9 (0.8–1.1)	.86
Nutrition initiation	0.9 (0.7–1.2)	0.9 (0.7–1.2)	0.9 (0.7–1.1)	.85
Nutrition interruption	N/A	N/A	0.7 (0.5–1.1)	N/A

N/A, not applicable.

TABLE 3 Nutrition Goal Achievement and Nutrition Timing Data for Children With Acute Viral Bronchiolitis With and Without Nutrition Interruptions on HFNC

Variables	All Subjects (N = 132)	No Interruptions (n = 120)	Interruption Cohort (n = 12)	P
Route of enteral nutrition, n (%)				
Nasogastric tube fed	4 (3)	3 (2.5)	1 (8.3)	.32
Bottle-fed	114 (86)	104 (87)	10 (83)	.67
Breastfed	14 (11)	13 (11)	1 (8.3)	.38
Nutrition started on admission, n (%)	29 (22)	26 (22)	3 (25)	.73
Nutrition initiation delay, h (IQR)	10.5 (6.9–16.3)	11 (6.9–16.2)	9.1 (5.2–10)	.25
All nutrition goals achieved, n (%)				
By PICU discharge	55 (42)	48 (40)	7 (58)	.24
During HFNC therapy	34 (26)	28 (23)	6 (50)	.04*
Time to 100% nutrition goals, d (IQR)	1.4 (1–2)	1.4 (1–1.8)	2.3 (1.7–2.8)	.03*

* Significant, $P < .05$.

The only literature to link enteral nutrition during HFNC therapy and aspiration are 2 studies ($n = 12$ and 29) assessing the presence of lipid-laden macrophages during blind laryngeal lavage in the acute phase of bronchiolitis.^{22,23} These publications noted resolution in aspiration symptoms by the 4-week follow-up evaluations. We suspect these findings are confounded by the presence of GERD. It is well established that, in the first year of life, gastroesophageal reflux has an estimated prevalence of 50% to 85%, which naturally decreases with age.^{24,25} In a prospective randomized pilot study comparing enteral nutrition via nasogastric tube with parenteral nutrition in acute bronchiolitis, there were no aspiration events recorded in the nasogastric tube cohort.²⁶ These studies, including our own, used a smaller sample size but nonetheless support our observations that aspiration-related respiratory failure is a relatively rare event and should not determine the practice of withholding nutrition.

Although we could not detect any differences between those with and without interruptions of enteral nutrition in terms of patient characteristics, viral pathogens, respiratory rates, or HFNC flow rates, there do appear to be consequences associated with nutrition interruption. The interruption cohort had a longer length of stay by 2.5 days and received an additional day of HFNC therapy. Could it be that providing children with nutrition is in and of itself therapeutic? Although we were not able to

explore the exact mechanisms behind these observations, we suspect that decreases in length of stay and HFNC therapy duration may be a consequence of improved patient comfort and decreased respiratory distress after nutrition initiation. We are not able to determine causality from our data, but answering this question in future investigations is warranted.

There are currently no comparative effectiveness data in nonintubated term children receiving noninvasive ventilatory support to suggest a lower incidence of aspiration events when receiving nutrition via nasogastric or post-pyloric tubes as opposed to by mouth feeding. Because our institutional practice was to provide enteral nutrition by mouth, we were unable to assess the advantage of a specific route of nutrition delivery as it relates to clinical aspiration events or nutrition achievement goals. We suspect there are specific populations of children, such as those with symptomatic GERD, who would most benefit from post-pyloric tube nutrition. Only 26% of children in our sample achieved all nutrition goals during HFNC therapy. This deficiency could be accounted for by a variety of variables. It may be that children in our sample were simply not provided enough time to achieve their nutrition goal because the duration of HFNC use was a median of 1.7 days. In addition, initial volume resuscitation, continuous intravenous fluids, or patient fatigue may have resulted in decreased appetite after admission. It is conceivable that nasogastric

or nasoduodenal tube nutrition could improve these observed nutrition deficits. A large, prospective, randomized controlled trial is needed to determine the superiority of the enteral nutrition route during HFNC therapy.

Finally, when comparing those admitted overnight with those admitted during the day, we noted an increased incidence in nutrition delay, 30% versus 11%, in subjects admitted overnight. These data represent specific nil per os orders placed by the PICU fellow or attending physician after admission assessment and may reflect a preference to defer the decision to start nutrition to morning rounding or, alternatively, to allow for a period of observation to gauge clinical trajectory. There are limited data to assist providers in predicting which children will fail to respond to HFNC and will require escalation of respiratory support to mechanical ventilation. Because half of the sample represented evening admissions, it is conceivable that nutrition was withheld due to normal patient sleep patterns. Yet, we conclude that, in the world of 24/7, in-house physician coverage, and given the lack of observed aspiration-related respiratory failure in our sample, the responsible admitting physician may want to rethink the approach of delaying the initiation of nutrition to morning rounds.

There are several limitations to our study. Although the rate of mechanical ventilation after a trial of HFNC therapy in bronchiolitis has been reported to be between 7% and 17%,^{7–9} we noted an incidence of 0.8% in our sample. This finding is likely a representation of our strict inclusion criteria. We aimed to evaluate aspiration and enteral nutrition tolerance in full-term, otherwise healthy children with bronchiolitis. This population accounts for 72% of bronchiolitis admissions requiring HFNC in our institution and has a similar prevalence reported in the literature.¹⁰ By choosing this unique population, we cannot draw conclusions regarding children with bronchiolitis who have comorbid chronic conditions, concurrent bacterial infection, or prematurity. It is possible that children excluded for never receiving enteral

nutrition represented a group at particular risk of aspiration-related respiratory failure and their exclusion may represent selection bias. The observed median weight-adjusted HFNC flow rate at the time of nutrition initiation was 0.9 (IQR: 0.7–1.2) L/kg per minute. Recent literature suggests flow rates of 1.6 to 2 L/kg per minute are needed to produce optimal HFNC therapeutic effects, such as consistent pressure generation throughout the respiratory cycle.^{27,28} Reduced weight-based flow rates, in combination with a lower observed intubation rate, could imply that our sample had milder bronchiolitis or a misrepresentation of severity of illness. Although bronchiolitis severity-of-illness scores have been used in the literature for cohort descriptive analyses, these scoring systems have limitations including: inadequate construct validity, high test-retest measurement errors, low inter-rater reliability, and validation primarily for the purposes of emergency department disposition.^{29–31} The inability to objectively measure the work of breathing as an additional means of assessing severity of illness is a limitation of our study. Our findings did not determine if the initiation of nutrition resulted in reductions in respiratory support, patient agitation, or respiratory rates. It is possible that these associations exist and account for observed lower weight-adjusted HFNC flow rates in our sample. Because the incidence of nutrition interruption was low and a detailed exploration into the etiology of nutritional interruptions was not possible, we cannot exclude an etiology of nutrition interruption as a covariate for the observed differences in PICU length of stay. Finally, HFNC and enteral nutrition practice patterns may vary widely across institutions, thus limiting the generalizability of these data.

CONCLUSIONS

These data are the first to describe the epidemiology of aspiration-related respiratory failure and nutrition interruptions for hospitalized children receiving enteral nutrition with acute bronchiolitis on HFNC. Our findings suggest that, in full-term children with bronchiolitis without superimposed bacterial infection or

chronic medical conditions, enteral nutrition is well tolerated across a range of HFNC flow rates and respiratory rates. We suggest that withholding enteral nutrition in this population is unwarranted, and delaying nutrition may lead to a longer length of hospital stay. Future study should include large, prospective, randomized controlled trials assessing the route of nutrition superiority, early versus late nutrition initiation, and potential risk factors for noninvasive ventilation failure.

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